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Progesterone/Tocolytics for Prevention of Preterm Birth

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1. Adjuvant 17-hydroxyprogesterone caproate in women with history-indicated cerclage: A systematic review and meta-analysis

Author(s): Eke A.C.; Sheffield J.; Graham E.M.

Source: Acta Obstetricia et Gynecologica Scandinavica; 2019; vol. 98 (no. 2); p. 139-153

Publication Date: 2019

Publication Type(s): Review

PubMedID: 30339274

Available at Acta obstetricia et gynecologica Scandinavica - from Wiley Online Library

Available at Acta obstetricia et gynecologica Scandinavica - from Unpaywall

Abstract: Introduction: The purpose of this study was to evaluate whether there are additional benefits of 17-hydroxyprogesterone caproate (17-OHPC) supplementation in preventing recurrent spontaneous preterm birth in women with a prophylactic cerclage. Material(s) and Method(s): Electronic databases (MEDLINE, Scopus, ClinicalTrials.gov, PROSPERO, EMBASE, Scielo and the Cochrane Central Register of Controlled Trials) were searched for studies published before June 2018. Keywords included "preterm birth", "prophylactic cerclage", "history-indicated cerclage", "pregnancy" and "17-hydroxyprogesterone caproate". Studies comparing history-indicated cerclage alone with cerclage+17-OHPC were included. The primary outcome measure was preterm birth at <24 weeks of gestation. Secondary outcome measures include preterm birth at <28 weeks, <32 weeks and <37 weeks of gestation, respiratory distress syndrome, necrotizing enterocolitis, fetal birthweight, neonatal intensive care unit stay, mean gestational age at delivery, fetal/neonatal death, neurological morbidity (intraventricular hemorrhage plus periventricular leukomalacia), neonatal sepsis and a composite of severe neonatal morbidity. Severe neonatal morbidity was defined as a composite measure of periventricular leukomalacia, intraventricular hemorrhage (grades III and IV), necrotizing enterocolitis or respiratory distress syndrome. Meta-analysis was performed using the random-effects model of DerSimonian and Laird. Risk of bias and quality assessment were performed using the ROBINS-I and GRADE tools, respectively. PROSPERO Registration Number: CRD42018094559. Result(s): Five studies met the inclusion criteria and were included in the final analysis. Of the 546 women, 357 (75%) received history-indicated cerclage alone

and 189 (35%) received adjuvant 17-OHPC. The composite endpoint, severe neonatal morbidity, was present in 84 of 1515 neonates. Though there was a trend toward a reduced risk of preterm birth, the summary estimate of effect was not statistically significant when comparing cerclage alone with cerclage+17-OHPC at <24 weeks (relative risk [RR].86, 95% confidence interval [CI].45-1.65). Similarly, we found no differences in preterm birth at <37 weeks (RR.90, 95% CI.70-1.17) and <28 weeks (RR.85, 95% CI.54-1.32) when comparing cerclage alone with cerclage+17-OHPC. There were no differences in fetal birthweight, respiratory distress syndrome or necrotizing enterocolitis comparing cerclage alone with cerclage+17-OHPC. Conclusion(s): Intramuscular 17-OHPC in combination with prophylactic cerclage in women with prior preterm birth had no synergistic effect in reducing spontaneous recurrent preterm birth or improving perinatal outcomes.

Database: EMBASE

2. Progesterone for the Prevention of Preterm Birth - An Update of Evidence-Based Indications

Author(s): Kuon R.-J.; Vobeta P.; Rath W.

Source: Geburtshilfe und Frauenheilkunde; 2019; vol. 79 (no. 8); p. 844-853

Publication Date: 2019

Publication Type(s): Review

Abstract: The prevention and treatment of preterm birth remains one of the biggest challenges in obstetrics. Worldwide, 11% of all children are born prematurely with far-reaching consequences for the children concerned, their families and the health system. Experimental studies suggest that progesterone inhibits uterine contractions, stabilises the cervix and has immunomodulatory effects. Recent years have seen the publication of numerous clinical trials using progestogens for the prevention of preterm birth. As a result of different inclusion criteria and the use of different progestogens and their methods of administration, it is difficult to draw comparisons between these studies. A critical evaluation of the available studies was therefore carried out on the basis of a search of the literature (1956 to 09/2018). Taking into account the most recent randomised, controlled studies, the following evidence-based recommendations emerge: In asymptomatic women with singleton pregnancies and a short cervical length on ultrasound of <= 25 mm before 24 weeks of gestation (WG), daily administration of vaginal progesterone (200 mg capsule or 90 mg gel) up until 36 + 6 WG leads to a significant reduction in the preterm birth rate and an improvement in neonatal outcome. The latest data also suggest positive effects of treatment with progesterone in cases of twin pregnancies with a short cervical length on ultrasound of <= 25 mm before 24 WG. The study data for the administration of progesterone in women with singleton pregnancies with a previous preterm birth have become much more heterogeneous, however. It is not possible to make a general recommendation for this indication at present, and decisions must therefore be made on a case-by-case basis. Even if progesterone use is considered to be safe in terms of possible long-term consequences, exposure should be avoided where it is not indicated. Careful patient selection is crucial for the success of treatment.

Database: EMBASE

3. Cyclooxygenase inhibitors for treating preterm labour: What is the molecular evidence?

Author(s): Urrego D.; Liwa A.C.; Cole W.C.; Slater D.M.; Wood S.L.

Source: Canadian Journal of Physiology and Pharmacology; 2019; vol. 97 (no. 3); p. 222-231

Publication Date: 2019

Publication Type(s): Review

PubMedID: 30661374

Abstract: Preterm birth (<37 weeks of gestation) significantly increases the risk of neonatal mortality and morbidity. As many as half of all preterm births occur following spontaneous preterm labour. Since in such cases there are no known reasons for the initiation of labour, treatment of preterm labour (tocolysis) has sought to stop labour contractions and delay delivery. Despite some success, the use of cyclooxygenase (COX) inhibitors is associated with maternal/fetal side effects, and possibly increased risk of preterm birth. Clinical use of these drugs predates the collection of molecular and biochemical evidence in vitro, examining the expression and activity of COX enzymes in pregnant uterine tissues with and without labour. Such evidence is important to the rationale that COX enzymes are, or are not, appropriate targets for the tocolysis. The current study systematically searched existing scientific evidence to address the hypothesis that COX expression/activity is increased with the onset of human labour, in an effort to determine whether there is a rationale for the use of COX inhibitors as tocolytics. Our review identified 44 studies, but determined that there is insufficient evidence to support or refute a role of COX-1/-2 in the onset of preterm labour that supports COX-targeted tocolysis.

Database: EMBASE

4. A systematic review and meta-analysis of randomized controlled trials comparing 17-alpha-hydroxyprogesterone caproate versus placebo for the prevention of recurrent preterm birth.

Author(s): Fernandez-Macias, Rosa; Martinez-Portilla, Raigam J; Cerrillos, Lucas; Figueras, Francesc; Palacio, Montse

Source: International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics; Nov 2019; vol. 147 (no. 2); p. 156-164

Publication Date: Nov 2019

Publication Type(s): Meta-analysis Journal Article Systematic Review

PubMedID: 31402445

Abstract:BACKGROUNDPreterm birth causes an increased risk for perinatal morbidity and mortality.OBJECTIVETo determine whether mid-trimester 17-alpha-hydroxyprogesterone caproate (17-OHPC) reduces the risk of recurrent preterm birth and adverse perinatal outcomes.SEARCH STRATEGYSystematic search to identify relevant studies published in different languages, registered after 2000, using appropriate MeSH terms.SELECTION CRITERIAInclusion criteria were women between 16 and 26+6 weeks of pregnancy with history of preterm delivery in any pregnancy randomized to either 17-OHPC or placebo/no treatment.DATA COLLECTION AND ANALYSISThe number of preterm births and adverse outcomes in the 17-OHPC and placebo arms over the total number of patients in each randomized group were used to calculate the risk ratio (RR) by random-effects models using the Mantel-Haenszel method. Between-study heterogeneity was assessed using tau2 , χ2 (Cochrane Q), and I2 statistics.MAIN RESULTSFour studies were included. There was a 29% (RR 0.71; 95% CI, 0.53-0.96; P=0.001), 26% (RR 0.74; 95% CI, 0.58-0.96; P=0.021), and 40% (RR 0.60; 95% CI, 0.42-0.85; P=0.004) reduction in recurrent preterm birth at <37, <35, and <32 weeks,

respectively, in the 17-OHPC group compared with placebo. The reduction in neonatal death was 68% (RR 0.32; 95% CI, 0.15-0.66; P=0.002).CONCLUSIONS17-OHPC could reduce the risk of recurrent preterm birth at <37, <35, and <28 weeks and neonatal death.PROSPEROCDR42017082190.

Database: Medline

5. Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy

Author(s): Dodd J.M.; Deussen A.R.; Grivell R.M.; OBrien C.M.; Dowswell T.

Source: Cochrane Database of Systematic Reviews; Nov 2019; vol. 2019 (no. 11)

Publication Date: Nov 2019

Publication Type(s): Review

PubMedID: 31745984

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Abstract: Background: Multiple pregnancy is a strong risk factor for preterm birth, and more than 50% of women with a twin pregnancy will give birth prior to 37 weeks' gestation. Infants born preterm are recognised to be at increased risk of many adverse health outcomes, contributing to more than half of overall perinatal mortality. Progesterone is produced naturally in the body and has a role in maintaining pregnancy, although it is not clear whether administering progestogens to women with multiple pregnancy at high risk of early birth is effective and safe. Since publication of this new review in Issue 10, 2017, we have now moved one study (El-Refaie 2016) from included to studies awaiting classification, pending clarification about the study data. Objective(s): To assess the benefits and harms of progesterone administration for the prevention of preterm birth in women with a multiple pregnancy. Search Method(s): We searched the Cochrane Pregnancy and Childbirth Group's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (1 November 2016) and reference lists of retrieved studies. Selection Criteria: We included randomised controlled trials examining the administration of a progestogen by any route for the prevention of preterm birth in women with multiple pregnancy. We did not include quasi-randomised or cross-over studies. Data Collection and Analysis: Two review authors independently assessed reports identified by the search for eligibility, extracted data, assessed risk of bias and graded the quality of the evidence. Main Result(s): We included 16 trials, which all compared either vaginal or intramuscular (IM) progesterone with a placebo or no treatment, and involved a total of 4548 women. The risk of bias for the majority of included studies was low, with the exception of three studies that had inadequate blinding, or significant loss to follow-up or both, or were not reported well enough for us to make a judgement. We graded the evidence low to high quality, with downgrading for statistical heterogeneity, design limitations in some of the studies contributing data, and imprecision of the effect estimate. 1 IM progesterone versus no treatment or placebo. More women delivered at less than 34 weeks' gestation in the IM progesterone group compared with placebo (risk ratio (RR) 1.54, 95% confidence interval (CI) 1.06 to 2.26; women = 399; studies = 2; low-quality evidence). Although the incidence of perinatal death in the progesterone group was higher, there was considerable uncertainty around the effect estimate and high heterogeneity between studies (average RR 1.45, 95% CI 0.60 to 3.51; infants = 3089; studies = 6; I2 = 71%; low-quality evidence). No studies reported maternal mortality or major neurodevelopmental disability at childhood follow-up. There were no clear group differences found in any of the other maternal or infant outcomes (preterm birth less than 37 weeks (RR 1.05, 95% CI 0.98 to 1.13; women = 2010; studies = 5; high-quality evidence); preterm birth less than 28 weeks (RR 1.08, 95% CI 0.75 to 1.55; women = 1920; studies = 5; moderate-quality evidence); infant birthweight less than 2500 g (RR 0.99, 95% CI 0.90 to 1.08; infants = 4071; studies = 5; I2 = 76%, moderate-quality evidence)). No childhood outcomes were reported in the trials. 2 Vaginal progesterone versus no treatment or

placebo by dose. There were no clear group differences in incidence of preterm birth before 34 weeks (average RR 0.90, 95% CI 0.66 to 1.23; women = 1503; studies = 5; I2 = 36%; low-quality evidence). Although fewer births before 34 weeks appeared to occur in the progesterone group, the CIs crossed the line of no effect. Incidence of perinatal death was higher in the progesterone group, although there was considerable uncertainty in the effect estimate and the quality of the evidence was low for this outcome (RR 1.23, 95% CI 0.74 to 2.06; infants = 2287; studies = 3; low-quality evidence). No studies reported maternal mortality or major neurodevelopmental disability at childhood follow-up. There were no clear group differences found in any of the other maternal or infant outcomes (preterm birth less than 37 weeks (average RR 0.97, 95% CI 0.89 to 1.06; women = 1597; studies = 6; moderate-quality evidence); preterm birth less than 28 weeks (RR 1.53, 95% CI 0.79 to 2.97; women = 1345; studies = 3; low-quality evidence); infant birthweight less than 2500 g (average RR 0.95, 95% CI 0.84 to 1.07; infants = 2640; studies = 3; I2 = 66%, moderate-quality evidence)). No childhood outcomes were reported in the trials. For secondary outcomes, there were no clear group differences found in any of the other maternal outcomes except for caesarean section, where women who received vaginal progesterone did not have as many caesarean sections as those in the placebo group, although the difference between groups was not large (8%) (RR 0.92, 95% CI 0.86 to 0.98; women = 1919; studies = 5; I2 = 0%). There were no clear group differences found in any of the infant outcomes except for mechanical ventilation, which was required by fewer infants whose mothers had received the vaginal progesterone (RR 0.70, 95% CI 0.52 to 0.94; infants = 2695; studies = 4). Authors' conclusions: Overall, for women with a multiple pregnancy, the administration of progesterone (either IM or vaginal) does not appear to be associated with a reduction in risk of preterm birth or improved neonatal outcomes. Future research could focus on a comprehensive individual participant data meta-analysis including all of the available data relating to both IM and vaginal progesterone administration in women with a multiple pregnancy, before considering the need to conduct trials in subgroups of high-risk women (for example, women with a multiple pregnancy and a short cervical length identified on ultrasound).

Database: EMBASE

6. Progestogens for the prevention of preterm birth and risk of developing gestational diabetes mellitus: a meta-analysis

Author(s): Pergialiotis V.; Bellos I.; Hatziagelaki E.; Antsaklis A.; Loutradis D.; Daskalakis G.

Source: American Journal of Obstetrics and Gynecology; Nov 2019; vol. 221 (no. 5); p. 429

Publication Date: Nov 2019

Publication Type(s): Review

PubMedID: 31132340

Abstract: Background: Several articles have implied that progestogen supplementation during pregnancy to reduce the risk of preterm birth may increase the risk for developing gestational diabetes mellitus. Objective(s): The purpose of the present meta-analysis was to accumulate existing evidence concerning this correlation. Data Sources: We searched Medline (1966-2019), Scopus (2004-2019), Clinicaltrials.gov (2008-2019), EMBASE (1980-2019), Cochrane Central Register of Controlled Trials CENTRAL (1999-2019), and Google Scholar (2004-2019) databases. Study Eligibility Criteria: Randomized trials and observational studies were considered eligible for inclusion in the present meta-analysis. To minimize the possibility of article losses, we avoided language, country, and date restrictions. Study Appraisal and Synthesis Methods: The methodological quality of included studies was evaluated with the Cochrane risk of bias and the Risk Of Bias In Non-Randomized Studies of Interventions (ROBINS-I) tool. Meta-analysis was performed with the RevMan 5.3 and secondary analysis with the Open Meta-Analyst software. Trial sequential analysis was conducted with the trial sequential analysis program. Result(s): Overall, 11 studies were included in the present meta-analysis that recruited 8085 women. The meta-analysis revealed that women who received 17-alpha hydroxyprogesterone caproate had increased the risk of developing gestational diabetes mellitus (risk ratio, 1.73, 95% confidence interval, 1.32-2.28), whereas women who received vaginal progesterone had a decreased risk, although the effect did not reach statistical significance because of the unstable estimate of confidence intervals (risk ratio, 0.82, 95% confidence interval, 0.50-1.12). Meta-regression analysis indicated that neither the methodological rationale for investigating the prevalence of gestational diabetes mellitus (incidence investigated as primary or secondary outcome) (coefficient of covariance, -0.36, 95% confidence interval, -0.85 to 0.13, P = .154) nor the type of investigated study (randomized controlled trial/observational) (coefficient of covariance -0.361, 95% confidence interval, -1.049 to 0.327, P = .304) significantly altered the results of the primary analysis. Trial sequential analysis suggested that the meta-analysis concerning the correlation of 17-alpha hydroxyprogesterone caproate was of adequate power to reach firm conclusions, whereas this was not confirmed in the case of vaginal progesterone. Conclusion(s): The results of the present meta-analysis clearly indicate that women who receive supplemental 17-alpha hydroxyprogesterone caproate for the prevention of preterm birth have an increased risk of developing gestational diabetes mellitus. On the other hand, evidence concerning women treated with vaginal progesterone remains inconclusive.

Database: EMBASE

7. Drugs for the Treatment and Prevention of Preterm Labor

Author(s): Patel S.S.; Ludmir J.

Source: Clinics in Perinatology; Jun 2019; vol. 46 (no. 2); p. 159-172

Publication Date: Jun 2019

Publication Type(s): Review

PubMedID: 31010553

Abstract: Preterm birth can be medically-indicated or spontaneous. Almost half of spontaneous preterm deliveries are preceded by preterm labor. Preterm labor is a clinical diagnosis characterized by regular uterine contractions (painful or painless) with concomitant cervical change. This article discusses the prevention and treatment of spontaneous preterm labor utilizing progesterone and tocolytic agents and provides management recommendations in patients with and without a history of prior spontaneous preterm birth.Copyright © 2019 Elsevier Inc.

Database: EMBASE

8. Primary and secondary prevention of preterm birth: a review of systematic reviews and ongoing randomized controlled trials

Author(s): Matei A.; Armson A.B.; Saccone G.; Vogel J.P.

Source: European Journal of Obstetrics and Gynecology and Reproductive Biology; May 2019; vol. 236 ; p. 224-239

Publication Date: May 2019

Publication Type(s): Review

PubMedID: 30772047

Abstract: Background: Preterm birth (PTB) is a leading cause of perinatal morbidity and mortality. Interventions aimed at preventing PTB can be classified as primary, secondary, or tertiary prevention. Objective(s): To conduct a review of systematic reviews on the effectiveness and safety of primary and secondary preterm birth prevention interventions. Search strategy: A systematic literature search of the Cochrane, PubMed/Medline, EMBASE and CINAHL databases was conducted on 2 September 2015, and updated on 21 November 2016. Selection Criteria: We included any published systematic review of randomized controlled trials (RCTs) or individual patient data (IPD) of RCTs related to primary or secondary prevention of PTB, published between 2005-2016 where gestational age at birth (of any interval) was a pre-specified outcome. Individual trials and non-systematic reviews were not eligible. Data Collection and Analysis: The population of interest was all pregnant women, regardless of PTB risk. The primary outcome was PTB < 37 weeks. Main Result(s): In total, 112 reviews were included in this study. Overall there were 49 Cochrane and 63 non-Cochrane reviews. Eight were individual participant data (IPD) reviews. Sixty reviews assessed the effect of primary prevention interventions on risk of PTB. Positive effects were reported for lifestyle and behavioural changes (including diet and exercise); nutritional supplements (including calcium and zinc supplementation); nutritional education; screening for lower genital tract infections. Eighty-three systematic reviews were identified relating to secondary PTB prevention interventions. Positive effects were found for low dose aspirin among women at risk of preeclampsia; clindamycin for treatment of bacterial vaginosis; treatment of vaginal candidiasis; progesterone in women with prior spontaneous PTB and in those with short midtrimester cervical length; L-arginine in women at risk for preeclampsia; levothyroxine among women with tyroid disease; calcium supplementation in women at risk of hypertensive disorders; smoking cessation; cervical length screening in women with history of PTB with placement of cerclage in those with short cervix; cervical pessary in singleton gestations with short cervix; and treatment of periodontal disease. Conclusion(s): The

overview serves as a guide to current evidence relevant to PTB prevention. Only a few interventions have been demononstrated to be effective, including cerclage, progesterone, low dose aspirin, and lifestyle and behavioural changes. For several of the interventions evaluated, there was insufficient evidence to assess whether they were effective or not.

Database: EMBASE

9. Systematic review and meta-analysis of randomized controlled trials of atosiban versus nifedipine for inhibition of preterm labor

Author(s): Ali A.A.; Sayed A.K.; El Sherif L.; Loutfi G.O.; Ahmed A.M.M.; Mohamed H.B.; Anwar A.T.; Taha A.S.; Yahia R.M.; Elgebaly A.; Abdel-Daim M.M.

Source: International Journal of Gynecology and Obstetrics; May 2019; vol. 145 (no. 2); p. 139-148

Publication Date: May 2019

Publication Type(s): Review

PubMedID: 30784056

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library

Abstract: Background: Two tocolytic drugs-atosiban and nifedipine-are currently used for first-line treatment of preterm labor (PTL). Objective(s): To compare the efficacy and safety of atosiban with nifedipine for PTL treatment. Search strategy: In May 2017, we searched PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Clinical Trials with search terms including "nifedipine", "atosiban", and "preterm labor". Selection Criteria: Randomized controlled trials of women with PTL. Data Collection and Analysis: Data were extracted for study design, patient characteristics, risk of bias domains, and study outcomes. A random-effects model was used to generate pooled risk ratios (RRs) and 95% confidence intervals (CIs). Result(s): We included seven studies that enrolled 992 patients. There was no significant difference between atosiban and nifedipine for pregnancy prolongation of 48 hours or more regarding efficacy (RR 1.06, 95% CI 0.92-1.22; P=0.440) or effectiveness (0.93, 0.84-1.03; P=0.177). Pregnancy prolongation for 7 days or more also did not differ between groups for efficacy (RR 1.04, 95% CI 0.89-1.21; P=0.656) or effectiveness (0.91, 0.79-1.05; P=0.177). Atosiban-however-was associated with fewer maternal side-effects than nifedipine. Conclusion(s): Atosiban resulted in fewer maternal side-effects than nifedipine, with no difference in pregnancy prolongation. PROSPERO registration: CRD42018090223.

Database: EMBASE

10. Prevention of spontaneous preterm birth

Author(s): Daskalakis G.; Antsaklis A.; Goya M.; Cabero L.; Pergialiotis V.; Kyvernitakis I.; Arabin B.

Source: Archives of Gynecology and Obstetrics; May 2019; vol. 299 (no. 5); p. 1261-1273

Publication Date: May 2019

Publication Type(s): Review

PubMedID: 30761417

Available at Archives of gynecology and obstetrics - from SpringerLink - Medicine

Abstract: Background: It is estimated that globally, approximately 13 million preterm infants are born annually and a much higher number of pregnancies are characterized by threatening preterm birth. Finding(s): A proportional inverse correlation between gestational age at delivery and neonatal mortality has been observed which is more prevalent in countries without high standard neonatal care. The socioeconomic burden of preterm birth is enormous, as preterm neonates are particularly prone to severe morbidity that may expand up to adulthood. Several strategies have been proposed for the prevention of preterm birth which can be sub-stratified as primary (when these apply to the general population), secondary (when they target women at risk), and tertiary (optimizing neonatal outcomes when preterm birth cannot any longer be prevented). The aim of this review is to summarize the most important strategies.Copyright © 2019, Springer-Verlag GmbH Germany, part of Springer Nature.

Database: EMBASE

11. Nifedipine alone or combined with sildenafil citrate for management of threatened preterm labour: a randomised trial.

Author(s): Maher, M A; Sayyed, T M; El-Khadry, S W

Source: BJOG : an international journal of obstetrics and gynaecology; May 2019; vol. 126 (no. 6); p. 729-735

Publication Date: May 2019

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 30315625

Available at BJOG : an international journal of obstetrics and gynaecology - from Wiley Online Library

Abstract:OBJECTIVETo study the tocolytic action of nifedipine combined with sildenafil citrate (SC) and if the combination is superior to nifedipine alone in inhibiting threatened preterm labour (PTL).DESIGNProspective randomised study.SETTINGAn Egyptian university hospital.POPULATIONWomen with threatened PTL who received either nifedipine with SC or nifedipine alone.METHODSPatients were randomly allocated to receive either (1) nifedipine 20 mg orally (stat dose), followed by 10 mg orally every 6-8 hours at the same time as vaginal administration of SC (25 mg at 8-hourly intervals) or (2) nifedipine alone. Medications were continued for 48-72 hours.MAIN OUTCOME MEASURESThe percentage of women who remained undelivered during hospitalisation.RESULTSFrom January 2015 to November 2016, 239 women were randomised. The baseline characteristics of participants were similar. Nifedipine combined with SC was associated with more women remaining undelivered (81.8 versus 68.6%; P = 0.018) during hospitalisation. Regarding secondary outcomes, the addition of SC was also associated with fewer deliveries within 7 days of admission (9.1 versus 20.3%; P = 0.014), prolonged latency (29 versus 7 days; P = 0.002), fewer admissions to neonatal intensive care units (31.4 versus 44.1%; P = 0.043), fewer very preterm deliveries (from 28 to <32 weeks, 20.7 versus 38.1%; P = 0.043), and increased neonatal birthweight (1900 versus 1500 g; P = 0.018).CONCLUSIONSVaginal SC combined with

nifedipine is an effective option for tocolytic therapy during threatened PTL.TWEETABLE ABSTRACTVaginal SC enhances the tocolytic effect of nifedipine.

Database: Medline

12. Effects of progestogens in women with preterm premature rupture of membranes.

Author(s): Di Sarno, Rossana; Raffone, Antonio; Saccone, Gabriele

Source: Minerva ginecologica; Apr 2019; vol. 71 (no. 2); p. 121-124

Publication Date: Apr 2019

Publication Type(s): Journal Article Review

PubMedID: 30318880

Abstract: Different strategies have been adopted for prevention of spontaneous preterm birth, including use of progestogens. So far, five randomized trials have been published evaluating the efficacy of progestogens in women with PPROM, including a total of 425 participants. All the five trials enrolled pregnant women with singleton pregnancies randomized between 20 and 34 weeks of gestation. In four trials women were randomized to either weekly intramuscular 250 mg 17α-hydroxyprogesterone-caproate or placebo, while Mirzaei et al. was a three arms trials in which women received weekly intramuscular 250 mg 17α-hydroxyprogesterone-caproate, or rectal progesterone 400 mg daily, or no treatment. In all the trials, latency antibiotics were used, and tocolysis was used permitted for first 48 hours at discretion of attending physician. Recently a meta-analysis including the five trials has been published. They found that when compared to placebo weekly intramuscular 250 mg 17α-hydroxyprogesterone-caproate did not alter the latency period to delivery in singleton gestations with PPROM. Additionally, there was no difference in gestational age at delivery between groups or in mode of delivery. No significant differences were reported in maternal or neonatal outcomes, with latency not significantly altered in sensitivity analyses. So far, no trials have been published evaluating natural vaginal progesterone in women with PPROM.

Database: Medline

13. Vaginal progesterone, oral progesterone, 17-OHPC, cerclage, and pessary for preventing preterm birth in at-risk singleton pregnancies: an updated systematic review and network meta-analysis.

Author(s): Jarde, A; Lutsiv, O; Beyene, J; McDonald, S D

Source: BJOG : an international journal of obstetrics and gynaecology; Apr 2019; vol. 126 (no. 5); p. 556-567

Publication Date: Apr 2019

Publication Type(s): Meta-analysis Journal Article Systematic Review

PubMedID: 30480871

Abstract:BACKGROUNDRecent progesterone trials call for an update of previous syntheses of interventions to prevent preterm birth.OBJECTIVESTo compare the relative effects of different types and routes of administration of progesterone, cerclage, and pessary at preventing preterm birth in at-risk women overall and in specific populations.SEARCH STRATEGYWe searched Medline, EMBASE, CINAHL, Cochrane CENTRAL, and Web of Science up to 1 January 2018.SELECTION CRITERIAWe included randomised trials of progesterone, cerclage or pessary for preventing preterm birth in at-risk singleton pregnancies.DATA COLLECTION AND ANALYSISWe used a piloted data extraction form and performed Bayesian random-effects network meta-analyses with 95% credibility intervals (CrI), as well as pairwise meta-analyses, rating the quality of the evidence using GRADE.MAIN RESULTSWe included 40 trials (11 311 women). In at-risk women overall, vaginal progesterone reduced preterm birth <34 (OR 0.43, 95% CrI 0.20-0.81) and <37 weeks (OR 0.51, 95% CrI 0.34-0.74), and neonatal death (OR 0.41, 95% CrI 0.20-0.83). In women with a previous preterm birth, vaginal progesterone reduced preterm birth <34 (OR 0.29, 95% CI 0.12-0.68) and <37 weeks (OR 0.43, 95% CrI 0.23-0.74), and 17α-hydroxyprogesterone caproate reduced preterm birth <37 weeks (OR 0.53, 95% CrI 0.27-0.95) and neonatal death (OR 0.39, 95% CI 0.16-0.95). In women with a short cervix (≤25 mm), vaginal progesterone reduced preterm birth <34 weeks (OR 0.45, 95% CI 0.24-0.84).CONCLUSIONSVaginal progesterone was the only intervention with consistent effectiveness for preventing preterm birth in singleton at-risk pregnancies overall and in those with a previous preterm birth.TWEETABLE ABSTRACTIn updated NMA, vaginal progesterone consistently reduced PTB in overall at-risk pregnancies and in women with previous PTB.

