West Middlesex University Hospital

Metformin in Pregnancy

Date of Search: 14/07/2016
Sources: Medline, Embase, The Cochrane Library

Search History:
1. EMBASE; *METFORMIN/; 12109 results.
2. EMBASE; metformin.ti; 10542 results.
3. EMBASE; 1 OR 2; 13013 results.
4. EMBASE; (pregn* OR "gestational diabetes" OR GDM).ti; 232347 results.
5. EMBASE; *PREGNANCY DIABETES MELLITUS/ OR *PREGNANCY/; 137102 results.
6. EMBASE; 4 OR 5; 271874 results.
7. EMBASE; 3 AND 6; 378 results.
8. EMBASE; 7 [Limit to: English Language]; 360 results.
9. Medline; *METFORMIN/; 6185 results.
10. Medline; metformin.ti; 6449 results.
11. Medline; 9 OR 10; 7355 results.
12. Medline; (pregn* OR "gestational diabetes" OR GDM).ti; 198748 results.
13. Medline; *PREGNANCY/; 30111 results.
14. Medline; *DIABETES, GESTATIONAL/; 5838 results.
15. Medline; 12 OR 13 OR 14; 208288 results.
16. Medline; 11 AND 15; 211 results.
17. Medline; 16 [Limit to: (Language English)]; 209 results.

Title: Metformin versus insulin in gestational diabetes mellitus: a meta-analysis of randomized clinical trials.

Citation: Irish journal of medical science, May 2016, vol. 185, no. 2, p. 371-381, 1863-4362 (May 2016)

Author(s): Zhu, B, Zhang, L, Fan, Y Y, Wang, L, Li, X G, Liu, T, Cao, Y S, Zhao, Z G

Abstract: Metformin is widely used in treatment of type 2 diabetes. However, whether it is safe for use in pregnancy is controversial. A search for relevant studies were performed using PubMed (1948-2014), Embase (1974-2014), the Web of knowledge (1950-2014), and the Cochrane database, included all randomized control trials published in English. Eight RCTs (1712 patients with gestational diabetes mellitus) were retrieved; of those 853 patients were given metformin, and 859 patients were given insulin. Our results showed that metformin does not increase risk of prematurity (RR = 1.26; 95 % CI [0.89, 1.79], P = 0.19). In addition, metformin can either decrease the total weight gain [MD = -1.49, 95 % CI (-2.66, -0.31), P = 0.01] or weight gain after randomization [MD = -1.23, 95 % CI (-1.75, -

0.71), P < 0.00001]. No significant differences were observed in patients with pre-eclampsia [RR = 0.82, 95 % CI (0.56, 1.2), P = 0.32] or caesarean section [RR = 0.93, 95 % CI (0.75, 1.16), P = 0.53]. Use of metformin also significantly decreased the risk of neonatal hypoglycemia [RR = 0.58, 95 % CI (0.43, 0.78), P = 0.0003] and admission rates to neonatal intensive care units [RR = 0.74, 95 % CI (0.61, 0.89), P = 0.002]. No other adverse effects were observed, such as hyperbilirubinaemia [RR = 0.83, 95 % CI (0.64, 1.08), P = 0.16], large for gestational age [RR = 0.85, 95 % CI (0.68, 1.05), P = 0.14], small for gestational age [RR = 0.92, 95 % CI (0.61, 1.39), P = 0.69], macrosomia [RR = 0.75, 95 % CI (0.54, 1.03), P = 0.07] or respiratory distress syndrome [RR = 0.88, 95 % CI (0.55, 1.41), P = 0.6]. **Metformin may be beneficial in treating gestational diabetes. However, even more studies are needed to provide more evidence for the future use of metformin.**

Source: Medline

Full Text:
Available from *Springer Link Journals* in Irish Journal of Medical Science

---

Title: Short-term antidiabetic treatment with insulin or metformin has a similar impact on the components of metabolic syndrome in women with gestational diabetes mellitus requiring antidiabetic agents: Results of a prospective, randomised study

Citation: Journal of Physiology and Pharmacology, April 2016, vol./is. 67/2(227-233), 0867-5910;1899-1505 (April 2016)

Author(s): Zawiejska A., Wender-Ozegowska E., Grewling-Szmit K., Brazert M., Brazert J.

Language: English

Abstract: Gestational diabetes mellitus (GDM) is associated with an increased prevalence of fetal and maternal complications primarily caused by maternal hyperglycemia, which results in abnormal fetal growth. Diet modification is a common first step in the treatment of GDM, followed by antidiabetic pharmacotherapy if this approach fails. Insulin therapy is generally accepted; however, oral hypoglycemic agents have been used in this population. In this prospective, randomised study, we compared maternal metabolic status after treatment with insulin or metformin. Pregnant women (gestational age: > 20 weeks) with GDM requiring medical hypoglycemic treatment were randomly allocated to the Metformin (n = 35) or Insulin (n = 43) Groups. Maternal metabolic status - assessed by glycated hemoglobin (HBA<inf>1c</inf>) level, glycemic profile, insulin concentration, Homeostatic Model Assessment - Insulin Resistance index, and lipids -was recorded at booking and throughout pregnancy. The characteristics of the study group were: maternal age 33.5 +/- 5.9 years, gestational age at baseline 28.5 +/- 3.5 weeks, prepregnancy body mass index (BMI) 32.2 +/- 3.5 kg/m², HbA<inf>1c</inf> at baseline 5.6 +/- 0.6%, and average daily glycemia 5.9 +/- 0.6 mmol/dl. Fasting glycemia at term was significantly lower in the Insulin Group but there were no significant differences in mean daily glycemia, HbA<inf>1c</inf> and BMI at term between the groups. Longitudinally, there was a small but significant increase in BMI and a significant increase in high-density lipoprotein-cholesterol in the Insulin Group and a significant increase in the atherogenic index of plasma (AIP) and a trend

towards higher triglycerides in the Metformin Group. Both fasting and average daily glycemia were significantly reduced following treatment in both groups. No such change was evident for HbA<inf>1c</inf>. In a relative risk analysis, metformin treatment was associated with an insignificant elevated risk of HbA<inf>1c</inf>, triglycerides and lipid indices falling within the highest quartile at term. The risk of gestational weight gain and total cholesterol falling within the highest quartile at term was insignificantly reduced in the Metformin Group. **In conclusion, short-term antidiabetic treatment with insulin or metformin has a similar impact on markers of metabolic syndrome in women with GDM requiring antidiabetic treatment. Secondly, treatment with metformin is associated with increased triglyceride levels and higher AIP in the third trimester in pregnant women with GDM.**

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Free Access Content* in Journal of Physiology and Pharmacology

---

Title: Retrospective analysis of maternal and neonatal outcomes following the introduction of metformin in the treatment of gestational diabetes

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, April 2016, vol./is. 123/(30-31), 1470-0328 (April 2016)

Author(s): Knight L., Fontaine T., Page J., Green E., Allwood A.

Language: English

Abstract: Introduction Uncontrolled maternal hyperglycaemia in gestational diabetes is well documented to result in poor fetal and maternal outcomes during pregnancy and in the peripartum period. Over the last 10 years, research has focused on the use of insulin and oral hypoglycaemic agents in the management of gestational diabetes (GDM) and their impact on pregnancy outcomes for mother and baby. Metformin was first advocated as a treatment for GDM by the National Institute for health and Care Excellence (NICE) in 2008. Methods Here we report the maternal and neonatal outcomes of 243 women with gestational diabetes managed with insulin or with metformin alone. Results Overall there were a higher proportion of people women undergoing caesarean section (CS) in the insulin-only group compared with the metformin group (46% versus 26%). Category I CS was much lower in the metformin group (<1% versus 20%). A higher proportion of macrosomic babies (>4.5 kg) were noted in the insulin group (3.6% versus 0%). There were no neonatal intensive care unit (NICU) admissions and all had an Apgar score of >9 at 5 minutes. No significant difference in neonatal hypoglycaemia (first blood sugar <2.6) was noted (12% insulinonly versus 11% metformin group). Admissions to NICU were equal in each group (7%). Premature delivery was slightly higher in the insulin group (62% versus 50**%).** **Conclusion Our results show metformin to be associated with fewer caesarean section deliveries (particularly category I) and a lower incidence of neonatal macrosomia.**

Metformin is shown to be a favourable alternative to insulin in terms of cost-effectiveness for healthcare service provision and maternal acceptability.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

---

Title: Randomised controlled trial of metformin treatment versus standard diabetes antenatal care in women with mild fasting hyperglycaemia diagnosed in pregnancy: A pilot study

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, April 2016, vol./is. 123/(28-29), 1470-0328 (April 2016)

Author(s): Mumby C., Bernatavicius G., Zhang J., Myers J.

Language: English

Abstract: Introduction Guidelines disagree on the diagnostic thresholds for gestational diabetes (GDM); treatment of women with mild fasting hyperglycaemia may not be cost effective and may increase unnecessary intervention. Methods Single-centre open-label randomised controlled feasibility trial (ISRCTN86503951). Intervention: 'Metformin' treatment (2 g/day) without home blood glucose monitoring compared with National Institute of Health and Care Excellence 'standard' diabetes antenatal care in women with fasting 5.1-5.4 mmol/L, 2-hour <8.5 mmol/L) at oral glucose tolerance test. Results Forty of 147 (27%) eligible women agreed to participate (noncompletion, n = 3). All women received dietary advice. Fifteen of the 19 women randomised to 'standard' care were prescribed metformin based on home blood glucose monitoring, two women required additional insulin. Overall, compliance was good; 30/35 reported missing tablets less than one to three times/ week. In the 'metformin' arm (n = 18), median compliance (returned packets) was 65% (0-98%); four women were unable to tolerate metformin. All women were satisfied with their treatment; 9/18 (metformin) would choose the same treatment in a future pregnancy. Clinical outcome: Data on glycaemic control were available for 16/19 women ('standard'). A reduction in fasting and postprandial glucose was achieved in 15/16. Baseline characteristics, including ethnicity, were not different between participants and nonparticipants (n = 133). Spontaneous labour was more frequent (51.5 versus 28.2%; P = 0.03) and there was an increased trend of large-for-gestational-age infants (24.8 versus 10.3% P = 0.07) in non-participants versus participants. **Conclusion Treatment with metformin in conjunction with routine care was acceptable to participating women. This study has generated important information regarding recruitment rates, pregnancy outcomes and treatment effects in women with mild fasting hyperglycaemia; a definitive multicentre study in this group is now justified.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

---

Title: Major malformation risk, pregnancy outcomes, and neurodevelopmental outcomes associated with metformin use during pregnancy.

Citation: The Journal of clinical psychiatry, Apr 2016, vol. 77, no. 4, p. e411., 1555-2101 (April 2016)

Author(s): Andrade, Chittaranjan

Abstract: There are several reasons why metformin treatment may be considered for women in neuropsychiatric practice. These include prevention or attenuation of antipsychotic-associated weight gain, prevention or treatment of gestational diabetes mellitus (GDM), treatment of type 2 diabetes mellitus, and improvement of conception chances and pregnancy outcomes in the presence of polycystic ovarian disease (PCOD). This article examines the benefits and risks associated with metformin use during pregnancy. The available data suggest that metformin exposure during the first trimester is not associated with major congenital malformations; that metformin reduces the risk of early pregnancy loss, preeclampsia, preterm delivery, and GDM in women with PCOD; that metformin is associated with at least comparable benefits relative to insulin treatment in women with mild GDM; and that neurodevelopmental outcomes at age 1.5-2.5 years are comparable after gestational exposure to metformin and insulin. Whereas study designs were not always ideal and sample sizes were mostly small to modest, the study findings are more encouraging than discouraging and can guide shared decision-making in women who are receiving or may need metformin during pregnancy.

Source: Medline

Title: Metformin versus Placebo in Obese Pregnant Women without Diabetes Mellitus.

Citation: The New England journal of medicine, Feb 2016, vol. 374, no. 5, p. 434-443, 1533-4406 (February 4, 2016)

Author(s): Syngelaki, Argyro, Nicolaides, Kypros H, Balani, Jyoti, Hyer, Steve, Akolekar, Ranjit, Kotecha, Reena, Pastides, Alice, Shehata, Hassan

Abstract: Obesity is associated with an increased risk of adverse pregnancy outcomes. Lifestyle-intervention studies have not shown improved outcomes. Metformin improves insulin sensitivity and in pregnant patients with gestational diabetes it leads to less weight

gain than occurs in those who do not take metformin. In this double-blind, placebo-controlled trial, we randomly assigned pregnant women without diabetes who had a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of more than 35 to receive metformin, at a dose of 3.0 g per day, or placebo (225 women in each group) from 12 to 18 weeks of gestation until delivery. The BMI was calculated at the time of study entry (12 to 18 weeks of gestation). The primary outcome was a reduction in the median neonatal birth-weight z score by 0.3 SD (equivalent to a 50% reduction, from 20% to 10%, in the incidence of large-for-gestational-age neonates). Secondary outcomes included maternal gestational weight gain and the incidence of gestational diabetes and of preeclampsia, as well as the incidence of adverse neonatal outcomes. Randomization was performed with the use of computer-generated random numbers. The analysis was performed according to the intention-to-treat principle. A total of 50 women withdrew consent during the trial, which left 202 women in the metformin group and 198 in the placebo group. There was no significant between-group difference in the median neonatal birth-weight z score (0.05 in the metformin group [interquartile range, -0.71 to 0.92] and 0.17 in the placebo group [interquartile range, -0.62 to 0.89], P=0.66). The median maternal gestational weight gain was lower in the metformin group than in the placebo group (4.6 kg [interquartile range, 1.3 to 7.2] vs. 6.3 kg [interquartile range, 2.9 to 9.2], P<0.001), as was the incidence of preeclampsia (3.0% vs. 11.3%; odds ratio, 0.24; 95% confidence interval, 0.10 to 0.61; P=0.001). The incidence of side effects was higher in the metformin group than in the placebo group. There were no significant between-group differences in the incidence of gestational diabetes, large-for-gestational-age neonates, or adverse neonatal outcomes**. Among women without diabetes who had a BMI of more than 35, the antenatal administration of metformin reduced maternal weight gain but not neonatal birth weight.** (Funded by the Fetal Medicine Foundation; ClinicalTrials.gov number, NCT01273584; EudraCT number, 2008-005892-83.).

Source: Medline

Full Text:
Available from *New England Journal of Medicine* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *Massachusetts Medical Society* in New England Journal of Medicine; Note: ; Notes: Please select 'Login via Athens or your institution' and enter your OpenAthens username and password.
Available from *ProQuest* in New England Journal of Medicine, The

---

Title: The effects of metformin treatment of gestational diabetes on maternal weight and glucose tolerance postpartum - A prospective follow-up study

Citation: Acta Obstetricia et Gynecologica Scandinavica, January 2016, vol./is. 95/1(79-87), 0001-6349;1600-0412 (01 Jan 2016)

Author(s): Pellonpera O., Ronnemaa T., Ekblad U., Vahlberg T., Tertti K.

