Sources Searched: Medline, Embase Cochrane Library.
Date of Search: 26 Jan 2017

Oral vs IM Dexamethasone for Preterm Labour

Summary

Despite the widespread use of antenatal corticosteroids to prevent respiratory distress syndrome in preterm infants, there is currently no consensus as to the type of corticosteroid to use; nor the dose, frequency, timing of use or the route of administration.

According to the conclusions of a Cochrane Systematic Review (Brownfoot F.C. et al, 2013 intramuscular administration of dexamethasone may have advantages over the oral route based upon the results observed from one small trial (Egerman R.S et al, 1998) which found that oral administration increased the incidence of neonatal sepsis. Therefore further studies in this area are warranted.

1. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth

Author(s): Brownfoot F.C.; Gagliardi D.I.; Bain E.; Middleton P.; Crowther C.A.

Source: The Cochrane database of systematic reviews; 2013; vol. 8

Publication Date: 2013

Publication Type(s): Journal: Review

Abstract: Despite the widespread use of antenatal corticosteroids to prevent respiratory distress syndrome in preterm infants, there is currently no consensus as to the type of corticosteroid to use; nor the dose, frequency, timing of use or the route of administration. To assess the effects of different corticosteroid regimens for women at risk of preterm birth. We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (13 February 2013). All identified published and unpublished randomised controlled trials or quasi-randomised control trials comparing any two corticosteroids (dexamethasone or betamethasone or any other corticosteroid that can cross the placenta), comparing different dose regimens (including frequency and timing of administration) in women at risk of preterm birth were included. We planned to exclude cross-over trials and cluster-randomised trials. We included studies published as abstracts only along with studies published as full-text manuscripts Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of included studies. Data were checked for accuracy. For this update, 12 trials (1557 women and 1661 infants) were included. Dexamethasone was associated with a reduced risk of intraventricular haemorrhage (IVH) compared with betamethasone (risk ratio (RR) 0.44, 95% confidence interval (CI) 0.21 to 0.92; four trials, 549 infants). No statistically significant differences were seen for other primary outcomes: respiratory distress syndrome (RDS) (RR 1.06, 95% CI 0.88 to 1.27; five trials, 753 infants) and perinatal death (neonatal death RR 1.41, 95% CI 0.54 to 3.67; four trials, 596 infants). Similarly, very few differences were seen for secondary outcomes such as rate of admission to the neonatal intensive care unit (NICU) although in one trial, those infants exposed to dexamethasone, compared with betamethasone, had a significantly shorter length of NICU admission (mean difference (MD) -0.91 days, 95% CI -1.77 to -0.05; 70 infants). Results for biophysical parameters were inconsistent, but mostly no clinically important differences were seen. Compared with intramuscular dexamethasone, oral dexamethasone significantly increased the

incidence of neonatal sepsis (RR 8.48, 95% CI 1.11 to 64.93) in one trial of 183 infants. No statistically significant differences were seen for other outcomes reported. Apart from a reduced maternal postpartum length of stay for women who received betamethasone at 12-hourly intervals compared to 24-hourly intervals in one trial (MD -0.73 days, 95% CI -1.28 to -0.18; 215 women), no differences in maternal or neonatal outcomes were seen between the different betamethasone dosing intervals assessed. Similarly, no significant differences in outcomes were seen when betamethasone acetate and phosphate was compared with betamethasone phosphate in one trial. It remains unclear whether one corticosteroid (or one particular regimen) has advantages over another. Dexamethasone may have some benefits compared with betamethasone such as less IVH, and a shorter length of stay in the NICU. The intramuscular route may have advantages over the oral route for dexamethasone, as identified in one small trial. Apart from the suggestion that 12-hour dosing may be as effective as 24-hour dosing of betamethasone based on one small trial, few other conclusions about optimal antenatal corticosteroid regimens were able to be made. No long-term results were available except for a small subgroup of 18 month old children in one trial. Trials comparing the commonly used corticosteroids are most urgently needed, as are trials of dosages and other variations in treatment regimens.

Database: EMBASE

2. Current controversies in perinatal steroid therapy

Author(s): Eventov-Friedman S.; Shinwell E.S.

Source: Acta Paediatrica, International Journal of Paediatrics; Nov 2008; vol. 97 (no. 11); p. 1492-1501

Publication Date: Nov 2008

Publication Type(s): Journal: Review

Available in full text at Acta Paediatrica - from John Wiley and Sons

Abstract: Few therapies in perinatal medicine have created as much controversy as corticosteroids. Despite five decades of extensive research and practice, major areas of uncertainty remain. In this article, we review the most current evidence on both antenatal and postnatal therapy. Conclusion: Overall, it is clear that we must continue to investigate the most appropriate doses of the ideal preparation in the most appropriate target populations before we can let the steroid issues rest. © 2008 The Author(s).