Database: Medline

14. Progestin therapy to prevent preterm birth: History and effectiveness of current strategies and development of novel approaches

Author(s): Mesiano S.A.; Peters G.A.; Amini P.; Wilson R.A.; Tochtrop G.P.; van Den Akker F.

Source: Placenta; Apr 2019; vol. 79 ; p. 46-52

Publication Date: Apr 2019

Publication Type(s): Review

PubMedID: 30745115

Abstract: In the 1930s the "progestin" hormone produced by the corpus luteum was isolated and found to be a DELTA4-keto-steroid. It was aptly named progesterone (P4)and in the following 30 years the capacity of P4 and derivatives to prevent preterm birth (PTB)was examined. Outcomes of multiple small studies suggested that progestin prophylaxis beginning at mid-gestation decreases the risk for PTB. Subsequent larger trials found that prophylaxis with weekly intramuscular injections of 17alpha-hydroxyprogesterone caproate (17HPC)beginning at mid-gestation decreased PTB risk in women with a history of PTB. Other trials found that daily vaginal P4 prophylaxis, also beginning at mid-gestation decreased PTB risk in women with a short cervix. Currently, prophylaxis with 17HPC (in women with a history of PTB)or vaginal P4 (in women with a short cervix)are used to prevent PTB. Recent advances in understanding the molecular biology of P4 signaling in uterine cells is revealing novel progestin-based targets for PTB prevention. One possibility is to use selective P4 receptor (PR)modulators (SPRMs)to boost PR anti-inflammatory activity that blocks labor, while simultaneously preventing PR phosphorylation that causes loss of P4/PR anti-inflammatory activity. This may be achieved by SPRMs that induce a specific PR conformation that prevents site-specific serine phosphorylation that inhibits anti-inflammatory activity. Further advances in understanding how P4 promotes uterine quiescence and how its labor blocking actions are withdrawn to trigger parturition will reveal novel therapeutic targets to more effectively prevent PTB.

Database: EMBASE

15. Oral progesterone for the prevention of recurrent preterm birth: systematic review and metaanalysis

Author(s): Boelig R.C.; Berghella V.; Della Corte L.; Saccone G.; Ashoush S.; McKenna D.; Rajaram S.

Source: American Journal of Obstetrics and Gynecology MFM; Mar 2019; vol. 1 (no. 1); p. 50-62

Publication Date: Mar 2019

Publication Type(s): Review

Abstract: Objective Data: The purpose of this study was to perform a systematic review and metaanalysis of randomized controlled trials on oral progesterone compared with placebo or other interventions for preterm birth prevention in singleton pregnancies with previous spontaneous preterm birth. The primary outcome was preterm birth at <37 weeks gestation; the secondary outcomes included preterm birth rate at <34 weeks gestation, neonatal morbidity/death, and maternal side-effects. Study: Searches were performed in PubMed, Scopus, ClinicalTrials.gov, PROSPERO, EMBASE, and the Cochrane Register with the use of a combination of words related to "preterm birth,""preterm delivery,""progesterone,""progestogens," and "oral" from inception of each database to April 2018. Additionally, systematic reviews on progesterone for preterm birth prevention that were identified in our search were also reviewed for additional studies. We included all randomized trials of asymptomatic singleton gestations with previous spontaneous singleton preterm birth that had been randomized to prophylactic treatment with oral progesterone vs placebo, no treatment, or other preterm birth intervention. Exclusion criteria included quasirandomized trials, trials that involved women with preterm labor/membrane rupture at the time of randomization or multiple gestations. Study Appraisal and Synthesis Methods: The risk of bias and quality of evidence were assessed for each study. All analyses were done with an intention-to-treat approach. The primary outcome was incidence of preterm birth at <37 weeks gestation; the secondary outcomes included preterm birth at <34 and <28 weeks gestation, maternal adverse events, maternal serum progesterone level, and neonatal morbidity and death. Summary measures were reported as relative risk or mean difference. I2>30% was used to identify heterogeneity. Result(s): The search strategy identified 79 distinct studies. Three trials on oral progesterone vs placebo (involved 386 patients: 196 in oral progesterone and 190 in placebo) met the inclusion criteria; there were no studies on oral progesterone vs other intervention that met inclusion criteria. Metaanalysis demonstrated a significantly decreased risk of preterm birth at <37 weeks gestation (42% vs 63%; P=.0005; relative risk, 0.68; 95% confidence interval, 0.55-0.84), preterm birth at <34 weeks gestation (29% vs 53%; P<.00001; relative risk, 0.55; 95% confidence interval, 0.43-0.71), and increased gestational age of delivery (mean difference, 1.71 weeks; 95% confidence interval, 1.11-2.30) with oral progesterone compared with placebo. There was a significantly lower rate of perinatal death (5% vs 17%; P=.001; relative risk 0.32; 95% confidence interval, 0.16-0.63), neonatal intensive care admission (relative risk, 0.39; 95% confidence interval, 0.25-0.61), respiratory distress syndrome (relative risk, 0.21; 95% confidence interval, 0.05-0.93), and higher birthweight (mean difference, 435.06 g; 95% confidence interval, 324.59-545.52) with oral progesterone. There was a higher rate of maternal adverse effects with oral progesterone that included dizziness (relative risk, 2.95; 95% confidence interval, 1.47-5.90), somnolence (relative risk, 2.06; 95% confidence interval, 1.29-3.30), and vaginal dryness (relative risk, 2.37; 95% confidence interval, 1.10-5.11); no serious adverse effects were noted. Conclusion(s): Oral progesterone appears to be effective for the prevention of recurrent preterm birth and a reduction in perinatal morbidity and mortality rates in asymptomatic singleton gestations with a history of previous spontaneous preterm birth compared with placebo. There were also increased adverse effects with oral progesterone therapy compared with placebo, although none were serious. Further randomized study on oral progesterone compared with other established therapies for the prevention of recurrent preterm birth are warranted.

Database: EMBASE

16. Tocolysis: A Review of the Literature.

Author(s): Hanley, Margaret; Sayres, Lauren; Reiff, Emily S; Wood, Amber; Grotegut, Chad A; Kuller, Jeffrey A

Source: Obstetrical & gynecological survey; Jan 2019; vol. 74 (no. 1); p. 50-55

Publication Date: Jan 2019

Publication Type(s): Journal Article Review

PubMedID: 30648727

Abstract: ImportancePreterm delivery represents an important cause of infant morbidity and mortality. Various tocolytics have been studied with the objective of stopping preterm labor, increasing gestational age at delivery, and preventing complications related to preterm birth.ObjectiveThis review aims to summarize the major classes of tocolytics and review the evidence regarding use of each.Evidence AcquisitionA PubMed search of the following terms was performed to gather relevant data: "tocolytic," "preterm labor," "preterm delivery," "PPROM," "magnesium," "indomethacin," "nifedipine," and "betamimetics."ResultsThe benefits and risks of nonsteroid anti-inflammatory drugs, calcium channel blockers, magnesium, and betamimetics are reviewed. Calcium channel blockers afford superior outcomes in terms of prolonging gestation and decreasing neonatal morbidity and mortality with the fewest adverse effects.Conclusions and RelevanceTocolytics, particularly calcium channel blockers, may provide benefit to pregnant women and their infants. Their use should be tailored to the particular clinical circumstances of the patient and used in conjunction with other management strategies (e.g., administration of corticosteroids for fetal lung maturation or magnesium for neuroprotection and transfer to a tertiary medical center). Further research and professional guidelines are needed on optimal use of these agents.

Database: Medline

17. Spontaneous preterm birth prevention in multiple pregnancy

Author(s): Murray S.R.; Stock S.J.; Norman J.E.; Cowan S.; Cooper E.S.

Source: Obstetrician and Gynaecologist; 2018; vol. 20 (no. 1); p. 57-63

Publication Date: 2018

Publication Type(s): Review

Available at The Obstetrician & Gynaecologist - from Wiley Online Library

Abstract: Key content: Twin pregnancies are associated with a three-fold greater perinatal mortality than singleton pregnancies. Prematurity is a main contributor, with 50% of twin pregnancies delivering before 37 weeks and 10% delivering before 32 weeks of gestation. The aetiology of preterm delivery in twin pregnancies is likely multifactorial and different from that of singletons. Cervical cerclage reduces preterm birth rates in singletons but has mixed results in twins with some studies showing harm. The use of progesterone to prevent preterm birth in singletons has conflicting results and has not been proven to prevent preterm birth in twins. Studies continue to determine whether the cervical pessary is effective in preventing preterm birth in multiple pregnancies. There is a paucity of data available on the prevention of preterm birth in triplets/higher order multiples but similar principles to twin pregnancy apply. Learning objectives: To review the burden of preterm birth in multiple pregnancy. To understand the methods available for preventing preterm birth in multiple pregnancies and the evidence surrounding the use of each one. To be aware of the use of the Arabin pessary.

Database: EMBASE

18. Interventions during pregnancy to prevent preterm birth: An overview of Cochrane systematic reviews

Author(s): Medley N.; Vogel J.P.; Care A.; Alfirevic Z.

Source: Cochrane Database of Systematic Reviews; Nov 2018; vol. 2018 (no. 11)

Publication Date: Nov 2018

Publication Type(s): Review

PubMedID: 30480756

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Available at The Cochrane database of systematic reviews - from Unpaywall

Abstract: Background: Preterm birth (PTB) is a major factor contributing to global rates of neonatal death and to longer-term health problems for surviving infants. Both the World Health Organization and the United Nations consider prevention of PTB as central to improving health care for pregnant women and newborn babies. Current preventative clinical strategies show varied efficacy in different populations of pregnant women, frustrating women and health providers alike, while researchers call for better understanding of the underlying mechanisms that lead to PTB. Objective(s): We aimed to summarise all evidence for interventions relevant to the prevention of PTB as reported in Cochrane systematic reviews (SRs). We intended to highlight promising interventions and to identify SRs in need of an update. Method(s): We searched the Cochrane Database of Systematic Reviews (2 November 2017) with key words to capture any Cochrane SR that prespecified or reported a PTB outcome. Inclusion criteria focused on pregnant women without signs of preterm labour or ruptured amniotic membranes. We included reviews of interventions for pregnant women irrespective of their risk status. We followed standard Cochrane methods. We applied GRADE criteria to evaluate the quality of SR evidence. We assigned graphic icons to classify the effectiveness of interventions as: clear evidence of benefit; clear evidence of harm; clear

evidence of no effect or equivalence; possible benefit; possible harm; or unknown benefit or harm. We defined clear evidence of benefit and clear evidence of harm to be GRADE moderate- or high-quality evidence with a confidence interval (CI) that does not cross the line of no effect. Clear evidence of no effect or equivalence is GRADE moderate- or high-quality evidence with a narrow CI crossing the line of no effect. Possible benefit and possible harm refer to GRADE low-quality evidence with a clear effect (CI does not cross the line of no effect) or GRADE moderate- or high-quality evidence with a wide CI. Unknown harm or benefit refers to GRADE low- or very low-quality evidence with a wide CI. Main Result(s): We included 83 SRs; 70 had outcome data. Below we highlight key results from a subset of 36 SRs of interventions intended to prevent PTB. Outcome(s): preterm birth Clear evidence of benefit Four SRs reported clear evidence of benefit to prevent specific populations of pregnant women from giving birth early, including midwife-led continuity models of care versus other models of care for all women; screening for lower genital tract infections for pregnant women less than 37 weeks' gestation and without signs of labour, bleeding or infection; and zinc supplementation for pregnant women without systemic illness. Cervical cerclage showed clear benefit for women with singleton pregnancy and high risk of PTB only. Clear evidence of harm No included SR reported clear evidence of harm. No effect or equivalence For pregnant women at high risk of PTB, bedrest for women with singleton pregnancy and antibiotic prophylaxis during the second and third trimester were of no effect or equivalent to a comparator. Possible benefit Four SRs found possible benefit in: group antenatal care for all pregnant women; antibiotics for pregnant women with asymptomatic bacteriuria; pharmacological interventions for smoking cessation for pregnant women who smoke; and vitamin D supplements alone for women without pre-existing conditions such as diabetes. Possible harm One SR reported possible harm (increased risk of PTB) with intramuscular progesterone, but this finding is only relevant to women with multiple pregnancy and high risk of PTB. Another review found possible harm with vitamin D, calcium and other minerals for pregnant women without pre-existing conditions. Outcome(s): perinatal death Clear evidence of benefit Two SRs reported clear evidence of benefit to reduce pregnant women's risk of perinatal death: midwife-led continuity models of care for all pregnant women; and fetal and umbilical Doppler for high-risk pregnant women. Clear evidence of harm No included SR reported clear evidence of harm. No effect or equivalence For pregnant women at high risk of PTB, antibiotic prophylaxis during the second and third trimester was of no effect or equivalent to a comparator. Possible benefit One SR reported possible benefit with cervical cerclage for women with singleton pregnancy and high risk of PTB. Possible harm One SR reported possible harm associated with a reduced schedule of antenatal visits for pregnant women at low risk of pregnancy complications; importantly, these women already received antenatal care in settings with limited resources. Outcome(s): preterm birth and perinatal death Unknown benefit or harm For pregnant women at high risk of PTB for any reason including multiple pregnancy, home uterine monitoring was of unknown benefit or harm. For pregnant women at high risk due to multiple pregnancy: bedrest, prophylactic oral betamimetics, vaginal progesterone and cervical cerclage were all of unknown benefit or harm. Authors' conclusions: Implications for practice The overview serves as a map and guide to all current evidence relevant to PTB prevention published in the Cochrane Library. Of 70 SRs with outcome data, we identified 36 reviews of interventions with the aim of preventing PTB. Just four of these SRs had evidence of clear benefit to women, with an additional four SRs reporting possible benefit. No SR reported clear harm, which is an important finding for women and health providers alike. The overview summarises no evidence for the clinically important interventions of cervical pessary, cervical length assessment and vaginal progesterone because these Cochrane Reviews were not current. These are active areas for PTB research. The graphic icons we assigned to SR effect estimates do not constitute clinical guidance or an endorsement of specific interventions for pregnant women. It remains critical for pregnant women and their healthcare providers to carefully consider whether specific strategies to prevent PTB will be of benefit for individual women, or for specific populations of women. Implications for research Formal consensus work is needed to establish standard language for overviews of reviews and to define the limits of

their interpretation. Clinicians, researchers and funders must address the lack of evidence for interventions relevant to women at high risk of PTB due to multiple pregnancy.

Database: EMBASE

19. Clinical guidelines for prevention and management of preterm birth: a systematic review.

Author(s): Medley, N; Poljak, B; Mammarella, S; Alfirevic, Z

Source: BJOG : an international journal of obstetrics and gynaecology; Oct 2018; vol. 125 (no. 11); p. 1361-1369

Publication Date: Oct 2018

Publication Type(s): Journal Article Systematic Review

PubMedID: 29460323

Available at BJOG : an international journal of obstetrics and gynaecology - from Wiley Online Library

Abstract:BACKGROUNDClinical practice guidelines (CPG) endorse multiple strategies to prevent or manage preterm birth (PTB).OBJECTIVESTo summarise CPG recommendations for PTB and identify areas of international consensus.SEARCH STRATEGYIn May 2017 we searched for all CPG relevant to PTB without language restrictions.SELECTION CRITERIACPG were eligible if the following criteria were met: (1) the guideline was published or current from June 2013; (2) the guideline recommended practices for the prevention or management of PTB relevant to our prespecified clinical questions for screening, medications or surgery and other interventions; (3) publications on methods of guideline development for eligible CPG were included to enable quality assessment.DATA COLLECTION AND ANALYSISTwo authors classified CPG recommendations relevant to prespecified clinical questions. When more than 70% of CPGs reporting on a topic recommended or rejected an intervention, we regarded this as consensus. We summarised recommendations in tables.MAIN RESULTSWe identified 49 guidelines from 16 guideline developers. We found consensus for several clinical practices: cervical length screening for high-risk women; short-term tocolysis; steroids for fetal lung maturation; and magnesium sulphate for fetal neuroprotection. We found discrepant recommendations for progesterone and fibronectin. No guideline identified an effective strategy for women with multiple pregnancy.CONCLUSIONSWe identified interventions for which there is an international consensus on benefit for PTB. Systematic reviews of CPG using standardised methodology will help avoid duplication and target scarce resources for guideline developers globally.TWEETABLE ABSTRACTInternational clinical guidelines agree on the benefits and harmful effects of several important interventions to prevent preterm birth.

Database: Medline

20. Efficacy of progesterone for prevention of preterm birth.

Author(s): Sykes, Lynne; Bennett, Phillip R

Source: Best practice & research. Clinical obstetrics & gynaecology; Oct 2018; vol. 52 ; p. 126-136

Publication Date: Oct 2018

Publication Type(s): Journal Article Review

PubMedID: 30266582

Available at Best practice & research. Clinical obstetrics & gynaecology - from Unpaywall

Abstract: Preterm birth (PTB) occurs in 5-18% of pregnancies and is the leading cause of neonatal morbidity, mortality and infant death. Up to 30% of PTBs are due to iatrogenic reasons, but the remainder are due to the spontaneous onset of labour or pre-labour premature rupture of membranes (P-PROM). During pregnancy, the uterus remains quiescent and the cervix remains long and closed. Although the exact mechanisms that lead to spontaneous PTB (sPTB) are not fully understood, it is likely that the terminal pathways that are common to term labour are activated prematurely. Despite continued research efforts to develop preventative strategies, there have been no major advances resulting in the reduction of sPTB rates. Progesterone is the most researched prophylactic agent, yet, there is lack of consistency in the reported beneficial effects for the prevention of PTB and improvement in neonatal outcome. This is likely to stem from the multifactorial aetiology of sPTB, the varied patient cohorts recruited and the use of different preparations and routes of administration for progesterone. This review summarises the scientific rationale supporting the efficacy of progesterone and the results of major randomised controlled trials and finally emphasizes how targeted studies with more detailed patient stratification are essential to understand which population would benefit.

Database: Medline

21. Rationale for current and future progestin-based therapies to prevent preterm birth.

Author(s): Weatherborn, Megan; Mesiano, Sam

Source: Best practice & research. Clinical obstetrics & gynaecology; Oct 2018; vol. 52 ; p. 114-125

Publication Date: Oct 2018

Publication Type(s): Journal Article Review

PubMedID: 29724668

Abstract: Preterm birth (PTB) is the leading cause of neonatal morbidity and mortality worldwide. The only medicinal therapy currently recommended to prevent PTB is prophylactic progestin therapy in the form of micronized progesterone (P4) administered daily via vaginal suppository from the 24th to the 34th week of gestation or 17α-hydroxyprogesterone caproate in oil administered weekly from the 16th to the 36th week of gestation via an intramuscular injection. These therapies decrease the risk of PTB in women with an elevated risk of PTB indicated by a history of PTB or by a short cervix measured by sonography at mid-gestation. The mechanism by which progestin therapy prevents PTB in some women is not clear but may involve non-progestin mechanism and/or supplementation of localized progestin deficiency. Advances in understanding the molecular biology and physiology of P4 signaling via the P4 receptor isoforms in uterine cells reveal novel therapeutic targets; this may improve the effectiveness of progestin therapy to prevent PTB in the majority of pregnancies by targeting key steps in the pathway leading to inflammation-induced parturition.

Database: Medline

22. Preventing preterm birth: New approaches to labour therapeutics using Nanoparticles.

Author(s): Paul, Jonathan W; Smith, Roger

Source: Best practice & research. Clinical obstetrics & gynaecology; Oct 2018; vol. 52 ; p. 48-59

Publication Date: Oct 2018

Publication Type(s): Journal Article Review

PubMedID: 29724667

Abstract: Preterm birth remains a major obstetric problem with ramifications that extend beyond immediate health and safety concerns for the newborn to include massive societal and economic burden. Although three quarters of preterm birth-related deaths could be prevented with cost-effective interventions, there has been little progress towards achieving sustained tocolysis that translates into improved outcomes for the newborn. With private enterprise reluctant to venture into the sphere of tocolysis, due to potential litigation, advances in the field may fall to new approaches using existing tocolytic resources more effectively. An emerging approach is the utilisation of nanoparticles, which have been established as versatile drug carriers with the power to modify the pharmacokinetics of entrapped therapeutics. In this article, we examine the development of nanoparticle-based drug delivery in pregnancy, with a focus on new approaches to therapeutics for preterm birth and modifying the labour process more generally.

Database: Medline

23. Progestogens in singleton gestations with preterm prelabor rupture of membranes: a systematic review and metaanalysis of randomized controlled trials.

Author(s): Quist-Nelson, Johanna; Parker, Pamela; Mokhtari, Neggin; Di Sarno, Rossana; Saccone, Gabriele; Berghella, Vincenzo

Source: American journal of obstetrics and gynecology; Oct 2018; vol. 219 (no. 4); p. 346

Publication Date: Oct 2018

Publication Type(s): Meta-analysis Journal Article Systematic Review

PubMedID: 29614278

Abstract:OBJECTIVE DATAPreterm prelabor rupture of membranes occurs in 3% of all pregnancies. Neonatal benefit is seen in uninfected women who do not deliver immediately after preterm prelabor rupture of membranes. The purpose of this study was to evaluate whether the administration of progestogens in singleton pregnancies prolongs pregnancy after preterm prelabor rupture of membranes.STUDYSearches were performed in MEDLINE, OVID, Scopus, EMBASE, ClinicalTrials.gov, and the Cochrane Central Register of Controlled Trials with the use of a combination of keywords and text words related to "progesterone," "progestogen," "prematurity," and "preterm premature rupture of membranes" from the inception of the databases until January 2018. We included all randomized controlled trials of singleton gestations after preterm prelabor rupture of membranes that were randomized to either progestogens or control (either placebo or no treatment). Exclusion criteria were trials that included women who had contraindications to expectant management after preterm prelabor rupture of membranes (ie, chorioamnionitis, severe preeclampsia, and nonreassuring fetal status) and trials on multiple gestations. We planned to include all progestogens, including but not limited to 17-α hydroxyprogesterone caproate, and natural progesterone.STUDY APPRAISAL AND SYNTHESIS METHODSThe primary outcome was latency from randomization to delivery. Metaanalysis was performed with the use of the random effects model of DerSimonian and Laird to produce relative risk with 95% confidence interval. Analysis was performed for each mode of progestogen administration separately.RESULTSSix randomized controlled trials (n=545 participants) were included. Four of the included trials assessed

the efficacy of 17-α hydroxyprogesterone caproate; 1 trial assessed rectal progestogen, and 1 trial had 3 arms that compared 17-α hydroxyprogesterone caproate, rectal progestogen, and placebo. The mean gestational age at time randomization was 26.9 weeks in the 17-α hydroxyprogesterone caproate group and 27.3 weeks in the control group. 17-α Hydroxyprogesterone caproate administration was not found to prolong the latency period between randomization and delivery (mean difference, 0.11 days; 95% confidence interval, -3.30 to 3.53). There were no differences in mean gestational age at delivery, mode of delivery, or maternal or neonatal outcomes between the 2 groups. Similarly, there was no difference in latency for those women who received rectal progesterone (mean difference, 4.00 days; 95% confidence interval, -0.72 to 8.72).CONCLUSIONProgestogen administration does not prolong pregnancy in singleton gestations with preterm prelabor rupture of membranes.

Database: Medline

24. Cervical Pessary Compared With Vaginal Progesterone for Preventing Early Preterm Birth: A Randomized Controlled Trial.

Author(s): Cruz-Melguizo, Sara; San-Frutos, Luis; Martínez-Payo, Cristina; Ruiz-Antorán, Belén; Adiego-Burgos, Begoña; Campillos-Maza, José Manuel; García-González, Celso; Martínez-Guisasola, Javier; Pérez-Carbajo, Esther; Teulón-González, María; Avendaño-Solá, Cristina; Pérez-Medina, Tirso

Source: Obstetrics and gynecology; Oct 2018; vol. 132 (no. 4); p. 907-915

Publication Date: Oct 2018

Publication Type(s): Research Support, Non-u.s. Gov't Comparative Study Randomized Controlled Trial Journal Article

PubMedID: 30204689

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Obstetrics and gynecology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

Abstract:OBJECTIVETo compare the effectiveness of a cervical pessary and vaginal progesterone to prevent spontaneous preterm births in pregnant women with cervical lengths 25 mm or less as measured by transvaginal ultrasonography.METHODSThis was a multicenter, open-label, randomized, noninferiority trial. Women with singleton pregnancies and a short cervix (25 mm or less) measured transvaginally at the second-trimester ultrasonogram were invited to participate. They were computer-randomized (one to one) into cervical pessary placement or treatment with vaginal progesterone (200 mg/24 hours). The primary outcome was spontaneous preterm delivery before 34 weeks of gestation. The noninferiority margin was set at 4% with a 0.025 one-sided α level and a statistical power of 80%. That is, if the 95% CI upper bound exceeded 4%, the pessary could not be deemed noninferior. A sample size of 254 women was required to show noninferiority of the pessary to progesterone.RESULTSThe trial was conducted from August 2012 to April 2016 with the participation of 27 Spanish hospitals. A total of 254 patients were enrolled and 246 included in the intention-to-treat analysis. Demographic and baseline characteristics were similar across groups. The rate of spontaneous delivery before 34 weeks of gestation was 14% (n=18/127) in the pessary group and 14% (n=17/119) in the progesterone group with a risk difference of -0.11% (95% CI -8.85% to 8.62%; P=.99), that is, noninferiority was not shown for the pessary. The incidence of increased vaginal discharge (87% vs 71%, P=.002) and discomfort (27% vs 3%, P<.001) was significantly higher in the pessary group.CONCLUSIONA cervical pessary was not noninferior to vaginal progesterone for preventing spontaneous birth before 34 weeks of gestation in pregnant women with short

cervixes.CLINICAL TRIAL REGISTRATIONEU Clinical Trials Register, 2012-000241-13; ClinicalTrials.gov, NCT01643980.

Database: Medline

25. A randomised trial to compare 200 mg micronised progesterone effervescent vaginal tablet daily with 250 mg intramuscular 17 alpha hydroxy progesterone caproate weekly for prevention of recurrent preterm birth.

Author(s): Shambhavi, Shruti; Bagga, Rashmi; Bansal, Pallavi; Kalra, Jasvinder; Kumar, Praveen

Source: Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology; Aug 2018; vol. 38 (no. 6); p. 800-806

Publication Date: Aug 2018

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 29557230

Abstract: For prevention of a recurrent preterm birth (PTB), intramuscular 17-α-hydroxy progesterone caproate (IM 17 OHPC) weekly is recommended. Vaginal progesterone is preferred for women at risk for PTB due to a short cervical length, but may be useful in women with a prior PTB. However, there is no consensus about the optimal vaginal formulation or its efficacy as compared to 17 OHPC to prevent recurrent PTB. We randomised 100 women with a singleton pregnancy between 16 and 24 weeks of gestation and ≥ one prior spontaneous PTB, of a singleton (>16 to <37 weeks of gestation) to receive the 200 mg vaginal progesterone effervescent tablet daily (Group A) or IM 17-OHPC, 250 mg weekly (Group B) till 37 weeks of gestation or delivery. The spontaneous PTB rate of <37 weeks was similar (20% in Group A and 20.8% in Group B, p = .918). The PTB rate of <34 weeks or <28 weeks were also comparable. The mean birth weight and other neonatal outcomes were similar in the two groups. Two neonates in Group A and four neonates in Group B required NICU admission, one of whom (Group B) died due to prematurity. Twenty percent of women in Group A and 29.2% in Group B reported adverse effects from their respective study medications (p = .408, NS). Thus, there did not appear to be a difference between vaginal progesterone and 17-OHPC when used for the prevention of a recurrent PTB. Impact statement What is already known on this subject? Progesterone administration is useful for prevention of a recurrent preterm birth (PTB) and these women are prescribed the intramuscular 17-α-hydroxy progesterone caproate (IM 17 OHPC), 250 mg, weekly. Some studies found that vaginal progesterone (once daily) is also beneficial in these women, but there is no consensus regarding its efficacy when compared to 17 OHPC, or its optimal formulation and dose. What do the results of this study add? In the present study, 100 women with a singleton pregnancy between 16 and 24 weeks of gestation and ≥ one prior spontaneous singleton PTB or mid-trimester abortion were randomised to receive 200 mg of vaginal progesterone effervescent tablet daily (Group A) or 250 mg IM 17-OHPC weekly (Group B) till 37 weeks of gestation or delivery. The spontaneous PTB rate <37 weeks was similar in the two groups (20% in Group A and 20.8% in Group B, p = .918). The PTB rate <34 weeks or <28 weeks were also comparable. The mean birth weight and other neonatal outcomes were similar. Twenty percent of women in Group A and 29.2% of women in Group B reported adverse effects from their respective study medications (p = .408, NS). Thus, there did not appear to be a difference between the vaginal progesterone effervescent tablet and 17-OHPC when used for the prevention of a recurrent PTB. What are the implications of these findings for clinical practice and/or further research? The vaginal progesterone effervescent tablet may be a suitable alternative to IM 17 OHPC to prevent recurrent PTB. Future studies should identify the most appropriate route (IM or vaginal) and vaginal progesterone formulation for PTB prevention in women at risk for a recurrent PTB and in women with a short cervical length.