Language: English

Abstract: Introduction. Metformin seems to reduce gestational weight gain compared with insulin in women with gestational diabetes (GDM). Women with GDM requiring insulin are more likely to develop abnormal glucose tolerance postpartum than women treated with diet only. In this prospective follow-up study of a randomized clinical trial, we investigated the effect of metformin treatment in women with GDM on weight gain and glucose tolerance postpartum. Materials and Methods. Women with GDM with two or more pathologic glucose values at 2-h 75-g oral glucose tolerance test (OGTT) were recruited. Those needing medication to achieve sufficient glycemic control were randomized at 22-34 weeks of gestation to either metformin (n = 110) or insulin (n = 107) treatment until delivery. A third GDM group (n = 128) requiring no medication had only diet treatment. Weight, OGTT and glycosylated hemoglobin (HbA1c) were determined at 6-8 weeks and 1 year postpartum. Results. At least one postpartum visit was attended by 104, 101 and 120 women in the metformin, insulin and diet-only groups, respectively. No significant differences were found in the change of weight, HbA1c or OGTT glucose values between the groups during the study ($p > 0.121$ in all comparisons). One year postpartum the diet-only group had less impaired glucose tolerance compared with the metformin and insulin groups (7.1%, 19.1% and 15.6%, respectively; overall $p = 0.039$) and a lower incidence of diabetes ($p = 0.027$). **Conclusions. Short-term metformin therapy does not affect weight, HbA1c or OGTT glucose values postpartum compared with insulin or diet-only treatments. Women with GDM requiring no medication are least likely to develop impaired glucose tolerance or diabetes postpartum**.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Acta Obstetricia et Gynecologica Scandinavica

---

Title: Metformin versus insulin for gestational diabetes mellitus: a meta-analysis.

Citation: British journal of clinical pharmacology, Nov 2015, vol. 80, no. 5, p. 1224-1234, 1365-2125 (November 2015)

Author(s): Zhao, Li-Ping, Sheng, Xiao-Yan, Zhou, Shuang, Yang, Ting, Ma, Ling-Yue, Zhou, Ying, Cui, Yi-Min

Abstract: The aim of the present meta-analysis was to determine the efficacy and safety of metformin for the treatment of women with gestational diabetes mellitus (GDM). We searched databases, including PubMed, Embase and the Cochrane Central Register of Controlled Trials, for randomized controlled trials (RCTs) comparing metformin and insulin treatments in women with GDM. We carried out statistical analyses using RevMan 2011 and used the Grading of Recommendations, Assessment, Development, and Evaluations profiler to rate the quality of evidence of the primary outcomes. We analysed eight studies involving 1592 subjects. Meta-analysis of the RCTs showed that metformin had statistically significant effects on pregnancy-induced hypertension [PIH; risk ratio (RR) 0.54; 95% confidence interval (CI) 0.31, 0.91]. However, its effects on neonatal hypoglycaemia (RR 0.80; 95% CI

0.62, 1.02), rate of large-for-gestational age infants (RR 0.77; 95% CI 0.55, 1.08), respiratory distress syndrome (RR 1.26; 95% CI 0.67, 2.37), phototherapy (RR 0.94; 95% CI 0.67, 1.31) and perinatal death (RR 1.01; 95% CI 0.11, 9.53) were not significant. **Our analyses suggest that there is no clinically relevant difference in efficacy or safety between metformin and insulin; however, metformin may be a good choice for GDM because of the lower risk of PIH. The advantages of metformin in terms of glycaemic control, PIH incidence and gestational age at birth are unclear, and should be verified in further trial**s.

Source: Medline

Full Text:
Available from *John Wiley and Sons* in British Journal of Clinical Pharmacology

---

Title: Efficacy of metformin on pregnancy complications in women with polycystic ovary syndrome: A meta-analysis

Citation: Gynecological Endocrinology, November 2015, vol./is. 31/11(833-839), 0951-3590;1473-0766 (02 Nov 2015)

Author(s): Feng L., Lin X.-F., Wan Z.-H., Hu D., Du Y.-K.

Language: English

Abstract: Objective: To evaluate the efficacy of metformin administration throughout pregnancy on pregnancy-related complications in women with polycystic ovary syndrome (PCOS).Study design: MEDLINE and ScienceDirect were searched to retrieve relevant trials. The endpoint was the incidence of complications of pregnancy, gestational diabetes mellitus (GDM), pre-eclampsia (PE), miscarriage and premature birth included.Results: Five studies with 502 PCOS patients with metformin administration throughout pregnancy and 427 controls who used metformin just to get conception were included in our meta-analysis. In study group, a significantly lower change of emerging miscarriage and premature birth was observed, the pooled relative risk (RR) was 0.32 (95% confidence interval (CI): 0.19-0.56) for miscarriage and 0.40 (95%CI: 0.18-0.91) for premature birth. No significant difference was demonstrated in emerging GDM and PE.Conclusions: **Metformin therapy throughout pregnancy can reduce the RR of miscarriage and premature birth incidence in PCOS patients with no serious side effects.**

Publication Type: Journal: Article

Source: EMBASE

Title: Use of metformin during pregnancy

Citation: Journal of Perinatal Medicine, October 2015, vol./is. 43/(no pagination), 0300-5577 (October 2015)

Author(s): Mejia Jimenez I., Montanez Quero D., Simon San Jose E., Calvo Luque E., Villar Ruiz O., Vallejo Perez P.

Language: English

Abstract: Introduction: Carbohydrate metabolism disorders (including insulin resistance, gestational diabetes or Type I-II pre gestational diabetes) are one of the most prevalent pathology during pregnancy and associate important adverse maternal and fetal outcomes. Traditionally, the control of glucose level has been achieved with diet, exercise and Insulin when needed, considered gold standard pharmacological treatment during gestation. However, an increasing number of studies proposing Metformin as a cheaper and more comfortable alternative for Insulin are showing similar outcomes and adverse effects between both drugs. Objective: Report the characteristics, clinical features and pregnancy outcomes of the patients that were elegible for the treatment with Metformin in our High Risk Obstetrical Unit. Case Report: Seven patients in our High Risk Obstetrical Unit had Metformin as a treatment before pregnancy and continued it after its onset. Of these seven patients, four had insulin resistance, one had insulin resistance and polycystic ovarian syndrome, one had Type II Diabetes Mellitus and one had Type I Diabetes Mellitus. Three of these patients only received Metformin in the first trimester, and four of them continued it throughout pregnancy. No hypoglycaemia episodes associated with the use of Metformin were reported, and only one of the patients required the addition of Insulin in the second trimester of pregnancy. Glycaemic control was acceptable in 6 of the 7 patients and Hb1C levels were normal in all of them. Three of these patients have already delivered, and no macrosomic newborns or neonatal hypoglycaemia were reported**. Conclusion: Metformin has been proposed as a cheaper and more comfortable alternative or adjuvant treatment of Insulin. However, there is still a lack of long term evidence of the adverse outcomes and security related with the use of this drug. This report describes the characteristics, the main reason for the drug start, the complications and outcomes of the seven patients that had Metformin during pregnancy in our High Risk Obstetrical Unit experience. Nevertheless, long-term, well-designed randomised controlled trials of the use of Metformin during pregnancy are required prior to generalize its use**.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWaR): a randomised, double-blind, placebo-controlled trial.

Citation: The lancet. Diabetes & endocrinology, Oct 2015, vol. 3, no. 10, p. 778-786, 2213-8595 (October 2015)

Author(s): Chiswick, Carolyn, Reynolds, Rebecca M, Denison, Fiona, Drake, Amanda J, Forbes, Shareen, Newby, David E, Walker, Brian R, Quenby, Siobhan, Wray, Susan, Weeks, Andrew, Lashen, Hany, Rodriguez, Aryelly, Murray, Gordon, Whyte, Sonia, Norman, Jane E

Abstract: Maternal obesity is associated with increased birthweight, and obesity and premature mortality in adult offspring. The mechanism by which maternal obesity leads to these outcomes is not well understood, but maternal hyperglycaemia and insulin resistance are both implicated. We aimed to establish whether the insulin sensitising drug metformin improves maternal and fetal outcomes in obese pregnant women without diabetes. We did this randomised, double-blind, placebo-controlled trial in antenatal clinics at 15 National Health Service hospitals in the UK. Pregnant women (aged ≥16 years) between 12 and 16 weeks' gestation who had a BMI of 30 kg/m(2) or more and normal glucose tolerance were randomly assigned (1:1), via a web-based computer-generated block randomisation procedure (block size of two to four), to receive oral metformin 500 mg (increasing to a maximum of 2500 mg) or matched placebo daily from between 12 and 16 weeks' gestation until delivery of the baby. Randomisation was stratified by study site and BMI band (30-39 vs ≥40 kg/m(2)). Participants, caregivers, and study personnel were masked to treatment assignment. The primary outcome was Z score corresponding to the gestational age, parity, and sex-standardised birthweight percentile of liveborn babies delivered at 24 weeks or more of gestation. We did analysis by modified intention to treat. This trial is registered, ISRCTN number 51279843. Between Feb 3, 2011, and Jan 16, 2014, inclusive, we randomly assigned 449 women to either placebo (n=223) or metformin (n=226), of whom 434 (97%) were included in the final modified intention-to-treat analysis. Mean birthweight at delivery was 3463 g (SD 660) in the placebo group and 3462 g (548) in the metformin group. The estimated effect size of metformin on the primary outcome was non-significant (adjusted mean difference -0·029, 95% CI -0·217 to 0·158; p=0·7597). The difference in the number of women reporting the combined adverse outcome of miscarriage, termination of pregnancy, stillbirth, or neonatal death in the metformin group (n=7) versus the placebo group (n=2) was not significant (odds ratio 3·60, 95% CI 0·74-17·50; p=0·11). **Metformin has no significant effect on birthweight percentile in obese pregnant women. Further follow-up of babies born to mothers in the EMPOWaR study will identify longer-term outcomes of metformin in this population; in the meantime, metformin should not be used to improve pregnancy outcomes in obese women without diabetes**. The Efficacy and Mechanism Evaluation (EME) Programme, a Medical Research Council and National Institute for Health Research partnership.

Source: Medline

Title: Metformin for the treatment of gestational diabetes: An updated meta-analysis

Citation: Diabetes Research and Clinical Practice, September 2015, vol./is. 109/3(521-532), 0168-8227;1872-8227 (01 Sep 2015)

Author(s): Kitwitee P., Limwattananon S., Limwattananon C., Waleekachonlert O., Ratanachotpanich T., Phimphilai M., Nguyen T.V., Pongchaiyakul C.

Language: English

Abstract: Objective: To assess the efficacy of metformin and insulin in the treatment of pregnant women with gestational diabetes mellitus (GDM). Methods: A meta-analysis was conducted by including randomized controlled trials comparing metformin and insulin in GDM. An electronic search was conducted to identify relevant studies. Data were synthesized by a random effects meta-analysis model. A Bayesian analysis was also performed to account for uncertainties in the treatment efficacy. Results: Eight clinical trials involving 1712 individuals were included in the final analysis. The pooled estimates of metformin-insulin differences were very small and statistically non-significant in fasting plasma glucose, postprandial plasma glucose and HbA1c, measured at 36-37 weeks of gestation. Notably, 14-46% of those receiving metformin required additional insulin. Compared with the insulin group, metformin treatment was associated with a lower incidence of neonatal hypoglycemia (relative risk, RR 0.74; 95% CI 0.58-0.93; P = 0.01) and of neonatal intensive care admission (RR 0.76; 95% CI 0.59-0.97; P = 0.03). Bayesian analysis revealed that the efficacy of metformin was consistently higher than insulin with a probability of over 98% on these two neonatal complications. Other outcomes were not significantly different between the two treatment groups**. Conclusion: In women with gestational diabetes, metformin use and insulin therapy have comparable glycemic control profile, but metformin use was associated with lower risk of neonatal hypoglycemia.**

Publication Type: Journal: Article

Source: EMBASE

Title: Metformin use in pregnancy and risks of birth defects

Citation: Pharmacoepidemiology and Drug Safety, September 2015, vol./is. 24/(399-400), 1053-8569 (September 2015)

Author(s): Van Bennekom C.M., Dukhovny S.E., Hernandez-Diaz S., Werler M.M., Anderka M., Gagnon D.R., Mitchell A.A.

Language: English

Abstract: Background: Diabetes is a common complication of pregnancy. Poor control is associated with maternal and neonatal morbidity, including increased risks for birth defects. Risks decrease with improved glucose control. Oral hypoglycemic agents are first-line treatment for diabetes in non-pregnant patients, but use in pregnancy (largely metformin) is controversial. Objectives: The aim of this study was to identify associations between metformin use and major birth defects. Methods: We used 1997-2009 data from the National Birth Defects Prevention Study, a population-based, case-control study, to assess the association between maternal first trimester metformin use for diabetes and risks for specific major birth defects. We calculated crude odds ratios and 95% confidence intervals (CIs) by exact logistic regression and, where numbers permitted (for example, heart defects and oral clefts), adjusted odds ratios and CIs using inverse probability weighting to control for potential confounders. Confounding by diabetes was assessed by comparing metformin

with both insulin use in diabetic women and metformin use for infertility in non-diabetic women. Results: Among 9355 controls, first trimester exposure prevalences of metformin for diabetes, insulin for diabetes, and metformin for infertility were 0.1%, 0.4%, and 0.3%, respectively. Compared with nondiabetic women with no metformin use, diabetic metformin users had elevated odds ratios (ORs) for heart defects, oral clefts, neural tube defects, and limb defects; these ORs were similar to those for insulin users. In contrast, metformin users for infertility had ORs of ~1.0 with the exception of limb defects, where the ORs for metformin-diabetes, insulin, and metformin- infertility, respectively, were 4.1 (1.1-12.5), 5.1 (2.7-9.2), and 2.9 (1.2-6.2**). Conclusions: As expected, insulin-dependent diabetes was strongly associated with a number of defects. For metformin, we could only partially adjust for diabetes severity. However, for most defects studied, there was no evidence that metformin is itself teratogenic, as risks were not elevated when used for a non-diabetic indication. The elevated risk for limb defects associated with metformin is a new finding, which may be due to chance, and requires further study.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Pharmacoepidemiology and Drug Safety

---

Title: Metformin for the management of gestational diabetes mellitus

Citation: Australian and New Zealand Journal of Obstetrics and Gynaecology, August 2015, vol./is. 55/4(303-308), 0004-8666;1479-828X (01 Aug 2015)

Author(s): Singh K.P., Rahimpanah F., Barclay M.

Language: English

Abstract: Introduction Glycaemic control in women with gestational diabetes mellitus (GDM) has typically been achieved with diet, exercise and insulin therapy. Controversy exists in the literature about a potential role for metformin. Methods A literature review was completed aiming to compare the glycaemic control, maternal and fetal out comes of metformin therapy with insulin. Searches were completed on databases, including Medline, PubMed and ScienceDirect. Seven randomised control trials (RCTs) fit the inclusion criteria, with a total sample size of 1514 women. Results The majority of studies found no difference in glycaemic control between metformin and insulin groups. When comparing maternal outcomes, those receiving metformin therapy recorded less maternal weight gain in four studies. A number of studies reported lower rates of neonatal hypoglycaemia, and one reported higher rates of preterm birth in the metformin group. There were no other differences in the recorded maternal and fetal outcomes. Discussion The Jadad score for assessing risk of bias for most included studies was either 3 or 4. The criteria for diagnosis of GDM, maternal and neonatal complications varied between studies. Only one study has published follow-up data, and most are single-centre trials with relatively small sample sizes. **Conclusion Though there is a growing body of evidence to suggest a role for metformin in**

GDM management, further large-scale, multicentre RCTs are needed before guidelines can be altered.