Database: EMBASE

3. A randomized, controlled trial of oral and intramuscular dexamethasone in the prevention of neonatal respiratory distress syndrome

Author(s): Egerman R.S.; Mercer B.M.; Doss J.L.; Sibai B.M.

Source: American Journal of Obstetrics and Gynecology; 1998; vol. 179 (no. 5); p. 1120-1123

Publication Date: 1998

Publication Type(s): Journal: Conference Paper

Abstract:OBJECTIVE: The study's objective was to compare the efficacies of oral and intramuscular antenatal administration of dexamethasone in reducing neonatal respiratory distress syndrome. STUDY DESIGN: Subjects at high risk for preterm delivery between 24 and 33 weeks' gestation were prospectively randomly assigned to receive either 6 mg intramuscular dexamethasone or 8 mg oral dexamethasone every 12 hours for 4 doses. The regimen was repeated weekly until 34 weeks' gestation if delivery had not yet occurred. A blinded data review was performed. The primary outcome of the trial was respiratory distress syndrome. Data were analyzed in an intent to treat fashion. Comparisons were made with an unpaired t test, chi2 or Fisher exact test, and survival analysis. P < .05 was considered significant. RESULTS: The study was discontinued at 39% enrollment after a blinded review of available outcomes. A total of 170 women with 188 fetuses were randomly assigned. The oral and intramuscular groups had similar mean gestational ages at enrollment (29.9 weeks vs 29.2 weeks) and similar median latencies (9.5 vs 10 days). No difference in the frequency of respiratory distress syndrome was found between the oral and intramuscular groups, (34,3% vs 29.8%). Neonatal sepsis (10.1% vs 1,2%, P = .01) and intraventricular hemorrhage (10.1% vs 2.4%, P = .04) were significantly higher in the oral group. There were no statistical differences in the frequencies of necrotizing enterocolitis or neonatal death. A subgroup analysis of 112 patients who were delivered at <34 weeks' gestation revealed no statistical difference in respiratory distress syndrome between the groups; however, oral dexamethasone was associated with a significant increase in sepsis (15.9% vs 1.6%, P = .009) and intraventricular hemorrhage (15.9% vs 3.3%, P = .03). CONCLUSION: Oral administration increases neonatal morbidity without demonstrable benefit and should not at this time be used clinically for induction of fetal pulmonary maturation.

Database: EMBASE

4. Comparison between oral and intramuscular dexamethasone in suppressing unconjugated estriol levels during the third trimester

Author(s): Egerman R.S.; Walker R.A.; Mercer B.M.; Doss J.L.; Sibai B.M.; Andersen R.A.

Source: American Journal of Obstetrics and Gynecology; 1998; vol. 179 (no. 5); p. 1234-1236

Publication Date: 1998

Publication Type(s): Journal: Conference Paper

Abstract:OBJECTIVES: Unconjugated estriol production depends on fetal adrenal androgen precursors. Fetal exposure to exogenous glucocorticoids results in adrenal suppression with a subsequent decrease in maternal serum unconjugated estriol levels. We compared the efficacy between oral and intramuscular dexamethasone in maternal serum unconjugated estriol suppression at 48 hours after the initial dose among women at risk for preterm delivery. STUDY DESIGN: Twenty-four gravidas at risk for preterm delivery were randomized to receive either 6 mg intramuscular or 8 mg oral dexamethasone every 12 hours for a total of 4 doses. Blood samples (9 mL) were obtained before the initial dexamethasone administration and again after the fourth dose. Serum was separated and frozen at -70degreeC and subsequently underwent batch analysis. Unconjugated estriol levels were determined by radioimmunoassay with intra- assay and interassay coefficients of variation of 7.9% and 5.5%, respectively. All values are reported as mean +/- SD. The primary statistical analysis was attest, with P .05). No difference in percent decrease in

unconjugated estriol levels was found between the intramuscular (0.67 +/- 0.24) and oral (0.65 +/- 0.39) groups. CONCLUSION: Oral dexamethasone (8 mg) produces similar maternal serum unconjugated estriol suppression compared with intramuscular dexamethasone (6 mg) when evaluated 48 hours after administration.

Database: EMBASE

5. A comparison of the bioavailability of oral and intramuscular dexamethasone in women in late pregnancy

Author(s): Egerman R.S.; Pierce IV W.F.; Andersen R.N.; Umstot E.S.; Carr T.L.; Sibai B.M.