Database: Medline

26. Vaginal progesterone is as effective as cervical cerclage to prevent preterm birth in women with a singleton gestation, previous spontaneous preterm birth, and a short cervix: updated indirect comparison meta-analysis.

Author(s): Conde-Agudelo, Agustin; Romero, Roberto; Da Fonseca, Eduardo; O'Brien, John M; Cetingoz, Elcin; Creasy, George W; Hassan, Sonia S; Erez, Offer; Pacora, Percy; Nicolaides, Kypros H

Source: American journal of obstetrics and gynecology; Jul 2018; vol. 219 (no. 1); p. 10-25

Publication Date: Jul 2018

Publication Type(s): Meta-analysis Research Support, N.i.h., Intramural Journal Article Systematic Review

PubMedID: 29630885

Abstract:BACKGROUNDAn indirect comparison meta-analysis published in 2013 reported that both vaginal progesterone and cerclage are equally efficacious for preventing preterm birth and adverse perinatal outcomes in women with a singleton gestation, previous spontaneous preterm birth, and a sonographic short cervix. The efficacy of vaginal progesterone has been challenged after publication of the OPPTIMUM study. However, this has been resolved by an individual patient-data meta-analysis (Am J Obstet Gynecol. 2018;218:161-180).OBJECTIVETo compare the efficacy of vaginal progesterone and cerclage in preventing preterm birth and adverse perinatal outcomes in women with a singleton gestation, previous spontaneous preterm birth, and a midtrimester sonographic short cervix.DATA SOURCESMEDLINE, EMBASE, LILACS, and CINAHL (from their inception to March 2018); Cochrane databases, bibliographies, and conference proceedings.STUDY ELIGIBILITY CRITERIARandomized controlled trials comparing vaginal progesterone to placebo/no treatment or cerclage to no cerclage in women with a singleton gestation, previous spontaneous preterm birth, and a sonographic cervical length <25 mm.STUDY APPRAISAL AND SYNTHESIS METHODSUpdated systematic review and adjusted indirect comparison meta-analysis of vaginal progesterone vs cerclage using placebo/no cerclage as the common comparator. The primary outcomes were preterm birth <35 weeks of gestation and perinatal mortality. Pooled relative risks (RRs) with 95% confidence intervals were calculated.RESULTSFive trials comparing vaginal progesterone vs placebo (265 women) and 5 comparing cerclage vs no cerclage (504 women) were included. Vaginal progesterone, compared to placebo, significantly reduced the risk of preterm birth <35 and <32 weeks of gestation, composite perinatal morbidity/mortality, neonatal sepsis, composite neonatal morbidity, and admission to the neonatal intensive care unit (RRs from 0.29 to 0.68). Cerclage, compared to no cerclage, significantly decreased the risk of preterm birth <37, <35, <32, and <28 weeks of gestation, composite perinatal morbidity/mortality, and birthweight <1500 g (RRs from 0.64 to 0.70). Adjusted indirect comparison meta-analyses did not show statistically significant differences between vaginal progesterone and cerclage in the reduction of preterm birth or adverse perinatal outcomes.CONCLUSIONVaginal progesterone and cerclage are equally effective for preventing preterm birth and improving perinatal outcomes in women with a singleton gestation, previous spontaneous preterm birth, and a midtrimester sonographic short cervix. The choice of treatment will depend on adverse events and cost-effectiveness of interventions and patient/physician's preferences.

Database: Medline

27. A Double-Blind, Randomized, Placebo-Controlled Trial of 17 Alpha-hydroxyprogesterone Caproate in the Management of Preterm Premature Rupture of Membranes.

Author(s): Langen, Elizabeth S; Sit, Anita; Sherwin, Katie; Lyell, Deirdre J; Blumenfeld, Yair J; El-Sayed, Yasser Y

Source: American journal of perinatology; Jul 2018; vol. 35 (no. 8); p. 779-784

Publication Date: Jul 2018

Publication Type(s): Research Support, Non-u.s. Gov't Research Support, N.i.h., Extramural Randomized Controlled Trial Multicenter Study Journal Article

PubMedID: 29298456

Abstract:OBJECTIVEThe objective of this study was to evaluate whether weekly administration of 17 α-hydroxyprogesterone caproate (17-OHPC) increases the number of women who achieve 34 weeks of gestation after preterm premature rupture of membranes (PPROM).STUDY DESIGNWe conducted a multicenter double-blind, randomized controlled trial of 17-OHPC versus placebo among women with PPROM. Women with singleton pregnancy, clinically confirmed PPROM, and without evidence of active infection or major fetal malformation between 240/7 and 320/7 weeks of pregnancy were offered enrollment. Women received weekly injections of 17-OHPC versus placebo until 340/7 weeks of gestation or delivery. The remainder of care was per hospital protocol. The primary outcome was achievement of 34 weeks of gestation. Secondary outcomes included length of latency and maternal and fetal outcomes.RESULTSIn this study, 21 women were enrolled. Eleven women received placebo and 10 received 17-OHPC. The study was closed prematurely secondary to poor enrollment. None of the women remained pregnant until 34 weeks of gestation. The median latency periods were 8 and 14.5 days for the placebo and 17-OHPC groups, respectively (p = 0.14). There were no differences in maternal or neonatal outcomes.CONCLUSIONWe did not identify any benefit from administration of 17-OHPC in pregnancies complicated by PPROM.

Database: Medline

28. Cervical pessary to reduce preterm birth <34 weeks of gestation after an episode of preterm labor and a short cervix: a randomized controlled trial.

Author(s): Pratcorona, Laia; Goya, Maria; Merced, Carme; Rodó, Carlota; Llurba, Elisa; Higueras, Teresa; Cabero, Luis; Carreras, Elena; Trial Group

Source: American journal of obstetrics and gynecology; Jul 2018; vol. 219 (no. 1); p. 99

Publication Date: Jul 2018

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 29704487

Abstract:BACKGROUNDTo date, no intervention has proved effective in reducing the spontaneous preterm birth rate in singleton pregnancies following an episode of threatened preterm labor and short cervix remaining.OBJECTIVEThis study was designed to ascertain whether cervical pessaries could be useful in preventing spontaneous preterm birth in women with singleton pregnancies and a short cervix after a threatened preterm labor episode.STUDY DESIGNThis open randomized controlled trial was conducted in 357 pregnant women (between 240-336 weeks) who had not delivered 48 hours after a threatened preterm labor episode and had a short cervix remaining (≤25 mm at 240-296 weeks; ≤15 mm at 300-336 weeks). Patients were randomly assigned to cervical pessary (179) or routine management (178). The primary outcome was the spontaneous preterm birth rate <34 weeks. Spontaneous preterm birth <28 and 37 weeks and neonatal morbidity and mortality were also evaluated in an intention-to-treat analysis.RESULTSNo significant differences between the pessary and routine management groups were observed in the spontaneous preterm

birth rate <34 weeks (19/177 [10.7%] in the pessary group vs 24/175 [13.7%] in the control group; relative risk, 0.78; 95% confidence interval, 0.45-1.38). Spontaneous preterm birth <37 weeks occurred less frequently in the pessary group (26/175 [14.7%] vs 44/175 [25.1%]; relative risk, 0.58; 95% confidence interval, 0.38-0.90; P = .01). Preterm premature rupture of membranes rate was significantly lower in pessary carriers (4/177 [2.3%] vs 14/175 [8.0%]; relative risk, 0.28; 95% confidence interval, 0.09-0.84; P = .01). The pessary group less frequently required readmission for new threatened preterm labor episodes (8/177 [4.5%] vs 35/175 [20.0%]; relative risk, 0.23; 95% confidence interval, 0.11-0.47; P < .0001). No serious adverse maternal events occurred; neonatal morbidity and mortality were similar in both groups.CONCLUSIONPessary use did not significantly lower the spontaneous preterm birth rate <34 weeks in women with a short cervix remaining after a threatened preterm labor episode but did significantly reduce the spontaneous preterm birth rate <37 weeks, threatened preterm labor recurrence, and the preterm premature rupture of membranes rate.

Database: Medline

29. Does progesterone prophylaxis to prevent preterm labour improve outcome? A randomised double-blind placebo-controlled trial (OPPTIMUM).

Author(s): Norman, Jane E; Marlow, Neil; Messow, Claudia-Martina; Shennan, Andrew; Bennett, Philip R; Thornton, Steven; Robson, Stephen C; McConnachie, Alex; Petrou, Stavros; Sebire, Neil J; Lavender, Tina; Whyte, Sonia; Norrie, John

Source: Health technology assessment (Winchester, England); Jun 2018; vol. 22 (no. 35); p. 1-304

Publication Date: Jun 2018

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Journal Article

PubMedID: 29945711

Available at Health technology assessment (Winchester, England) - from Unpaywall

Abstract:BACKGROUNDProgesterone prophylaxis is widely used to prevent preterm birth but is not licensed and there is little information on long-term outcome.OBJECTIVETo determine the effect of progesterone prophylaxis in women at high risk of preterm birth on obstetric, neonatal and childhood outcomes.DESIGNDouble-blind, randomised placebo-controlled trial.SETTINGObstetric units in the UK and Europe between February 2009 and April 2013.PARTICIPANTSWomen with a singleton pregnancy who are at high risk of preterm birth because of either a positive fibronectin test or a negative fibronectin test, and either previous spontaneous birth at ≤ 34 weeks+0 of gestation or a cervical length of ≤ 25 mm.INTERVENTIONSFibronectin test at 18+0 to 23+0 weeks of pregnancy to determine risk of preterm birth. Eligible women were allocated (using a web-based randomisation portal) to 200 mg of progesterone or placebo, taken vaginally daily from 22+0 to 24+0 until 34+0 weeks' gestation. Participants, caregivers and those assessing the outcomes were blinded to group assignment until data collection was complete.MAIN OUTCOME MEASURESThere were three primary outcomes, as follows: (1) obstetric - fetal death or delivery before 34+0 weeks' gestation; (2) neonatal - a composite of death, brain injury on ultrasound scan (according to specific criteria in the protocol) and bronchopulmonary dysplasia; and (3) childhood - the Bayley-III cognitive composite score at 22-26 months of age.RESULTSIn total, 96 out of 600 (16%) women in the progesterone group and 108 out of 597 (18%) women in the placebo group had the primary obstetric outcome [odds ratio (OR) 0.86, 95% confidence interval (CI) 0.61 to 1.22]. Forty-six out of 589 (8%) babies of women in the progesterone group and 62 out of 587 (11%) babies of women in the placebo group experienced the primary neonatal outcome [OR 0.72, 95% CI 0.44 to 1.17]. The mean Bayley-III cognitive composite score of the children at 2 years of age was 97.3 points [standard deviation (SD) 17.9 points; n = 430] in the progesterone group and 97.7 points (SD 17.5 points; n = 439) in the placebo group (difference in means -0.48, 95% CI -2.77 to 1.81).LIMITATIONSOverall

compliance with the intervention was 69%.HARMSThere were no major harms, although there was a trend of more deaths from trial entry to 2 years in the progesterone group (20/600) than in the placebo group (16/598) (OR 1.26, 95% CI 0.65 to 2.42).CONCLUSIONSIn this study, progesterone had no significant beneficial or harmful effects on the primary obstetric, neonatal or childhood outcomes.The OPPTIMUM trial is now complete. We intend to participate in a comprehensive individual patient-level data meta-analysis examining women with a singleton pregnancy with a variety of risk factors for preterm birth.TRIAL REGISTRATIONCurrent Controlled Trials ISRCTN14568373.FUNDINGThis trial was funded by the Medical Research Council (MRC) and managed by the National Institute for Health Research (NIHR) on behalf of the MRC-NIHR partnership.

Database: Medline

30. Vaginal progesterone for preventing preterm birth and adverse perinatal outcomes in singleton gestations with a short cervix: a meta-analysis of individual patient data.

Author(s): Romero, Roberto; Conde-Agudelo, Agustin; Da Fonseca, Eduardo; O'Brien, John M; Cetingoz, Elcin; Creasy, George W; Hassan, Sonia S; Nicolaides, Kypros H

Source: American journal of obstetrics and gynecology; Feb 2018; vol. 218 (no. 2); p. 161-180

Publication Date: Feb 2018

Publication Type(s): Research Support, Non-u.s. Gov't Meta-analysis Journal Article Review Systematic Review

PubMedID: 29157866

Available at American journal of obstetrics and gynecology - from Unpaywall

Abstract:BACKGROUNDThe efficacy of vaginal progesterone for preventing preterm birth and adverse perinatal outcomes in singleton gestations with a short cervix has been questioned after publication of the OPPTIMUM study.OBJECTIVETo determine whether vaginal progesterone prevents preterm birth and improves perinatal outcomes in asymptomatic women with a singleton gestation and a midtrimester sonographic short cervix.STUDY DESIGNWe searched MEDLINE, EMBASE, LILACS, and CINAHL (from their inception to September 2017); Cochrane databases; bibliographies; and conference proceedings for randomized controlled trials comparing vaginal progesterone vs placebo/no treatment in women with a singleton gestation and a midtrimester sonographic cervical length ≤25 mm. This was a systematic review and meta-analysis of individual patient data. The primary outcome was preterm birth <33 weeks of gestation. Secondary outcomes included adverse perinatal outcomes and neurodevelopmental and health outcomes at 2 years of age. Individual patient data were analyzed using a 2-stage approach. Pooled relative risks with 95% confidence intervals were calculated. Quality of evidence was assessed using the GRADE methodology.RESULTSData were available from 974 women (498 allocated to vaginal progesterone, 476 allocated to placebo) with a cervical length ≤25 mm participating in 5 high-quality trials. Vaginal progesterone was associated with a significant reduction in the risk of preterm birth <33 weeks of gestation (relative risk, 0.62; 95% confidence interval, 0.47-0.81; P = .0006; high-quality evidence). Moreover, vaginal progesterone significantly decreased the risk of preterm birth <36, <35, <34, <32, <30, and <28 weeks of gestation; spontaneous preterm birth <33 and <34 weeks of gestation; respiratory distress syndrome; composite neonatal morbidity and mortality; birthweight <1500 and <2500 g; and admission to the neonatal intensive care unit (relative risks from 0.47-0.82; high-quality evidence for all). There were 7 (1.4%) neonatal deaths in the vaginal progesterone group and 15 (3.2%) in the placebo group (relative risk, 0.44; 95% confidence interval, 0.18-1.07; P = .07; low-quality evidence). Maternal adverse events, congenital anomalies, and adverse neurodevelopmental and health outcomes at 2 years of age did not differ between groups.CONCLUSIONVaginal progesterone decreases the risk of preterm birth and improves perinatal outcomes in singleton

gestations with a midtrimester sonographic short cervix, without any demonstrable deleterious effects on childhood neurodevelopment.

Database: Medline

31. Recent advances in the prevention of preterm birth

Author(s): Keelan J.A.; Newnham J.P.

Source: F1000Research; 2017; vol. 6

Publication Date: 2017

Publication Type(s): Review

PubMedID: 28781747

Available at F1000Research - from Europe PubMed Central - Open Access

Available at F1000Research - from Unpaywall

Abstract: Preterm birth (PTB) remains a major obstetric healthcare problem and a significant contributor to perinatal morbidity, mortality, and long-term disability. Over the past few decades, the perinatal outcomes of preterm neonates have improved markedly through research and advances in neonatal care, whereas rates of spontaneous PTB have essentially remained static. However, research into causal pathways and new diagnostic and treatment modalities is now bearing fruit and translational initiatives are beginning to impact upon PTB rates. Successful PTB prevention requires a multifaceted approach, combining public health and educational programs, lifestyle modification, access to/optimisation of obstetric healthcare, effective prediction and diagnostic modalities, and the application of effective, targeted interventions. Progress has been made in some of these areas, although there remain areas of controversy and uncertainty. Attention is now being directed to areas where greater gains can be achieved. In this mini-review, we will briefly and selectively review a range of PTB prevention strategies and initiatives where progress has been made and where exciting opportunities await exploitation, evaluation, and implementation.

Database: EMBASE

32. Progesterone for prevention of preterm birth shortcomings and unintended consequences of the orphan drug act

Author(s): Gee R.E.; Kuy S.; Karas L.O.

Source: Obstetrics and Gynecology; 2017; vol. 130 (no. 6); p. 1202-1206

Publication Date: 2017

Publication Type(s): Review

PubMedID: 29112651

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: Preterm birth is a problem of major public health significance that continues to plague our country despite the existence of a therapy, 17a-hydroxyprogesterone caproate, with known efficacy in reducing the risk of spontaneous preterm birth among high-risk women. Over the past several years, the Louisiana Department of Health has undertaken a robust, multifaceted initiative to improve access to 17a-hydroxyprogesterone caproate, which resulted in a 3.5-fold increase in the percentage of eligible high-risk pregnant women in the Medicaid program who received the therapy between 2013 and 2016. Yet despite Louisiana's progress, the vast majority of the eligible population still fails to receive 17a-hydroxyprogesterone caproate. In this Current Commentary, we argue that the high price of progesterone since U.S. Food and Drug Administration approval has unnecessarily complicated access, and our nation has potentially suffered nearly 60,000 avoidable premature births as a consequence. We present the history of the orphan drug approval and manufacturer-imposed price increase for injectable progesterone, the interplay between the drug's high price and the persistence of racial and ethnic disparities in preterm birth, which are particularly germane in Louisiana, and Louisiana's broadreaching efforts to improve progesterone coverage. The story of 17a-hydroxyprogesterone caproate highlights the durable barriers that high prices place in the way of access and helps illuminate the shortcomings and unintended consequences of the Orphan Drug Act. This case, however, is not an outlier; it is the fartoo- common product of monopoly pricing in the U.S. pharmaceutical market, inadvertently bolstered by existing law, at the expense of affordability and patient access.

Database: EMBASE

33. Tocolysis: Present and future treatment options.

Author(s): Younger, Joshua D; Reitman, Elena; Gallos, George

Source: Seminars in perinatology; Dec 2017; vol. 41 (no. 8); p. 493-504

Publication Date: Dec 2017

Publication Type(s): Journal Article Review

PubMedID: 29191291

Abstract: In the United States, the generally accepted indication for tocolytic therapy centers on suppression of preterm labor. This may be in the form of preventative therapy with progesterone in women with prior spontaneous preterm birth or as an acute intervention to suppress established uterine contractions associated with cervical change occurring at less than 37 weeks gestation. This article seeks to apply this perspective to tocolytic therapy. Here, we provide a review of current tocolytic options and what the last decade of discovery has revealed about the regulation of myometrial excitability and quiescence. Moving forward, we must incorporate the emerging molecular data that is amassing in order to develop novel and effective tocolytic therapeutic options to prevent preterm labor and spontaneous preterm birth (sPTB).

Database: Medline

34. Maintaining and repeating tocolysis: A reflection on evidence.

Author(s): Dehaene, Isabelle; Bergman, Lina; Turtiainen, Paula; Ridout, Alexandra; Mol, Ben Willem; Lorthe, Elsa; from the International Spontaneous Preterm birth Young Investigators group (I-SPY)

Source: Seminars in perinatology; Dec 2017; vol. 41 (no. 8); p. 468-476

Publication Date: Dec 2017

Publication Type(s): Journal Article Review

PubMedID: 28943054

Abstract: It is inherent to human logic that both doctors and patients want to suppress uterine contractions when a woman presents in threatened preterm labor. Tocolysis is widely applied in women with threatened preterm labor with a variety of drugs. According to literature, tocolysis is indicated to enable transfer to a tertiary center as well as to ensure the administration of corticosteroids for fetal maturation. There is international discrepancy in the content and the implementation of guidelines on preterm labor. Tocolysis is often maintained or repeated. Nevertheless, the benefit of prolonging pregnancy has not yet been proven, and it is not impossible that prolongation of the pregnancy in a potential hostile environment could harm the fetus. Here we reflect on the use of tocolysis, focusing on maintenance and repeated tocolysis, and compare international guidelines and practices to available evidence. Finally, we propose strategies to improve the evaluation and use of tocolytics, with potential implications for future research.

Database: Medline

35. Current options for mechanical prevention of preterm birth.

Author(s): Boelig, Rupsa C; Berghella, Vincenzo

Source: Seminars in perinatology; Dec 2017; vol. 41 (no. 8); p. 452-460

Publication Date: Dec 2017

Publication Type(s): Journal Article Review

PubMedID: 29033106

Abstract: Cervical insufficiency can be defined by a combination of obstetric history, cervical dilation on exam, and/or short cervical length in women with prior preterm birth. Options for mechanical intervention include cerclage and pessary. There is evidence to support the benefit of a cervical cerclage in women with singleton gestations who have a diagnosis of cervical insufficiency either based on second trimester painless cervical dilatation leading to recurrent early preterm births, or a history of early spontaneous preterm birth and a second trimester transvaginal ultrasound short cervical length or cervical dilation on exam. For women with multiple gestations, the benefit of a cerclage is uncertain, and further study is warranted. The pessary has also been studied for mechanical prevention of preterm birth in various populations, however the results so far have been mixed and warrants further study prior to routine use.

Database: Medline

36. The More, the Better? Combining Interventions to Prevent Preterm Birth in Women at Risk: a Systematic Review and Meta-Analysis.

Author(s): Jarde, Alexander; Lewis-Mikhael, Anne-Mary; Dodd, Jodie M; Barrett, Jon; Saito, Shigeru; Beyene, Joseph; McDonald, Sarah D

Source: Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC; Dec 2017; vol. 39 (no. 12); p. 1192-1202

Publication Date: Dec 2017

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 29197486

Abstract:OBJECTIVESTo systematically examine the evidence around the combination of interventions to prevent preterm birth.METHODSWithout language restrictions, we searched clinicaltrials.gov and five electronic databases (Medline, EMBASE, CINAHL, Cochrane CENTRAL, and Web of Science) up to July 7, 2016. We included randomized and non-randomized studies where asymptomatic women at risk of preterm birth received any combination of progesterone, cerclage, or pessary compared with either one or no intervention. Primary outcomes were preterm birth <34 and <37 weeks and neonatal death. Two independent reviewers extracted data using a piloted form and assessed risk and direction of bias. We pooled data with unlikely or unclear bias using random-effects meta-analyses. Comparisons with likely bias (e.g., confounding by indication) were not pooled.RESULTSWe screened 1335 results and assessed 154 full texts, including seven studies. In singletons, we found no differences in preterm birth <34 weeks when comparing pessary & progesterone with pessary alone (RR 1.30, 95% CI 0.70-2.42) or progesterone alone (RR 1.16, 95% CI 0.79-1.72). Similarly, we found no differences in preterm birth <37 weeks when comparing cerclage & progesterone with cerclage alone (RR 1.04, 95% CI 0.56-1.93) or with progesterone alone (RR 0.82, 95% CI 0.57-1.19) nor between pessary & progesterone and pessary alone (RR 1.04, 95% CI 0.62-1.74). No data were available for neonatal death in singletons.CONCLUSIONSDespite being a common clinical practice, evidence to support the combined use of multiple versus single interventions for preventing preterm birth is scarce.

Database: Medline

37. Effect of Cervical Pessary on Spontaneous Preterm Birth in Women With Singleton Pregnancies and Short Cervical Length: A Randomized Clinical Trial.

Author(s): Saccone, Gabriele; Maruotti, Giuseppe Maria; Giudicepietro, Antonia; Martinelli, Pasquale; Italian Preterm Birth Prevention (IPP) Working Group

Source: JAMA; Dec 2017; vol. 318 (no. 23); p. 2317-2324

Publication Date: Dec 2017

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 29260226

Abstract: ImportanceSpontaneous preterm birth is a major cause of perinatal morbidity and mortality. It is unclear if a cervical pessary can reduce the risk of spontaneous preterm delivery.ObjectiveTo test whether in asymptomatic women with singleton pregnancies and no prior spontaneous preterm birth but with short cervical length on transvaginal ultrasound, use of a cervical pessary would reduce the rate of spontaneous preterm birth at less than 34 weeks of gestation.Design, Setting, and ParticipantsParallel-group, nonblinded, randomized clinical trial conducted from March 1, 2016, to May 25, 2017, at a single center in Italy. Asymptomatic women with singleton gestations, no previous spontaneous preterm births, and cervical lengths of 25 mm or less at 18 weeks 0 days to 23 weeks 6 days of gestation were eligible.InterventionsPatients were randomized 1:1 to receive either cervical pessary (n = 150) or no pessary (n = 150). The pessary was removed between 37 weeks 0 days and 37 weeks 6 days of gestation or earlier if clinically indicated. The control group received standard care. For cervical length of 20 mm or shorter, women in both groups were prescribed vaginal progesterone, 200 mg/d, until 36 weeks 6 days of gestation. No bed rest or activity restriction was recommended.Main Outcomes and MeasuresThe primary end point was spontaneous preterm birth at less than 34 weeks of gestation. Secondary outcomes were adverse events.ResultsAmong 300 women who were randomized (mean age, 29 [SD, 6.3] years; mean gestational age, 22 [SD, 1.3] weeks), 100% completed the trial. The primary end point occurred in 11 women (7.3%) in the pessary group and 23 women (15.3%) in the control group (between-group difference, -8.0% [95% CI, -15.7% to -0.4]; relative risk, 0.48 [95% CI, 0.24-0.95]). During follow-up, the pessary group had a higher rate of increased or new vaginal discharge (86.7% vs 46.0%; between-group difference, +40.7% [95% CI, +30.1%-+50.3%]; relative risk, 1.88 [95% CI, 1.57-2.27]).Conclusions and RelevanceAmong women without prior spontaneous preterm birth who had asymptomatic singleton pregnancies and short transvaginal cervical length, use of a cervical pessary, compared with no pessary use, resulted in a lower rate of spontaneous preterm birth at less than 34 weeks of gestation. The results of this single-center, nonblinded study among selected pregnant women require confirmation in multicenter clinical trials.Trial Registrationclinicaltrials.gov Identifier: NCT02716909.

Database: Medline

38. Use of progesterone supplement therapy for prevention of preterm birth: review of literatures.

Author(s): Choi, Suk-Joo

Source: Obstetrics & gynecology science; Sep 2017; vol. 60 (no. 5); p. 405-420

Publication Date: Sep 2017

Publication Type(s): Journal Article Review

PubMedID: 28989916

Available at Obstetrics & gynecology science - from Europe PubMed Central - Open Access

Abstract: Preterm birth (PTB) is one of the most common complications during pregnancy and it primarily accounts for neonatal mortality and numerous morbidities including long-term sequelae including cerebral palsy and developmental disability. The most effective treatment of PTB is prediction and prevention of its risks. Risk factors of PTB include history of PTB, short cervical length (CL), multiple pregnancies, ethnicity, smoking, uterine anomaly and history of curettage or cervical conization. Among these risk factors, history of PTB, and short CL are the most important predictive factors. Progesterone supplement therapy is one of the few proven effective methods to prevent PTB in women with history of spontaneous PTB and in women with short CL. There are 2 types of progesterone therapy currently used for prevention of PTB: weekly intramuscular injection of 17-alpha hydroxyprogesterone caproate and daily administration of natural micronized progesterone vaginal gel, vaginal suppository, or oral capsule. However, the efficacy of progesterone therapy to prevent PTB may vary depending on the administration route, form, dose of progesterone and indications for the treatment. This review aims to summarize the efficacy and safety of progesterone supplement therapy on prevention of PTB according to different indication, type, route, and dose of progesterone, based on the results of recent randomized trials and meta-analysis.

Database: Medline

39. Vaginal progesterone pessaries for pregnant women with a previous preterm birth to prevent neonatal respiratory distress syndrome (the PROGRESS Study): A multicentre, randomised, placebo-controlled trial.