Publication Type: Journal: Review

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Australian and New Zealand Journal of Obstetrics and Gynaecology

---

Title: Effect comparison of metformin with insulin treatment for gestational diabetes: a meta-analysis based on RCTs.

Citation: Archives of gynecology and obstetrics, Jul 2015, vol. 292, no. 1, p. 111-120, 1432-0711 (July 2015)

Author(s): Li, Genxia, Zhao, Shujun, Cui, Shihong, Li, Lei, Xu, Yajuan, Li, Yuanyuan

Abstract: To compare the effects of metformin with insulin on maternal and neonatal outcomes in gestational diabetes mellitus (GDM). A literature search in PUBMED, EMBASE, Science Direct, Springer link, and Cochrane library was conducted using the following search terms: "Gestational Diabetes" or "GDM", and "insulin" and "metformin". Quality assessment of included studies was determined with Quality Assessment of Diagnostic Accuracy Studies. Review Manger 5.2 was used to analyze mean difference (MD)/risk ratio (RR) and 95 % confidence interval (CI) in random-effects model or fixed-effects model depending on the level of heterogeneity. A total of 11 studies were identified. There was no significant difference of the effect on maternal outcomes between the two treatments in glycohemoglobin A1c levels (P = 0.37), fasting blood glucose (P = 0.66), and the incidence of preeclampsia (P = 0.26); whereas, significantly reduced results were found in the metformin group in pregnancy-induced hypertension (PIH) rate (RR = 0.53, 95 % CI 0.31-0.90, P = 0.02), average weight gains after enrollment (MD = -1.28, 95 % CI -1.54 to -1.01, P < 0.0001), and average gestational ages at delivery (MD = 0.94, 95 % CI -0.21 to -0.01, P = 0.03). Regarding neonatal outcomes, when compared with insulin group, metformin presented significantly lower average birth weights (MD = -44.35, 95 % CI -85.79 to -2.90, P = 0.04), incidence of hypoglycemia (RR = 0.69, 95 % CI 0.55-0.87, P = 0.001) and neonatal intensive care unit (NICU) (RR = 0.82, 95 % CI 0.67-0.99, P = 0.04). **Metformin can significantly reduce several adverse maternal and neonatal outcomes including PIH rate, incidence of hypoglycemia and NICU, thus it may be an effective and safe alternative or additional treatment to insulin for GDM women.**

Source: Medline

Full Text:
Available from *Springer Link Journals* in Archives of Gynecology and Obstetrics

---

Title: A follow-up of a randomised study of metformin and insulin in gestational diabetes mellitus: growth and development of the children at the age of 18 months.

Citation: BJOG : an international journal of obstetrics and gynaecology, Jun 2015, vol. 122, no. 7, p. 994-1000, 1471-0528 (June 2015)

Author(s): Ijäs, H, Vääräsmäki, M, Saarela, T, Keravuo, R, Raudaskoski, T

Abstract: To compare the growth and development of children born to mothers with gestational diabetes mellitus (GDM) requiring pharmacological treatment, and randomised to treatment with metformin or insulin. Follow-up of a randomised controlled trial (RCT) comparing metformin and insulin treatment of GDM. Data were gathered during routine visits to child welfare clinics at the ages of 6, 12, and 18 months, including weight and height measurements, and assessment of motor, social, and linguistic development. The children of mothers with GDM randomised to metformin (n = 47) or insulin (n = 50) treatment during pregnancy. Data were collected from the structured questionnaire filled in at the child welfare clinics. The growth and development of the children until the age of 18 months. Children exposed to metformin were significantly heavier (10.47 versus 9.85 kg, 95% CI 0.04-1.20) at the age of 12 months and taller and heavier (83.9 vs 82.2 cm, 95% CI 0.23-3.03, 12.05 vs 11.32 kg, 95% CI 0.04-1.43) at the age of 18 months. The mean ponderal index (PI) did not differ significantly. The motor, social, or linguistic development evaluated at the age of 18 months did not differ between the groups. Children prenatally exposed to metformin were heavier at the 12 months measurements and taller and heavier at the 18 months measurements than those exposed to insulin, but their body composition defined by PI did not differ. **Over the short term, metformin does not seem to be harmful with regards to early motor, linguistic, or social development**. © 2014 Royal College of Obstetricians and Gynaecologists.

Source: Medline

Title: Comparison of glyburide with metformin in treating gestational diabetes mellitus: a systematic review and meta-analysis.

Citation: Clinical drug investigation, Jun 2015, vol. 35, no. 6, p. 343-351, 1179-1918 (June 2015)

Author(s): Amin, Muhammad, Suksomboon, Naeti, Poolsup, Nalinee, Malik, Obaidullah

Abstract: Controversy has surrounded the treatment of gestational diabetes mellitus (GDM) for a long time. Although the use of both glyburide and metformin are recommended as an alternate to insulin if dietary therapy fails in GDM patients, it remains unclear whether both drugs are equally safe and efficacious. Therefore, in this review we compared the efficacy and safety of glyburide with metformin in treating GDM. A systematic review and meta-

analysis of randomized controlled trials was conducted that compared the efficacy and safety of glyburide with metformin in GDM patients. Electronic databases were used to conduct the literature search for study identification along with a hand search of pertinent journals and conference proceedings. The effect measure used to present the results was risk ratio (RR) with 95% confidence interval (CI). A fixed-effects model was used to pool the data if no significant heterogeneity was reported and a random-effects model was used in the case of significant heterogeneity being reported for an outcome. Three studies involving 508 patients met the inclusion criteria of this review. A significant increase in the risk of the composite outcome, i.e., macrosomia and large for gestational age (LGA) births (RR 1.94; 95% CI 1.03-3.66, p = 0.04), was observed in the glyburide group, whereas a non-significant increase in the risk of neonatal hypoglycemia (RR 1.92; 95% CI 0.31-12.02) was also noticed. Results remained statistically non-significant for preterm births (RR 0.65; 95% CI 0.24-1.77), neonatal birth weight (mean difference (MD) 120.63 g; 95% CI -62.08 to 303.33), and cesarean section (RR 0.86; 95% CI 0.55-1.34). A significant decrease in fasting glucose levels (MD -2.40 mg/dL; 95% CI -4.60 to -0.21; p = 0.03) was noticed in glyburide group while the difference was non-significant for postprandial glucose levels (MD -0.84 mg/dL; 95% CI -4.03 to 2.35). **Metformin seems to be a superior choice to glyburide if oral antidiabetic drug therapy is to be initiated in GDM patients.**

Source: Medline

Full Text:
Available from *ProQuest* in Clinical Drug Investigation

Title: Blood pressure measurement at two years in offspring of women randomized to a trial of metformin for GDM: Follow up data from the MiG trial

Citation: BMC Pediatrics, May 2015, vol./is. 15/1(no pagination), 1471-2431 (May 06, 2015)

Author(s): Battin M.R., Obolonkin V., Rush E., Hague W., Coat S., Rowan J.

Language: English

Abstract: Background: Offspring born following maternal gestational diabetes are at risk of excessive childhood weight gain and Type 2 diabetes in childhood, which in turn is associated with an increased rate of hypertension. Methods: The offspring of women who had gestational diabetes and had been assigned to either open treatment with metformin (with supplemental insulin if required) or insulin in the MiG trial were followed up at 2 years of age. Oscillometric measurement of BP in the right arm was performed by a researcher using an appropriately sized cuff. Results: A total of 489 measurement blood pressure measurements were obtained in 170 of the 222 children who were seen at a median (range) age of 29 (22-38) months corrected gestational age. At the time of assessment the mean (SD) weight and height was 13.8(2) kg and 90 (4.2) cm respectively. For the whole group the mean (SD) systolic pressure was 90.9 (9.9) mmHg and mean (SD) diastolic pressure was 55.7 (8.1) mmHg. No difference was found between the metformin and insulin treatment arms. In a regression model, height and weight were only two factors associated with the levels of systolic blood pressure. For each additional kg the systolic blood pressure increased by 1.0

mmHg. For each additional cm of height the systolic blood pressure increased by 0.42 mmHg. **Conclusions: Blood pressure data was obtained at approximately two years of age in a substantial cohort of children whose mothers received treatment for GDM. These novel data compare favorably with published norms**.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *BioMed Central* in BMC Pediatrics
Available from *National Library of Medicine* in BMC Pediatrics
Available from *National Library of Medicine* in BMC Pediatrics
Available from *ProQuest* in BMC Pediatrics

Title: Comparative efficacy and safety of OADs in management of GDM: Network meta-analysis of randomized controlled trials

Citation: Journal of Clinical Endocrinology and Metabolism, May 2015, vol./is. 100/5(2071-2080), 0021-972X;1945-7197 (01 May 2015)

Author(s): Jiang Y.-F., Chen X.-Y., Ding T., Wang X.-F., Zhu Z.-N., Su S.-W.

Language: English

Abstract: Objective: We conducted a network meta-analysis to evaluate the efficacy and safety of oral antidiabetic drugs (OADs) for gestational diabetes. Data Sources: We searched PubMed, the Cochrane Library, ClinicalTrials.gov, and related reviews from inception to October 2014. Study Selection: We included randomized clinical trials comparing efficacy and safety between different OADs or OADs vs insulin in patients with gestational diabetes. Data Synthesis: We included 18 randomized clinical trials. Traditional and network meta-analyses were performed to compare different OADs or OADs vs insulin. Traditional meta-analyses confirmed that there was no significant difference in maternal fasting blood glucose or glycated hemoglobin levels in patients treated with insulin, metformin, and glyburide. Compared to insulin, metformin was associated with lower maternal weight gain (weighted mean difference [WMD], -1.49 kg; 95% confidence interval [CI], -2.26 to -0.31), shorter gestational age (WMD, -0.16 wk; 95% CI, -0.30 to -0.03), and increased incidence of premature birth (odds ratio [OR], 1.63; 95% CI, 1.07 to 2.48). Compared to insulin, glyburide was associated with higher neonatal birth weight (WMD, 130.68 g; 95% CI, 55.98 to 205.38), increased incidence of neonatal hypoglycemia (OR, 2.64; 95% CI, 1.59 to 4.38), and increased incidence of macrosomia (OR, 3.09; 95% CI, 1.59 to 6.04). Network meta-analysis revealed that glyburide was associated with higher maternal weight gain, higher neonatal birth weight, increased incidence of neonatal hypoglycemia, and increased incidence of macrosomia than was metformin. **Conclusion: Both metformin and glyburide are suitable for use in the management of gestational diabetes because of good glycemic control. However, glyburide treatment is associated with increased risk of neonatal hypoglycemia, high maternal weight gain, high neonatal birth weight, and macrosomia.**

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Free Access Content* in Journal of Clinical Endocrinology and Metabolism

---

Title: Has metformin revolutionised the management of GDM?

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, April 2015, vol./is. 122/(389-390), 1470-0328 (April 2015)

Author(s): Rudra T., Balasubramanium S., Lawton J.

Language: English

Abstract: Introduction North West London Hospitals, London, is a busy unit with 5400 deliveries annually and has 35-42% high risk pregnancies with diverse ethnic groups. GDM is highly prevalent in these women. Metformin was introduced for management of diabetes in pregnancy since 2010. Objective To analyse whether introduction of Metformin for the Management of GDM had influenced the outcome of pregnancy. Setting This study was conducted in the Obstetrics Unit of North West London Hospitals NHS Trust between 2011 to 2013. Methodology All pregnant women who were diagnosed to have GDM were included in this study. The data was collected retrospectively. Mothers with GDM were grouped into Diet, Metformin only, Metformin and Insulin and Insulin only as Groups 1, 2, 3 and 4 respectively. Primary outcome measures were Intra partum fetal problems, Mode of Delivery, BW, Apgar, cord gases and neonatal admission. Secondary outcome measures were postpartum complications. Results 175 mothers who were included in this analysis of GDM on Diet, Metformin only, Metformin with Insulin and Insulin only 53, 90, 25 and 7 respectively. Corresponding CS rates were 30.7%, 17.8%, 64.1% and 42.2%. Instrumental delivery rate varied between 12-14% without significant difference in the groups. CTG abnormalities or Meconium liquor were found in 28.3%, 36.7%, 20%, 43.9% in the Groups 1, 2, 3 and 4 correspondingly. Shoulder dystocia was encountered in 9.4% in Diet Controlled and 3.3% in Metformin only Group. Neither mothers who had Metformin and Insulin nor only Insulin had babies with shoulder dystocia. Macrosomic baby with 4.26 kg was born only in one diet controlled mother. Mean Birth weights in kilograms for the groups were 3.7, 3.2, 3.3 and 3.4 respectively. 13.2%, 7.8%, 12% and 14.3% of babies had low Apgar at birth as well low cord pH: 22.6%,13.3%,20% and 14.3% in Groups 1, 2, 3 and 4 respectively. All babies born to mothers who had only Insulin needed special care admission for hypoglycaemia or respiratory support in contrast to 35.6% in the Metformin only group. Maternal complications were 11.3%.11.1%, 24%, and 28.6% in the respective groups mostly due to PPH or postpartum sepsis. **Conclusions Metformin is a suitable and safe alternative to insulin for management of GDM achieving good perinatal and maternal outcomes.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

---

Title: Retrospective analysis of maternal and neonatal outcomes following the introduction of metformin in the treatment of gestational diabetes

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, April 2015, vol./is. 122/(281), 1470-0328 (April 2015)

Author(s): Knight L.J., Page J., Green E.