Source: Obstetrics and Gynecology; Feb 1997; vol. 89 (no. 2); p. 276-280

Publication Date: Feb 1997

Publication Type(s): Journal: Article

Available in print at Patricia Bowen Library and Knowledge Service West Middlesex university Hospital - from Obstetrics and Gynecology

Available in full text at Obstetrics and Gynecology - from Ovid

Abstract: Objective: To compare the bioavailability of oral and intramuscular (IM) dexamethasone in third-trimester pregnant women. Methods: Oral and IM dexamethasone levels were compared in a randomized, parallel, crossover bioavailability study involving 11 gravid women in the third trimester of pregnancy. Subjects were randomized to receive either 6 mg of IM or 8 mg of oral dexamethasone. The following week, the alternative regimen was administered. Serial blood samples were obtained after drug administration. Dexamethasone concentrations were measured by radioimmunoassay. Total area under the curve was compared for the oral and IM groups using a paired t test. Results: Eight of the 11 women completed the study through 12 hours; all 11 women completed the study through 6 hours. Among the 11 women, peak levels of dexamethasone occurred 30 minutes after IM injection (mean +/- standard deviation, 101.7 +/- 19.2 ng/mL) and 120 minutes after oral administration (65.9 +/- 20.5 ng/mL). Area under the curve did not differ significantly between those receiving IM dexamethasone (258.3 +/- 50.0 ng/minute/mL) and those receiving oral dexamethasone (251.8 +/- 59.7 ng/minute/mL) when measured 6 hours after administration of the drug. Terminal half-lives were similar in the IM and oral groups. Similar findings were noted among the eight women who were studied through 12 hours. This study had a power of 87% to detect a 20% difference in area under the curve between the two groups. Conclusion: The bioavailability of 8 mg of oral dexamethasone is similar to that of a 6-mg IM dose, as determined by the area under the curve.

Database: EMBASE

6. The pharmacokinetics of oral and intramuscular administration of dexamethasone in late pregnancy

Author(s): Elliott C.L.; Wallace E.M.; Read G.F.

Source: Acta Obstetricia et Gynecologica Scandinavica; 1996; vol. 75 (no. 3); p. 213-216

Publication Date: 1996

Publication Type(s): Journal: Article

Abstract: Background. To compare the pharmacokinetics of orally administered dexamethasone with intramuscular administration in antenatal patients at risk of preterm delivery. Method. Ten antenatal patients at risk for preterm delivery were given two intramuscular and then one oral dose of dexamethasone. Plasma which was collected at set intervals following the first intramuscular dose and the oral dose was assayed for dexamenthasone. The results were analyzed using pharmacokinetic data-fitting software and pharmacokinetic parameters calculated. Results. After oral administration of dexamethasone the mean maximum plasma concentration obtained was 65% that of the intramuscular dose and the bioavailability of the oral route was calculated as 72% of the intramuscular route. The terminal half-lives of dexamethasone were similar for both routes. Conclusions. These limited data would suggest that if dexamethasone is to be administered orally, which would be both preferable to patients and more economic, then a proportionately increased dose of oral dexamethasone would be required to provide similar maternal plasma pharmacokinetics to the intramuscular dose in current use. Further, larger studies are now required to confirm this.

Strategy 124579

#	Database	Search term	Results
1	EMBASE	exp DEXAMETHASONE/po	5929
2	EMBASE	(dexamethasone ADJ3 oral*).ti,ab	1467
3	EMBASE	exp DEXAMETHASONE/im	995
4	EMBASE	(dexamethasone ADJ3 intramuscul*).ti,ab	242
5	EMBASE	(1 OR 2)	6942
6	EMBASE	(3 OR 4)	1173
7	EMBASE	((premature OR pre term OR "pre term") ADJ3 (labour OR labor)).ti,ab	4311
8	EMBASE	exp "PREMATURE LABOR"/	41399
9	EMBASE	(7 OR 8)	42688
10	EMBASE	(5 AND 6 AND 9)	8
11	EMBASE	(5 AND 6)	207
12	EMBASE	(pregnan*).ti,ab	533055
13	EMBASE	exp PREGNANCY/	719286
14	EMBASE	(12 OR 13)	854147
15	EMBASE	(11 AND 14)	15
16	Medline	(dexamethasone ADJ3 oral*).ti,ab	1159
17	Medline	exp DEXAMETHASONE/	46909
19	Medline	("Administration, Oral").ti,ab,af	125379

20	Medline	exp "INTRAMUSCULAR ABSORPTION"/	5
21	Medline	(dexamethasone ADJ3 intramuscul*).ti,ab	238
22	Medline	(dexamethasone ADJ3 IM).ti,ab	131
29	Medline	("premature labor" OR "premature labour " OR "preterm labor" OR "pre term labour").ti,ab	7884
30	Medline	("OBSTETRIC LABOR, PREMATURE" OR "premature birth").ti,ab,af	23199
31	Medline	(29 OR 30)	26318
32	Medline	(17 AND 19)	708
33	Medline	(16 OR 32)	1637
34	Medline	exp "INJECTIONS, INTRAMUSCULAR"/	28918
35	Medline	(17 AND 34)	320
36	Medline	(21 OR 22 OR 35)	596
37	Medline	(31 AND 33 AND 36)	4