Author(s): Crowther, Caroline A; Ashwood, Pat; McPhee, Andrew J; Flenady, Vicki; Tran, Thach; Dodd, Jodie M; Robinson, Jeffrey S; PROGRESS Study Group

Source: PLoS medicine; Sep 2017; vol. 14 (no. 9); p. e1002390

Publication Date: Sep 2017

Publication Type(s): Randomized Controlled Trial Multicenter Study Journal Article

PubMedID: 28949973

Available at PLoS medicine - from Europe PubMed Central - Open Access

Available at PLoS medicine - from Public Library of Science (PLoS)

Available at PLoS medicine - from ProQuest (Health Research Premium) - NHS Version

Available at PLoS medicine - from Unpaywall

Abstract:BACKGROUNDNeonatal respiratory distress syndrome, as a consequence of preterm birth, is a major cause of early mortality and morbidity. The withdrawal of progesterone, either actual or functional, is thought to be an antecedent to the onset of labour. There remains limited information on clinically relevant health outcomes as to whether vaginal progesterone may be of benefit for pregnant women with a history of a previous preterm birth, who are at high risk of a recurrence. Our primary aim was to assess whether the use of vaginal progesterone pessaries in women with a history of previous spontaneous preterm birth reduced the risk and severity of respiratory distress

syndrome in their infants, with secondary aims of examining the effects on other neonatal morbidities and maternal health and assessing the adverse effects of treatment.METHODSWomen with a live singleton or twin pregnancy between 18 to <24 weeks' gestation and a history of prior preterm birth at less than 37 weeks' gestation in the preceding pregnancy, where labour occurred spontaneously or in association with cervical incompetence or following preterm prelabour rupture of the membranes, were eligible. Women were recruited from 39 Australian, New Zealand, and Canadian maternity hospitals and assigned by randomisation to vaginal progesterone pessaries (equivalent to 100 mg vaginal progesterone) (n = 398) or placebo (n = 389). Participants and investigators were masked to the treatment allocation. The primary outcome was respiratory distress syndrome and severity. Secondary outcomes were other respiratory morbidities; other adverse neonatal outcomes; adverse outcomes for the woman, especially related to preterm birth; and side effects of progesterone treatment. Data were analysed for all the 787 women (100%) randomised and their 799 infants.FINDINGSMost women used their allocated study treatment (740 women, 94.0%), with median use similar for both study groups (51.0 days, interquartile range [IQR] 28.0-69.0, in the progesterone group versus 52.0 days, IQR 27.0-76.0, in the placebo group). The incidence of respiratory distress syndrome was similar in both study groups-10.5% (42/402) in the progesterone group and 10.6% (41/388) in the placebo group (adjusted relative risk [RR] 0.98, 95% confidence interval [CI] 0.64-1.49, p = 0.912)-as was the severity of any neonatal respiratory disease (adjusted treatment effect 1.02, 95% CI 0.69-1.53, p = 0.905). No differences were seen between study groups for other respiratory morbidities and adverse infant outcomes, including serious infant composite outcome (155/406 [38.2%] in the progesterone group and 152/393 [38.7%] in the placebo group, adjusted RR 0.98, 95% CI 0.82-1.17, p = 0.798). The proportion of infants born before 37 weeks' gestation was similar in both study groups (148/406 [36.5%] in the progesterone group and 146/393 [37.2%] in the placebo group, adjusted RR 0.97, 95% CI 0.81-1.17, p = 0.765). A similar proportion of women in both study groups had maternal morbidities, especially those related to preterm birth, or experienced side effects of treatment. In 9.9% (39/394) of the women in the progesterone group and 7.3% (28/382) of the women in the placebo group, treatment was stopped because of side effects (adjusted RR 1.35, 95% CI 0.85-2.15, p = 0.204). The main limitation of the study was that almost 9% of the women did not start the medication or forgot to use it 3 or more times a week.CONCLUSIONSOur results do not support the use of vaginal progesterone pessaries in women with a history of a previous spontaneous preterm birth to reduce the risk of neonatal respiratory distress syndrome or other neonatal and maternal morbidities related to preterm birth. Individual participant data meta-analysis of the relevant trials may identify specific women for whom vaginal progesterone might be of benefit.TRIAL REGISTRATIONCurrent Clinical Trials ISRCTN20269066.

Database: Medline

40. Progesterone in women with arrested premature labor, a report of a randomised clinical trial and updated meta-analysis.

Author(s): Wood, Stephen; Rabi, Yacov; Tang, Selphee; Brant, Rollin; Ross, Susan

Source: BMC pregnancy and childbirth; Aug 2017; vol. 17 (no. 1); p. 258

Publication Date: Aug 2017

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 28768474

Available at BMC pregnancy and childbirth - from BioMed Central

Abstract:BACKGROUNDProgesterone may be effective in prevention of premature birth in some high risk populations. Women with arrested premature labor are at risk of recurrent labor and maintenance therapy with standard tocolytics has not been successful.METHODSRandomized double blinded clinical trial of daily treatment with 200 mg vaginal progesterone in women with arrested premature labor and an updated meta-analysis.RESULTSThe clinical trial was terminated early after 41 women were enrolled. Vaginal progesterone treatment did not change the median gestational age at delivery: 36+2 weeks versus 36+4 weeks, p = .865 nor increase the mean latency to delivery: 44.5 days versus 46.6 days, p = .841. In the updated meta-analysis, progesterone treatment did reduce delivery <37 weeks gestation and increase latency to delivery, but this treatment effect was not evident in the high quality trials: (OR 1.23, 95% CI 0.91, 1.67) and (-0.95 days, 95% CI -5.54, 3.64) respectively.CONCLUSIONProgesterone is not effective for preventing preterm birth following arrested preterm labor.

Database: Medline

41. Meta-analysis of randomized controlled trials comparing 17α-hydroxyprogesterone caproate and vaginal progesterone for the prevention of recurrent spontaneous preterm delivery.

Author(s): Oler, Elizabeth; Eke, Ahizechukwu C; Hesson, Ashley

Source: International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics; Jul 2017; vol. 138 (no. 1); p. 12-16

Publication Date: Jul 2017

Publication Type(s): Meta-analysis Comparative Study Journal Article Review

PubMedID: 28369874

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library

Abstract:BACKGROUNDVaginal progesterone and 17α-hydroxyprogesterone (17α-OHP) are both used to prevent preterm delivery in women who have experienced spontaneous preterm delivery (SPTD) previously. Randomized trial data of the comparative effectiveness of these interventions have been mixed.OBJECTIVESTo compare the efficacy of intramuscular 17α-OHP and vaginal progesterone in the prevention of recurrent SPTD.SEARCH STRATEGYCochrane Central Register of Controlled Trials, African Journals Online, Embase, Google Scholar, ISI Web of Science, LILACS, CINAHL, PubMed, and registers of ongoing trials were searched using keywords related to 17α-OHP, vaginal progesterone, and preterm delivery.SELECTION CRITERIARandomized controlled trials published between January 1, 1966, and November 30, 2016, comparing 17α-OHP and vaginal progesterone for the prevention of recurrent SPTD during singleton pregnancies were included.DATA COLLECTION AND ANALYSISStudy data were extracted and meta-analyses were performed when outcomes were comparable.MAIN RESULTSThe meta-analyses included data from three randomized trials. Lower rates of SPTD before 34 weeks (relative risk 0.71, 95% confidence interval 0.53-0.95) and before 32 weeks (relative risk 0.62, 95% confidence interval 0.40-0.94) of

pregnancy were observed among patients treated with vaginal progesterone.CONCLUSIONSVaginal progesterone and 17α-OHP were comparable for the prevention of recurrent SPTD in singleton pregnancies; vaginal progesterone could be superior.

Database: Medline

42. Effectiveness of progesterone, cerclage and pessary for preventing preterm birth in singleton pregnancies: a systematic review and network meta-analysis.

Author(s): Jarde, A; Lutsiv, O; Park, C K; Beyene, J; Dodd, J M; Barrett, J; Shah, P S; Cook, J L; Saito, S; Biringer, A B; Sabatino, L; Giglia, L; Han, Z; Staub, K; Mundle, W; Chamberlain, J; McDonald, S D

Source: BJOG : an international journal of obstetrics and gynaecology; Jul 2017; vol. 124 (no. 8); p. 1176-1189

Publication Date: Jul 2017

Publication Type(s): Meta-analysis Comparative Study Journal Article Systematic Review

PubMedID: 28276151

Available at BJOG : an international journal of obstetrics and gynaecology - from Wiley Online Library

Available at BJOG : an international journal of obstetrics and gynaecology - from Unpaywall

Abstract:BACKGROUNDPreterm birth (PTB) is the leading cause of infant death, but it is unclear which intervention is best to prevent it.OBJECTIVESTo compare progesterone, cerclage and pessary, determine their relative effects and rank them.SEARCH STRATEGYWe searched Medline, EMBASE, CINAHL, Cochrane CENTRAL and Web of Science (to April 2016), without restrictions, and screened references of previous reviews.SELECTION CRITERIAWe included randomised trials of progesterone, cerclage or pessary for preventing PTB in women with singleton pregnancies at risk as defined by each study.DATA COLLECTION AND ANALYSISWe extracted data by duplicate using a piloted form and performed Bayesian random-effects network meta-analyses and pairwise meta-analyses. We rated evidence quality using GRADE, ranked interventions using SUCRA and calculated numbers needed to treat (NNT).MAIN RESULTSWe included 36 trials (9425 women; 25 low risk of bias trials). Progesterone ranked first or second for most outcomes, reducing PTB < 34 weeks [odds ratio (OR) 0.44; 95% credible interval (CrI) 0.22-0.79; NNT 9; low quality], <37 weeks (OR 0.58; 95% CrI 0.41-0.79; NNT 9; moderate quality), and neonatal death (OR 0.50; 95% CrI 0.28-0.85; NNT 35; high quality), compared with control, in women overall at risk. We found similar results in the subgroup with previous PTB, but only a reduction of PTB < 34 weeks in women with a short cervix. Pessary showed inconsistent benefit and cerclage did not reduce PTB < 37 or <34 weeks.CONCLUSIONSProgesterone was the best intervention for preventing PTB in singleton pregnancies at risk, reducing PTB < 34 weeks, <37 weeks, neonatal demise and other sequelae.TWEETABLE ABSTRACTProgesterone was better than cerclage and pessary to prevent preterm birth, neonatal death and more in network meta-analysis.

Database: Medline

43. Preterm birth prevention in twin pregnancies with progesterone, pessary, or cerclage: a systematic review and meta-analysis.

Author(s): Jarde, A; Lutsiv, O; Park, C K; Barrett, J; Beyene, J; Saito, S; Dodd, J M; Shah, P S; Cook, J L; Biringer, A B; Giglia, L; Han, Z; Staub, K; Mundle, W; Vera, C; Sabatino, L; Liyanage, S K; McDonald, S D

Source: BJOG : an international journal of obstetrics and gynaecology; Jul 2017; vol. 124 (no. 8); p. 1163-1173

Publication Date: Jul 2017

Publication Type(s): Meta-analysis Journal Article Systematic Review

PubMedID: 28176485

Abstract:BACKGROUNDAbout half of twin pregnancies deliver preterm, and it is unclear whether any intervention reduces this risk.OBJECTIVESTo assess the evidence for the effectiveness of progesterone, cerclage, and pessary in twin pregnancies.SEARCH STRATEGYWe searched Medline, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials, and ISI Web of Science, without language restrictions, up to 25 January 2016.SELECTION CRITERIARandomised controlled trials of progesterone, cerclage, or pessary for preventing preterm birth in women with twin pregnancies, without symptoms of threatened preterm labour.DATA COLLECTION AND ANALYSISTwo independent reviewers extracted data using a piloted form. Study quality was appraised with the Cochrane Risk of Bias tool. We performed pairwise inverse variance random-effects meta-analyses.MAIN RESULTSWe included 23 trials (all but three were considered to have a low risk of bias) comprising 6626 women with twin pregnancies. None of the interventions significantly reduced the risk of preterm birth overall at <34 or <37 weeks of gestation, or neonatal death, our primary outcomes, compared to a control group. In women receiving vaginal progesterone, the relative risk (RR) of preterm birth <34 weeks of gestation was 0.82 (95% CI 0.64-1.05, seven studies, I2 36%), with a significant reduction in some key secondary outcomes, including very low birthweight (<1500 g, RR 0.71, 95% CI 0.52-0.98, four studies, I2 46%) and mechanical ventilation (RR 0.61, 95% CI 0.45-0.82, four studies, I2 22%).CONCLUSIONIn twin gestations, although no overarching intervention was beneficial for the prevention of preterm birth and its sequelae, vaginal progesterone improved some important secondary outcomes.TWEETABLE ABSTRACTVaginal progesterone may be beneficial in twin pregnancies, but not 17-OHPC, cerclage, or pessary.

Database: Medline

44. Progestogens for Maintenance Tocolysis in Women With a Short Cervix: A Randomized Controlled Trial.

Author(s): Facchinetti, Fabio; Vergani, Patrizia; Di Tommaso, Mariarosaria; Marozio, Luca; Acaia, Barbara; Vicini, Roberto; Pignatti, Lucrezia; Locatelli, Anna; Spitaleri, Marina; Benedetto, Chiara; Zaina, Barbara; D'Amico, Roberto

Source: Obstetrics and gynecology; Jul 2017; vol. 130 (no. 1); p. 64-70

Publication Date: Jul 2017

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 28594783

Abstract:OBJECTIVETo assess the efficacy of progestogens for maintenance tocolysis in women undelivered after their first preterm labor episode.METHODSWomen with singleton pregnancies between 22 0/7 and 31 6/7 weeks of gestation with arrested preterm labor and a cervical length 25 mm or less at hospital discharge were eligible. Patients with a previous preterm birth were excluded. In a randomized controlled trial conducted in five university hospitals, women were randomized to receive vaginal progesterone (200 mg per day) or intramuscular 17α-hydroxyprogesterone caproate (341 mg per week) or to an observation groups (control group). The primary outcome was the proportion of women with preterm birth at less than 37 weeks of gestation. A sample size of 160 per group (n=480) was planned to compare vaginal progesterone and 17α-hydroxyprogesterone caproate groups with those in the control group. The sample size estimation was based on the hypothesis that the risk of experiencing preterm birth in the control group would be 30% and that 17α-hydroxyprogesterone caproate or progesterone would decrease this risk to 15%. A P value of <.025 was defined as statistically significant. At planned interim analysis (n=254), the trial was stopped for futility.RESULTSBetween July 2010 and June 2015, 257 women were eligible and 254 were subsequently randomly assigned to vaginal progesterone (n=86), 17α-hydroxyprogesterone caproate (n=87), or observation (n=81). Nineteen (8%) were excluded from the analysis because they either dropped out or information was missing, leaving 235 women available for analysis. Demographic characteristics were similar across groups. The preterm birth rate did not differ significantly between groups: 23% in the 17α-hydroxyprogesterone caproate group, 39% in the vaginal progesterone group, and 22% in the women in the control group (P=.949 for 17α-hydroxyprogesterone caproate compared with the women in the control group and P=.027 for vaginal progesterone compared with women in the control group).CONCLUSIONThe use of progestogens for maintenance tocolysis in women with a short cervix did not reduce the rate of preterm birth.CLINICAL TRIAL REGISTRATIONClinicalTrials.gov, NCT01178788.

Database: Medline

45. Vaginal progesterone vs intramuscular 17α-hydroxyprogesterone caproate for prevention of recurrent spontaneous preterm birth in singleton gestations: systematic review and meta-analysis of randomized controlled trials.

Author(s): Saccone, G; Khalifeh, A; Elimian, A; Bahrami, E; Chaman-Ara, K; Bahrami, M A; Berghella, V

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Mar 2017; vol. 49 (no. 3); p. 315-321

Publication Date: Mar 2017

Publication Type(s): Meta-analysis Comparative Study Journal Article Review Systematic Review

PubMedID: 27546354

Available at Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology - from Wiley Online Library

Abstract:OBJECTIVERandomized controlled trials (RCTs) have recently compared intramuscular 17α-hydroxyprogesterone caproate (17-OHPC) with vaginal progesterone for reducing the risk of spontaneous preterm birth (SPTB) in singleton gestations with prior SPTB. The aim of this systematic review and meta-analysis was to evaluate the efficacy of vaginal progesterone compared with 17-OHPC in prevention of SPTB in singleton gestations with prior SPTB.METHODSSearches of electronic databases were performed to identify all RCTs of asymptomatic singleton gestations with prior SPTB that were randomized to prophylactic treatment with either vaginal progesterone (intervention group) or intramuscular 17-OHPC (comparison group). No restrictions for language or geographic location were applied. The primary outcome was SPTB < 34 weeks. Secondary outcomes were SPTB < 37 weeks, < 32 weeks, < 28 weeks and < 24 weeks, maternal adverse drug reaction and neonatal outcomes. The summary measures were reported as relative risk (RR) with 95% CI. Risk of bias for each included study was assessed.RESULTSThree RCTs (680 women) were included. The mean gestational age at randomization was about 16 weeks. Women were given progesterone until 36 weeks or delivery. Regarding vaginal progesterone, one study used 90 mg gel daily, one used 100 mg suppository daily and one used 200 mg suppository daily. All included RCTs used 250 mg intramuscular 17-OHPC weekly in the comparison group. Women who received vaginal progesterone had significantly lower rates of SPTB < 34 weeks (17.5% vs 25.0%; RR, 0.71 (95% CI, 0.53-0.95); low quality of evidence) and < 32 weeks (8.9% vs 14.5%; RR, 0.62 (95% CI, 0.40-0.94); low quality of evidence) compared with women who received 17-OHPC. There were no significant differences in the rates of SPTB < 37 weeks, < 28 weeks and < 24 weeks. The rate of women who reported adverse drug reactions was significantly lower in the vaginal progesterone group compared with the 17-OHPC group (7.1% vs 13.2%; RR, 0.53 (95% CI, 0.31-0.91); very low quality of evidence). Regarding neonatal outcomes, vaginal progesterone was associated with a lower rate of neonatal intensive care unit admission compared with 17-OHPC (18.7% vs 23.5%; RR, 0.63 (95% CI, 0.47-0.83); low quality of evidence). For the comparison of 17-OHPC vs vaginal progesterone, the quality of evidence was downgraded for all outcomes by at least one degree due to imprecision (the optimal information size was not reached) and by at least one degree due to indirectness (different interventions).CONCLUSIONSDaily vaginal progesterone (either suppository or gel) started at about 16 weeks' gestation is a reasonable, if not better, alternative to weekly 17-OHPC injection for prevention of SPTB in women with singleton gestations and prior SPTB. However, the quality level of the summary estimates was low or very low as assessed by GRADE, indicating that the true effect may be, or is likely to be, substantially different from the estimate of the effect. Copyright © 2016 ISUOG. Published by John Wiley & Sons Ltd. COMPARACIÓN ENTRE LA PROGESTERONA VAGINAL Y EL 17A-HIDROXIPROGESTERONA CAPROATO INTRAMUSCULAR PARA LA PREVENCIÓN DEL PARTO PRETÉRMINO ESPONTÁNEO RECURRENTE EN EMBARAZOS CON FETO ÚNICO: REVISIÓN SISTEMÁTICA Y METAANÁLISIS DE ENSAYOS CONTROLADOS ALEATORIOS: RESUMEN OBJETIVO: Recientemente se han realizado varios ensayos controlados aleatorios (ECA) que comparaban el

caproato de 17α-hidroxiprogesterona (17-OHPC, por sus siglas en inglés) por vía intramuscular con la progesterona por vía vaginal para la reducción del riesgo de parto pretérmino espontáneo (PPTE) en embarazos con feto único de gestantes con historial de PPTE. El objetivo de esta revisión sistemática y metaanálisis fue evaluar la eficacia de la progesterona vaginal en comparación con la 17-OHPC en la prevención de embarazos con feto único de gestantes con historial de PPTE. MÉTODOS: Se realizaron búsquedas en bases de datos electrónicas para identificar todos los ECA con embarazos de feto único asintomáticos con historial de PPTE antes de ser asignados al azar a un tratamiento profiláctico, ya fuera con progesterona vaginal (grupo de intervención) o con 17-OHPC intramuscular (grupo de control). No se aplicaron restricciones respecto al idioma o la ubicación geográfica. El resultado primario fue PPTE < 34 semanas. Los resultados secundarios fueron PPTE <37 semanas, < 32 semanas, < 28 semanas y < 24 semanas, la reacción materna adversa al fármaco y los resultados neonatales. Las medidas del resumen se reportaron como riesgo relativo (RR) con IC del 95%. Para cada estudio incluido se evaluó el riesgo de sesgo.RESULTADOSSe incluyeron tres ECA (680 mujeres). La media de la edad gestacional en el momento de la aleatorización fue de 16 semanas. A las mujeres se les administró progesterona hasta la semana 36 o hasta el parto. Con respecto a la progesterona vaginal, un estudio utilizó gel de 90 mg diariamente, otro utilizó un supositorio diario de 100 mg y el otro utilizó un supositorio diario de 200 mg. Todos los ECA incluidos en el grupo de comparación utilizaron 250 mg semanales de 17-OHPC por vía intramuscular. Las mujeres que recibieron progesterona vaginal tuvieron tasas significativamente más bajas de PPTE < 34 semanas (17,5% vs. 25,0%; RR 0,71 (IC 95%, 0,53-0,95); calidad de la evidencia baja) y < 32 semanas (8,9% vs. 14,5%; RR 0,62 (IC 95%, 0,40-0,94); calidad de evidencia baja), en comparación con las mujeres que recibieron 17-OHPC. No hubo diferencias significativas en las tasas de PPTE < 37 semanas, < 28 semanas y < 24 semanas. La tasa de mujeres que reportaron reacciones adversas a los medicamentos fue significativamente menor en el grupo de progesterona vaginal en comparación con el grupo de 17-OHPC (7,1% vs. 13,2%; RR 0,53 (IC 95%, 0,31-0,91); calidad de la evidencia muy baja). En cuanto a los resultados neonatales, la progesterona vaginal se asoció a una menor tasa de admisiones en la unidad neonatal de cuidados intensivos en comparación con la 17-OHPC (18,7% vs. 23,5%; RR 0,63 (IC 95%, 0,47-0,83); calidad de evidencia baja). Para la comparación del 17-OHPC con la progesterona vaginal se rebajó la calidad de las pruebas para todos los resultados en al menos un grado debido a imprecisiones (no se alcanzó el tamaño óptimo de la información) y en al menos un grado debido al carácter indirecto de los estudios (diferentes intervenciones).CONCLUSIONESLa progesterona vaginal administrada diariamente (ya fuera como supositorio o como gel) desde la semana 16 de gestación es una alternativa razonable, si no mejor, a una inyección semanal de 17-OHPC para la prevención de PPTE en mujeres con embarazos de feto único e historial de PPTE. Sin embargo, el nivel de calidad de las estimaciones del resumen fue bajo o muy bajo según lo evaluado por GRADE, lo que indica que el verdadero efecto puede ser, o es probable que sea, sustancialmente diferente de la estimación del efecto. 17A-:META: : (randomized controlled trials,RCTs)(spontaneous preterm birth,SPTB)17α-(intramuscular 17α-hydroxyprogesterone caproate,17-OHPC)SPTB。metaSPTB17-OHPCSPTB。 : ,SPTBRCTs,RCTs()17-OHPC()。。34SPTB。37、32、2824SPTB,。(relative risk,RR)95%CI。。 : 3RCTs(680)。16。,36。,90 mg,100 mg,200 mg。,RCTs250 mg 17-OHPC。17-OHPC,34 [17.5%25.0%;RR,0.71(95% CI,0.53 ~ 0.95);]32[8.9%14.5%;RR,0.62(95% CI,0.40 ~ 0.94);]SPTB。37、2824SPTB。17-OHPC,[7.1%13.2%;RR,0.53(95% CI,0.31 ~ 0.91);]。,17-OHPC,[18.7%23.5%;RR,0.63(95% CI,0.47 ~ 0.83);]。17-OHPC,(),()。 : SPTBSPTB,16()17-OHPC,。,GRADE,,。.

Database: Medline

46. Vaginal progesterone decreases preterm birth and neonatal morbidity and mortality in women with a twin gestation and a short cervix: an updated meta-analysis of individual patient data.

Author(s): Romero, R; Conde-Agudelo, A; El-Refaie, W; Rode, L; Brizot, M L; Cetingoz, E; Serra, V; Da Fonseca, E; Abdelhafez, M S; Tabor, A; Perales, A; Hassan, S S; Nicolaides, K H

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Mar 2017; vol. 49 (no. 3); p. 303-314

Publication Date: Mar 2017

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 28067007

Abstract:OBJECTIVETo assess the efficacy of vaginal progesterone for the prevention of preterm birth and neonatal morbidity and mortality in asymptomatic women with a twin gestation and a sonographic short cervix (cervical length ≤ 25 mm) in the mid-trimester.METHODSThis was an updated systematic review and meta-analysis of individual patient data (IPD) from randomized controlled trials comparing vaginal progesterone with placebo/no treatment in women with a twin gestation and a mid-trimester sonographic cervical length ≤ 25 mm. MEDLINE, EMBASE, POPLINE, CINAHL and LILACS (all from inception to 31 December 2016), the Cochrane Central Register of Controlled Trials, Research Registers of ongoing trials, Google Scholar, conference proceedings and reference lists of identified studies were searched. The primary outcome measure was preterm birth < 33 weeks' gestation. Two reviewers independently selected studies, assessed the risk of bias and extracted the data. Pooled relative risks (RRs) with 95% confidence intervals (CI) were calculated.RESULTSIPD were available for 303 women (159 assigned to vaginal progesterone and 144 assigned to placebo/no treatment) and their 606 fetuses/infants from six randomized controlled trials. One study, which included women with a cervical length between 20 and 25 mm, provided 74% of the total sample size of the IPD meta-analysis. Vaginal progesterone, compared with placebo/no treatment, was associated with a statistically significant reduction in the risk of preterm birth < 33 weeks' gestation (31.4% vs 43.1%; RR, 0.69 (95% CI, 0.51-0.93); moderate-quality evidence). Moreover, vaginal progesterone administration was associated with a significant decrease in the risk of preterm birth < 35, < 34, < 32 and < 30 weeks' gestation (RRs ranging from 0.47 to 0.83), neonatal death (RR, 0.53 (95% CI, 0.35-0.81)), respiratory distress syndrome (RR, 0.70 (95% CI, 0.56-0.89)), composite neonatal morbidity and mortality (RR, 0.61 (95% CI, 0.34-0.98)), use of mechanical ventilation (RR, 0.54 (95% CI, 0.36-0.81)) and birth weight < 1500 g (RR, 0.53 (95% CI, 0.35-0.80)) (all moderate-quality evidence). There were no significant differences in neurodevelopmental outcomes at 4-5 years of age between the vaginal progesterone and placebo groups.CONCLUSIONAdministration of vaginal progesterone to asymptomatic women with a twin gestation and a sonographic short cervix in the mid-trimester reduces the risk of preterm birth occurring at < 30 to < 35 gestational weeks, neonatal mortality and some measures of neonatal morbidity, without any demonstrable deleterious effects on childhood neurodevelopment. Published 2017. This article is a U.S. Government work and is in the public domain in the USA.

Database: Medline

47. The safety of progestogen in the prevention of preterm birth: Meta-analysis of neonatal mortality

Author(s): Ahn K.H.; Bae N.-Y.; Hong S.-C.; Cho G.-J.; Oh M.-J.; Kim H.-J.; Lee J.-S.; Lee E.H.; Jee H.-J.

Source: Journal of Perinatal Medicine; Jan 2017; vol. 45 (no. 1); p. 11-20

Publication Date: Jan 2017

Publication Type(s): Review

PubMedID: 27124668

Abstract: The safety of preventive progestogen therapy for preterm birth remains to be established. This meta-analysis aimed to evaluate the effects of preventive progestogen therapy on neonatal mortality. Randomized controlled trials (RCTs) on the preventive use of progestogen therapy, published between October 1971 and November 2015, were identified by searching MEDLINE/PubMed, EMBASE, Scopus, ClinicalTrials.gov, Cochrane Library databases, CINAHL, POPLINE, and LILACS using "progesterone" and "preterm birth" as key terms. We conducted separate analyses according to the type of progestogen administered and plurality of the pregnancy. Twenty-two RCTs provided data on 11,188 neonates. Preventive progestogen treatment in women with a history of preterm birth or short cervical length was not associated with increased risk of neonatal death compared to placebo in all analyzed progestogen types and pregnancy conditions. The pooled relative risks (95% confidence interval) of neonatal mortality were 0.69 (0.31-1.54) for vaginal progestogen in singleton pregnancies, 0.6 (0.33-1.09) for intramuscular progestogen in singleton pregnancies, 0.96 (0.51-1.8) for vaginal progestogen in multiple pregnancies, and 0.96 (0.49-1.9) for intramuscular progestogen in multiple pregnancies. The results of this meta-analysis suggest that administration of preventive progestogen treatment to women at risk for preterm birth does not appear to negatively affect neonatal mortality in single or multiple pregnancies regardless of the route of administration.

Database: EMBASE

48. Management of preterm labor

Author(s): Simhan H.N.

Source: Obstetrics and Gynecology; 2016; vol. 127 (no. 1)

Publication Date: 2016

Publication Type(s): Review

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Obstetrics and gynecology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

Abstract: Preterm birth is the leading cause of neonatal mortality and the most common reason for antenatal hospitalization (1-4). In the United States, approximately 12% of all live births occur before term, and preterm labor preceded approximately 50% of these preterm births (5, 6). Although the causes of preterm labor are not well understood, the burden of preterm births is clear-preterm births account for approximately 70% of neonatal deaths and 36% of infant deaths as well as 25-50% of cases of long-term neurologic impairment in children (7-9). A 2006 report from the Institute of Medicine estimated the annual cost of preterm birth in the United States to be 26.2 billion or more than 51,000 per premature infant (10). However, identifying women who will give birth preterm is an inexact process. The purpose of this document is to present the various methods proposed to manage preterm labor and to review the evidence for the roles of these methods in clinical practice. Identification and management of risk factors for preterm labor are not addressed in this document.