Language: English

Abstract: Introduction Multiple, ground-breaking studies in the last 10 years have demonstrated the effects of maternal hyperglycaemia on poor fetal and maternal outcomes during pregnancy and in the peripartum period. The multi-national Hyperglycaemia and Pregnancy Outcome (HAPO) study in 2008 demonstrated how fetal growth can be modified by glucose-lowering therapies, with diet and lifestyle intervention often being successful. The Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) established that treatment of gestational diabetes with insulin improved pregnancy outcomes. Subsequent research has demonstrated that treatment with metformin results in similar outcomes to initial insulin treatment in gestational diabetes. Metformin was first advocated as a treatment for Gestational Diabetes by the National Institute for Clinical Excellence (NICE) in 2008. Methods Here we report the maternal and neonatal outcomes of 243 women with gestational diabetes managed with insulin-alone (pre-metformin) and with metformin alone following its introduction within our unit in 2011. The maternal outcomes recorded were course of labour onset, gestation and mode of delivery. Fetal outcomes include the fetal weight, cord gas results, Apgar scores and whether an admission to Neonatal Intensive Care (NICU) was needed. Results Overall there were a higher proportion of women undergoing caesarean section (CS) in the insulin only group compared with the metformin group (46% versus 26%). Category I CS was much lower in the metformin group (<1% versus 20%). Instrumental deliveries were equivocal; 14% and 11% for insulin and metformin groups respectively. A higher proportion of macrosomic babies (>4.5 kg) were noted in the insulin group (3.6% versus 0%). One of these babies delivered vaginally, the others by planned CS. There were no NICU admissions and all had an Apgar score of >9 at 5 min. Admissions to NICU were equivocal in each group (7%). Of note 62% of these patients within the insulin group delivered prematurely (<37 weeks) and 50% underwent a category I CS. In the metformin group 50% delivered before 37 weeks gestation with no caesarean sections in this group. Conclusion Our results with metformin have so far shown positive fetal and maternal outcomes, fewer caesarean section deliveries (particularly category I) and neonatal macrosomia. **This analysis shows metformin to be a favourable alternative to insulin in terms of cost-effectiveness for healthcare service and provision and maternal acceptability. An interesting extension to this study will be the comparative incidence of**

neonatal hypoglycaemia in the metformin compared with insulin group, the results of which will be available in due course.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

---

Title: The effect of lifestyle intervention and metformin on preventing or delaying diabetes among women with and without gestational diabetes: the Diabetes Prevention Program outcomes study 10-year follow-up.

Citation: The Journal of clinical endocrinology and metabolism, Apr 2015, vol. 100, no. 4, p. 1646-1653, 1945-7197 (April 2015)

Author(s): Aroda, V R, Christophi, C A, Edelstein, S L, Zhang, P, Herman, W H, Barrett-Connor, E, Delahanty, L M, Montez, M G, Ackermann, R T, Zhuo, X, Knowler, W C, Ratner, R E, Diabetes Prevention Program Research Group

Abstract: Gestational diabetes (GDM) confers a high risk of type 2 diabetes. In the Diabetes Prevention Program (DPP), intensive lifestyle (ILS) and metformin prevented or delayed diabetes in women with a history of GDM. The objective of the study was to evaluate the impact of ILS and metformin intervention over 10 years in women with and without a history of GDM in the DPP/Diabetes Prevention Program Outcomes Study. This was a randomized controlled clinical trial with an observational follow-up. The study was conducted at 27 clinical centers. Three hundred fifty women with a history of GDM and 1416 women with previous live births but no history of GDM participated in the study. The participants had an elevated body mass index and fasting glucose and impaired glucose tolerance at study entry. Interventions included placebo, ILS, or metformin. Outcomes measure was diabetes mellitus. Over 10 years, women with a history of GDM assigned to placebo had a 48% higher risk of developing diabetes compared with women without a history of GDM. In women with a history of GDM, ILS and metformin reduced progression to diabetes compared with placebo by 35% and 40%, respectively. Among women without a history of GDM, ILS reduced the progression to diabetes by 30%, and metformin did not reduce the progression to diabetes. Women with a history of GDM are at an increased risk of developing diabetes. **In women with a history of GDM in the DPP/Diabetes Prevention Program Outcomes Study, both lifestyle and metformin were highly effective in reducing progression to diabetes during a 10-year follow-up period. Among women without a history of GDM, lifestyle but not metformin reduced progression to diabetes.**

Source: Medline

Full Text:
Available from *Free Access Content* in Journal of Clinical Endocrinology and Metabolism

Title: The effects of metformin on weight loss in women with gestational diabetes: a pilot randomized, placebo-controlled trial.

Citation: American journal of obstetrics and gynecology, Mar 2015, vol. 212, no. 3, p. 389.e1, 1097-6868 (March 2015)

Author(s): Refuerzo, Jerrie S, Viteri, Oscar A, Hutchinson, Maria, Pedroza, Claudia, Blackwell, Sean C, Tyson, Jon E, Ramin, Susan M

Abstract: We sought to compare weight loss in the first 6 weeks postpartum among women with gestational diabetes mellitus (GDM) treated with metformin or placebo, a promising therapy to reduce later risk of progression to diabetes mellitus. We conducted a pilot, randomized trial of metformin vs placebo in postpartum women with GDM. Women with pre-GDM, unable to tolerate metformin, resumed on insulin or oral hypoglycemic agent, delivered <34 weeks' gestation, or with a body mass index <20 kg/m(2) were excluded. Women were randomized to either metformin 850 mg daily for 7 days, then metformin 850 mg twice a day for the next 5 weeks or placebo prescribed in a similar frequency. The subject, health care provider, and research staff were blinded to the treatment. The primary outcome was weight change from delivery to 6 weeks postpartum. Secondary outcomes included the percentage of women achieving their self-reported prepregnancy weight, reported medication adherence, adverse effects, and satisfaction. Differences in weight change between groups were determined by Wilcoxon rank sum test and in achieving prepregnancy weight by χ(2) test. Of 114 women randomized, 79 (69.3%) completed the 6 weeks; 36 (45.6%) were randomized to metformin and 43 (54.4%) to placebo. Metformin and placebo groups were similar in median weight loss (6.3 kg [range, -0.3 to 19.8] vs 6.5 kg [range, -0.3 to 12.1], P = .988) and percentage of women achieving reported prepregnancy weight (41.7 vs 37.2%, P = .69). Self-reported adherence in taking >50% of medication was 75% at 3 weeks and 97% at 6 weeks. Nausea, diarrhea, and hypoglycemia were reported in approximately 11-17% of women and 56-63% reported dissatisfaction with the medication. Women with GDM lost approximately 6 kg by 6 weeks' postpartum. This was similar in both groups and resulted in <50% of women achieving their prepregnancy weight. Although the reported adherence and satisfaction with the medication was high, adverse effects were reported with nearly 1 in 5 women including nausea, diarrhea, and hypoglycemia. **Contrary to expectation, we found no evidence of benefit from metformin. However, longer treatment periods and larger studies with minimal attrition may be warranted.**

Source: Medline

Title: Comparison of neonatal outcomes in women with gestational diabetes with moderate hyperglycaemia on metformin or glibenclamide - A randomised controlled trial

Citation: Australian and New Zealand Journal of Obstetrics and Gynaecology, February 2015, vol./is. 55/1(47-52), 0004-8666;1479-828X (01 Feb 2015)

Author(s): George A., Mathews J.E., Sam D., Beck M., Benjamin S.J., Abraham A., Antonisamy B., Jana A.K., Thomas N.

Language: English

Abstract: Background: Two oral hypoglycaemic agents, metformin and glibenclamide, have been compared with insulin in separate large randomised controlled trials and have been found to be as effective as insulin in gestational diabetes. However, very few trials have compared metformin with glibenclamide. Materials and Methods: Of 159 South Indian women with fasting glucose >5.5 mmol/l and <7.2 mmol/l and/or 2-h post-prandial value >6.7 mmol/l and <13.9 mmol/l after medical nutritional therapy consented to be randomised to receive either glibenclamide or metformin. 80 women received glibenclamide and 79 received metformin. Neonatal outcomes were assessed by neonatologists who were unaware that the mother was part of a study and were recorded by assessors blinded to the medication the mother was given. The primary outcome was a composite of neonatal outcomes namely macrosomia, hypoglycaemia, need for phototherapy, respiratory distress, stillbirth or neonatal death and birth trauma. Secondary outcomes were birthweight, maternal glycaemic control, pregnancy induced hypertension, preterm birth, need for induction of labour, mode of delivery and complications of delivery. Results: Baseline characteristics were similar but for the higher fasting triglyceride levels in women on metformin. The primary outcome was seen in 35% of the glibenclamide group and 18.9% of the metformin group [95% CI 16.1 (2.5, 29.7); P = 0.02]. The difference in outcome related to a higher rate of neonatal hypoglycaemia in the glibenclamide group (12.5%) versus none in the metformin group [95% CI 12.5(5.3, 19.7); P = 0.001]. Secondary outcomes in both groups were similar. **Conclusion: In a south Indian population with gestational diabetes, metformin was associated with better neonatal outcomes than glibenclamide.**

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Australian and New Zealand Journal of Obstetrics and Gynaecology

---

Title: A pilot randomized, controlled trial of metformin versus insulin in women with type 2 diabetes mellitus during pregnancy

Citation: American journal of perinatology, February 2015, vol./is. 30/2(163-170), 1098-8785 (01 Feb 2015)

Author(s): Refuerzo J.S., Gowen R., Pedroza C., Hutchinson M., Blackwell S.C., Ramin S.

Language: English

Abstract: OBJECTIVE: Few studies support oral diabetic treatment in pregnant women with type 2 diabetes mellitus (T2DM). The objective of this study was to compare the effects of metformin versus insulin on achieving glycemic control and improving maternal and neonatal outcomes in pregnant women with T2DM.STUDY DESIGN: A pilot randomized, controlled trial was conducted of metformin versus insulin for the treatment of T2DM during pregnancy. The primary outcome was glycemic control measured with hemoglobin A1c<7% at delivery. Maternal and neonatal outcomes were compared between groups.RESULTS: In this study, 8 women received metformin and 11 received insulin. All women in both groups achieved glycemic control by delivery (HgbA1c: metformin 5.96+/-5.88 vs. insulin 6.34+/-0.92%). There were similar rates of cesarean delivery, birth weights, neonatal intensive care unit admissions, respiratory distress syndrome, and neonatal dextrose treatment between groups. There was one case of fetal macrosomia in the insulin group, one case of shoulder dystocia in the metformin group and no cases of failed metformin therapy.**CONCLUSION: In this pilot study, glycemic control was achieved in women who received metformin and insulin. Larger studies are needed to determine whether metformin can be considered a reasonable alternative to insulin in pregnant women with T2DM.**

Publication Type: Journal: Article

Source: EMBASE

Title: Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis.

Citation: BMJ (Clinical research ed.), Jan 2015, vol. 350, p. h102., 1756-1833 (2015)

Author(s): Balsells, Montserrat, García-Patterson, Apolonia, Solà, Ivan, Roqué, Marta, Gich, Ignasi, Corcoy, Rosa

Abstract: To summarize short term outcomes in randomized controlled trials comparing glibenclamide or metformin versus insulin or versus each other in women with gestational diabetes requiring drug treatment. Systematic review and meta-analysis. Randomized controlled trials that fulfilled all the following: (1) published as full text; (2) addressed women with gestational diabetes requiring drug treatment; (3) compared glibenclamide v insulin, metformin v insulin, or metformin v glibenclamide; and (4) provided information on maternal or fetal outcomes. Medline, CENTRAL, and Embase were searched up to 20 May 2014. We considered 14 primary outcomes (6 maternal, 8 fetal) and 16 secondary (5 maternal, 11 fetal) outcomes. We analyzed 15 articles, including 2509 subjects. Significant differences for primary outcomes in glibenclamide v insulin were obtained in birth weight (mean difference 109 g (95% confidence interval 35.9 to 181)), macrosomia (risk ratio 2.62 (1.35 to 5.08)), and neonatal hypoglycaemia (risk ratio 2.04 (1.30 to 3.20)). In metformin v insulin, significance was reached for maternal weight gain (mean difference -1.14 kg (-2.22 to -0.06)), gestational age at delivery (mean difference -0.16 weeks (-0.30 to -0.02)), and preterm birth (risk ratio 1.50 (1.04 to 2.16)), with a trend for neonatal hypoglycaemia (risk ratio 0.78 (0.60 to 1.01)). In metformin v glibenclamide, significance was reached for

maternal weight gain (mean difference -2.06 kg (-3.98 to -0.14)), birth weight (mean difference -209 g (-314 to -104)), macrosomia (risk ratio 0.33 (0.13 to 0.81)), and large for gestational age newborn (risk ratio 0.44 (0.21 to 0.92)). Four secondary outcomes were better for metformin in metformin v insulin, and one was worse for metformin in metformin v glibenclamide. Treatment failure was higher with metformin than with glibenclamide. **At short term, in women with gestational diabetes requiring drug treatment, glibenclamide is clearly inferior to both insulin and metformin, while metformin (plus insulin when required) performs slightly better than insulin. According to these results, glibenclamide should not be used for the treatment of women with gestational diabetes if insulin or metformin is available.Systematic review registration NCT01998113.**

Source: Medline

Full Text:
Available from *British Medical Journal (BMJ)* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *Highwire Press* in The BMJ

Title: Efficacy of metformin in pregnant obese women: a randomised controlled trial.

Citation: BMJ open, Jan 2015, vol. 5, no. 1, p. e006854., 2044-6055 (2015)

Author(s): Chiswick, Carolyn A, Reynolds, Rebecca M, Denison, Fiona C, Whyte, Sonia A, Drake, Amanda J, Newby, David E, Walker, Brian R, Forbes, Shareen, Murray, Gordon D, Quenby, Siobhan, Wray, Susan, Norman, Jane E

Abstract: Increasing evidence suggests obesity has its origins prior to birth. There is clear correlation between maternal obesity, high birthweight and offspring risk of obesity in later life. It is also clear that women who are obese during pregnancy are at greater risk of adverse outcomes, including gestational diabetes and stillbirth. The mechanism(s) by which obesity causes these problems is unknown, although hyperglycaemia and insulin resistance are strongly implicated. We present a protocol for a study to test the hypothesis that metformin will improve insulin sensitivity in obese pregnant women, thereby reducing the incidence of high birthweight babies and other pregnancy complications. The Efficacy of Metformin in Pregnant Obese Women, a Randomised controlled (EMPOWaR) trial is a double-masked randomised placebo-controlled trial to determine whether metformin given to obese (body mass index >30 kg/m(2)) pregnant women from 16 weeks' gestation until delivery reduces the incidence of high birthweight babies. A secondary aim is to test the mechanism(s) of any effect. Obese women with a singleton pregnancy and normal glucose tolerance will be recruited prior to 16 weeks' gestation and prescribed study medication, metformin or placebo, to be taken until delivery. Further study visits will occur at 28 and 36 weeks' gestation for glucose tolerance testing and to record anthropometric measurements. Birth weight and other measurements will be recorded at time of delivery. Anthropometry of mother and baby will be performed at 3 months postdelivery. As of January 2014, 449 women had been randomised across the UK. The study will be conducted in accordance with the principles of Good Clinical Practice. A favourable ethical opinion was obtained from Scotland A Research Ethics Committee, reference number 10/MRE00/12. Results will be

disseminated at conferences and published in peer-reviewed journals. ISRCTN51279843.

Source: Medline

Full Text:
Available from *ProQuest* in BMJ Open
Available from *National Library of Medicine* in BMJ Open
Available from *Highwire Press* in BMJ Open

Title: Metformin treatment in type 2 diabetes in pregnancy: an active controlled, parallel-group, randomized, open label study in patients with type 2 diabetes in pregnancy.