Database: EMBASE

49. Progesterone as a tocolytic agent for preterm labor: a systematic review.

Author(s): Navathe, Reshama; Berghella, Vincenzo

Source: Current opinion in obstetrics & gynecology; Dec 2016; vol. 28 (no. 6); p. 464-469

Publication Date: Dec 2016

Publication Type(s): Journal Article Review Systematic Review

PubMedID: 27764015

Available at Current opinion in obstetrics & gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract:PURPOSE OF REVIEWTocolytic agents have been used for over 60 years in the fight against preterm labor, which ultimately can lead to preterm birth. Currently, clinicians can choose from a variety of drug classes to achieve the primary goal of delaying delivery by 48 h, thereby allowing time for administration of corticosteroids for fetal lung maturity, and if appropriate, starting magnesium sulfate for fetal neuroprotection. However, there are currently no known therapies to maintain the tocolytic effect beyond those initial 48 h.RECENT FINDINGSProgesterone, which has been used in the prevention of preterm birth for over 10 years, has long been known to have the effect of uterine quiescence. It was first studied as a tocolytic agent in the 1960s. In the last several years, more studies have been done that suggest a potential use for maintenance tocolysis after the successful arrest of preterm labor. Although the studies are conflicting, the meta-analyses on progesterone show some promise in different outcomes of delayed delivery, reduced incidence of preterm birth, and reduced neonatal morbidity.SUMMARYProgesterone is currently the most promising agent for

maintenance tocolysis. Although further trials are certainly needed, this is an exciting advancement in the realm of tocolysis.

Database: Medline

50. Progestogens as Maintenance Treatment in Arrested Preterm Labor: A Systematic Review and Meta-analysis.

Author(s): Palacio, Montse; Ronzoni, Stefania; Sánchez-Ramos, Luis; Murphy, Kellie E

Source: Obstetrics and gynecology; Nov 2016; vol. 128 (no. 5); p. 989-1000

Publication Date: Nov 2016

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 27741193

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Obstetrics and gynecology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

Abstract:OBJECTIVETo evaluate the efficacy of maintenance tocolysis with progestogens compared with placebo or no treatment in women with singleton pregnancies and arrested preterm labor.DATA SOURCESStudies without language restrictions were identified from MEDLINE, EMBASE, PubMed, Scopus, the Cochrane Pregnancy and Childbirth Group's Trials Register, the Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from inception to June 2015. MeSH headings for progestogens were combined with terms regarding labor, tocolysis, or preterm birth. Reference lists of included studies and GoogleSearch were also reviewed.METHODS OF STUDY SELECTIONRandomized controlled trials that compared progestogens as a maintenance treatment after arrested preterm labor in singleton pregnancies with placebo or no treatment were identified. Selected studies evaluated delivery before 37 or 34 weeks of gestation or the latency period from randomization to delivery. Excluded studies used progestogens as prevention in asymptomatic women at risk. Risk of bias assessment, subgroup analysis on type of progestogens used, and sensitivity analysis by high-quality studies were performed.TABULATION, INTEGRATION, AND RESULTSSixteen randomized controlled trials consisting of 1,917 participants were included. Study characteristics and quality were recorded. Preterm delivery at less than 37 weeks of gestation was decreased (38.2% compared with 44.3%; relative risk 0.79, 95% confidence interval [CI] 0.65-0.97) and pregnancy was prolonged (mean difference 8.1 days; 95% CI 3.8-12.4) when women treated with progestogens were compared with placebo or no treatment. There were no differences in the outcome of delivery at less than 34 weeks of gestation (15.6% compared with 18.3%; relative risk 0.77, 95% CI 0.53-1.12). However, sensitivity analysis including five high-quality studies showed no significant differences for preterm delivery at less than 37 weeks of gestation (37.2% compared with 36.9%; relative risk 0.91, 95% CI 0.67-1.25) or latency period (mean difference 0.6 days; 95% CI -3.7 to 4.9).CONCLUSIONThere is insufficient high-quality data to inform clinicians and patients about the use of progestogens as maintenance treatment after arrested preterm labor to reduce the incidence of preterm birth or pregnancy prolongation.

Database: Medline

51. Progestogens as Maintenance Treatment in Arrested Preterm Labor

Author(s): Palacio M.; Ronzoni S.; Sanchez-Ramos L.; Murphy K.E.

Source: Obstetrics and Gynecology; Nov 2016; vol. 128 (no. 5); p. 989-1000

Publication Date: Nov 2016

Publication Type(s): Review

Abstract:OBJECTIVE: To evaluate the efficacy of maintenance tocolysis with progestogens compared with placebo or no treatment in women with singleton pregnancies and arrested preterm labor. DATA SOURCES: Studies without language restrictions were identified from MEDLINE, EMBASE, PubMed, Scopus, the Cochrane Pregnancy and Childbirth Group's Trials Register, the Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from inception to June 2015. MeSH headings for progestogens were combined with terms regarding labor, tocolysis, or preterm birth. Reference lists of included studies and GoogleSearch were also reviewed. METHODS OF STUDY SELECTION: Randomized controlled trials that compared progestogens as a maintenance treatment after arrested preterm labor in singleton pregnancies with placebo or no treatment were identified. Selected studies evaluated delivery before 37 or 34 weeks of gestation or the latency period from randomization to delivery. Excluded studies used progestogens as prevention in asymptomatic women at risk. Risk of bias assessment, subgroup analysis on type of progestogens used, and sensitivity analysis by high-quality studies were performed. TABULATION, INTEGRATION, AND RESULTS: Sixteen randomized controlled trials consisting of 1,917 participants were included. Study characteristics and quality were recorded. Preterm delivery at less than 37 weeks of gestation was decreased (38.2% compared with 44.3%; relative risk 0.79, 95% confidence interval [CI] 0.65-0.97) and pregnancy was prolonged (mean difference 8.1 days; 95% CI 3.8-12.4) when women treated with progestogens were compared with placebo or no treatment. There were no differences in the outcome of delivery at less than 34 weeks of gestation (15.6% compared with 18.3%; relative risk 0.77, 95% CI 0.53-1.12). However, sensitivity analysis including five high-quality studies showed no significant differences for preterm delivery at less than 37 weeks of gestation (37.2% compared with 36.9%; relative risk 0.91, 95% CI 0.67-1.25) or latency period (mean difference 0.6 days; 95% CI -3.7 to 4.9). CONCLUSION(S): There is insufficient high-quality data to inform clinicians and patients about the use of progestogens as maintenance treatment after arrested preterm labor to reduce the incidence of preterm birth or pregnancy prolongation.

Database: EMBASE

52. Nifedipine maintenance tocolysis and perinatal outcome: an individual participant data meta-analysis.

Author(s): van Vliet, Eog; Dijkema, G H; Schuit, E; Heida, K Y; Roos, C; van der Post, Jam; Parry, E C; McCowan, L; Lyell, D J; El-Sayed, Y Y; Carr, D B; Clark, A L; Mahdy, Z A; Uma, M; Sayin, N C; Varol, G F; Mol, B W; Oudijk, M A

Source: BJOG : an international journal of obstetrics and gynaecology; Oct 2016; vol. 123 (no. 11); p. 1753-1760

Publication Date: Oct 2016

Publication Type(s): Meta-analysis Journal Article Review

PubMedID: 27550838

Abstract:BACKGROUNDPreterm birth is the leading cause of neonatal mortality and morbidity in developed countries. Whether continued tocolysis after 48 hours of rescue tocolysis improves neonatal outcome is unproven.OBJECTIVESTo evaluate the effectiveness of maintenance tocolytic therapy with oral nifedipine on the reduction of adverse neonatal outcomes and the prolongation of pregnancy by performing an individual patient data meta-analysis (IPDMA).SEARCH STRATEGYWe searched PubMed, Embase, and Cochrane databases for randomised controlled trials of maintenance tocolysis therapy with nifedipine in preterm labour.SELECTION CRITERIAWe selected trials including pregnant women between 24 and 36(6/7) weeks of gestation (gestational age, GA) with imminent preterm labour who had not delivered after 48 hours of initial tocolysis, and compared maintenance nifedipine tocolysis with placebo/no treatment.DATA COLLECTION AND ANALYSISThe primary outcome was perinatal mortality. Secondary outcome measures were intraventricular haemorrhage (IVH), necrotising enterocolitis (NEC), infant respiratory distress syndrome (IRDS), prolongation of pregnancy, GA at delivery, birthweight, neonatal intensive care unit admission, and number of days on ventilation support. Pre-specified subgroup analyses were performed.MAIN RESULTSSix randomised controlled trials were included in this IPDMA, encompassing data from 787 patients (n = 390 for nifedipine; n = 397 for placebo/no treatment). There was no difference between the groups for the incidence of perinatal death (risk ratio, RR 1.36; 95% confidence interval, 95% CI 0.35-5.33), intraventricular haemorrhage (IVH) ≥ grade II (RR 0.65; 95% CI 0.16-2.67), necrotising enterocolitis (NEC) (RR 1.15; 95% CI 0.50-2.65), infant respiratory distress syndrome (IRDS) (RR 0.98; 95% CI 0.51-1.85), and prolongation of pregnancy (hazard ratio, HR 0.74; 95% CI 0.55-1.01).CONCLUSIONMaintenance tocolysis is not associated with improved perinatal outcome and is therefore not recommended for routine practice.TWEETABLE ABSTRACTNifedipine maintenance tocolysis is not associated with improved perinatal outcome or pregnancy prolongation.

Database: Medline

53. Practice Bulletin No. 171: Management of Preterm Labor

Author(s): Simhan H.N.

Source: Obstetrics and Gynecology; Oct 2016; vol. 128 (no. 4)

Publication Date: Oct 2016

Publication Type(s): Review

PubMedID: 27661654

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Obstetrics and gynecology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

Abstract: Preterm birth is the leading cause of neonatal mortality and the most common reason for antenatal hospitalization(1-4). In the United States, approximately 12% of all live births occur before term, and preterm labor preceded approximately 50% of these preterm births(5, 6). Although the causes of preterm labor are not well understood, the burden of preterm births is clear - preterm births account for approximately 70% of neonatal deaths and 36% of infant deaths as well as 25-50% of cases of long-term neurologic impairment in children(7-9). A 2006 report from the Institute of Medicine estimated the annual cost of preterm birth in the United States to be $26.2 billion or more than $51,000 per premature infant(10). However, identifying women who will give birth preterm is an inexact process. The purpose of this document is to present the various methods proposed to manage preterm labor and to review the evidence for the roles of these methods in clinical practice. Identification and management of risk factors for preterm labor are not addressed in this document.

Database: EMBASE

54. Prevention of preterm delivery: Current challenges and future prospects

Author(s): Van Zijl M.D.; Koullali B.; Pajkrt E.; Oudijk M.A.; Mol B.W.J.

Source: International Journal of Women's Health; Oct 2016; vol. 8 ; p. 633-645

Publication Date: Oct 2016

Publication Type(s): Review

Available at International Journal of Women's Health - from Europe PubMed Central - Open Access

Available at International Journal of Women's Health - from Free Medical Journals . com

Available at International Journal of Women's Health - from Unpaywall

Abstract: Preterm birth (PTB), defined as delivery at <37 weeks of gestation, is the most important cause of neonatal morbidity and mortality. Therefore, preventing PTB is one of the main goals in obstetric care. In this review, we provide an overview of the current available literature on screening for risk factors for PTB and a summary of preventive strategies in both low-risk and high-risk women with singleton or multiple gestations. Furthermore, current challenges and future prospects on PTB are discussed. For an optimal prevention of PTB, risk stratification should be based on a combination of (maternal) risk factors, obstetric history, and screening tools. Cervical length measurements can help identify women at risk. Thereafter, preventive strategies such as progesterone, pessaries, and cerclage may help prevent PTB. Effective screening and prevention of PTB vary between the different pregnancy populations. In singleton or multiple pregnancies with a short cervix, without previous PTB, a pessary or progesterone might prevent PTB. In women with a (recurrent) PTB in the

past, progesterone and a cerclage may prevent recurrence. The effect of a pessary in these high-risk women is currently being studied. A strong collaboration between doctors, patients' organizations, pharmaceutical companies, and (international) governments is needed to reduce the morbidity and mortality as a result of spontaneous PTB.

Database: EMBASE

55. Nifedipine versus placebo in the treatment of preterm prelabor rupture of membranes: a randomized controlled trial: Assessment of perinatal outcome by use of tocolysis in early labor-APOSTEL IV trial.

Author(s): Nijman, Tobias A J; van Vliet, Elvira O G; Naaktgeboren, Christiana A; Oude Rengerink, Katrien; de Lange, Thomas S; Bax, Caroline J; Bloemenkamp, Kitty W M; van Eyck, Jim; Kok, Marjolein; Scheepers, Hubertina C J; Woiski, Mallory; Franx, Arie; Mol, Ben Willem J; Oudijk, Martijn A

Source: European journal of obstetrics, gynecology, and reproductive biology; Oct 2016; vol. 205 ; p. 79-84

Publication Date: Oct 2016

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 27567363

Abstract:OBJECTIVEPreterm birth is the most common cause of neonatal morbidity and mortality. Around one third of preterm deliveries starts with preterm prelabor rupture of membranes (PPROM). The aim of this trial was to study the effect of prolonged tocolysis with nifedipine versus placebo in women with PPROM on perinatal outcome and prolongation of pregnancy.STUDY DESIGNThe Apostel IV was a nationwide multicenter randomized placebo controlled trial. We included women with PPROM without contractions between 24(+0) and 33(+6) weeks of gestation. Participants were randomly allocated to daily 80mg nifedipine or placebo, until the start of labor, with a maximum of 18 days. The primary outcome measure was a composite of poor neonatal outcome, including perinatal death, bronchopulmonary dysplasia, periventricular leukomalacia>grade 1, intraventricular hemorrhage>grade 2, necrotizing enterocolitis>stage 1 and culture proven sepsis. Secondary outcomes were gestational age at delivery and prolongation of pregnancy. Analysis was by intention to treat. To detect a reduction of poor neonatal outcome from 30% to 10%, 120 women needed to be randomized.TRIAL REGISTRYNTR 3363.RESULTSBetween October 2012 and December 2014 we randomized 25 women to nifedipine and 25 women to placebo. Due to slow recruitment the study was stopped prematurely. The median gestational age at randomization was 29.9 weeks (IQR 27.7-31.3) in the nifedipine group and 27.0 weeks (IQR 24.7-29.9) in the placebo group. Other baseline characteristics were comparable. The adverse perinatal outcome occurred in 9 neonates (33.3%) in the nifedipine group and 9 neonates (32.1%) in the placebo group (RR 1.04, 95% CI 0.49-2.2). Two perinatal deaths occurred, both in the nifedipine group. Bronchopulmonary dysplasia was seen less frequently in the nifedipine group (0% versus 17.9%; p=0.03). Prolongation of pregnancy did not differ between the nifedipine and placebo group (median 11 versus 8 days, HR 1.02; 95% CI 0.58-1.79).CONCLUSIONThis randomized trial did not show a beneficial effect of prolonged tocolysis on neonatal outcomes or prolongation of pregnancy in women with PPROM without contractions. However, since results are based on a small sample size, a difference in effectiveness cannot be excluded.

Database: Medline

56. Vaginal progesterone decreases preterm birth ≤ 34 weeks of gestation in women with a singleton pregnancy and a short cervix: an updated meta-analysis including data from the OPPTIMUM study.

Author(s): Romero, R; Nicolaides, K H; Conde-Agudelo, A; O'Brien, J M; Cetingoz, E; Da Fonseca, E; Creasy, G W; Hassan, S S

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Sep 2016; vol. 48 (no. 3); p. 308-317

Publication Date: Sep 2016

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 27444208

Abstract:OBJECTIVETo evaluate the efficacy of vaginal progesterone administration for preventing preterm birth and perinatal morbidity and mortality in asymptomatic women with a singleton gestation and a mid-trimester sonographic cervical length (CL) ≤ 25 mm.METHODSThis was an updated systematic review and meta-analysis of randomized controlled trials comparing the use of vaginal progesterone to placebo/no treatment in women with a singleton gestation and a mid-trimester sonographic CL ≤ 25 mm. Electronic databases, from their inception to May 2016, bibliographies and conference proceedings were searched. The primary outcome measure was preterm birth ≤ 34 weeks of gestation or fetal death. Two reviewers independently selected studies, assessed the risk of bias and extracted the data. Pooled relative risks (RRs) with 95% confidence intervals (CI) were calculated.RESULTSFive trials involving 974 women were included. A meta-analysis, including data from the OPPTIMUM study, showed that vaginal progesterone significantly decreased the risk of preterm birth ≤ 34 weeks of gestation or fetal death compared to placebo (18.1% vs 27.5%; RR, 0.66 (95% CI, 0.52-0.83); P = 0.0005; five studies; 974 women). Meta-analyses of data from four trials (723 women) showed that vaginal progesterone administration was associated with a statistically significant reduction in the risk of preterm birth occurring at < 28 to < 36 gestational weeks (RRs from 0.51 to 0.79), respiratory distress syndrome (RR, 0.47 (95% CI, 0.27-0.81)), composite neonatal morbidity and mortality (RR, 0.59 (95% CI, 0.38-0.91)), birth weight < 1500 g (RR, 0.52 (95% CI, 0.34-0.81)) and admission to the neonatal intensive care unit (RR, 0.67 (95% CI, 0.50-0.91)). There were no significant differences in neurodevelopmental outcomes at 2 years of age between the vaginal progesterone and placebo groups.CONCLUSIONThis updated systematic review and meta-analysis reaffirms that vaginal progesterone reduces the risk of preterm birth and neonatal morbidity and mortality in women with a singleton gestation and a mid-trimester CL ≤ 25 mm, without any deleterious effects on neurodevelopmental outcome. Clinicians should continue to perform universal transvaginal CL screening at 18-24 weeks of gestation in women with a singleton gestation and to offer vaginal progesterone to those with a CL ≤ 25 mm. Published 2016. This article is a U.S. Government work and is in the public domain in the USA.

Database: Medline

57. The safety of tocolytics used for the inhibition of preterm labour.

Author(s): Lamont, Callum D; Jørgensen, Jan Stener; Lamont, Ronald F

Source: Expert opinion on drug safety; Sep 2016; vol. 15 (no. 9); p. 1163-1173

Publication Date: Sep 2016

Publication Type(s): Journal Article Review Systematic Review

PubMedID: 27159501

Abstract:INTRODUCTIONPreterm birth is the major cause of neonatal mortality and morbidity worldwide and a huge cost burden on healthcare. Between 22 and 26 completed weeks of gestation, for every day that delivery is delayed, survival increases by 3%.AREAS COVEREDFollowing a systematic review of the literature, we have provided an overview of the use of tocolytics for the prevention of preterm birth and have examined the fetal and maternal adverse effects of the various tocolytic agents currently in use.EXPERT OPINIONNo tocolytic currently in use was developed specifically to treat preterm labour so most have multi-organ side effects. β2-agonists are relatively safe for the fetus but have rare and potentially serious maternal adverse effects. In contrast, prostaglandin synthetase inhibitors have potentially serious side effects for the fetus and neonate but have mild maternal gastrointestinal side effects. In Europe, the choice of first line therapy is either atosiban or nifedipine. The evidence base for atosiban is much more robust than for nifedipine. While their efficacy is similar, atosiban has placebo level side effects and is safer than nifedipine but is much more expensive.

Database: Medline

58. What we have learned about the role of 17-alpha-hydroxyprogesterone caproate in the prevention of preterm birth.

Author(s): Caritis, Steve N; Feghali, Maisa N; Grobman, William A; Rouse, Dwight J; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network

Source: Seminars in perinatology; Aug 2016; vol. 40 (no. 5); p. 273-280

Publication Date: Aug 2016

Publication Type(s): Journal Article Review

PubMedID: 27105940

Abstract: Despite major advances in neonatal care, the burden of preterm birth remains high. This is not unexpected since strategies to identify and treat risk factors in early pregnancy have not been very effective in reducing the preterm birth rate. Initial studies suggested a potential benefit for 17-alpha-hydroxyprogesterone caproate (17-OHPC) in decreasing the risk of recurrent preterm birth women with a singleton gestation. However, the use of 17-OHPC has not conferred benefit for other categories of women at high risk for preterm delivery (twins, triplets, and short cervical length). The increasing body of evidence suggests that preterm birth is a complex condition with variable mechanisms of disease and significant individual heterogeneity. This review will examine the plausibility of 17-OHPC in preventing preterm birth and the investigation of its clinical efficacy. We will also highlight factors to explain variations in clinical trial outcomes and outline the trajectory needed for future investigations.

Database: Medline

59. Progestogens and prevention of preterm birth in women at risk

Author(s): anonymous

Source: Prescrire International; Jul 2016; vol. 25 (no. 173); p. 185-188

Publication Date: Jul 2016

Publication Type(s): Review

Abstract:* The natural hormone progesterone and the progesterone derivative hydroxyprogesterone have been proposed for the prevention of preterm birth in pregnant women considered at high risk due to a history of prior preterm birth or a short cervix on ultrasound examination. * What are the results of the evaluation of these progestogens in the prevention of preterm birth in women at high risk? And what are the adverse effects on the mother and the unborn child? We identified a Cochrane systematic review and searched the literature for more recent data. * Four randomised trials evaluated the administration of intramuscular hydroxyprogesterone, beginning in the second trimester of pregnancy, in about 650 women with a history of preterm birth. The data on perinatal mortality and on the incidence of preterm birth were uninterpretable due to heterogeneity between the placebo groups. * Seven randomised placebocontrolled trials evaluated oral or vaginal progesterone in about 1300 women with a history of preterm birth. Delivery before 34 weeks' gestation was less frequent with progesterone (10% of births versus 26% with placebo), with no impact on perinatal mortality. The results on neonatal health outcomes are undermined by reporting bias. * In five randomised trials in women found to have a short cervix midway through pregnancy, there was no firm evidence that either vaginal progesterone or intramuscular hydroxyprogesterone reduce the incidence of preterm birth before 37 weeks. * Progesterone and hydroxyprogesterone were evaluated in 16 randomised trials in women with a multiple pregnancy, with no evidence of a reduction in the risk of preterm birth. * At the doses evaluated, the adverse effects of these progestogens are moderate for the mother, although women at risk for deep vein thrombosis were excluded from several trials. Exposure to progesterone or hydroxyprogesterone after the first trimester of pregnancy does not appear to increase the risk of congenital defects in the newborn. The long-term effects of these progestogens are unknown. * In practice, the efficacy of progesterone and hydroxyprogesterone administered from the second trimester of pregnancy for the prevention of preterm birth is highly uncertain. As of early 2016, the evaluation results are not sufficiently convincing to justify progestogen exposure as soon as the risk of preterm birth appears high. They do, however, justify continued evaluation of progesterone in clinical trials for women with a history of recurrent preterm birth with no identified cause.

Database: EMBASE

60. Progesterone and nifedipine for maintenance tocolysis after arrested preterm labor: A systematic review and meta-analysis of randomized controlled trial.

Author(s): Ding, Ming-Xia; Luo, Xin; Zhang, Xue-Mei; Bai, Bing; Sun, Ju-Xiang; Qi, Hong-Bo

Source: Taiwanese journal of obstetrics & gynecology; Jun 2016; vol. 55 (no. 3); p. 399-404

Publication Date: Jun 2016

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 27343323

Abstract:OBJECTIVENo treatment is recommended for routine maintenance tocolysis after an arrested preterm birth. Our present study aimed to evaluate the effect of progesterone and nifedipine as maintenance tocolysis therapy after an arrested preterm birth.MATERIALS AND METHODSFor relevant studies, we systematically searched the literature in databases of PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library. Only randomized controlled trials were included.RESULTSNine trials were included in our review. Nifedipine and progesterone were used for maintenance tocolysis. Compared to placebo treatment or no treatment, maintenance tocolysis with progesterone could significantly prolong the delivery gestational weeks [standard mean difference (SMD) 1.64; 95% confidence interval (CI), 1.21, 2.07; $p < 0.00001$], reduce the proportion of patients with delivery before 37 weeks (risk ratio 0.63; 95% CI, 0.47, 0.83; $p = 0.001$), and increase the birth weight (SMD 317.71; 95% CI, 174.89, 460.53; $p < 0.0001$). However, no such benefits were observed after maintenance tocolysis with nifedipine. Both nifedipine and progesterone had no significant influences on the following outcomes: neonatal intensive care unit stay, proportion of neonatal intensive care unit admission, neonatal mortality, and incidence of respiratory distress syndrome.CONCLUSIONOur results with maintenance tocolysis with progesterone may be useful for patients who had an episode of threatened preterm labor successfully treated with acute tocolytic therapy.

Database: Medline

61. Vaginal progesterone prophylaxis for preterm birth (the OPPTIMUM study): a multicentre, randomised, double-blind trial.

Author(s): Norman, Jane Elizabeth; Marlow, Neil; Messow, Claudia-Martina; Shennan, Andrew; Bennett, Phillip R; Thornton, Steven; Robson, Stephen C; McConnachie, Alex; Petrou, Stavros; Sebire, Neil J; Lavender, Tina; Whyte, Sonia; Norrie, John; OPPTIMUM study group

Source: Lancet (London, England); May 2016; vol. 387 (no. 10033); p. 2106-2116

Publication Date: May 2016

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Multicenter Study Journal Article

PubMedID: 26921136

Abstract:BACKGROUNDProgesterone administration has been shown to reduce the risk of preterm birth and neonatal morbidity in women at high risk, but there is uncertainty about longer term effects on the child.METHODSWe did a double-blind, randomised, placebo-controlled trial of vaginal progesterone, 200 mg daily taken from 22-24 to 34 weeks of gestation, on pregnancy and infant outcomes in women at risk of preterm birth (because of previous spontaneous birth at ≤34 weeks and 0 days of gestation, or a cervical length ≤25 mm, or because of a positive fetal fibronectin test combined with other clinical risk factors for preterm birth [any one of a history in a previous pregnancy of preterm birth, second trimester loss, preterm premature fetal membrane rupture, or a history of a cervical procedure to treat abnormal smears]). The objective of the study was to determine whether vaginal progesterone prophylaxis given to reduce the risk of preterm birth affects neonatal and childhood outcomes. We defined three primary outcomes: fetal death or birth before 34 weeks and 0 days gestation (obstetric), a composite of death, brain injury, or bronchopulmonary dysplasia (neonatal), and a standardised cognitive score at 2 years of age (childhood), imputing values for deaths. Randomisation was done through a web portal, with participants, investigators, and others involved in giving the intervention, assessing outcomes, or analysing data masked to treatment allocation until the end of the study. Analysis was by intention to treat. This trial is registered at ISRCTN.com, number ISRCTN14568373.FINDINGSBetween Feb 2, 2009, and April 12, 2013, we randomly assigned 1228 women to the placebo group (n=610) and the progesterone group (n=618). In the placebo group, data from 597, 587, and 439 women or babies were available for analysis of obstetric, neonatal, and childhood outcomes, respectively; in the progesterone group the corresponding numbers were 600, 589, and 430. After correction for multiple outcomes, progesterone had no significant effect on the primary obstetric outcome (odds ratio adjusted for multiple comparisons [OR] 0·86, 95% CI 0·61-1·22) or neonatal outcome (OR 0·62, 0·38-1·03), nor on the childhood outcome (cognitive score, progesterone group vs placebo group, 97·3 [SD 17·9] vs 97·7 [17·5]; difference in means -0·48, 95% CI -2·77 to 1·81). Maternal or child serious adverse events were reported in 70 (11%) of 610 patients in the placebo group and 59 (10%) of 616 patients in the progesterone group (p=0·27).INTERPRETATIONVaginal progesterone was not associated with reduced risk of preterm birth or composite neonatal adverse outcomes, and had no long-term benefit or harm on outcomes in children at 2 years of age.FUNDINGEfficacy and Mechanism Evaluation (EME) Programme, a Medical Research Council (MRC) and National Institute for Health Research (NIHR) partnership. The EME Programme is funded by the MRC and NIHR, with contributions from the Chief Scientist Office in Scotland and National Institute for Social Care and Research in Wales.

Database: Medline

62. Effectiveness of Tocolytic Agents on Prevention of Preterm Delivery, Neonatal Morbidity, and Mortality: Is There a Consensus? A Review of the Literature.

Author(s): Petousis, Stamatios; Margioula-Siarkou, Chrysoula; Kalogiannidis, Ioannis

Source: Obstetrical & gynecological survey; Apr 2016; vol. 71 (no. 4); p. 243-252

Publication Date: Apr 2016

Publication Type(s): Journal Article Review

PubMedID: 27065070

Abstract: Preterm delivery presents the main cause of neonatal morbidity and mortality worldwide. The rate of preterm delivery is 12% to 13% in the United States, of which 29% concerns preterm deliveries before 34 weeks of gestation. Basic parameter of prevention strategy is implementation of tocolytic therapy in cases of threatened preterm labor. Several therapeutic approaches have been proposed, among which betamimetic agonists, calcium channel blockers, magnesium sulfate, oxytocin receptor blockers, nitrates, and prostaglandin inhibitors, whereas new alternatives such as usage of thiocolchicoside have also been reported. This article is one among few that aims to review the comparative effectiveness of various tocolytic agents regarding prevention of preterm delivery, impact on perinatal morbidity and mortality, neonatal health status, and maternal complications. Main conclusions of recent randomized control trials and meta-analyses are summarized to assess about which agents consensus already exists on their effectiveness, which agents should be further studied to achieve conclusions, as well as those that are rather unlikely to have significant tocolytic impact or any other benefit on neonatal outcome.

Database: Medline

63. 17-Hydroxyprogesterone caproate in triplet pregnancy: an individual patient data meta-analysis.