Citation: Journal of diabetes research, Jan 2015, vol. 2015, p. 325851., 2314-6753 (2015)

Author(s): Ainuddin, Jahan Ara, Karim, Nasim, Zaheer, Sidra, Ali, Syed Sanwer, Hasan, Anjum Ara

Abstract: To assess the effect of metformin and to compare it with insulin treatment in patients with type 2 diabetes in pregnancy in terms of perinatal outcome, maternal complications, additional insulin requirement, and treatment acceptability. In this randomized, open label study, 206 patients with type 2 diabetes in pregnancy who met the eligibility criteria were selected from the antenatal clinics. Insulin was added to metformin treatment when required, to maintain the target glycemic control. The patients were followed up till delivery. Maternal, and perinatal outcomes and pharmacotherapeutic characteristics were recorded on a proforma. Maternal characteristics were comparable in metformin and insulin treated group. 84.9% patients in metformin group required add-on insulin therapy at mean gestational age of 26.58 ± 3.85 weeks. Less maternal weight gain ($P < 0.001$) and pregnancy induced hypertension ($P = 0.029$) were observed in metformin treated group. Small for date babies were more in metformin group ($P < 0.01$). Neonatal hypoglycemia was significantly less and so was NICU stay of >24 hours in metformin group ($P < 0.01$). Significant reduction in cost of treatment was found in metformin group. **Metformin alone or with add-on insulin is an effective and cheap treatment option for patients with type 2 diabetes in pregnancy.** This trial is registered with clinical trial registration number: Clinical trials.gov NCT01855763.

Source: Medline

Full Text:
Available from *National Library of Medicine* in Journal of Diabetes Research

---

Title: A comparison between two oral hypoglycemics: Glyburide and metformin and their combination for the treatment of gestational diabetes mellitus e a prospective randomized controlled study

Citation: American Journal of Obstetrics and Gynecology, January 2015, vol./is. 212/1 SUPPL. 1(S23), 0002-9378 (January 2015)

Author(s): Nachum Z., Zafran N., Salim R., Hissin N., Hasanein J., Ze Letova Y.G., Suleiman A.

Language: English

Abstract: OBJECTIVE: To compare the efficacy and safety of glyburide vs. metformin in the treatment of gestational diabetes mellitus (GDM), and to evaluate the improvement in glycemic control after their replacement due to adverse effects, or after the addition of the second drug due to failure of the first STUDY DESIGN: Prospective randomized controlled open label study. We recruited GDM patients 13 to 33 weeks, who were not well controlled by diet (fasting glucose>95mg%, 90min postprandial> 130mg% or daily average glucose > 100mg%). Power analysis: assuming 80% well glycemic control with glyburide vs 55% with metformin, 52 women were needed in each group with alpha=0.05 and beta=0.2. Women provided daily glucose levels 7 times a day. If optimal glycemic control was not achieved, the other drug was added. If adverse effects occurred, the drug was replaced. If both failed, insulin was given. Maximal dose of glyburide was 20 mg and metformin 2550 mg per day. RESULTS: Glyburide was started in 55 and metformin in 51 patients at a comparable gestational week. In the glyburide group, 18 (33%) were failures: 6 (11%) because of adverse effects (mainly hypoglycemia) and 12 (22%) due to a lack of glycemic control. In the metformin group, 15 (29%) were failures: 1 (2%) because of adverse effects (gastrointestinal) and 14 (28%) due to lack of glycemic control (all comparisons were NS). In the glyburide group, 9 (16%) were treated eventually with insulin, compared with 2 (4%) of the metformin group (P=0.054). Combination of the drugs reduced the need for insulin from 33 (31%) to 11 (10%) patients (P=0.0003). Other obstetrical and neonatal outcomes were comparable between the groups, including anthropometric measures and cord blood insulin and C-peptide. **CONCLUSION: Glyburide and metformin are comparable oral treatments for GDM regarding glucose control or adverse effects. Their combination allows higher efficacy rate with significant reduced need for insulin.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Efficacy and safety of oral antidiabetic drugs in comparison to insulin in treating gestational diabetes mellitus: A meta-analysis

Citation: PLoS ONE, October 2014, vol./is. 9/10(no pagination), 1932-6203 (10 Oct 2014)

Author(s): Poolsup N., Suksomboon N., Amin M.

Language: English

Abstract: Objective: To assess the efficacy and safety of oral antidiabetic drugs (OADs) in gestational diabetes mellitus (GDM) in comparison to insulin. Methods: A meta-analysis of

randomized controlled trials was conducted. The efficacy and safety of OADs in comparison to insulin in GDM patients were explored. Studies were identified by conducting a literature search using the electronic databases of Medline, CENTRAL, CINAHL, LILACS, Scopus and Web of Science in addition to conducting hand search of relevant journals from inception until October 2013. Results: Thirteen studies involving 2,151 patients met the inclusion criteria. These studies were randomized controlled trials of metformin and glyburide in comparison to insulin therapy. Our results indicated a significant increase in the risk for preterm births (RR, 1.51; 95% CI, 1.04-2.19, p = 0.03) with metformin compared to insulin. However, a significant decrease in the risk for gestational hypertension (RR, 0.54; 95% CI, 0.31-0.91, p = 0.02) was found. Postprandial glucose levels also decreased significantly in patients receiving metformin (MD, -2.47 mg/dL; 95% CI, -4.00, -0.94, p = 0.002). There was no significant difference between the two groups for the remaining outcomes. There were significant increases in the risks of macrosomia (RR, 2.34; 95% CI, 1.18-4.63, p = 0.03) and neonatal hypoglycemia (RR, 2.06; 95% CI, 1.27-3.34, p = 0.005) in the glyburide group compared to insulin whereas results for the other analyzed outcomes remained non-significant. **Conclusion: The available evidence suggests favorable effects of metformin in treating GDM patients. Metformin seems to be an efficacious alternative to insulin and a better choice than glyburide especially those with mild form of disease.**

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in PLoS ONE
Available from *ProQuest* in PLoS One
Available from *National Library of Medicine* in PLoS ONE
Available from *Allen Press* in PLoS One

Title: Neonatal outcomes in women with gestational diabetes mellitus treated with metformin in compare with insulin: A randomized clinical trial.

Citation: Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences, Oct 2014, vol. 19, no. 10, p. 970-975, 1735-1995 (October 2014)

Author(s): Ruholamin, Safura, Eshaghian, Safieh, Allame, Zahra

Abstract: The objective of this study was to compare neonatal outcomes in women with gestational diabetes mellitus (GDM) treated with either metformin or insulin. A randomized clinical trial carried out on year 2011 on 109 women with GDM who did not adequately control by dietary measures. They received metformin 500 mg once or twice daily or insulin 0.2 IU/kg/day initially. The dose was titrated to achieve target blood glucose values. Neonatal outcomes such as hypoglycemia, birth weight, Apgar score, umbilical artery pH, and hyperbilirubinemia in the 50 women who remained exclusively on metformin were compared with 50 women who treated with insulin. Two groups were similar in mean fasting blood sugar (P = 0.7) and postprandial measurements (P = 0.8) throughout GDM treatment. Pregnancy complications or preterm labor were not different significantly

between two groups. Considering neonatal outcomes between insulin and metformin groups, such as hypoglycemia (2 [4%] and 0 [0%], respectively), birth weight (3342 ± 506 mg and 3176 ± 438 mg, respectively), 5(th) min Apgar score <7 (no one in either group), umbilical artery pH <7.05 (no one in either group) and hyperbilirubinemia (1 [2%] and 0 [0%], respectively), no significant statistical differences were seen. **Based on these preliminary data, considering neonatal outcomes, metformin appears to be a safe as insulin in the treatment of GDM.**

Source: Medline

Full Text:
Available from *National Library of Medicine* in Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences
Available from *Free Access Content* in Journal of Research in Medical Sciences
Available from *ProQuest* in Journal of Research in Medical Sciences

---

Title: Review of metformin and glyburide in the management of gestational diabetes.

Citation: Pharmacy practice, Oct 2014, vol. 12, no. 4, p. 528., 1885-642X (October 2014)

Author(s): Carroll, Dana G, Kelley, Kristi W

Abstract: Worldwide, gestational diabetes affects 15% of pregnancies. It is recommended in patients with gestational diabetes to initiate diet therapy and if this is not adequate, insulin is the next treatment modality. While insulin is the preferred drug therapy to manage gestational diabetes in the majority of women, it may not always be the best option for all women. The purpose of this review is to assess the efficacy and safety of oral agents for treatment of gestational diabetes. A literature search of the MEDLINE, Ovid databases and Google Scholar was performed using the search term "gestational diabetes" combined with each "metformin" and "glyburide". The time frame for the search was inception through August 2014. Randomized controlled trials and cohort (both prospective and retrospective) trials, published in English, with human participants were included. Studies included only pregnant women diagnosed with gestational diabetes. There were no significant differences in preterm deliveries, delivery modes, macrosomia, and birth weights and large for gestational age when utilizing glyburide vs insulin for gestational diabetes management. There were significantly higher neonatal intensive care unit admissions as well as longer lengths of stay for hypoglycemia and respiratory distress in babies whose mothers were treated with glyburide versus insulin. For the studies comparing metformin to insulin, there are no significant differences reported for birth weight, gestational age, delivery mode, prematurity and perinatal deaths**. Women taking metformin may require supplemental insulin more frequently than those taking glyburide. Glyburide and metformin appear to be safe and effective to manage blood glucose in patients with gestational diabetes who prefer to not utilize insulin or who cannot afford insulin therapy. All other oral therapies to manage blood glucose levels during gestational diabetes should be reserved until additional evidence is available regarding safety and efficacy to both mother and fetus.**

Source: Medline

Full Text:
Available from *National Library of Medicine* in Pharmacy Practice
Available from *ProQuest* in Pharmacy Practice; Granada

Title: Gestational diabetes mellitus: A randomized study comparing insulin therapy to a combination of half maximal dosages of metformin and glyburide

Citation: Canadian Journal of Diabetes, October 2014, vol./is. 38/(S23), 1499-2671 (October 2014)

Author(s): Ardilouze J.-L., Menard J., Hivert M.-F., Houde G., Perron P., Moutquin J.-M., Ouellet A., Baillargeon J.-P.

Language: English

Abstract: Controlled trials have demonstrated that GDM can be treated with Metformin (Met, Glucophage) or glyburide (Gly, Diabeta) with a 9 to 55% treatment failure leading to insulinotherapy. Our aim is to show that a combination of both drugs decreases this failure rate. We performed a randomized study comparing a Met-Gly combination of half maximal dosage (Met 1250 mg/day, Gly 10 mg/ day) to intensive insulin therapy using Aspart (NovoRapid) and NPH (Novolin NPH) in women with GDM not achieving treatment goals under diet therapy. When treatments started (at 29.3+/-3.8/30.1+/-3.1 weeks), there was no difference between the Met-Gly (n=35) and the insulin (n=33) groups in age (31.1+/-4.7/30.7+/-4.4 years), weight (85.3+/-17.5/ 85.3+/-22.9 kg) and GC assessed during the previous 2 weeks (capillary glucose was measured fasting and 2 hours after each meal): 5.3+/-0.7/5.3+/-0.6; 6.3+/-0.8/6.3+/-0.7; 6.6+/-0.8/6.4+/-0.6; 6.8+/-0.8/6.8+/-0.9 mmol/L, respectively. At delivery, in the Met-Gly group, 8women were taking Met alone (844+/-265 mg/day),14 were taking Met (1179+/-153 mg) and Gly (3.9+/-1.9 mg), 10 were on Met-Gly+insulin (1333+/-250 mg, 8.6+/-2.2 mg, 12.7+/-9.9 units) and 3 were on insulin alone. In these 13 women taking insulin (37%), injections were initiated 4.2+/-2.1 weeks after Met-Gly treatment start. During the 2 weeks prior to delivery, no difference was observed in GC (4.7+/-0.3/4.8+/-0.3; 5.8+/-0.4/5.9+/-0.5; 5.8+/-0.5/ 5.9+/-0.5; 6.0+/-0.5/6.1+/-0.5 mmol/L). At delivery, we found no difference in neonatal outcomes**. Our data suggest that a combination of mild doses of Met-Gly successfully controlled GDM without insulinotherapy in >60% women, with neonatal outcomes comparable to those of neonates born to women on insulin therapy.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *Free Access Content* in Canadian Journal of Diabetes

---

Title: Metformin in gestational diabetes mellitus. Outcomes in an Irish cohort

Citation: Irish Journal of Medical Science, October 2014, vol./is. 183/9 SUPPL. 1(S445-S446), 0021-1265 (October 2014)

Author(s): Hameed A., Ryan G., McCarthy A., Daly S., Kinsley B.

Language: English

Abstract: Metformin (MF) use in Gestational diabetes mellitus (GDM) is increasing. Studies to date suggest that its use is safe and effective (MiG Trial). MF use in GDM results in a reduction in the proportion of GDM requiring insulin therapy. The use of MF in GDM commenced in our service in March, 2013. This retrospective review reports on pregnancy outcomes of the first 50 GDM pregnancies treated with MF. Outcomes are compared with 50 randomly chosen GDM pregnancies treated with insulin in 2012 (prior to the introduction of MF). We compared a number of maternal and fetal variables in the MF treated group (MFG) with the insulin treated group (IG). Results: Mean weight and BMI at booking was higher in MFG compared to IG (86 +/- 16 kg vs 78 +/- 18 kg, p 0.01 and 33 +/- 13 vs 30 +/- 7 kg/m², p = 0.1). The mean weight gain during pregnancy did not differ significantly between groups (6.8 +/- 5 vs 7.5 +/- 4.7 kg, p 0.5). FPG in diagnostic OGTT was lower in MFG (5.2 vs 5.8 mmol/ l, p<0.05) as were 1 and 2 h values (p<0.01) and HBA1c at diagnosis (35 +/- 3 vs 39 +/- 6 mmol/mol (p<0.01). Rate of macrosomia (birth weight >4 kg), polyhydramnios, caesarian section, gestation at delivery and birth weight at delivery (3.4 +/- 0.6 vs 3.5 +/- 0.4 kg did not differ between groups. Reported rates of ante partum haemorrhage were higher in theMFG(5 cases) vs. no cases in IG and NNICU admits were 4 cases in MFG compared to zero cases in IG. There were no Intrauterine or Neonatal Deaths in either group**. Based on 50 cases metformin use appears safe and effective for GDM when compared to insulin therapy. The higher rates of antepartum haemorrhage and NNICU admission noted in the metformin group merits further review.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *Springer Link Journals* in Irish Journal of Medical Science

---

Title: Metformin vs insulin in the management of gestational diabetes: a systematic review and meta-analysis.

Citation: Diabetes research and clinical practice, Jun 2014, vol. 104, no. 3, p. 353-357, 1872-8227 (June 2014)

Author(s): Su, D F, Wang, X Y

Abstract: To evaluate the effectiveness of metformin compared with insulin in achieving glycemic control and investigate the maternal and neonatal outcomes in gestational diabetes mellitus. We searched four electronic databases from inception through December 2012. Terms for Gestational diabetes/gestational diabetes mellitus/diabetes pregnancy

AND/OR Metformin/hypoglycemic drugs/Hypoglycemic Agents/Antidiabetic Medications were used in the search. Two investigators independently reviewed titles and abstracts, performed data abstraction on full articles, and assessed study quality. Meanwhile, manual search of other resources and the search on Google Scholar were also carried out to identify more related articles .Rev Man 5.0 was used to analyze the data. Six randomized clinical trials involving 1420 subjects were included. **The current limited data suggested that using metformin in gestational diabetes subjects did not significantly increase adverse maternal outcomes and neonatal outcomes, also with less weight gain and neonatal hypoglycemia, but a higher incidence of premature birth. Metformin will not increase the incidence of adverse maternal outcomes and neonatal outcomes.**

Source: Medline

Title: Metformin throughout pregnancy in women with polycystic ovary syndrome: Safety and advantages

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, April 2014, vol./is. 121/(21), 1470-0328 (April 2014)

Author(s): Dalal R., Pai H., Palshetkar N., Takhtani M., Bansal B., Saxena N.

Language: English

Abstract: Introduction To study the incidence of miscarriage, congenital malformations, neonatal and maternal hypoglycemia after metformin therapy in pregnancy. Methods Prospective study. Setting: Outpatient. Patient(s): 56 women previously oligomenorrheic, nondiabetic women with polycystic ovarian syndrome, who conceived while on metformin. Intervention(s): Metformin 1 to 1.5 g/day throughout pregnancy. Main outcome: Incidence of first trimester miscarriage, gestational diabetes, teratogenicity and maternal complications, like gastritis and hypoglycemia. Results On metformin, the incidence of first trimester miscarriage was 11% and the incidence of gestational diabetes was 7%, which is much lower than the incidence otherwise cited for PCOS women. No major congenital abnormalities were observed. **Conclusion Metformin therapy in pregnancy reduces the otherwise high incidence of first trimester miscarriage, and gestational diabetes in PCOS women is tolerated well and is not found to be teratogenic.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

---

Title: The Role of Metformin in Metabolic Disturbances during Pregnancy: Polycystic Ovary Syndrome and Gestational Diabetes Mellitus.

Citation: International journal of reproductive medicine, Jan 2014, vol. 2014, p. 797681., 2356-7104 (2014)

Author(s): Rojas, Joselyn, Chávez-Castillo, Mervin, Bermúdez, Valmore

Abstract: Maintenance of gestation implicates complex function of multiple endocrine mechanisms, and disruptions of the global metabolic environment prompt profound consequences on fetomaternal well-being during pregnancy and postpartum. Polycystic Ovary Syndrome (PCOS) and gestational diabetes mellitus (GDM) are very frequent conditions which increase risk for pregnancy complications, including early pregnancy loss, pregnancy-induced hypertensive disorders, and preterm labor, among many others. Insulin resistance (IR) plays a pivotal role in the pathogenesis of both PCOS and GDM, representing an important therapeutic target, with metformin being the most widely prescribed insulin-sensitizing antidiabetic drug. Although traditional views neglect use of oral antidiabetic agents during pregnancy, increasing evidence of safety during gestation has led to metformin now being recognized as a valuable tool in prevention of IR-related pregnancy complications and management of GDM. Metformin has been demonstrated to reduce rates of early pregnancy loss and onset of GDM in women with PCOS, and it appears to offer better metabolic control than insulin and other oral antidiabetic drugs during pregnancy. This review aims to summarize key aspects of current evidence concerning molecular and epidemiological knowledge on metformin use during pregnancy in the setting of PCOS and GDM.

Source: Medline

Title: Efficacy and safety of oral antidiabetic drugs in comparison to insulin in treating gestational diabetes mellitus: a meta-analysis.

Citation: PloS one, Jan 2014, vol. 9, no. 10, p. e109985., 1932-6203 (2014)

Author(s): Poolsup, Nalinee, Suksomboon, Naeti, Amin, Muhammad

Abstract: To assess the efficacy and safety of oral antidiabetic drugs (OADs) in gestational diabetes mellitus (GDM) in comparison to insulin. A meta-analysis of randomized controlled trials was conducted. The efficacy and safety of OADs in comparison to insulin in GDM patients were explored. Studies were identified by conducting a literature search using the electronic databases of Medline, CENTRAL, CINAHL, LILACS, Scopus and Web of Science in addition to conducting hand search of relevant journals from inception until October 2013. Thirteen studies involving 2,151 patients met the inclusion criteria. These studies were randomized controlled trials of metformin and glyburide in comparison to insulin therapy.

Our results indicated a significant increase in the risk for preterm births (RR, 1.51; 95% CI, 1.04-2.19, p = 0.03) with metformin compared to insulin. However, a significant decrease in the risk for gestational hypertension (RR, 0.54; 95% CI, 0.31-0.91, p = 0.02) was found. Postprandial glucose levels also decreased significantly in patients receiving metformin (MD, -2.47 mg/dL; 95% CI, -4.00, -0.94, p = 0.002). There was no significant difference between the two groups for the remaining outcomes. There were significant increases in the risks of macrosomia (RR, 2.34; 95% CI, 1.18-4.63, p = 0.03) and neonatal hypoglycemia (RR, 2.06; 95% CI, 1.27-3.34, p = 0.005) in the glyburide group compared to insulin whereas results for the other analyzed outcomes remained non-significant. The available evidence suggests favorable effects of metformin in treating GDM patients. **Metformin seems to be an efficacious alternative to insulin and a better choice than glyburide especially those with mild form of disease.**

Source: Medline

Full Text:
Available from *National Library of Medicine* in PLoS ONE
Available from *ProQuest* in PLoS One
Available from *National Library of Medicine* in PLoS ONE
Available from *Allen Press* in PLoS One

Title: Effect of metformin intervention during pregnancy on the gestational diabetes mellitus in women with polycystic ovary syndrome: a systematic review and meta-analysis

Citation: Journal of diabetes research, 2014, vol./is. 2014/(381231), 2314-6753 (2014)

Author(s): Zhuo Z., Wang A., Yu H.

Language: English

Abstract: Metformin is an effective insulin sensitizer treating type 2 diabetes mellitus. However, the functional consequences of metformin administration throughout pregnancy on gestational diabetes mellitus (GDM) with polycystic ovary syndrome (PCOS) have not been assessed. We therefore performed a meta-analysis and system review to determine the effect of metformin on GDM in PCOS. A meta-analysis was performed on the published studies before December, 2013. Meta-analysis examined whether metformin could reduce GDM occurrence in PCOS with a fixed effect model. The odds ratio (OR) with 95% confidence interval (95% CI) was calculated to estimate the strength of association. A total of 13 studies including 5 RCTs and 8 non-RCTs were enrolled. Ultimately, effectiveness analysis demonstrated that, in total, there was no significant availability of metformin on GDM in PCOS in contrast to placebo (OR=1.07, 95% CI 0.60-1.92) in RCTs and significant availability of metformin on GDM (OR=0.19, 95% CI 0.13-0.27) was indicated in non-RCTs. **In summary, according to the results of our meta-analysis, strictly, metformin did not significantly effect on GDM with PCOS, though more multicenters RCTs still need to be investigated.**

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in Journal of Diabetes Research

---

Title: Neonatal outcomes in women with gestational diabetes mellitus treated with metformin in compare with insulin: A randomized clinical trial

Citation: Journal of Research in Medical Sciences, 2014, vol./is. 19/10(970-975), 1735-1995;1735-7136 (2014)

Author(s): Ruholamin S., Eshaghian S., Allame Z.

Language: English

Abstract: Background: The objective of this study was to compare neonatal outcomes in women with gestational diabetes mellitus (GDM) treated with either metformin or insulin.Materials and Methods: A randomized clinical trial carried out on year 2011 on 109 women with GDM who did not adequately control by dietary measures. They received metformin 500 mg once or twice daily or insulin 0.2 IU/kg/day initially. The dose was titrated to achieve target blood glucose values. Neonatal outcomes such as hypoglycemia, birth weight, Apgar score, umbilical artery pH, and hyperbilirubinemia in the 50 women who remained exclusively on metformin were compared with 50 women who treated with insulin.Results: Two groups were similar in mean fasting blood sugar (P = 0.7) and postprandial measurements (P = 0.8) throughout GDM treatment. Pregnancy complications or preterm labor were not different significantly between two groups. Considering neonatal outcomes between insulin and metformin groups, such as hypoglycemia (2 [4%] and 0 [0%], respectively), birth weight (3342 +/- 506 mg and 3176 +/- 438 mg, respectively), 5th min Apgar score <7 (no one in either group), umbilical artery pH <7.05 (no one in either group) and hyperbilirubinemia (1 [2%] and 0 [0%], respectively), no significant statistical differences were seen.**Conclusion: Based on these preliminary data, considering neonatal outcomes, metformin appears to be a safe as insulin in the treatment of GDM.**

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences
Available from *Free Access Content* in Journal of Research in Medical Sciences
Available from *ProQuest* in Journal of Research in Medical Sciences

---

Title: Efficacy and safety of metformin during pregnancy in women with gestational diabetes mellitus or polycystic ovary syndrome: A systematic review

Citation: Metabolism: Clinical and Experimental, November 2013, vol./is. 62/11(1522-1534), 0026-0495;1532-8600 (November 2013)

Author(s): Lautatzis M.-E., Goulis D.G., Vrontakis M.

Language: English

Abstract: Background Metformin is an effective oral anti-hyperglycemic agent that is widely used to manage diabetes mellitus type 2 in the general population and more recently, in pregnancy. However, as metformin crosses the placenta, its use during pregnancy raises concerns regarding potential adverse effects on the mother and fetus. Objective i) To provide background for the use of metformin during pregnancy through a narrative review and ii) to critically appraise the published evidence on the efficacy and safety of using metformin during pregnancy through a systematic review. Results Metformin appears to be effective and safe for the treatment of gestational diabetes mellitus (GDM), particularly for overweight or obese women. However, patients with multiple risk factors for insulin resistance may not meet their treatment goals with metformin alone and may require supplementary insulin. Evidence suggests that there are potential advantages for the use of metformin over insulin in GDM with respect to maternal weight gain and neonatal outcomes. Furthermore, patients are more accepting of metformin than insulin. The use of metformin throughout pregnancy in women with polycystic ovary syndrome reduces the rates of early pregnancy loss and preterm labor and protects against fetal growth restriction. There have been no demonstrable teratogenic effects, intra-uterine deaths or developmental delays with the use of metformin. Conclusions The publications reviewed in this paper support the efficacy and safety of metformin during pregnancy with respect to immediate pregnancy outcomes. Because there are no guidelines for the continuous use of metformin in pregnancy, the duration of treatment is based on clinical judgment and experience on a case-by-case basis.

Publication Type: Journal: Review

Source: EMBASE

Title: Effectiveness of metformin in gestational diabetes: Systematic review and meta-analysis

Citation: Diabetologia, September 2013, vol./is. 56/(S504), 0012-186X (September 2013)

Author(s): Khin M.O., Vatish M., Gates S., Saravanan P.

Language: English

Abstract: Background and aims: Gestational diabetes (GDM) is a common condition and contributes to significant maternal and neonatal morbidity. The prevalence of GDM will triple, from ~5% to 16-18%, if universal screening and the new IADPSG (International Association of Diabetes and Pregnancy Study Groups) cut-off for diagnosis are adopted.

Management of GDM is time and resource intensive. Because of the concerns of diluting the existing resources, these guidelines are not yet universally followed. Treatment involves dietary control, followed by insulin therapy if dietary control is ineffective. Oral hypoglycaemic agents, metformin or glibenclamide, are considered safe but used as second line to insulin and are not widely used. Glibenclamide has shown to be effective but does increase the risk of hypoglycaemia. In one large "non-inferiority", open label, randomised controlled trial (RCT) metformin was shown to be as effective as insulin but not routinely prescribed probably due to lack of superiority trials. We conducted a methodologically robust systematic review to evaluate whether metformin is superior over insulin or glibenclamide in GDM. Materials and methods: Five databases were searched by two independent reviewers without any restriction along with hand searching of relevant references in the primary publications. All primary studies comparing metformin to insulin or glibenclamide and reporting maternal and neonatal outcomes of GDM were included. Nine studies compared with insulin (4 RCTs and 5 non-RCTs/NRCTs) and two RCTs with glibenclamide were identified. Quality assessment of the RCTs and NRCTs used separate risk of bias tools, in line with PRISMA and MOOSE guidelines. Results: In the meta-analysis of RCTs with insulin, metformin appeared superior to insulin in preventing neonatal hypoglycaemia (odds ratio (OR): 0.67; 95% confidence interval (CI): 0.48,0.94) and minimising maternal weight gain (weighted mean difference (WMD): -1.80kg; CI:-2.57,-1.02). Similar effects were observed in the meta-analysis of NRCTs (neonatal hypoglycaemia: OR: 0.42; CI: 0.27,0.64; maternal weight gain: WMD: -1.77kg; CI: -1.91,-1.64), along with reduction in macrosomia (OR: 0.63; CI: 0.42,0.93) and neonatal intensive care admissions (OR: 0.57; CI: 0.40,0.82). Compared to glibenclamide, metformin reduces the risk of macrosomia (OR: 0.32; CI: 0.08, 1.19) and birth weight (WMD: -249.13g; CI: -355.88,-142.38). There are no differences in the risks of other outcomes. **Conclusion: Metformin in GDM appears to be superior to insulin and glibenclamide in a number of maternal and neonatal outcomes. Metformin is likely to improve the compliance and is less expensive compared to insulin. Therefore, using metformin as a first line therapy for GDM after diet and lifestyle might offer an effective strategy and less strain on the existing resources. This may also enable to manage more mothers with GDM if the new IADPSG guidelines are adopted. However, an adequately powered randomised controlled, superiority trial based on the IADPSG criteria, to demonstrate the differences in the key maternal and neonatal outcomes is urgently warranted.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Randomized trial of metformin vs insulin in the management of gestational diabetes

Citation: American Journal of Obstetrics and Gynecology, July 2013, vol./is. 209/1(34e1-34e7), 0002-9378;1097-6868 (July 2013)

Author(s): Spaulonci C.P., Bernardes L.S., Trindade T.C., Zugaib M., Francisco R.P.V.

Language: English

Abstract: OBJECTIVE: To evaluate glycemic control in women receiving metformin or insulin for gestational diabetes, and to identify factors predicting the need for supplemental insulin in women initially treated with metformin. STUDY DESIGN: Women with gestational diabetes who failed to achieve glycemic control with diet and exercise were randomized to receive metformin (n = 47) or insulin (n = 47). Criteria for inclusion were singleton pregnancy, diet, and exercise for a minimum period of 1 week without satisfactory glycemic control, absence of risk factors for lactic acidosis, and absence of anatomic and/or chromosome anomalies of the conceptus. Patients who were lost to prenatal followup were excluded. RESULTS: Comparison of mean pretreatment glucose levels showed no significant difference between groups (P = .790). After introduction of the drug, lower mean glucose levels were observed in the metformin group (P = .020), mainly because of lower levels after dinner (P = .042). Women using metformin presented less weight gain (P=.002) and a lower frequency of neonatal hypoglycemia (P= .032). Twelve women in the metformin group (26.08%) required supplemental insulin for glycemic control. Early gestational age at diagnosis (odds ratio, 0.71; 95% confidence interval, 0.52e0.97; P = .032) and mean pretreatment glucose level (odds ratio, 1.061; 95% confidence interval, 1.001e1.124; P =.046) were identified as predictors of the need for insulin. **CONCLUSION: Metformin was found to provide adequate glycemic control with lower mean glucose levels throughout the day, less weight gain and a lower frequency of neonatal hypoglycemia. Logistic regression analysis showed that gestational age at diagnosis and mean pretreatment glucose level were predictors of the need for supplemental insulin therapy in women initially treated with metformin.** © 2013 Mosby, Inc. All rights reserved.