Author(s): Combs, C A; Schuit, E; Caritis, S N; Lim, A C; Garite, T J; Maurel, K; Rouse, D; Thom, E; Tita, A T; Mol, Bwj; Global Obstetrics Network (GONet) collaboration

Source: BJOG : an international journal of obstetrics and gynaecology; Apr 2016; vol. 123 (no. 5); p. 682-690

Publication Date: Apr 2016

Publication Type(s): Meta-analysis Journal Article Review

PubMedID: 26663620

Abstract:BACKGROUNDPreterm birth complicates almost all triplet pregnancies and no preventive strategy has proven effective.OBJECTIVETo determine, using individual patient data (IPD) meta-analysis, whether the outcome of triplet pregnancy is affected by prophylactic administration of 17-hydroxyprogesterone caproate (17OHPc).SEARCH STRATEGYWe searched literature databases, trial registries and references in published articles.SELECTION CRITERIARandomised controlled trials (RCTs) of progestogens versus control that included women with triplet pregnancies.DATA COLLECTION AND ANALYSISInvestigators from identified RCTs collaborated on the protocol and contributed their IPD. The primary outcome was a composite measure of adverse perinatal outcome. The secondary outcome was the rate of birth before 32 weeks of gestation. Other pre-specified outcomes included randomisation-to-delivery interval and rates of birth at <24, <28 and <34 weeks of gestation.MAIN RESULTSThree RCTs of 17OHPc versus placebo included 232 mothers with triplet pregnancies and their 696 offspring. Risk-of-bias scores and between-study heterogeneity were low. Baseline characteristics were comparable between 17OHPc and placebo groups. The rate of the composite adverse perinatal outcome was similar among those treated with 17OHPc and those treated with placebo (34 and 35%, respectively; risk ratio [RR] 0.98, 95% confidence interval [95% CI] 0.79-1.2). The rate of birth at <32 weeks was also similar in the two groups (35 and 38%, respectively; RR 0.92, 95% CI 0.55-1.56). There were no significant between-group differences in perinatal mortality rate, randomisation-to-delivery interval, or other specified outcomes.CONCLUSIONProphylactic 17OHPc given to mothers with triplet pregnancies had no significant impact on perinatal outcome or pregnancy duration.TWEETABLE ABSTRACT17-Hydroxyprogesterone caproate had no significant impact on the outcome or duration of triplet pregnancy.

Database: Medline

64. Clinical Application of Progesterone for the Prevention of Preterm Birth, 2016.

Author(s): Goodnight, William

Source: American journal of perinatology; Feb 2016; vol. 33 (no. 3); p. 253-257

Publication Date: Feb 2016

Publication Type(s): Journal Article Review

PubMedID: 26788788

Available at American journal of perinatology - from Unpaywall

Abstract: While the preterm neonate continues to benefit from improved perinatal care, the rate of preterm birth in the United States remains significant. An increasing body of scientific literature has demonstrated the benefits of maternal progesterone administration in reducing primary and recurrent preterm birth. Intramuscular hydroxyprogesterone caproate is indicated in singleton pregnancies in women with a prior spontaneous preterm birth, while vaginal progesterone demonstrates similar efficacy in prolonging pregnancy in women with asymptomatic cervical shortening in the midtrimester. Given these favorable benefits, the use of progesterone has been expanded to other clinical situations at risk for preterm birth with less rigorous scientific evidence. This review highlights the current evidence-based clinical applications of progesterone for prevention of preterm birth.

Database: Medline

65. Tocolysis for Acute Preterm Labor: Where Have We Been, Where Are We Now, and Where are We Going?

Author(s): Navathe, Reshama; Berghella, Vincenzo

Source: American journal of perinatology; Feb 2016; vol. 33 (no. 3); p. 229-235

Publication Date: Feb 2016

Publication Type(s): Journal Article Review

PubMedID: 26808195

Abstract: Tocolytics have been used for over 60 years for women with preterm labor, which ultimately can lead to preterm birth (PTB). Diagnosing preterm labor is challenging, but use of objective tests such as transvaginal ultrasound of cervical length assists in the identification of women at the highest risk for PTB. Once preterm labor has been diagnosed, clinicians can choose from a variety of drug classes (cyclooxygenase inhibitors, calcium channel blockers, and betamimetics) to achieve the primary goal of delaying delivery by 48 hours, thereby allowing time for administration of corticosteroids for fetal lung maturity, and if appropriate, starting magnesium sulfate for fetal neuroprotection. Cyclooxygenase inhibitors are the only class of tocolytics proven to decrease PTB < 37 weeks. Knowledge of the safety and effectiveness of these medications is paramount. Several additional agents (e.g., oxytocin receptor antagonists) have significant promise, but further studies are required before these medications can be approved for tocolysis in the United States. As we look into the future of tocolysis, we anticipate that deeper understanding of the complex physiology of preterm labor will allow us to uniquely target different etiologies that lead to the final path resulting in spontaneous preterm delivery.

Database: Medline

66. Vaginal progesterone to prevent preterm birth in pregnant women with a sonographic short cervix: Clinical and public health implications

Author(s): Conde-Agudelo A.; Romero R.

Source: American Journal of Obstetrics and Gynecology; Feb 2016; vol. 214 (no. 2); p. 235-242

Publication Date: Feb 2016

Publication Type(s): Review

PubMedID: 26450404

Abstract: Vaginal progesterone administration to women with a sonographic short cervix is an efficacious and safe intervention used to prevent preterm birth and neonatal morbidity and mortality. The clinical and public health implications of this approach in the United States have been critically appraised and compared to other therapeutic interventions in obstetrics. Vaginal progesterone administration to women with a transvaginal sonographic cervical length (CL) <=25 mm before 25 weeks of gestation is associated with a significant and substantial reduction of the risk for preterm birth from <28 to <35 weeks of gestation, respiratory distress syndrome, composite neonatal morbidity and mortality, admission to the neonatal intensive care unit, and mechanical ventilation. These beneficial effects have been achieved in women with a singleton gestation, with or without a history of spontaneous preterm birth, and did not differ significantly as a function of CL (<10 mm, 10-20 mm, or 21-25 mm). The number of patients required for treatment to prevent 1 case of preterm birth or adverse neonatal outcomes ranges from 10-19 women. The number needed to screen for the prevention of 1 case of preterm birth before 34 weeks of gestation is 125 women, and 225 for the prevention of 1 case of major neonatal morbidity or neonatal mortality. Several cost-effectiveness and decision analyses have shown that the combination of universal transvaginal CL screening and vaginal progesterone administration to women with a short cervix is a cost-effective intervention that prevents preterm birth and associated perinatal morbidity and mortality. Universal assessment of CL and treatment with vaginal progesterone for singleton gestations in the United States would result in an annual reduction of approximately 30,000 preterm births before 34 weeks of gestation and of 17,500 cases of major neonatal morbidity or neonatal mortality. In summary, there is compelling evidence to recommend universal transvaginal CL screening at 18-24 weeks of gestation in women with a singleton gestation and to offer vaginal progesterone to those with a CL <=25 mm, regardless of the history of spontaneous preterm birth, with the goal of preventing preterm birth and neonatal morbidity and mortality.

Database: EMBASE

67. What is New in the Management of Acute Preterm Labor?

Author(s): Malone F.D.

Source: Obstetrics and Gynecology; Feb 2016; vol. 127 (no. 2); p. 398-399

Publication Date: Feb 2016

Publication Type(s): Review

PubMedID: 26942371

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Obstetrics and gynecology - from Patricia Bowen Library & Knowledge Service West Middlesex University Hospital NHS Trust (lib302631) Local Print Collection [location] : Patricia Bowen Library and Knowledge Service West Middlesex university Hospital.

Abstract: This month we focus on current research in the management of acute preterm labor. Dr. Malone discusses four recent publications, which are concluded with a "bottom line" that is the take-home message. The complete reference for each can be found inBox 1on this page, along with direct links to the abstracts.Copyright © 2016 by The American College of Obstetricians and Gynecologists.

Database: EMBASE

68. Cervical pessary to prevent preterm birth in women with twin gestation and sonographic short cervix: a multicenter randomized controlled trial (PECEP-Twins).

Author(s): Goya, Maria; de la Calle, Maria; Pratcorona, Laia; Merced, Carme; Rodó, Carlota; Muñoz, Begoña; Juan, Miquel; Serrano, Ariana; Llurba, Elisa; Higueras, Teresa; Carreras, Elena; Cabero, Luis; PECEP-Twins Trial Group

Source: American journal of obstetrics and gynecology; Feb 2016; vol. 214 (no. 2); p. 145-152

Publication Date: Feb 2016

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Multicenter Study Twin Study Journal Article

PubMedID: 26627728

Abstract:BACKGROUNDSpontaneous preterm birth (SPB) is the leading cause of perinatal morbidity and mortality. In twins, the rate of preterm birth is higher than in singletons; interventions to prevent preterm birth are needed in this high-risk population.OBJECTIVEWe sought to test whether a cervical pessary reduces the preterm birth rate in twin pregnancies with sonographic short cervix.STUDY DESIGNA prospective, open-label, multicenter, randomized clinical trial was conducted in 5 hospitals in Spain. The ethics committees of all participating hospitals approved the protocol. The trial was registered as ClinicalTrials.gov, number NCT01242410. Eligible women were scanned in Spain. The primary outcome was SPB <34 weeks of gestation. Neonatal morbidity and mortality were also evaluated.RESULTSCervical length was measured in 2287 women; 137 pregnant women with a sonographic cervical length ≤25 mm (of 154 detected with a short cervix) were randomly assigned to receive a cervical pessary or expectant management (1:1 ratio). SPB <34 weeks of gestation was significantly less frequent in the pessary group than in the expectant management group (11/68 [16.2%] vs 26/66 [39.4%]; relative risk, 0.41; 95% confidence interval, 0.22-0.76). Pessary use was associated with a significant reduction in the rate of birthweight <2500 g (P = .01). No significant differences were observed in composite neonatal morbidity outcome (8/136 [5.9%] vs 12/130 [9.1%]; relative risk, 0.64; 95% confidence interval, 0.27-1.50) or neonatal mortality (none) between the groups. No serious adverse effects associated with the use of a cervical pessary were observed.CONCLUSIONThe insertion of a cervical pessary was associated with a significant reduction

in the SPB rate. We propose the use of a cervical pessary for preventing preterm birth in twin pregnancies of mothers with a short cervix.

Database: Medline

69. Tocolysis for inhibiting preterm birth in extremely preterm birth, multiple gestations and in growth-restricted fetuses: a systematic review and meta-analysis.

Author(s): Miyazaki, Celine; Moreno Garcia, Ralf; Moreno, Ralfh Garcia; Ota, Erika; Swa, Toshiyuki; Oladapo, Olufemi T; Mori, Rintaro

Source: Reproductive health; Jan 2016; vol. 13 ; p. 4

Publication Date: Jan 2016

Publication Type(s): Research Support, Non-u.s. Gov't Meta-analysis Journal Article Review Systematic Review

PubMedID: 26762152

Available at Reproductive health - from BioMed Central

Available at Reproductive health - from SpringerLink - Medicine

Available at Reproductive health - from ProQuest (Health Research Premium) - NHS Version

Available at Reproductive health - from Unpaywall

Abstract: This systematic review was to identify available evidence on the effectiveness of tocolysis in inhibiting preterm delivery for women with threatened extremely preterm birth, multiple gestations, and growth-restricted babies, and their infants' outcomes. A comprehensive search using MEDLINE, Embase, the Cochrane Library, CINAHL, POPLINE and the WHO Global Health Library databases was conducted on 14 February 2014. For selection criteria, randomized controlled trials and non-randomized studies that compared tocolysis treatment to placebo or no treatment were considered. Selection of eligible studies, critical appraisal of the included studies, data collection, meta-analyses, and assessment of evidence quality were performed in accordance with the Cochrane Collaboration's guidance and validated assessment criteria. The search identified seven studies for extremely preterm birth, in which three were randomized controlled trials (RCTs) and four were non-randomized studies (non-RCTs). There were no eligible studies identified for women with multiple pregnancy and growth-restricted fetuses. Meta-analyses indicated no significant difference was found for the relative effectiveness of tocolytics versus placebo for prolonging pregnancy in women with extremely preterm birth (RR 1.04, 95% CI 0.83 to 1.31) or reducing the rate of perinatal deaths (RR 2.22, 95% CI 0.26 to 19.24). In summary, there is no evidence to draw conclusions on the effectiveness of tocolytic therapy for women with threatened extremely preterm birth, multiple gestations, and growth-restricted babies.

Database: Medline

70. A systematic review and meta-analysis of progestogen use for maintenance tocolysis after preterm labor in women with intact membranes.

Author(s): Eke, Ahizechukwu C; Chalaan, Tina; Shukr, Ghadear; Eleje, George U; Okafor, Charles I

Source: International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics; Jan 2016; vol. 132 (no. 1); p. 11-16

Publication Date: Jan 2016

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 26489489

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library

Abstract:BACKGROUNDThe use of progestogens for maintenance tocolysis remains controversial, with randomized controlled trials having conflicting results on their efficacy.OBJECTIVESTo evaluate the use of progestational agents for maintenance tocolysis after preterm labor in a systematic review of randomized controlled trials.SEARCH STRATEGYElectronic databases were searched for reports published before December 2014. Keywords included "tocolysis," "progesterone," "preterm labor," "17-alpha-hydroxyprogesterone," and "vaginal progesterone."SELECTION CRITERIAOnly randomized controlled trials involving progestational agents for maintenance tocolysis were included.DATA COLLECTION AND ANALYSISOutcomes were analyzed on an intent-to-treat basis and meta-analysis was performed where appropriate. Relative risks and mean differences with 95% confidence intervals were calculated.MAIN RESULTSFour studies (362 women) were included. There were no significant differences between progestational agents and placebo/no treatment in terms of delivery before 34weeks or before 37weeks of pregnancy, time from randomization to delivery, and respiratory distress syndrome. Progestogens were associated with an increase in the neonatal birth weight (mean difference 203.32g, 95% confidence interval 110.85-295.80; P=0.032).CONCLUSIONSThe current evidence does not support the routine use of progestational agents for maintenance tocolysis after an episode of preterm labor.

Database: Medline

71. Prevention of preterm birth with vaginal progesterone or 17-alpha-hydroxyprogesterone caproate: a critical examination of efficacy and safety.

Author(s): O'Brien, John M; Lewis, David F

Source: American journal of obstetrics and gynecology; Jan 2016; vol. 214 (no. 1); p. 45-56

Publication Date: Jan 2016

Publication Type(s): Journal Article Review

PubMedID: 26558340

Abstract: Progestogens are the first drugs to demonstrate reproducibly a reduction in the rate of early preterm birth. The efficacy and safety of progestogens are related to individual pharmacologic properties of each drug within this class of medication and characteristics of the population that is treated. The synthetic 17-hydroxyprogesterone caproate and natural progesterone have been studied with the use of a prophylactic strategy in women with a history of preterm birth and in women with a multiple gestation. Evidence from a single large comparative efficacy trial suggests that vaginal natural progesterone is superior to 17-hydroxyprogesterone caproate as a prophylactic treatment in women with a history of mid-trimester preterm birth. Progestogen therapy is indicated for women with this highest risk profile based on evidence from 2 trials. A therapeutic approach based on the identification of a sonographic short cervix has been studied in several phase III trials. Independent phase III trials and an individual patient metaanalysis suggest that vaginal progesterone is efficacious and safe in women with a singleton and a short cervix. Two trials that tested 17-hydroxyprogesterone caproate in women with a short cervix showed no benefit. No consistent benefit for the prophylactic or therapeutic use of progestogens has been demonstrated in larger trials of women whose pregnancies were complicated by a multiple gestation (twins or triplets), preterm labor, or preterm rupture of membranes. Unfortunately, several large randomized trials in multiple gestations have identified harm related to 17-hydroxyprogesterone caproate exposure, and the synthetic drug is contraindicated in this population. The current body of evidence is evaluated by the Grading of Recommendations Assessment, Development, and Evaluation guidelines to derive the strength of recommendation in each of these populations. A large confirmatory trial that is testing 17-hydroxyprogesterone caproate exposure in women with a singleton pregnancy and a history of preterm birth is near completion. Additional study of the efficacy and safety of progestogens is suggested in well-selected populations based on the presence of biomarkers.

Database: Medline

72. Vaginal progesterone for prevention of preterm labor in asymptomatic twin pregnancies with sonographic short cervix: a randomized clinical trial of efficacy and safety.

Author(s): El-Refaie, Waleed; Abdelhafez, Mohamed S; Badawy, Ahmed

Source: Archives of gynecology and obstetrics; Jan 2016; vol. 293 (no. 1); p. 61-67

Publication Date: Jan 2016

Publication Type(s): Randomized Controlled Trial Twin Study Journal Article

PubMedID: 26044148

Abstract:PURPOSETo evaluate the value of vaginal progesterone therapy for reduction of preterm labor in asymptomatic women with twin pregnancies and sonographic short cervix.METHODSThis randomized controlled study was conducted in Mansoura University Hospital and private practice settings in Mansoura, Egypt. Of 322 women with dichorionic twin pregnancy, 250 asymptomatic women with cervical length of 20-25 mm at 20-24 weeks of gestation were included in the study. All women were randomly divided into two groups; the study group (n = 125) received vaginal progesterone suppositories in a dose of 400 mg daily starting at 20-24 weeks of gestation while the control group (n = 125) received no treatment. The primary outcome measure was preterm labor before 34 weeks of gestation and the secondary outcome measures were neonatal respiratory distress syndrome (RDS) and early neonatal death (END).RESULTS224 women (116 in the study group and 108 in the control group) were subjected to final analysis. The duration of pregnancy was significantly longer in the study group and the incidence of preterm labor before 34 and 32 weeks of gestation was significantly lower in the study group. The neonatal morbidities and mortality were significantly lower in the study group as shown by lower incidence of very low (<1500 gm) birth weight, neonatal RDS, the need for mechanical ventilation and END.CONCLUSIONSVaginal progesterone administration in asymptomatic twin pregnancies with sonographic short cervix (20-25 mm) at 20-24 weeks of gestation is effective and safe treatment for reducing the incidence of preterm labor with subsequent reduction in the neonatal morbidities and mortality associated with preterm birth.

Database: Medline

73. Different treatment regimens of magnesium sulphate for tocolysis in women in preterm labour.

Author(s): McNamara, Helen C; Crowther, Caroline A; Brown, Julie

Source: The Cochrane database of systematic reviews; Dec 2015 (no. 12); p. CD011200

Publication Date: Dec 2015

Publication Type(s): Research Support, Non-u.s. Gov't Meta-analysis Journal Article Review Systematic Review

PubMedID: 26662716

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Abstract:BACKGROUNDMagnesium sulphate has been used to inhibit preterm labour to prevent preterm birth. There is no consensus as to the safety profile of different treatment regimens with respect to dose, duration, route and timing of administration.OBJECTIVESTo assess the efficacy and safety of alternative magnesium sulphate regimens when used as single agent tocolytic therapy during pregnancy.SEARCH METHODSWe searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2015) and reference lists of retrieved studies.SELECTION CRITERIARandomised trials comparing different magnesium sulphate treatment regimens when used as single agent tocolytic therapy during pregnancy in women in preterm labour. Quasi-randomised trials were eligible for inclusion but none were identified. Cross-over and cluster trials were not eligible for inclusion. Health outcomes were considered at the level of the mother, the infant/child and the health service.INTERVENTIONintravenous or oral magnesium sulphate given alone for tocolysis.Comparison: alternative dosing regimens of magnesium sulphate given alone for tocolysis.DATA COLLECTION AND ANALYSISTwo review authors independently assessed trial eligibility and quality and extracted data.MAIN RESULTSThree trials including 360 women and their infants were identified as eligible for inclusion in this review. Two trials were rated as low risk of bias for random sequence generation and concealment of allocation. A third trial was assessed as unclear risk of bias for these domains but did not report data for any of the outcomes examined in this review. No trials were rated to be of high quality overall.Intravenous magnesium sulphate was administered according to low-dose regimens (4 g loading dose followed by 2 g/hour continuous infusion and/or increased by 1 g/hour hourly until successful tocolysis or failure of treatment), or high-dose regimens (4 g loading dose followed by 5 g/hour continuous infusion and increased by 1 g/hour hourly until successful tocolysis or failure of treatment, or 6 g loading dose followed by 2 g/hour continuous infusion and increased by 1 g/hour hourly until successful tocolysis or failure of treatment).There were no differences seen between high-dose magnesium sulphate regimens compared with low-dose magnesium sulphate regimens for the primary outcome of fetal, neonatal and infant death (risk ratio (RR) 0.43, 95% confidence interval (CI) 0.12 to 1.56; one trial, 100 infants). Using the GRADE approach, the evidence for fetal, neonatal and infant death was considered to be VERY LOW quality. No data were reported for any of the other primary maternal and infant health outcomes (birth less than 48 hours after trial entry; composite serious infant outcome; composite serious maternal outcome).There were no clear differences seen between high-dose magnesium sulphate regimens compared with low-dose magnesium sulphate regimens for the secondary infant health outcomes of fetal death; neonatal death; and rate of hypocalcaemia, osteopenia or fracture; and secondary maternal health outcomes of rate of caesarean birth; pulmonary oedema; and maternal self-reported adverse effects. Pulmonary oedema was reported in two women given high-dose magnesium sulphate, but not in any of the women given low-dose magnesium sulphate.In a single trial of high and low doses of magnesium sulphate for tocolysis including 100 infants, the risk of respiratory distress syndrome was lower with use of a high-dose regimen compared with a low-dose regimen (RR 0.31, 95% CI 0.11 to 0.88; one trial, 100 infants). Using the GRADE approach, the evidence for respiratory distress syndrome was judged to be LOW quality. No difference was seen in the rate of admission to the neonatal intensive care unit.

However, for those babies admitted, a high-dose regimen was associated with a reduction in the length of stay in the neonatal intensive care unit compared with a low-dose regimen (mean difference -3.10 days, 95% confidence interval -5.48 to -0.72).We found no data for the majority of our secondary outcomes.AUTHORS' CONCLUSIONSThere are limited data available (three studies, with data from only two studies) comparing different dosing regimens of magnesium sulphate given as single agent tocolytic therapy for the prevention of preterm birth. There is no evidence examining duration of therapy, timing of therapy and the role for repeat dosing.Downgrading decisions for our primary outcome of fetal, neonatal and infant death were based on wide confidence intervals (crossing the line of no effect), lack of blinding and a limited number of studies. No data were available for any of our other important outcomes: birth less than 48 hours after trial entry; composite serious infant outcome; composite serious maternal outcome. The data are limited by volume and the outcomes reported. Only eight of our 45 pre-specified primary and secondary maternal and infant health outcomes were reported on in the included studies. No long-term outcomes were reported. Downgrading decisions for the evidence on the risk of respiratory distress were based on wide confidence intervals (crossing the line of no effect) and lack of blinding.There is some evidence from a single study suggesting a reduction in the length of stay in the neonatal intensive care unit and a reduced risk of respiratory distress syndrome where a high-dose regimen of magnesium sulphate has been used compared with a low-dose regimen. However, given that evidence has been drawn from a single study (with a small sample size), these data should be interpreted with caution.Magnesium sulphate has been shown to be of benefit in a wide range of obstetric settings, although it has not been recommended for tocolysis. In clinical settings where health benefits are established, further trials are needed to address the lack of evidence regarding the optimal dose (loading dose and maintenance dose), duration of therapy, timing of therapy and role for repeat dosing in terms of efficacy and safety for mothers and their children. Ongoing examination of different regimens with respect to important health outcomes is required.

Database: Medline

74. Vaginal progesterone for maintenance tocolysis: a systematic review and metaanalysis of randomized trials.

Author(s): Suhag, Anju; Saccone, Gabriele; Berghella, Vincenzo

Source: American journal of obstetrics and gynecology; Oct 2015; vol. 213 (no. 4); p. 479-487

Publication Date: Oct 2015

Publication Type(s): Meta-analysis Journal Article Review Systematic Review

PubMedID: 25797233

Abstract:OBJECTIVEWe sought to evaluate the efficacy of maintenance tocolysis with vaginal progesterone compared to control (placebo or no treatment) in singleton gestations with arrested preterm labor (PTL) in a metaanalysis of randomized controlled trials.STUDY DESIGNSearches were performed in MEDLINE, OVID, Scopus, ClinicalTrials.gov, and the Cochrane Central Register of Controlled Trials with the use of a combination of key words and text words related to "progesterone," "tocolysis," and "preterm labor" from 1966 through November 2014. We included all randomized trials of singleton gestations that had arrested PTL and then were randomized to maintenance tocolysis treatment with either vaginal progesterone or control (either placebo or no treatment). All published randomized studies on progesterone tocolysis were carefully reviewed. Exclusion criteria included maintenance tocolysis in women with preterm premature rupture of membrane, maintenance tocolysis with 17-alpha-hydroxyprogesterone caproate, and maintenance tocolysis with oral progesterone. The summary measures were reported as relative risks (RRs) with 95% confidence interval (CI). The primary outcome was preterm birth (PTB) <37 weeks.RESULTSFive randomized trials, including 441 singleton gestations, were analyzed. Women who received vaginal progesterone maintenance tocolysis for arrested PTL had a significantly lower rate of PTB <37 weeks (42% vs 58%; RR, 0.71; 95% CI, 0.57-0.90; 3 trials, 298 women). Women who received vaginal progesterone had significantly longer latency (mean difference 13.80 days; 95% CI, 3.97-23.63; 4 trials, 368 women), later gestational age at delivery (mean difference 1.29 weeks; 95% CI, 0.43-2.15; 4 trials, 368 women), lower rate of recurrent PTL (24% vs 46%; RR, 0.51; 95% CI, 0.31-0.84; 2 trials, 122 women), and lower rate of neonatal sepsis (2% vs 7%; RR, 0.34; 95% CI, 0.12-0.98; 4 trials, 368 women).CONCLUSIONMaintenance tocolysis with vaginal progesterone is associated with prevention of PTB, significant prolongation of pregnancy, and lower neonatal sepsis. However, given the frequent lack of blinding and the generally poor quality of the trials, we do not currently suggest a change in clinical care of women with arrested PTL. We suggest instead well-designed placebo-controlled randomized trials to confirm the findings of our metaanalysis.

Database: Medline

75. Tocolytics used as adjunctive therapy at the time of cerclage placement: a systematic review.

Author(s): Smith, J; DeFranco, E A

Source: Journal of perinatology : official journal of the California Perinatal Association; Aug 2015; vol. 35 (no. 8); p. 561-565

Publication Date: Aug 2015

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review Systematic Review

PubMedID: 25905689

Abstract:OBJECTIVETo review the published literature on whether the use of empiric perioperative tocolytic medications could provide additional benefit when used in combination with cerclage.STUDY DESIGNSystematic review of published medical literature reporting the efficacy of empiric tocolytics used as a perioperative adjunct to vaginal cerclage in high-risk patients. A PubMed search without date criteria of various tocolytics and cerclage yielded 42 studies. Review articles were excluded, as were reports of abdominal cerclage, emergent cerclage, or cerclage for the purpose of delayed interval delivery in twin gestations.RESULTOnly five publications on the topic of perioperative tocolytic use at the time of history or ultrasound-indicated vaginal cerclage placement were identified. These included zero clinical trials, three retrospective cohort studies, one case series and one case report. Only one cohort study compared cerclage with indomethacin and cerclage without indomethacin and suggested no difference between the groups. The other two published cohort studies had no referent group who received cerclage without tocolysis. One case series and one case report were also published reporting cerclage with empiric beta-mimetic and progesterone adjunctive therapy.CONCLUSIONThere is a paucity of published data on the topic of adjunctive perioperative tocolytics with cerclage. Adequately powered clinical trials on perioperative use of tocolysis with cerclage compared with a standard cerclage placement alone are needed to establish efficacy. Until adequately studied, this practice should be considered investigational.

Database: Medline

76. Preventing Preterm Birth with Progesterone in Women with a Short Cervical Length from a Low-Risk Population: A Multicenter Double-Blind Placebo-Controlled Randomized Trial.

Author(s): van Os, Melanie A; van der Ven, A Jeanine; Kleinrouweler, C Emily; Schuit, Ewoud; Kazemier, Brenda M; Verhoeven, Corine J; de Miranda, Esteriek; van Wassenaer-Leemhuis, Aleid G; Sikkema, J Marko; Woiski, Mallory D; Bossuyt, Patrick M; Pajkrt, Eva; de Groot, Christianne J M; Mol, Ben Willem J; Haak, Monique C

Source: American journal of perinatology; Aug 2015; vol. 32 (no. 10); p. 993-1000

Publication Date: Aug 2015

Publication Type(s): Randomized Controlled Trial Multicenter Study Journal Article

PubMedID: 25738790

Abstract:OBJECTIVEThe objective of this study was to evaluate the effectiveness of vaginal progesterone in reducing adverse neonatal outcome due to preterm birth (PTB) in low-risk pregnant women with a short cervical length (CL).STUDY DESIGNWomen with a singleton pregnancy without a history of PTB underwent CL measurement at 18 to 22 weeks. Women with a CL ≤ 30 mm received vaginal progesterone or placebo. Primary outcome was adverse neonatal outcome, defined as a composite of respiratory distress syndrome, bronchopulmonary dysplasia, intracerebral hemorrhage > grade II, necrotizing enterocolitis > stage 1, proven sepsis, or death before discharge. Secondary outcomes included time to delivery, PTB before 32, 34, and 37 weeks of gestation. Analysis was by intention to treat.RESULTSBetween 2009 and 2013, 20,234 women were screened. A CL of 30 mm or less was seen in 375 women (1.8%). In 151 women, a CL ≤ 30 mm was confirmed with a second measurement and 80 of these women agreed to participate in the trial. We randomly allocated 41 women to progesterone and 39 to placebo. Adverse neonatal outcomes occurred in two (5.0%) women in the progesterone and in four (11%) women in the control group (relative risk [RR], 0.47; 95% confidence interval [CI], 0.09-2.4). The use of progesterone resulted in a nonsignificant reduction of PTB < 32 weeks (2.0 vs. 8.0%; RR, 0.33; 95% CI, 0.04-3.0) and < 34 weeks (7.0 vs. 10%; RR, 0.73; 95% CI, 0.18-3.1) but not on PTB < 37 weeks (15 vs. 13%; RR, 1.2; 95% CI, 0.39-3.5).CONCLUSIONIn women with a short cervix, who are otherwise low risk, we could not show a significant benefit of progesterone in reducing adverse neonatal outcome and PTB.

Database: Medline

77. Vaginal progesterone for the prevention of preterm birth in twin gestations: a randomized placebo-controlled double-blind study.

Author(s): Brizot, Maria L; Hernandez, Wagner; Liao, Adolfo W; Bittar, Roberto E; Francisco, Rossana P V; Krebs, Vera L J; Zugaib, Marcelo

Source: American journal of obstetrics and gynecology; Jul 2015; vol. 213 (no. 1); p. 82

Publication Date: Jul 2015

Publication Type(s): Randomized Controlled Trial Journal Article

PubMedID: 25731690

Abstract:OBJECTIVEThe purpose of this study was to investigate the use of vaginal progesterone for the prevention of preterm delivery in twin pregnancies.STUDY DESIGNWe conducted a prospective, randomized, double-blind, placebo-controlled trial that involved 390 naturally conceived twin pregnancies among mothers with no history of preterm delivery who were receiving antenatal care at a single center. Women with twin pregnancies between 18 and 21 weeks and 6 days' gestation were assigned randomly to daily vaginal progesterone (200 mg) or placebo ovules until 34 weeks and 6 days' gestation. The primary outcome was the difference in mean gestational age at delivery; the secondary outcomes were the rate of spontaneous delivery at <34 weeks' gestation and the rate of neonatal composite morbidity and mortality in the treatment and nontreatment groups.RESULTSThe baseline characteristics were similar in both groups. The final analysis included 189 women in the progesterone group and 191 in the placebo group. No difference (P = .095) in the mean gestational age at delivery was observed between progesterone (35.08 ± 3.19 [SD]) and placebo groups (35.55 ± 2.85). The incidence of spontaneous delivery at <34 weeks' gestation was 18.5% in the progesterone group and 14.6% in the placebo group (odds ratio, 1.32; 95% confidence interval, 0.24-2.37). No difference in the composite neonatal morbidity and mortality was observed between the progesterone (15.5%) and placebo (15.9%) groups (odds ratio, 1.01; 95% confidence interval, 0.58-1.75).CONCLUSIONIn nonselected twin pregnancies, vaginal progesterone administration does not prevent preterm delivery and does not reduce neonatal morbidity and death.

Database: Medline

78. Cyclo-oxygenase (COX) inhibitors for treating preterm labour

Author(s): Reinebrant H.E.; Flenady V.; Pileggi-Castro C.; Romero C.L.T.; dos Santos R.A.N.; Kumar S.; Souza J.P.

Source: Cochrane Database of Systematic Reviews; Jun 2015; vol. 2015 (no. 6)

Publication Date: Jun 2015

Publication Type(s): Review

PubMedID: 26042617

Abstract: Background: Preterm birth is a major cause of perinatal mortality and morbidity. Cyclo-oxygenase (COX) inhibitors inhibit uterine contractions, are easily administered and appear to have few maternal side effects. However, adverse effects have been reported in the fetus and newborn as a result of exposure to COX inhibitors. Objective(s): To assess the effects on maternal and neonatal outcomes of COX inhibitors administered as a tocolytic agent to women in preterm labour when compared with (i) placebo or no intervention and (ii) other tocolytics. In addition, to compare the effects of non-selective COX inhibitors with COX-2 selective inhibitors. Search Method(s): We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (24 August 2014). We also contacted recognised experts and searched reference lists of retrieved studies. Selection Criteria: All published and unpublished randomised trials in which COX inhibitors were used for tocolysis for women in labour between 20 and 36 completed weeks' gestation. Data Collection and Analysis: Two review authors independently evaluated methodological quality and extracted data. We sought additional information from study authors. Results are presented using risk ratio (RR; dichotomous data) and mean difference (MD; continuous data) with 95% confidence interval (CI). The number needed to treat for benefit (NNTB) and the number needed to treat for harm (NNTH) were calculated for statistically different categorical outcomes. Main Result(s): With the addition of seven studies with a total of 684 women, this review now includes outcome data from 20 studies including 1509 women. The non-selective COX inhibitor indomethacin was used in 15 studies. The overall quality of the included studies was considered moderate to low. Three small studies (102 women), two of which were conducted in the 1980's, compared COX inhibition (indomethacin only) with placebo. No difference was shown in birth less than 48 hours after trial entry (average RR 0.20, 95% CI 0.03 to 1.28; two studies with 70 women). Indomethacin resulted in a reduction in preterm birth (before completion of 37 weeks of gestation) in one small study (36 women) (RR 0.21, 95% CI 0.07 to 0.62; NNTB 2, 95% CI 2 to 4); and an increase in gestational age at birth (average MD 3.59 weeks, 95% CI 0.65 to 6.52; two studies with 66 women) and birthweight (MD 716.34 g, 95% CI 425.52 to 1007.16; two studies with 67 infants). No difference was shown in measures of neonatal morbidity or neonatal mortality. Compared with betamimetics, COX inhibitors resulted in a reduction in birth less than 48 hours after trial entry (RR 0.27, 95% CI 0.08 to 0.96; NNTB 7, 95% CI 6 to 120; two studies with 100 women) and preterm birth (before completion of 37 weeks of gestation) (RR 0.53, 95% CI 0.28 to 0.99; NNTB 6, 95% CI 4 to 236; two studies with 80 women) although no benefit was shown in terms of neonatal morbidity or mortality. COX inhibition was also associated with fewer maternal adverse affects compared with betamimetics (RR 0.19, 95% CI 0.11 to 0.31; NNTB 3, 95% CI 2 to 3; five studies with 248 women) and maternal adverse effects requiring cessation of treatment (average RR 0.09, 95% CI 0.02 to 0.49; NNTB 5, CI 95% 5 to 9; three studies with 166 women). No differences were shown when comparing COX inhibitors with magnesium sulphate (MgSO4) (seven studies with 792 women) or calcium channel blockers (CCBs) (two studies with 230 women) in terms of prolonging pregnancy or for any fetal/neonatal outcomes. There were also no differences in very preterm birth (before completion of 34 weeks of gestation) and no maternal deaths occurred in the one study that reported on this outcome. However COX inhibitors resulted in fewer maternal adverse affects when compared with MgSO4 (RR 0.39, 95% CI 0.25 to 0.62; NNTB 11, 95% CI 9 to 17;

five studies with 635 women). A comparison of non-selective COX inhibitors versus any COX-2 inhibitor (two studies with 54 women) did not demonstrate any differences in maternal, fetal or neonatal outcomes. No data were available to assess COX inhibitors compared with oxytocin receptor antagonists (ORAs). Further, no data were available on extremely preterm birth (before 28 weeks of gestation), longer-term infant outcomes or costs. Authors' conclusions: In this review, no clear benefit for COX inhibitors was shown over placebo or any other tocolytic agents. While some benefit was demonstrated in terms of postponement of birth for COX inhibitors over placebo and betamimetics and also maternal adverse effects over betamimetics and MgSO4, due to the limitations of small numbers, minimal data on safety, lack of longer-term outcomes and generally low quality of the studies included in this review, we conclude that there is insufficient evidence on which to base decisions about the role of COX inhibition for women in preterm labour. Further well-designed tocolytic studies are required to determine short- and longer-term infant benefit of COX inhibitors over placebo and other tocolytics, particularly CCBs and ORAs. Another important focus for future studies is identifying whether COX-2 inhibitors are superior to non-selective COX inhibitors. All future studies on tocolytics for women in preterm labour should assess longer-term effects into early childhood and also costs.

Database: EMBASE

79. 17 alpha-hydroxyprogesterone caproate does not prolong pregnancy or reduce the rate of preterm birth in women at high risk for preterm delivery and a short cervix: a randomized controlled trial.

Author(s): Winer, Norbert; Bretelle, Florence; Senat, Marie-Victoire; Bohec, Caroline; Deruelle, Philippe; Perrotin, Frank; Connan, Laure; Vayssière, Christophe; Langer, Bruno; Capelle, Marianne; Azimi, Shohreh; Porcher, Raphael; Rozenberg, Patrick; Groupe de Recherche en Obstétrique et Gynécologie

Source: American journal of obstetrics and gynecology; Apr 2015; vol. 212 (no. 4); p. 485

Publication Date: Apr 2015

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Multicenter Study Journal Article

PubMedID: 25448515

Abstract:OBJECTIVEThe objective of the study was to evaluate the efficacy of 17 alpha-hydroxyprogesterone caproate (17OHP-C) in prolonging gestation in patients with a short cervix and other risk factors for preterm delivery, such as previous preterm birth, cervical surgery, uterine anomalies, or prenatal diethylstilbestrol (DES) exposure.STUDY DESIGNThis open-label, multicenter, randomized controlled trial included asymptomatic singleton pregnancies from 20(+0) through 31(+6) weeks of gestation with a cervical length less than 25 mm and a history of preterm delivery or cervical surgery or uterine malformation or prenatal DES exposure. Randomization assigned them to receive (or not) 500 mg of intramuscular 17OHP-C weekly until 36 weeks. The primary outcome was time from randomization to delivery.RESULTSAfter enrolling 105 patients, an interim analysis demonstrated the lack of efficacy of 17OHP-C in prolonging pregnancy. The study was discontinued because of futility. The groups were similar for maternal age, body mass index, parity, gestational age at inclusion, history of uterine anomalies, DES syndrome, previous preterm delivery or midtrimester abortion, and cervical length at randomization. The enrollment-to-delivery interval did not differ between patients allocated to 17OHP-C (n = 51) and those allocated to the control group (n = 54) (median [interquartile range] time to delivery: 77 [54-103] and 74 [52-99] days, respectively). The rate of preterm delivery less than 37 (45% vs 44%, P > .99), less than 34 (24% vs 30%, P = .51), or less than 32 (14% vs 20%, P = .44) weeks was similar in patients allocated to 17OHP-C and those in the control group.CONCLUSION17OHP-C did not prolong pregnancy in women with

singleton gestations, a sonographic short cervix, and other risk factors of preterm delivery (prior history, uterine malformations, cervical surgery, or prenatal DES exposure).

Database: Medline

80. Tocolysis for acute preterm labor: does anything work.

Author(s): Haram, Kjell; Mortensen, Jan Helge Seglem; Morrison, John C

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; Mar 2015; vol. 28 (no. 4); p. 371-378

Publication Date: Mar 2015

Publication Type(s): Journal Article Review

PubMedID: 24990666

Abstract: The central rationale of tocolysis for preterm labor (PTL) is to delay delivery for at least 48 h to allow for transfer of the mother to a tertiary facility and for corticosteroids to induce surfactant production in fetal lungs. Beta-mimetics decrease the number of women in preterm labor giving birth within 48 h without reducing adverse neonatal outcomes. Calcium channel blockers inclusive of nifedipine decrease the adverse neonatal outcomes by significantly delaying delivery. Atosiban has the best maternal and fetal safety profile but does not seem to reduce neonatal complications. Magnesium sulfate is controversial as a tocolytic, but is valuable as a neuroprotective agent and for treatment of eclamptic seizures. Indomethacin may be a reasonable first choice for acute tocolytsis in gestational ages less than 32 weeks' gestation. Prolonged use (>48 h) should be avoided. Transdermal nitroglycerin can reduce neonatal morbidity and mortality as a result of decreased risk of birth before 28 weeks' gestation. Nifedipine may be a reasonable first choice because it is easy to administer and also of limited side effects relative to β2-mimetics. Tocolysis does not appear to significantly lengthen the gestational age beyond seven days.

Database: Medline

81. Effectiveness of progestogens to improve perinatal outcome in twin pregnancies: An individual participant data meta-analysis

Author(s): Schuit E.; Zuithoff N.P.A.; Groenwold R.H.H.; Moons K.G.M.; Lim A.C.; Stock S.; Norman J.E.; Rode L.; Tabor A.; Rouse D.J.; Nassar A.H.; Awwad J.; Usta I.M.; Serra V.; Combs C.A.; Vayssiere C.; Aboulghar M.M.; Aboulghar M.A.; Amin Y.M.; Wood S.; Ross S.; Cetingoz E.; Cam C.; Karateke A.; Briery C.M.; Fonseca E.B.; Worda K.; Thom E.A.; Caritis S.N.; Perales A.; Meseguer J.; Maurel K.; Garite T.; Morrison J.C.; Magann E.F.; Nicolaides K.H.; Kwee A.; Mol B.W.J.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Jan 2015; vol. 122 (no. 1); p. 27-37

Publication Date: Jan 2015

Publication Type(s): Review

PubMedID: 25145491

Abstract: Background In twin pregnancies, the rates of adverse perinatal outcome and subsequent long-term morbidity are substantial, and mainly result from preterm birth (PTB). Objectives To assess the effectiveness of progestogen treatment in the prevention of neonatal morbidity or PTB in twin pregnancies using individual participant data meta-analysis (IPDMA). Search strategy We searched international scientific databases, trial registration websites, and references of identified articles. Selection criteria Randomised clinical trials (RCTs) of 17-hydroxyprogesterone caproate (17Pc) or vaginally administered natural progesterone, compared with placebo or no treatment. Data collection and analysis Investigators of identified RCTs were asked to share their IPD. The primary outcome was a composite of perinatal mortality and severe neonatal morbidity. Prespecified subgroup analyses were performed for chorionicity, cervical length, and prior spontaneous PTB. Main results Thirteen trials included 3768 women and their 7536 babies. Neither 17Pc nor vaginal progesterone reduced the incidence of adverse perinatal outcome (17Pc relative risk, RR 1.1; 95% confidence interval, 95% CI 0.97-1.4, vaginal progesterone RR 0.97; 95% CI 0.77-1.2). In a subgroup of women with a cervical length of <=25 mm, vaginal progesterone reduced adverse perinatal outcome when cervical length was measured at randomisation (15/56 versus 22/60; RR 0.57; 95% CI 0.47-0.70) or before 24 weeks of gestation (14/52 versus 21/56; RR 0.56; 95% CI 0.42-0.75). Author's conclusions In unselected women with an uncomplicated twin gestation, treatment with progestogens (intramuscular 17Pc or vaginal natural progesterone) does not improve perinatal outcome. Vaginal progesterone may be effective in the reduction of adverse perinatal outcome in women with a cervical length of <=25 mm; however, further research is warranted to confirm this finding.

Database: EMBASE

82. A randomised controlled double-blind clinical trial of 17-hydroxyprogesterone caproate for the prevention of preterm birth in twin gestation (PROGESTWIN): evidence for reduced neonatal morbidity.

Author(s): Awwad, J; Usta, I M; Ghazeeri, G; Yacoub, N; Succar, J; Hayek, S; Saasouh, W; Nassar, A H

Source: BJOG : an international journal of obstetrics and gynaecology; Jan 2015; vol. 122 (no. 1); p. 71-79

Publication Date: Jan 2015

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Journal Article

PubMedID: 25163819

Available at BJOG : an international journal of obstetrics and gynaecology - from Wiley Online Library

Abstract:OBJECTIVETo determine whether 17 alpha-hydroxyprogesterone caproate (17OHPC) prolongs gestation beyond 37 weeks of gestation (primary outcome) and reduces neonatal morbidity (secondary outcome) in twin pregnancy.DESIGNRandomised controlled double-blind clinical trial.SETTINGTertiary-care university medical centre.POPULATIONUnselected women with twin pregnancies.METHODSParticipants received weekly injections of 250 mg 17OHPC (n = 194) or placebo (n = 94), from 16-20 to 36 weeks of gestation. Randomisation was performed using the permuted-block randomisation method. Data were analysed on an intention-to-treat basis.MAIN OUTCOME MEASUREPreterm birth (PTB) rate before 37 weeks of gestation.RESULTSThere were no significant differences in the average gestational age at delivery, or in the rates of PTB before 37, 32, and 28 weeks of gestation, between the two groups. The proportion of very-low-birthweight neonates (<1500 g) was significantly lower in the 17OHPC group (7.6%) compared with placebo (14.3%) (relative risk, RR 0.5; 95% confidence interval, 95% CI 0.3-0.9; P = 0.01). Progestogen-treated neonates had a significantly lower composite neonatal morbidity (19.1%) compared with placebo (30.9%) (odds ratio, OR 0.53; 95% CI 0.31-0.90; P = 0.02), with significantly lower odds for respiratory distress syndrome (14.4 versus 23.4%; OR 0.55; 95% CI 0.31-0.98; P = 0.04), retinopathy of prematurity (1.1 versus 4.6%; OR 0.21; 95% CI 0.05-0.96; P = 0.04), and culture-confirmed sepsis (3.4 versus 12.8%; OR 0.24; 95% CI 0.10-0.57; P = 0.00).CONCLUSIONSIntramuscular 17OHPC therapy did not reduce PTB before 37 weeks of gestation in unselected twin pregnancies. Nonetheless, 17OHPC significantly reduced neonatal morbidity parameters and increased birthweight.

Database: Medline

83. Short-term tocolytics for preterm delivery - current perspectives.

Author(s): Haas, David M; Benjamin, Tara; Sawyer, Renata; Quinney, Sara K

Source: International journal of women's health; 2014; vol. 6 ; p. 343-349

Publication Date: 2014

Publication Type(s): Journal Article Review

PubMedID: 24707187

Available at International journal of women's health - from Europe PubMed Central - Open Access

Available at International journal of women's health - from Free Medical Journals . com

Available at International journal of women's health - from Unpaywall

Abstract: Administration of short-term tocolytic agents can prolong pregnancy for women in preterm labor. Prolonging pregnancy has many benefits because it allows for other proven interventions, such as antenatal corticosteroid administration, to be accomplished. This review provides an overview of currently utilized tocolytic agents and the evidence demonstrating their efficacy for prolonging pregnancy by at least 48 hours. General pharmacological principles for the clinician regarding drugs in pregnancy are also briefly discussed. In general, while the choice of the best first-line short-term tocolytic drug is not clear, it is evident that use of these agents has a clear place in current obstetric therapeutics.

Database: Medline

84. Prevention of preterm delivery with 17-hydroxyprogesterone caproate: pharmacologic considerations.

Author(s): Feghali, Maisa; Venkataramanan, Raman; Caritis, Steve

Source: Seminars in perinatology; Dec 2014; vol. 38 (no. 8); p. 516-522

Publication Date: Dec 2014

Publication Type(s): Research Support, N.i.h., Extramural Journal Article Review

PubMedID: 25256193

Available at Seminars in perinatology - from Unpaywall

Abstract: Despite advances in neonatal care, the burden of preterm birth remains high. Preterm birth is a multifactorial problem, and strategies to identify and treat medical risk factors in early pregnancy have not been effective in reducing preterm birth rates. In a sentinel clinical trial, prophylactic therapy with 17-hydoxyprogesterone caproate (17-OHPC) reduced the risk of recurrent, spontaneous preterm birth in 34% of women. As a result, clinical practice changed and extensive research on 17-OHPC followed. The increasing body of evidence demonstrated a variable efficacy of the drug. This review will examine the plausibility, pharmacology, clinical efficacy, and safety of 17-OHPC when used in the setting of preterm birth prevention. We will also discuss pharmacokinetic and pharmacodynamics data to highlight drug metabolism and mechanism of action, which will help clarify the variability in clinical outcomes and efficacy.

Database: Medline

85. Cerclage, progesterone and α-hydroxyprogeterone caproate treatment in women at risk for preterm delivery.

Author(s): Haram, Kjell; Mortensen, Jan Helge; Morrison, John C

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; Nov 2014; vol. 27 (no. 16); p. 1710-1715

Publication Date: Nov 2014

Publication Type(s): Journal Article Review

PubMedID: 24678618

Abstract: The most significant action of progesterone appears to be on the cervix and in prevention rather than on treatment of preterm delivery. In women with singleton gestations, no prior PTB, and CL <20 mm at <24 weeks, vaginal progesterone, either 90 mg gel or 200 mg suppository, is associated with reduction of both preterm birth (PTB) and perinatal morbidity/mortality. Cerclage is as effective as vaginal progesterone in women with CL <25 mm. Treatment of women with previous PTB with 17OHP-C from 16 to 20 weeks' gestation until 36 weeks could reduce significantly both the risk of delivery at <37, <35 and <32 weeks' gestation, as well as the rates of NEC, the need for supplemental oxygen and IVH. In women successfully treated with tocolytics progesterone combined with corticosteroid therapy lengthens pregnancy, reduces occurrence of respiratory distress syndrome and low birth weight. However, there is currently insufficient evidence on the role of progesterone after arrested preterm labor. It is reasonable to support an approach with CL screening of women with prior PTB starting at 16 to 19 weeks and administration of progesterone to women with a short cervix. Cerclage may be offered to those with a CL<25 mm. A combination of traditional tocolytics, corticosteroids and progesterone might be beneficial.

Database: Medline

86. Acute and chronic tocolysis.

Author(s): Bolden, Janelle R

Source: Clinical obstetrics and gynecology; Sep 2014; vol. 57 (no. 3); p. 568-578

Publication Date: Sep 2014

Publication Type(s): Journal Article Review

PubMedID: 25029339

Available at Clinical obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: Preterm birth occurs in 12% of all births in the United States. Preterm labor precedes approximately half of these births. Tocolysis is used in the short term to prolong pregnancy long enough to administer corticosteroids and/or facilitate transfer to a tertiary care center. A number of agents have been used for this therapy, which will be discussed in the following chapter.

Database: Medline

87. Progesterone.

Author(s): Maggio, Lindsay; Rouse, Dwight J

Source: Clinical obstetrics and gynecology; Sep 2014; vol. 57 (no. 3); p. 547-556

Publication Date: Sep 2014

Publication Type(s): Journal Article Review

PubMedID: 24936913

Available at Clinical obstetrics and gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: Progestogens are a promising treatment in the prevention of spontaneous preterm birth in high-risk women. In women with a prior history of spontaneous preterm delivery and in women with a sonographic shortened cervix, there is considerable evidence supporting a benefit of progestogen therapy in the reduction of preterm delivery. In women with multifetal gestations, progestogen therapy has not been shown to be beneficial. Data are inconclusive in women with arrested preterm labor. Questions remain about the mechanism of progestogen action, the optimal type of progestogen, the best mode of administration, and the ideal dosing regimen.

Database: Medline

88. Magnesium sulphate for preventing preterm birth in threatened preterm labour

Author(s): Crowther C.A.; Brown J.; Mckinlay C.J.D.; Middleton P.

Source: Cochrane Database of Systematic Reviews; Aug 2014; vol. 2014 (no. 8)

Publication Date: Aug 2014

Publication Type(s): Review

PubMedID: 25126773

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Abstract: Background: Magnesium sulphate has been used in some settings as a tocolytic agent to inhibit uterine activity in women in preterm labour with the aim of preventing preterm birth. Objective(s): To assess the effects of magnesium sulphate therapy given to women in threatened preterm labour with the aim of preventing preterm birth and its sequelae. Search Method(s): We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (last searched 31 January 2014). Selection Criteria: Randomised controlled trials of magnesium sulphate as the only tocolytic, administered by any route, compared with either placebo, no treatment or alternative tocolytic therapy (not magnesium sulphate) to women considered to be in preterm labour. Data Collection and Analysis: At least two review authors assessed trial eligibility and risk of bias and undertook data extraction independently. Main Result(s): The 37 included trials (total of 3571 women and over 3600 babies) were generally of moderate to high risk of bias. Antenatal magnesium sulphate was compared with either placebo, no treatment, or a range of alternative tocolytic agents. For the primary outcome of giving birth within 48 hours after trial entry, no significant differences were seen between women who received magnesium sulphate and women who did not (whether placebo/no alternative tocolytic drug, betamimetics, calcium channel blockers, cox inhibitors, prostaglandin inhibitors, or human chorionic gonadotropin) (19 trials, 1913 women). Similarly for the primary outcome of serious infant outcome, there were no significant differences between the infants exposed to magnesium sulphate and those not (whether placebo/no alternative tocolytic drug, betamimetics, calcium channel blockers, cox inhibitors, prostaglandin inhibitors, human chorionic gonadotropin or various tocolytic drugs) (18 trials; 2187 babies). No trials reported the outcome of extremely preterm birth. In the seven trials that reported serious maternal outcomes, no events were recorded. In the group treated with magnesium sulphate compared with women receiving

antenatal placebo or no alternative tocolytic drug, a borderline increased risk of total death (fetal, neonatal, infant) was seen (risk ratio (RR) 4.56, 95% confidence interval (CI) 1.00 to 20.86; two trials, 257 babies); none of the comparisons between magnesium sulphate and other classes of tocolytic drugs showed differences for this outcome (10 trials, 991 babies). The outcomes of neonatal and/or infant deaths and of fetal deaths did not show differences between magnesium sulphate and no magnesium sulphate, whether compared with placebo/no alternative tocolytic drug, or any specific class of tocolytic drug. For most of the other secondary outcomes, there were no significant differences between magnesium sulphate and the control groups for risk of preterm birth (except for a significantly lower risk with magnesium sulphate when compared with barbiturates in one trial of 65 women), gestational age at birth, interval between trial entry and birth, other neonatal morbidities, or neurodevelopmental outcomes. Duration of neonatal intensive care unit stay was significantly increased in the magnesium sulphate group compared with the calcium channel blocker group, but not when compared with cox inhibitors or prostaglandin inhibitors. No maternal deaths were reported in the four trials reporting this outcome. Significant differences between magnesium sulphate and controls were not seen for maternal adverse events severe enough to stop treatment, except for a significant benefit of magnesium sulphate compared with betamimetics in a single trial. Authors' conclusions: Magnesium sulphate is ineffective at delaying birth or preventing preterm birth, has no apparent advantages for a range of neonatal and maternal outcomes as a tocolytic agent and its use for this indication may be associated with an increased risk of total fetal, neonatal or infant mortality (in contrast to its use in appropriate groups of women for maternal, fetal, neonatal and infant neuroprotection where beneficial effects have been demonstrated).