Publication Type: Journal: Article

Source: EMBASE

Title: Metformin compared with insulin in the treatment of pregnant women with overt diabetes: a randomized controlled trial.

Citation: American journal of perinatology, Jun 2013, vol. 30, no. 6, p. 483-490, 1098-8785 (June 2013)

Author(s): Hickman, M Ashley, McBride, Ryan, Boggess, Kim A, Strauss, Robert

Abstract: To compare the safety and tolerability of metformin to insulin for glycemic control among women with preexisting type 2 and early A2 gestational diabetes. Women with preexisting type 2 diabetes and those diagnosed with gestational diabetes who required medical management prior to 20 weeks were randomly assigned to metformin or insulin. Glycemic control, defined as >50% capillary blood glucose within target range, was compared between groups. Other outcomes included patient tolerance, neonatal and obstetric complications, maternal weight gain, neonatal cord blood C-peptide, and patient

satisfaction with therapy. Twenty-eight women completed the study, with 14 in each group. Of the 15 women assigned to metformin, 100% continued to receive metformin until delivery, although 43% required supplemental insulin to achieve glycemic control. Glucose measures did not differ between the groups, and the proportion who met fasting and postprandial glycemic target values did not differ between the groups. Women treated with metformin had significantly fewer subjective episodes of hypoglycemia compared with those using insulin (0% versus 36%; p = 0.04) as well as reported glucose values < 60 mg/dL (7.1% versus 50%; p = 0.03). Metformin should be considered for treatment of overt diabetes and early A2 gestational diabetes in pregnancy. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

Source: Medline

Title: Metformin vs Insulin in the Management of Gestational Diabetes: A Meta-Analysis

Citation: PLoS ONE, May 2013, vol./is. 8/5(no pagination), 1932-6203 (27 May 2013)

Author(s): Gui J., Liu Q., Feng L.

Language: English

Abstract: Background:Nowadays, there have been increasing studies comparing metformin with insulin. But the use of metformin in pregnant women is still controversial, therefore, we aim to examine the efficiency and safety of metformin by conducting a meta-analysis of randomized controlled trials (RCTs) comparing the effects of metformin with insulin on glycemic control, maternal and neonatal outcomes in gestational diabetes mellitus (GDM).Methods:We used the key words "gestational diabetes" in combination with "metformin" and searched the databases including Pubmed, the Cochrane Library, Web of knowledge, and Clinical Trial Registries. A random-effects model was used to compute the summary risk estimates.Results:Meta-analysis of 5 RCTs involving 1270 participants detected that average weight gains after enrollment were much lower in the metformin group (n = 1006, P = 0.003, SMD = -0.47, 95%CI [-0.77 to -0.16]); average gestational ages at delivery were significantly lower in the metformin group (n = 1270, P = 0.02, SMD = -0.14, 95%CI [-0.25 to -0.03]); incidence of preterm birth was significantly more in metformin group (n = 1110, P = 0.01, OR = 1.74, 95%CI [1.13 to 2.68]); the incidence of pregnancy induced hypertension was significantly less in the metformin group (n = 1110, P = 0.02, OR = 0.52, 95%CI [0.30 to 0.90]). The fasting blood sugar levels of OGTT were significantly lower in the metformin only group than in the supplemental insulin group (n = 478, P = 0.0006, SMD = -0.83, 95%CI [-1.31 to -0.36]).**Conclusions:Metformin is comparable with insulin in glycemic control and neonatal outcomes. It might be more suitable for women with mild GDM. This meta-analysis also provides some significant benefits and risks of the use of metformin in GDM and help to inform further development of management guidelines.** © 2013 Gui et al.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in PLoS ONE
Available from *ProQuest* in PLoS One
Available from *National Library of Medicine* in PLoS ONE
Available from *Allen Press* in PLoS One

Title: Metformin for women who are obese during pregnancy versus standard care for improving maternal and infant outcomes - a systematic review

Citation: Journal of Paediatrics and Child Health, April 2013, vol./is. 49/(94), 1034-4810 (April 2013)

Author(s): Eames A.J., Grivell R.M., Dodd J.M., Deussen A.

Language: English

Abstract: Background: The prevalence of obesity is rising globally and is associated with a higher risk of maternal and infant health complications in pregnancy. There is little evidence surrounding effective interventions to limit gestational weight gain (GWG). Some evidence exists to suggest a role for metformin in treating not only diabetes and PCOS but also obesity. A small number of studies have suggested metformin may be effective in promoting weight loss in non-pregnant obese women. Our aim was to conduct a systematic review of the literature to evaluate the effect of metformin on insulin sensitivity and limiting GWG in obese women, and its effect on clinical maternal and infant outcomes. Method: Types of Participants: Pregnant women with a BMI > 30 kg/m². Types of Studies: Randomized controlled trials which compared the use of metformin alone or in combination with any other treatment modality to limit gestational weight gain to improve maternal and infant health outcomes. Search Terms: We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (February 2012), PUBMED, and the Australian (ACTR) and International (ICTN) Clinical Trials Registry. Primary Outcome: infant birth weight above 4 kg. Results: No published trials were identified. An ongoing UK-based trial comparing metformin with placebo in 400 obese pregnant women was identified. **Conclusions: Further evaluation of the role of metformin in limiting gestational weight gain and the effect on maternal and infant clinical outcomes in women who are obese is warranted. An Australian-based randomized trial is about to commence recruitment.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Journal of Paediatrics and Child Health
Available from *John Wiley and Sons* in Journal of Paediatrics and Child Health

---

Title: Evaluation of metformin in gestational diabetes: Systematic review and metaanalysis

Citation: Diabetic Medicine, March 2013, vol./is. 30/(12), 0742-3071 (March 2013)

Author(s): Khin M.O., Vatish M., Gates S., Saravanan P.

Language: English

Abstract: Background: Gestational diabetes (GDM) is common and contributes to significant maternal and neonatal morbidity. Despite being considered safe in pregnancy, metformin is still not used universally as first line therapy. This may be due to lack of studies designed to show that it is superior to insulin treatment. Aim: To evaluate the efficacy of metformin in GDM compared with insulin. Design and methods: Five databases were searched without any restriction together with hand searching of relevant references in the primary publications. All primary studies comparing metformin to insulin and reporting maternal and neonatal outcomes of GDM were included. Four randomized trials (RCTs) and five nonrandomized studies (NRCTs) were identified. Quality assessment of the RCTs and NRCTs used separate risk of bias tools, in line with PRISMA and MOOSE guidelines. The pooled effect estimates were computed separately either using fixed or random effect models depending on clinical and statistical heterogeneities. Results: In the meta-analysis of RCTs, metformin appeared superior to insulin for preventing neonatal hypoglycaemia [odds ratio (OR) 0.41; 95% confidence interval (CI) 0.25, 0.67] and lesser maternal weight gain [weighted mean difference (WMD) - 1.88kg; CI -2.24, -1.52). In NRCTs, similar effects were seen (neonatal hypoglycaemia, OR 0.42; CI 0.28, 0.64; maternal weight gain, WMD -1.77kg; CI -1.91, -1.64) along with reduction in macrosomia (OR 0.63; CI 0.42, 0.93), intensive care admission (OR 0.57; CI 0.40, 0.81) and lower risk of neonatal jaundice (OR 0.45; CI 0.27, 0.73). **Conclusion: Metformin inGDMis likely to be superior to insulin in reducing the risks of neonatal hypoglycaemia and maternal weight gain. Initiation of metformin along with diet and lifestyle management should be considered early in the management of GDM.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Diabetic Medicine

Title: Metformin versus insulin in gestational diabetes: A meta-analysis

Citation: Reproductive Sciences, March 2013, vol./is. 20/3 SUPPL. 1(311A), 1933-7191 (March 2013)

Author(s): Varrey A., Brady J.E., Hume H., Gelber S.E.

Language: English

Abstract: Introduction: Gestational diabetes (GDM) is an important complication of pregnancy, affecting 2-10 % of pregnant women. Insulin has been the gold standard for the

treatment of GDM. However, the use of oral hypoglycemics has been increasing due to their low cost and ease of administration. Metformin (MET) increases insulin sensitivity. Due to this effect, the use of MET has also been evaluated in GDM. Objective: To determine maternal and neonatal outcomes of pregnancies treated with metformin versus insulin for GDM. The outcomes were cesarean section (CS), large for gestational age (LGA), neonatal hypoglycemia, gestational hypertension, pre- eclampsia and hyperbilirubinemia. Methods: We systematically searched PubMed, Medline, Embase, Cochrane, International trials registry, pharmaceutical industry registries using the search terms "metformin" and "gestational diabetes". We included RCT and casecontrolled studies on patients with GDM being treated with metformin or insulin that measured more than one of the outcomes. The data was abstracted by two authors and was evaluated for the presence of bias, study confounders and number of patients. We examined heterogeneity among studies and calculated a summary effect estimate for each outcome. Results: 206 relevant references were identified. From these, 8 eligible studies were selected - 2 randomized trials and 6 case-control studies. Among women who received metformin, we found a decreased incidence of hyperbilirubinemia, (odds ratio (OR) 0.68, 95% confidence interval (CI) 0.48-0.96), LGA (OR 0.76, 95% CI 0.61- 0.95) and neonatal hypoglycemia (OR = 0.48, 95%CI 0.35 - 0.67). There was no statistically significant difference in gestational hypertension (OR:1.12, 95% CI 0.79-1.58) pre-eclampsia (OR:0.82 95% CI 0.57-1.17), or CS (OR = 0.96 95% CI 0.78-1.55). No significant heterogeneity existed between studies for the above outcomes. **Conclusions: This meta-analysis evaluating the use of metformin compared to insulin for GDM demonstrated a decreased incidence of hyperbilirubinemia, LGA and neonatal hypoglycemia. Further evaluation of metformin for treatment of gestational diabetes is warranted.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Comparison of newborn outcomes in women with gestational diabetes mellitus treated with metformin or insulin: a randomised blinded trial.

Citation: International journal of preventive medicine, Mar 2013, vol. 4, no. 3, p. 327-333, 2008-7802 (March 2013)

Author(s): Mesdaghinia, Elahe, Samimi, Mansoureh, Homaei, Zhila, Saberi, Farzaneh, Moosavi, Seyyed Gholam Abbas, Yaribakht, Mohammad

Abstract: Few studies have been done on the use of metformin in pregnancy and their results were not similar, therefore this research is performed to compare neonatal outcomes of metformin and insulin in the treatment of gestational diabetes. In this prospective randomized trial, 200 pregnant women within their 24(th) to 34(th) weeks of gestation with gestational diabetes, single fetus pregnancy, and in need of hyperglycemia treatment were entered and grouped as either metformin or insulin. Data related to maternal and neonatal outcomes were recorded and analyzed. Considering data recorded of HbA1c at the beginning of pregnancy, pregnancy induced hypertension, preeclampsia, birth

weight, dystocia, first and 5(th) min APGAR, neonatal sepsis, rout of delivery, liver function tests of neonate, hypoglycemia, anomaly, and still birth, there were no significant statistical differences between groups. The end pregnancy HbA1c, maternal weight gain during pregnancy, preterm labor, neonatal jaundice, respiratory distress and hospitalization of infants were higher in insulin group. **Considering data from this study, metformin is efficient to control hyperglycemia in pregnancy. It is suggested performing more studies to evaluate long term side effects of metformin in pregnancy with higher sample size and longer follow-up of newborns.**

Source: Medline

Full Text:
Available from *National Library of Medicine* in International Journal of Preventive Medicine
Available from *Free Access Content* in International Journal of Preventive Medicine
Available from *ProQuest* in International Journal of Preventive Medicine

---

Title: Metformin vs insulin in the management of gestational diabetes: a meta-analysis

Citation: PloS one, 2013, vol./is. 8/5(e64585), 1932-6203 (2013)

Author(s): Gui J., Liu Q., Feng L.

Language: English

Abstract: BACKGROUND: Nowadays, there have been increasing studies comparing metformin with insulin. But the use of metformin in pregnant women is still controversial, therefore, we aim to examine the efficiency and safety of metformin by conducting a meta-analysis of randomized controlled trials (RCTs) comparing the effects of metformin with insulin on glycemic control, maternal and neonatal outcomes in gestational diabetes mellitus (GDM).METHODS: We used the key words "gestational diabetes" in combination with "metformin" and searched the databases including Pubmed, the Cochrane Library, Web of knowledge, and Clinical Trial Registries. A random-effects model was used to compute the summary risk estimates.RESULTS: Meta-analysis of 5 RCTs involving 1270 participants detected that average weight gains after enrollment were much lower in the metformin group (n = 1006, P = 0.003, SMD = -0.47, 95%CI [-0.77 to -0.16]); average gestational ages at delivery were significantly lower in the metformin group (n = 1270, P = 0.02, SMD = -0.14, 95%CI [-0.25 to -0.03]); incidence of preterm birth was significantly more in metformin group (n = 1110, P = 0.01, OR = 1.74, 95%CI [1.13 to 2.68]); the incidence of pregnancy induced hypertension was significantly less in the metformin group (n = 1110, P = 0.02, OR = 0.52, 95%CI [0.30 to 0.90]). The fasting blood sugar levels of OGTT were significantly lower in the metformin only group than in the supplemental insulin group (n = 478, P = 0.0006, SMD = -0.83, 95%CI [-1.31 to -0.36]).CONCLUSIONS: Metformin is comparable with insulin in glycemic control and neonatal outcomes. It might be more suitable for women with mild GDM. This meta-analysis also provides some significant benefits and risks of the use of metformin in GDM and help to inform further development of management guidelines.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in PLoS ONE
Available from *ProQuest* in PLoS One
Available from *National Library of Medicine* in PLoS ONE
Available from *Allen Press* in PLoS One

Title: Metformin compared with insulin in the treatment of pregnant women with overt diabetes: A randomized controlled trial

Citation: American Journal of Perinatology, 2013, vol./is. 30/6(483-489), 0735-1631;1098-8785 (2013)

Author(s): Hickman M.A., McBride R., Boggess K.A., Strauss R.

Language: English

Abstract: Objective To compare the safety and tolerability of metformin to insulin for glycemic control among women with preexisting type 2 and early A2 gestational diabetes. Study Design Women with preexisting type 2 diabetes and those diagnosed with gestational diabetes who required medical management prior to 20 weeks were randomly assigned to metformin or insulin. Glycemic control, defined as >50% capillary blood glucose within target range, was compared between groups. Other outcomes included patient tolerance, neonatal and obstetric complications, maternal weight gain, neonatal cord blood C-peptide, and patient satisfaction with therapy. Results Twenty-eight women completed the study, with 14 in each group. Of the 15 women assigned to metformin, 100% continued to receive metformin until delivery, although 43% required supplemental insulin to achieve glycemic control. Glucose measures did not differ between the groups, and the proportion who met fasting and postprandial glycemic target values did not differ between the groups. Women treated with metformin had significantly fewer subjective episodes of hypoglycemia compared with those using insulin (0% versus 36%; p = 0.04) as well as reported glucose values < 60 mg/dL (7.1% versus 50%; p = 0.03). **Conclusion Metformin should be considered for treatment of overt diabetes and early A2 gestational diabetes in pregnancy**. © 2013 by Thieme Medical Publishers, Inc.