Database: EMBASE

89. Combination of tocolytic agents for inhibiting preterm labour.

Author(s): Vogel, Joshua P; Nardin, Juan Manuel; Dowswell, Therese; West, Helen M; Oladapo, Olufemi T

Source: The Cochrane database of systematic reviews; Jul 2014 (no. 7); p. CD006169

Publication Date: Jul 2014

Publication Type(s): Research Support, Non-u.s. Gov't Meta-analysis Journal Article Review Systematic Review

PubMedID: 25010869

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Abstract:BACKGROUNDPreterm birth represents the single largest cause of mortality and morbidity for newborns and a major cause of morbidity for pregnant women. Tocolytic agents include a wide range of drugs that can inhibit labour to prolong pregnancy. This may gain time to allow the fetus to mature further before being born, permit antenatal corticosteroid administration for lung maturation, and allow time for intra-uterine transfer to a hospital with neonatal intensive care facilities. However, some tocolytic drugs are associated with severe side effects. Combinations of tocolytic drugs may be more effective over single tocolytic agents or no intervention, without adversely affecting the mother or neonate.OBJECTIVESTo assess the effects on maternal, fetal and neonatal outcomes of any combination of tocolytic drugs for the treatment of preterm labour when compared with any other treatment, no treatment or placebo.SEARCH METHODSWe searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 January 2014) and reference lists of retrieved studies.SELECTION CRITERIAWe included randomised controlled trials comparing a combination of tocolytic agents, administered by any route or any dose, for inhibiting preterm labour versus any other treatment (including other combinations of tocolytics or single tocolytics), no intervention or placebo.DATA COLLECTION AND ANALYSISTwo review authors independently

assessed study reports for eligibility, carried out data extraction and assessed risk of bias.MAIN RESULTSEleven studies met our inclusion criteria. Two studies did not report any outcome data relevant to the review, so the results of the review are based on nine trials that contributed data. Primary outcomes were perinatal mortality, serious maternal or infant outcomes, adverse drug reactions, birth before 48 hours of trial entry, birth before 34 weeks' gestation and preterm neonates delivered without a full course of antenatal steroids completed 24 hours before birth. The quality of evidence in included trials was mixed; only three of the trials were placebo controlled.The included trials examined seven different comparisons: intravenous (IV) ritodrine plus oral or IV magnesium (sulphate or gluconate) versus IV ritodrine alone (three trials, 231 women); IV ritodrine plus indomethacin suppositories versus IV ritodrine alone (one trial, 208 women); IV ritodrine plus vaginal progesterone versus IV ritodrine alone (one trial, 83 women); IV hexoprenaline sulphate plus IV magnesium hydrochloride versus IV hexoprenaline sulphate alone (one trial, 24 women); IV fenoterol plus oral naproxen versus IV fenoterol alone (one trial, 72 women); oral pentoxifylline plus IV magnesium sulphate plus IV fenoterol versus IV magnesium sulphate plus IV fenoterol (one trial, 125 women); and, IV terbutaline plus oral metoprolol versus IV terbutaline alone (one trial, 17 women). Few studies with small numbers of women were available for each comparison, hence very little data were pooled in meta-analysis. In all trials, not many of the primary outcomes were reported.Three trials examined intravenous (IV) ritodrine plus IV or oral magnesium (sulphate or gluconate) compared with IV ritodrine alone. One study, with 41 women, reported more adverse drug reactions in the group receiving the combined tocolytics (risk ratio (RR) 7.79, 95% confidence interval (CI) 1.11 to 54.80). Two trials reported discontinuation of therapy due to severe side effects (results were not combined due to high statistical heterogeneity, $I^2 = 83\%$); one trial reported increased severe side effects in the group receiving IV ritodrine alone (RR 7.79, 95% CI 1.11 to 54.80, 41 women); in the other trial there was no clear difference between groups (RR 0.23, 95% CI 0.03 to 1.97, 107 women). Other primary outcomes were not reported.One trial assessed IV ritodrine plus indomethacin suppositories versus IV ritodrine alone. There were no significant differences between groups for perinatal mortality or serious neonatal morbidity. Results for other primary outcomes were not reported.There were no significant differences between groups receiving IV ritodrine plus vaginal progesterone compared with IV ritodrine alone for most outcomes reported, although the latency period (time from recruitment to delivery) was increased in the group receiving the combination of tocolytics.For other combinations of tocolytic agents, primary outcomes were rarely reported and for secondary outcomes results did not demonstrate differences between groups.AUTHORS' CONCLUSIONSIt is unclear whether a combination of tocolytic drugs for preterm labour is more advantageous for women and/or newborns due to a lack of large, well-designed trials including the outcomes of interest. There are no trials of combination regimens using widely used tocolytic agents, such as calcium channel blockers (nifedipine) and/or oxytocin receptor antagonists (atosiban). Further trials are needed before specific conclusions on use of combination tocolytic therapy for preterm labour can be made.

Database: Medline

90. Identification of candidates for progesterone: why, who, how, and when?

Author(s): Iams, Jay D

Source: Obstetrics and gynecology; Jun 2014; vol. 123 (no. 6); p. 1317-1326

Publication Date: Jun 2014

Publication Type(s): Journal Article Review

PubMedID: 24807317

Available at Obstetrics and gynecology - from Ovid (Journals @ Ovid) - Remote Access

Available at Obstetrics and gynecology - from Unpaywall

Abstract: Recognition of preterm birth as the major underlying cause of infant mortality in the United States has placed responsibility for prevention in the hands of obstetrician-gynecologists. The advent of effective methods to identify and treat women with increased risk is a major advance that will alter the focus of prenatal care. Adoption of research findings into clinical practice, never an easy task, will be particularly challenging for efforts to reduce the risk of preterm birth. Historical risk factors for preterm birth are numerous and variably defined. Measurement of the length of the cervix with ultrasonography requires unique personnel and facilities. Care algorithms exist but lack the detailed information that comes with experience. This review offers perspective and detail to aid health care practitioners in developing a prematurity prevention strategy appropriate to their practice population.

Database: Medline

91. Oxytocin receptor antagonists for inhibiting preterm labour

Author(s): Flenady V.; Reinebrant H.E.; Liley H.G.; Tambimuttu E.G.; Papatsonis D.N.M.

Source: Cochrane Database of Systematic Reviews; Jun 2014; vol. 2014 (no. 6)

Publication Date: Jun 2014

Publication Type(s): Review

PubMedID: 24903678

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Available at The Cochrane database of systematic reviews - from Unpaywall

Abstract: Background: Preterm birth, defined as birth between 20 and 36 completed weeks, is a major contributor to perinatal morbidity and mortality globally. Oxytocin receptor antagonists (ORA), such as atosiban, have been specially developed for the treatment of preterm labour. ORA have been proposed as effective tocolytic agents for women in preterm labour to prolong pregnancy with fewer side effects than other tocolytic agents. Objective(s): To assess the effects on maternal, fetal and neonatal outcomes of tocolysis with ORA for women with preterm labour compared with placebo or any other tocolytic agent. Search Method(s): We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (1 December 2013). Selection Criteria: We included all randomised controlled trials (published and unpublished) of ORA for tocolysis of labour between 20 and 36 completed weeks' gestation. Data Collection and Analysis: Two review authors independently evaluated methodological quality and extracted trial data. When required, we sought additional data from trial authors. Results are presented as risk ratio (RR) for categorical and mean difference (MD) for continuous data with the 95% confidence intervals (CI). Where appropriate, the number needed to treat for benefit (NNTB) and the number needed to treat for harm (NNTH) were calculated. Main Result(s): This review update includes eight additional studies (790 women), giving a total of 14 studies involving 2485 women. Four studies (854 women) compared ORA (three used atosiban and one barusiban) with placebo. Three studies were considered at low risk of bias in general (blinded

allocation to treatment and intervention), the fourth study did not adequately blind the intervention. No difference was shown in birth less than 48 hours after trial entry (average RR 1.05, 95% CI 0.15 to 7.43; random-effects, (two studies, 152 women), perinatal mortality (RR 2.25, 95% CI 0.79 to 6.38; two studies, 729 infants), or major neonatal morbidity. ORA (atosiban) resulted in a small reduction in birthweight (MD -138.86 g, 95% CI -250.53 to -27.18; two studies with 676 infants). In one study, atosiban resulted in an increase in extremely preterm birth (before 28 weeks' gestation) (RR 3.11, 95% CI 1.02 to 9.51; NNTH 31, 95% CI 8 to 3188) and infant deaths (up to 12 months) (RR 6.13, 95% CI 1.38 to 27.13; NNTH 28, 95% CI 6 to 377). However, this finding may be confounded due to randomisation of more women with pregnancy less than 26 weeks' gestation to atosiban. ORA also resulted in an increase in maternal adverse drug reactions requiring cessation of treatment in comparison with placebo (RR 4.02, 95% CI 2.05 to 7.85; NNTH 12, 95% CI 5 to 33). No differences were shown in preterm birth less than 37 weeks' gestation or any other adverse neonatal outcomes. No differences were evident by type of ORA, although data were limited. Eight studies (1402 women) compared ORA (atosiban only) with betamimetics; four were considered of low risk of bias (blinded allocation to treatment and to intervention). No statistically significant difference was shown in birth less than 48 hours after trial entry (RR 0.89, 95% CI 0.66 to 1.22; eight studies with 1389 women), very preterm birth (RR 1.70, 95% CI 0.89 to 3.23; one study with 145 women), extremely preterm birth (RR 0.84, 95% CI 0.37 to 1.92; one study with 244 women) or perinatal mortality (RR 0.55, 95% CI 0.21 to 1.48; three studies with 816 infants). One study (80 women), of unclear methodological quality, showed an increase in the interval between trial entry and birth (MD 22.90 days, 95% CI 18.03 to 27.77). No difference was shown in any reported measures of major neonatal morbidity (although numbers were small). ORA (atosiban) resulted in less maternal adverse effects requiring cessation of treatment (RR 0.05, 95% CI 0.02 to 0.11; NNTB 6, 95% CI 6 to 6; five studies with 1161 women). Two studies including (225 women) compared ORA (atosiban) with calcium channel blockers (CCB) (nifedipine only). The studies were considered as having high risk of bias as neither study blinded the intervention and in one study it was not known if allocation was blinded. No difference was shown in birth less than 48 hours after trial entry (average RR 1.09, 95% CI 0.44 to 2.73, random-effects; two studies, 225 women) and extremely preterm birth (RR 2.14, 95% CI 0.20 to 23.11; one study, 145 women). No data were available for the outcome of perinatal mortality. One small trial (145 women), which did not employ blinding of the intervention, showed an increase in the number of preterm births (before 37 weeks' gestation) (RR 1.56, 95% CI 1.13 to 2.14; NNTH 5, 95% CI 3 to 19), a lower gestational age at birth (MD -1.20 weeks, 95% CI -2.15 to -0.25) and an increase in admission to neonatal intensive care unit (RR 1.70, 95% CI 1.17 to 2.47; NNTH 5, 95% CI 3 to 20). ORA (atosiban) resulted in less maternal adverse effects (RR 0.38, 95% CI 0.21 to 0.68; NNTB 6, 95% CI 5 to 12; two studies, 225 women) but not maternal adverse effects requiring cessation of treatment (RR 0.36, 95% CI 0.01 to 8.62; one study, 145 women). No longer-term outcome data were included. Authors' conclusions: This review did not demonstrate superiority of ORA (largely atosiban) as a tocolytic agent compared with placebo, betamimetics or CCB (largely nifedipine) in terms of pregnancy prolongation or neonatal outcomes, although ORA was associated with less maternal adverse effects than treatment with the CCB or betamimetics. The finding of an increase in infant deaths and more births before completion of 28 weeks of gestation in one placebo-controlled study warrants caution. However, the number of women enrolled at very low gestations was small. Due to limitations of small numbers studied and methodological quality, further well-designed randomised controlled trials are needed. Further comparisons of ORA versus CCB (which has a better side-effect profile than betamimetics) are needed. Consideration of further placebo-controlled studies seems warranted. Future studies of tocolytic agents should measure all important short- and long-term outcomes for women and infants, and costs.

Database: EMBASE

92. The NIFTY study: a multicentre randomised double-blind placebo-controlled trial of nifedipine maintenance tocolysis in fetal fibronectin-positive women in threatened preterm labour.

Author(s): Parry, Emma; Roos, Carolien; Stone, Peter; Hayward, Lynsey; Mol, Ben Willem; McCowan, Lesley

Source: The Australian & New Zealand journal of obstetrics & gynaecology; Jun 2014; vol. 54 (no. 3); p. 231-236

Publication Date: Jun 2014

Publication Type(s): Research Support, Non-u.s. Gov't Randomized Controlled Trial Multicenter Study Journal Article

PubMedID: 24506318

Abstract:OBJECTIVEIn an unselected group of women with signs of preterm labour, maintenance tocolysis is not effective in the prevention of preterm birth and does not improve neonatal outcome. Among women with signs of preterm labour, those who are fetal fibronectin positive have an increased risk of preterm birth. We investigated whether maintenance tocolysis with nifedipine would delay delivery and improve neonatal outcome in women with threatened preterm labour and a positive fetal fibronectin status.STUDY DESIGNWomen with a singleton pregnancy in threatened preterm labour (24(+0) to 33(+6) weeks) with a positive fetal fibronectin test were randomised to nifedipine or placebo. Study medication was continued until 36 completed weeks' gestation. The primary endpoint was prolongation of pregnancy of seven days. Secondary endpoints were gestational age at delivery and length of NICU admission.RESULTSOf the 60 participants, 29 received nifedipine and 31 placebo. Prolongation of pregnancy by >7 days occurred in 22/29 (76%) in the nifedipine group and 25/31 (81%) in the placebo group (relative risks, RR 0.94 [0.72-1.2]). Gestational age at delivery was 36.1 ± 5.1 weeks for nifedipine and 36.8 ± 3.6 weeks for placebo (P = 0.027). Length of NICU admission [median (interquartile ranges, IQR)] was 27 (24-41) days and 16 (8-37) days in nifedipine and placebo groups, respectively (P = 0.17).CONCLUSIONIn women with threatened preterm labour who are fetal fibronectin positive, maintenance tocolysis with nifedipine does not seem to prolong pregnancy, nor reduce length of NICU admission.

Database: Medline

93. A comparison of three tocolytics for preterm labor: a randomized clinical trial.

Author(s): Klauser, Chad K; Briery, Christian M; Martin, Rick W; Langston, LeDon; Magann, Everett F; Morrison, John C

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; May 2014; vol. 27 (no. 8); p. 801-806

Publication Date: May 2014

Publication Type(s): Comparative Study Randomized Controlled Trial Journal Article

PubMedID: 24090282

Abstract:OBJECTIVETo compare the efficacy and maternal side effects of nifedipine (N), magnesium sulfate (M), and indomethacin (I) for acute tocolysis.METHODSIn this single center randomized trial, women in preterm labor 24-32 weeks' gestation received intravenous M, oral N, or I suppositories. The primary outcomes of interest were arrest of preterm labor (>48 h, ≥7 days), gestational age at delivery, and maternal side effects.RESULTSOver a 38-month period, 301 women were allocated to receive M (90), N (114), or I (90). Gestational age at delivery (p = 0.551) or arrest of labor >48 h, >7 days were similar between the three groups (p = 0.199, 0.654). Hypotension and tachycardia were more common in N patients compared to women receiving M or I (p = 0.003, 0.009). Patients receiving I had more fetal ductal constriction or oligohydramnios compared to M or N (p = 0.001, 0.020) but, I women were tested more often. There was one case of pulmonary edema in the M group and one with plural effusion in the N group.CONCLUSIONThere were no differences in efficacy or in major maternal safety issues between the three tocolytic agents. Since there is no FDA approved tocolytic to treat preterm labor, clinicians should use the tocolytic that has afforded them the best results with the least maternal/neonatal side effects.

Database: Medline

94. Preterm labor: current pharmacotherapy options for tocolysis.

Author(s): van Vliet, Elvira O G; Boormans, Elisabeth M; de Lange, Thomas S; Mol, Ben W; Oudijk, Martijn A

Source: Expert opinion on pharmacotherapy; Apr 2014; vol. 15 (no. 6); p. 787-797

Publication Date: Apr 2014

Publication Type(s): Journal Article Review

PubMedID: 24533566

Abstract:INTRODUCTIONIn the developed world, preterm birth is in quantity and in severity the most important issue in obstetric care. Adverse neonatal outcome is strongly related to gestational age at delivery. Since the pathophysiological mechanism of preterm birth is not yet completely unraveled, the development of successful preventive strategies is hampered. When preterm labor is actually threatening, current pharmacological therapies focus on inhibition of preterm contractions. This allows for transportation of the mother to a center with a neonatal intensive care unit and administration of corticosteroids to enhance fetal lung maturation. Globally, however, large practice variation exists.AREAS COVEREDThe aim of this review is to provide an overview of current pharmacological therapies for preterm labor.EXPERT OPINIONFor the initial tocolysis, the use of atosiban or nifedipine for 48 h is recommended based on the largest effectiveness and most favorable side effect profile. However, since data that convincingly indicate the beneficial effect of tocolytics on neonatal outcome are lacking, it might well be that tocolytics are ineffective. The role of progesterone in treatment of acute tocolysis is limited, but it might play a role in the prevention of preterm labor or as sensitizer for other tocolytic agents.

Database: Medline

95. Tocolysis for preterm labor: expert opinion.

Author(s): Hösli, Irène; Sperschneider, Christiane; Drack, Gero; Zimmermann, Roland; Surbek, Daniel; Irion, Olivier; Swiss Society of Obstetrics and Gynecology

Source: Archives of gynecology and obstetrics; Apr 2014; vol. 289 (no. 4); p. 903-909

Publication Date: Apr 2014

Publication Type(s): Practice Guideline Journal Article Review

PubMedID: 24385286

Available at Archives of gynecology and obstetrics - from SpringerLink - Medicine

Available at Archives of gynecology and obstetrics - from Unpaywall

Abstract: Tocolysis is an important treatment in the improvement of outcome in preterm labor and preterm birth, provided that its use follows clear evidence-based recommendations. In this expert opinion, the most recent evidence about efficacy and side effects of different tocolytics is being reviewed and evidence-based recommendation about diagnosis and treatment of preterm labor is given. Further aspects such as progesterone administration or antibiotic treatment for the prevention of preterm birth are included. Our review demonstrates that an individualized choice of different tocolytics and additional treatments is necessary to improve short- and long-term neonatal outcome in preterm labor and preterm birth.

Database: Medline

96. Preterm labor: Current tocolytic options for the treatment of preterm labor

Author(s): Jorgensen J.S.; Weile L.K.K.; Lamont R.F.

Source: Expert Opinion on Pharmacotherapy; Apr 2014; vol. 15 (no. 5); p. 585-588

Publication Date: Apr 2014

Publication Type(s): Review

PubMedID: 24456411

Available at Expert opinion on pharmacotherapy - from Unpaywall

Abstract: While tocolytic therapy may not be indicated in all cases of spontaneous preterm labor (SPTL), the evidence that they are superior to placebo is robust. The perfect tocolytic that is 100% efficacious and 100% safe does not exist and efforts should continue to develop and introduce safer and more effective agents. A reduction in the rate of neonatal mortality and morbidity using tocolysis has not been shown but no tocolytic study has been powered by numbers sufficient to demonstrate such an effect. Tocolytics can delay delivery long enough to administer a course of antepartum glucocorticoids and arrange in utero transfer to a center with neonatal intensive care facilities, both of which reduce neonatal mortality and morbidity. Few tocolytics (beta2-agonists and atosiban) are licensed for use as tocolytics and only one was developed specifically to treat preterm labor (atosiban). Accordingly, most tocolytics have multi-organ adverse effects. Currently, based on the evidence of safety and efficacy, atosiban should be the first-choice tocolytic for the treatment of SPTL to prevent or delay preterm birth. © 2014 Informa UK, Ltd.

Database: EMBASE

97. Nifedipine versus atosiban in the treatment of threatened preterm labour (Assessment of Perinatal Outcome after Specific Tocolysis in Early Labour: APOSTEL III-Trial).

Author(s): van Vliet, Elvira Og; Schuit, Ewoud; Heida, Karst Y; Opmeer, Brent C; Kok, Marjolein; Gyselaers, Wilfried; Porath, Martina M; Woiski, Mallory; Bax, Caroline J; Bloemenkamp, Kitty Wm; Scheepers, Hubertina Cj; Jaquemyn, Yves; van Beek, Erik; Duvekot, Hans Jj; Franssen, Maureen Tm; Bijvank, Bas N; Kok, Joke H; Franx, Arie; Mol, Ben Willem J; Oudijk, Martijn A

Source: BMC pregnancy and childbirth; Mar 2014; vol. 14 ; p. 93

Publication Date: Mar 2014

Publication Type(s): Research Support, Non-u.s. Gov't Comparative Study Randomized Controlled Trial Multicenter Study Journal Article Clinical Trial, Phase Iii

PubMedID: 24589124

Abstract:BACKGROUNDPreterm birth is the most common cause of neonatal morbidity and mortality. Postponing delivery for 48 hours with tocolytics to allow for maternal steroid administration and antenatal transportation to a centre with neonatal intensive care unit facilities is the standard treatment for women with threatening preterm delivery in most centres. However, there is controversy as to which tocolytic agent is the drug of first choice. Previous trials have focused on tocolytic efficacy and side effects, and are probably underpowered to detect clinically meaningfull differences in neonatal outcome. Thus, the current evidence is inconclusive to support a balanced recommendation for clinical practice. This multicenter randomised clinical trial aims to compare nifedipine and atosiban in terms of neonatal outcome, duration of pregnancy and maternal side effects.METHODS/DESIGNThe Apostel III trial is a nationwide multicenter randomised controlled study. Women with threatened preterm labour (gestational age 25 - 34 weeks) defined as at least 3 contractions per 30 minutes, and 1) a cervical length of ≤ 10 mm or 2) a cervical length of 11-30 mm and a positive Fibronectin test or 3) ruptured membranes will be randomly allocated to treatment with nifedipine or atosiban. Primary outcome is a composite measure of severe neonatal morbidity and mortality. Secondary outcomes will be time to delivery, gestational age at delivery, days on ventilation support, neonatal intensive care (NICU) admittance, length admission in neonatal intensive care, total days in hospital until 3 months corrected age, convulsions, apnoea, asphyxia, proven meningitis, pneumothorax, maternal side effects and costs. Furthermore, an economic evaluation of the treatment will be performed. Analysis will be by intention to treat principle. The power calculation is based on an expected 10% difference in the prevalence of adverse neonatal outcome. This implies that 500 women have to be randomised (two sided test, β 0.2 at alpha 0.05).DISCUSSIONThis trial will provide evidence on the optimal drug of choice in acute tocolysis in threatening preterm labour.TRIAL REGISTRATIONCLINICAL TRIAL REGISTRATIONNTR2947, date of registration: June 20th 2011.

Database: Medline

98. Progesterone to prevent spontaneous preterm birth.

Author(s): Romero, Roberto; Yeo, Lami; Chaemsaithong, Piya; Chaiworapongsa, Tinnakorn; Hassan, Sonia S

Source: Seminars in fetal & neonatal medicine; Feb 2014; vol. 19 (no. 1); p. 15-26

Publication Date: Feb 2014

Publication Type(s): Research Support, N.i.h., Extramural Research Support, N.i.h., Intramural Journal Article Review

PubMedID: 24315687

Available at Seminars in fetal & neonatal medicine - from Unpaywall

Abstract: Preterm birth is the leading cause of perinatal morbidity and mortality worldwide, and its prevention is an important healthcare priority. Preterm parturition is one of the 'great obstetrical syndromes' and is caused by multiple etiologies. One of the mechanisms of disease is the untimely decline in progesterone action, which can present as a clinically silent sonographic short cervix in the midtrimester. The detection of a short cervix in the midtrimester is a powerful risk factor for preterm delivery. Vaginal progesterone can reduce the rate of preterm delivery by 45% and the rate of neonatal morbidity (admission to the neonatal intensive care unit, respiratory distress syndrome, need for mechanical ventilation, etc.). To prevent one case of spontaneous preterm birth <33 weeks of gestation, 11 patients with a short cervix would need to be treated (based on an individual patient meta-analysis). Vaginal progesterone reduces the rate of spontaneous preterm birth in women with a short cervix, both with and without a prior history of preterm birth. In patients with a prior history of preterm birth, vaginal progesterone is as effective as cervical cerclage to prevent preterm delivery. 17α-Hydroxyprogesterone caproate has not been shown to be effective in reducing the rate of spontaneous preterm birth in women with a short cervix.

Database: Medline

99. Betamimetics for inhibiting preterm labour

Author(s): Neilson J.P.; West H.M.; Dowswell T.

Source: Cochrane Database of Systematic Reviews; Feb 2014; vol. 2014 (no. 2)

Publication Date: Feb 2014

Publication Type(s): Review

PubMedID: 24500892

Available at Cochrane Database of Systematic Reviews - from Cochrane Collaboration (Wiley)

Abstract: Background: Preterm birth is a major contributor to perinatal mortality and morbidity worldwide. Tocolytic agents are drugs used to inhibit uterine contractions. Betamimetics are tocolytic agents that have been widely used, especially in resource-poor countries. Objective(s): To assess the effects of betamimetics given to women with preterm labour. Search Method(s): We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 December 2013) and reference lists of retrieved studies. Selection Criteria: Randomised controlled trials of betamimetics, administered by any route or any dose, in the treatment of women in preterm labour where betamimetics were compared with other betamimetics, placebo or no treatment. Data Collection and Analysis: Two review authors assessed risk of bias and extracted the data independently. Main Result(s): Twenty-eight trials were assessed as eligible for inclusion in the review, but eight did not report any outcome data relevant to the review. Results are based on the 20 trials that contributed data. Twelve trials, involving 1367 women, compared betamimetics with placebo. Betamimetics decreased the number of women in preterm labour giving birth within 48 hours (average risk ratio (RR) 0.68, 95% confidence interval (CI) 0.53 to 0.88, 10 trials, 1209 women). There was a decrease in

the number of births within seven days (average RR 0.80; 95% CI 0.65 to 0.98, five trials, 911 women) but there was no evidence of a reduction in preterm birth (before 37 weeks' gestation) (RR 0.95; 95% CI 0.88 to 1.03, 10 trials, 1212 women). No benefit was demonstrated for betamimetics for perinatal death (RR 0.84; 95% CI 0.46 to 1.55, 11 trials, 1332 infants), or neonatal death (RR 0.90; 95% CI 0.27 to 3.00, six trials, 1174 infants). No significant effect was demonstrated for respiratory distress syndrome (RR 0.87; 95% CI 0.71 to 1.08, eight trials, 1239 infants). A few trials reported on cerebral palsy, infant death and necrotising enterocolitis; no significant differences between groups were identified for any of these outcomes. Betamimetics were significantly associated with the following outcomes: withdrawal from treatment due to adverse effects; maternal chest pain; dyspnoea; palpitation; tremor; headaches; hypokalaemia; hyperglycaemia; nausea or vomiting; nasal stuffiness; and fetal tachycardia. Nine trials compared different types of betamimetics. Other betamimetics were compared with ritodrine in five trials (n = 948). Other comparisons were examined in single trials: hexoprenaline compared with salbutamol (n = 140), slow versus moderate release salbutamol (n = 52) and salbutamol compared with terbutaline (n = 200). Trials were small, varied, and of insufficient quality to delineate any consistent patterns of effect. Authors' conclusions: Betamimetics help to delay birth, which may give time to allow women to be transferred to tertiary care or to complete a course of antenatal corticosteroids. However, multiple adverse effects must be considered. The data are too few to support the use of any particular betamimetic.

Database: EMBASE

100. Progestational agents for treating threatened or established preterm labour.

Author(s): Su, Lin-Lin; Samuel, Miny; Chong, Yap-Seng

Source: The Cochrane database of systematic reviews; Jan 2014 (no. 1); p. CD006770

Publication Date: Jan 2014

Publication Type(s): Research Support, Non-u.s. Gov't Meta-analysis Journal Article Review Systematic Review

PubMedID: 24482121

Available at The Cochrane database of systematic reviews - from Cochrane Collaboration (Wiley)

Abstract:BACKGROUNDPrematurity is not only the leading cause of perinatal morbidity and mortality but is associated with long-term impairment. Studies of various tocolytic agents have shown mixed results with little effect in improving pregnancy duration and insufficient data to confirm a definite beneficial effect on neonatal morbidity or mortality. Progesterone is known to have an inhibitory effect on uterine contractility and is thought to play a key role in the maintenance of pregnancy until term.OBJECTIVESTo determine if the use of progestational agents is effective as a form of treatment or co-treatment for women with threatened or established preterm labour with intact membranes.SEARCH METHODSWe searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 August 2013), CENTRAL (The Cochrane Library 2013, Issue 10), MEDLINE (1966 to August 31 2013) and Embase (1974 to 31 August 2013). We checked the reference lists of all included studies to identify any additional studies and communicated with authors and the pharmaceutical industry.SELECTION CRITERIARandomised controlled trials that compared progestational agents, given either alone or in combination with other tocolytics, with a control group receiving another tocolytic, placebo or no treatment, for the treatment of preterm labour.DATA COLLECTION AND ANALYSISTwo review authors independently extracted data and assessed trial quality.MAIN RESULTSEight studies were included in this review, involving 563 women, but only seven studies, involving 538 women, contributed data for analyses. There are some data suggesting that the use of progestational agents results in a reduction of preterm deliveries at less than 37 weeks of gestation and an increase in birthweight. The use of a progestational agent may

also reduce the frequency of uterine contractions, prolong pregnancy and attenuate the shortening of cervical length. However, the analysis was limited by the relatively small number of available studies. The power of the meta-analysis was also limited by the varying types, dosages and routes of administration of progesterone.AUTHORS' CONCLUSIONSThere is insufficient evidence to advocate progestational agents as a tocolytic for women presenting with preterm labour.

Database: Medline

Strategy 799015

#	Database	Search term	Results
1	Medline	(progesterone*).ti	24658
2	Medline	exp PROGESTERONE/	69540
3	Medline	(1 OR 2)	75202
4	Medline	((premature OR preterm OR "pre term") ADJ2 (labor OR labour OR birth* OR childbirth* OR deliver*)).ti	13624
5	Medline	exp "OBSTETRIC LABOR, PREMATURE"/	25423
6	Medline	(tocolytic* OR Tocolysis).ti	1157
7	Medline	exp TOCOLYSIS/	896
8	Medline	(4 OR 5)	28861
9	Medline	(6 OR 7)	1662
10	Medline	(8 AND 9)	1099
11	Medline	(3 AND 8)	959
12	Medline	(10 OR 11)	2020
13	Medline	12 [Document type Review] [Languages English]	321
14	EMBASE	(progesterone*).ti	25935
15	EMBASE	exp PROGESTERONE/	86741
17	EMBASE	(tocolytic* OR Tocolysis).ti	1485
18	EMBASE	exp TOCOLYSIS/ OR exp "TOCOLYTIC AGENT"/	137368
19	EMBASE	(14 OR 15 OR 17 OR 18)	229301

20	EMBASE	((premature OR preterm OR "pre term") ADJ2 (labor OR labour OR birth* OR childbirth* OR deliver*)).ti	17107
21	EMBASE	exp "PREMATURE LABOR"/	44375
22	EMBASE	(20 OR 21)	49332
23	EMBASE	(19 AND 22)	6033
25	EMBASE	23 [DT FROM 2014] [Publication types Review] [English language]	234
26	Medline	12 [Document type Randomized Controlled Trial] [Languages English]	207