Publication Type: Journal: Article

Source: EMBASE

Title: Metformin compared with insulin in the management of gestational diabetes mellitus: a randomized clinical trial.

Citation: Diabetes research and clinical practice, Dec 2012, vol. 98, no. 3, p. 422-429, 1872-8227 (December 2012)

Author(s): Niromanesh, Shirin, Alavi, Azin, Sharbaf, Fatemeh Rahimi, Amjadi, Nooshin, Moosavi, Sanaz, Akbari, Soheila

Abstract: To evaluate the effect of metformin and insulin in glycemic control and compare pregnancy outcome in women with gestational diabetes mellitus (GDM). This randomized controlled trial was conducted in GDM women with singleton pregnancy and gestational age between 20 and 34 weeks who did not achieve glycemic control on diet were assigned randomly to receive either metformin (n=80) or insulin (n=80). The primary outcomes were maternal glycemic control and birth weight. The secondary outcomes were neonatal and obstetric complications. Two groups were comparable regarding the maternal characteristics. Two groups were similar in mean FBS (P=0.68) and postprandial measurements (P=0.87) throughout GDM treatment. The neonates of metformin group had less rate of birth weight centile >90 than insulin group (RR: 0.5, 95% CI: 0.3-0.9, P=0.012). Maternal weight gain was reduced in the metformin group (P<0.001). Two groups were comparable according to neonatal and obstetric complications (P>0.05). In metformin group 14% of women needed to supplemental insulin to achieve euglycemia. **Metformin is an effective and safe alternative treatment to insulin for women with GDM. This study does not show significant risk of maternal or neonatal adverse outcome with the use of metformin.**

Source: Medline

Title: Metformin: A safe alternative to insulin therapy in gestational diabetes

Citation: International Journal of Gynecology and Obstetrics, October 2012, vol./is. 119/(S270), 0020-7292 (October 2012)

Author(s): Ainuddin J.

Language: English

Abstract: Objectives: To assess the efficacy of Metformin treatment in gestational diabetes pregnancies compared with insulin treatment. Materials: Human subjects, Pregnant patients having a diagnosis of GDM, Metformin tablets and human isulen. Methods: Interventional study, Randomized clinical trial A total of 150 patients with gestational diabetes between 20-35 weeks of gestation were selected for pharmacological treatment using metformin or insulin during the study period form 20-12-08 till 20-12-10 from Antenatal OPD after screaning with 75grams OGTT. The primary outcomes were neonatal morbidity and fetal macrosomia. Secondary outcome measures were glycaemic control and treatment acceptability including cost benefit. Results: Patients on metformin and insulin were matched in age, parity, BMI and gestational age at study entry. Mean birth weight did not differ in both groups but fetal macrosomia was less in metformin group than in insulin group 18.67% V/S 10. 65% P < 0.05. Neonatal morbidity and NICU admissions were less in

metformin group. 40% pts required supplemental insulin with metformin for tight glycaemic control. **Conclusions: Metformin is a safe and effective alternative to insulin in gestational diabetes. Metformin treatment resulted in less fetal macrosomia and fewer NICU admissions and neonatal morbidity with advantages of cheap oral therapy in our resource poor setting**.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Effectiveness of metformin versus insulin for treating diabetes in pregnancy - A retrospective cohort study to compare maternal and perinatal outcomes

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, June 2012, vol./is. 119/(95), 1470-0328 (June 2012)

Author(s): Hashmi F., Malik A., Sheikh L., Ismail H.

Language: English

Abstract: Introduction: Metformin is increasingly being used to treat gestational diabetes mellitus (GDM) in our population either alone or in combination with insulin. The numbers of studies reporting on metformin use in GDM are still few and most are from the western world. This study was undertaken to compare the use of metformin with insulin for treating GDM in an urban Pakistani population. Methods: A retrospective cohort study was performed among women with singleton pregnancies diagnosed as GDM who were booked at the AKUH from January 2009 to June 2010. Maternal and neonatal outcomes and complications were assessed for women being treated with metformin and those being treated with insulin. Results: In our study of 110 patients, 53 had received metformin and 56 patients received insulin as the first line drug of treatment for GDM. The mean birthweight was similar in both the groups; that is, 2.9 kg in the metformin group and 2.88 kg in the insulin group. Frequency of SGA was comparable; 5.7% in the metformin group and 9.3% in the insulin group (P-value = 0.71). A higher percentage of women in the insulin group developed gestational hypertension, 22.2% vs. 13.7%, though, it did not reach statistical significance (P-value = 0.31). One neonate in the metformin group developed respiratory distress syndrome versus none in the insulin group. 7.8% of neonate in the metformin group and 3.6% in the insulin group were shifted to NICU (P-value = 0.42). **Conclusion: Metformin is as effective as insulin in treatment of diabetes in pregnancy.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

---

Title: Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition at 2 years of age.

Citation: Diabetes care, Oct 2011, vol. 34, no. 10, p. 2279-2284, 1935-5548 (October 2011)

Author(s): Rowan, Janet A, Rush, Elaine C, Obolonkin, Victor, Battin, Malcolm, Wouldes, Trecia, Hague, William M

Abstract: In women with gestational diabetes mellitus, who were randomized to metformin or insulin treatment, pregnancy outcomes were similar (Metformin in Gestational diabetes [MiG] trial). Metformin crosses the placenta, so it is important to assess potential effects on growth of the children. In Auckland, New Zealand, and Adelaide, Australia, women who had participated in the MiG trial were reviewed when their children were 2 years old. Body composition was measured in 154 and 164 children whose mothers had been randomized to metformin and insulin, respectively. Children were assessed with anthropometry, bioimpedance, and dual energy X-ray absorptiometry (DEXA), using standard methods. The children were similar for baseline maternal characteristics and pregnancy outcomes. In the metformin group, compared with the insulin group, children had larger mid-upper arm circumferences (17.2 ± 1.5 vs. 16.7 ± 1.5 cm; P = 0.002) and subscapular (6.3 ± 1.9 vs. 6.0 ± 1.7 mm; P = 0.02) and biceps skinfolds (6.03 ± 1.9 vs. 5.6 ± 1.7 mm; P = 0.04). Total fat mass and percentage body fat assessed by bioimpedance (n = 221) and DEXA (n = 114) were not different. **Children exposed to metformin had larger measures of subcutaneous fat, but overall body fat was the same as in children whose mothers were treated with insulin alone. Further follow-up is required to examine whether these findings persist into later life and whether children exposed to metformin will develop less visceral fat and be more insulin sensitive. If so, this would have significant implications for the current pandemic of diabetes.**

Source: Medline

Title: Metformin should be considered in the treatment of gestational diabetes: A prospective randomised study

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, June 2011, vol./is. 118/7(880-885), 1470-0328;1471-0528 (June 2011)

Author(s): Ijas H., Vaarasmaki M., Morin-Papunen L., Keravuo R., Ebeling T., Saarela T., Raudaskoski T.

Language: English

Abstract: Objective To examine if oral metformin is as effective as insulin in the prevention of fetal macrosomy in pregnancies complicated with gestational diabetes mellitus (GDM). Design Open-label prospective randomised controlled study. Setting Maternity outpatient clinics in a secondary and tertiary level hospital in Finland. Sample One hundred women with GDM who did not attain euglycaemia with diet. Methods Women were randomised to therapy with insulin (n = 50) or oral metformin (n = 50). Main outcome measures Incidence of large-for-gestational-age (LGA) infants and neonatal morbidity. Results There were no statistically significant differences in the incidence of LGA (8.5 versus 10.0%, P = 0.97), mean birthweight, mean cord artery pH or neonatal morbidity between the insulin and metformin groups. Fifteen (31.9%) of the 47 women randomised to metformin needed supplemental insulin. They were more obese (with a body mass index of 36 versus 30 kg/m², P = 0.002), had higher fasting blood glucose levels in an oral glucose tolerance test (6.1 versus 5.0 mmol/l, P = 0.001) and needed medical treatment for GDM earlier (26 versus 31 gestational weeks, P = 0.002) than women who were normoglycemic with metformin. There was a tendency to a higher rate of caesarean sections in the metformin group than in the insulin group (RR 1.9; 95% CI 0.99-3.71). **Conclusions Metformin seems to be suitable for the prevention of fetal macrosomy, especially in lean or moderately overweight women developing GDM in late gestation. Women with considerable obesity, high fasting blood glucose and an early need for pharmacological treatment may be more suitable for insulin therapy.** © 2011 RCOG.

Publication Type: Journal: Review

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

---

Title: Oral hypoglycemic agents vs insulin in management of gestational diabetes: a systematic review and metaanalysis.

Citation: American journal of obstetrics and gynecology, Nov 2010, vol. 203, no. 5, p. 457.e1, 1097-6868 (November 2010)

Author(s): Dhulkotia, Jaya Saxena, Ola, Bolarinde, Fraser, Robert, Farrell, Tom

Abstract: The objective of this review was to provide pooled estimates of randomized controlled trials comparing the effects of oral hypoglycemic agents with insulin in achieving glycemic control and to study the maternal and perinatal outcomes in gestational diabetes mellitus. A protocol for the study was developed. All metaanalyses were performed using Stats Direct statistical software (Stats Direct Ltd, Cheshire, UK). Six studies comprising 1388 subjects were analyzed. No significant differences were found in maternal fasting (weighted

mean difference [WMD], 1.31; 95% confidence interval [CI], 0.81-3.43) or postprandial (WMD, 0.80; 95% CI, -3.26 to 4.87) glycemic control. Use of oral hypoglycemic agents (OHAs) was not associated with risk of neonatal hypoglycemia (odds ratio [OR], 1.59; 95% CI, 0.70-3.62), increased birthweight (WMD, 56.11; 95% CI, -42.62 to 154.84), incidence of caesarean section (OR, 0.91; 95% CI, -0.68 to 1.22), or incidence of large-for-gestational-age babies (OR, 1.01; 95% CI, 0.61-1.68). **Our study demonstrates that there are no differences in glycemic control or pregnancy outcomes when OHAs were compared with insulin.**

Source: Medline

Title: A randomized study comparing metformin and insulin in the treatment of gestational diabetes mellitus. interim results

Citation: Journal of Maternal-Fetal and Neonatal Medicine, May 2010, vol./is. 23/(381), 1476-7058 (May 2010)

Author(s): Martinez Piccole S., Abdulhaj Martinez M., Andres Nunez P., Garcia Leon P., Lopez Sanchez E.J., Gonzalez Ramirez A.R.

Language: English

Abstract: Brief Introduction: Oral metformin may be a good alternative to insulin regarding patient compliance in the treatment of gestational diabetes mellitus (GDM). We studied neonatal and maternal outcome in patients with GDM treated with metformin or insulin. Materials and Methods: We report interim data of a noninferior design, randomized prospective trial consisting of 100 first patients (final number 278) requiring pharmacological therapy for GDM. We randomly assigned patients to metformin or insulin treatment. Primary endpoints were neonatal hypoglycemia and birth weight standardized for gestational weeks. Clinical Cases or Summary Results: There were no significant differences in neonatal hypoglycemia or birth weight percentile between insulin and metformin groups. In the insulin group, there were statistically significantly more neonatal breathing problems than in the metformin group ($p < 0.05$). There were no significant differences between groups in transmission to neonatal intensive care unit, in 5 min Apgar scores or umbilical artery pH. Maternal demographic or obstetric data did not differ between the groups. There were statistically significantly more vacuum assisted deliveries in the insulin group than in the metformin group ($p < 0.05$). 20% of mothers treated with metformin needed supplementary insulin. **Conclusions: Metformin is as effective as insulin in treating GDM. Metformin may reduce some neonatal risks compared to insulin. However, one-fifth of metformin-treated mothers need additional insulin.**

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Title: Metformin compared with glyburide in gestational diabetes: a randomized controlled trial.

Citation: Obstetrics and gynecology, Jan 2010, vol. 115, no. 1, p. 55-59, 1873-233X (January 2010)

Author(s): Moore, Lisa E, Clokey, Diana, Rappaport, Valerie J, Curet, Luis B

Abstract: To compare the efficacy of metformin with glyburide for glycemic control in gestational diabetes. Patients with gestational diabetes who did not achieve glycemic control on diet were randomly assigned to metformin (n=75) or glyburide (n=74) as single agents. The primary outcome was glycemic control. Secondary outcomes were drug failure rate and neonatal and obstetric complications. In the patients who achieved adequate glycemic control, the mean fasting and 2-hour postprandial blood glucose levels were not statistically different between the two groups. However, 26 patients in the metformin group (34.7%) and 12 patients in the glyburide group (16.2%) did not achieve adequate glycemic control and required insulin therapy (P=.01). **In this study, the failure rate of metformin was 2.1 times higher than the failure rate of glyburide when used in the management of gestational diabetes (95% confidence interval 1.2-3.9).** ClinicalTrials.gov, www.clinicaltrials.gov, NCT00965991. I.

Source: Medline

Title: Does continuous use of metformin throughout pregnancy improve pregnancy outcomes in women with polycystic ovarian syndrome?

Citation: The journal of obstetrics and gynaecology research, Oct 2008, vol. 34, no. 5, p. 832-837, 1341-8076 (October 2008)

Author(s): Nawaz, Fauzia Haq, Khalid, Roha, Naru, Tahira, Rizvi, Javed

Abstract: Polycystic ovarian syndrome (PCOS) is one of the most common endocrinopathies in women of reproductive age. It is associated with hyperinsulinemia and insulin resistance which is further aggravated during pregnancy. This mechanism has a pivotal role in the development of various complications during pregnancy. In the past few years, metformin, an insulin sensitizer, has been extensively evaluated for induction of ovulation. Its therapeutic use during pregnancy is, however, a recent strategy and is a debatable issue. At present, evidence is inadequate to support the long-term use of insulin-sensitizing agents during pregnancy. It is a challenge for both clinicians and researchers to provide good

evidence of the safety of metformin for long-term use and during pregnancy. This study aimed to evaluate pregnancy outcomes in women with PCOS who conceived while on metformin treatment, and continued the medication for a variable length of time during pregnancy. This case-control study was conducted from January 2005 to December 2006 at the antenatal clinics of the Department of Obstetrics and Gynecology, Aga Khan University, Karachi, Pakistan. The sample included 137 infertile women with PCOS; of these, 105 conceived while taking metformin (cases), while 32 conceived spontaneously without metformin (controls). Outcomes were measured in three groups of cases which were formed according to the duration of use of metformin during pregnancy. Comparison was made between these groups and women with PCOS who conceived spontaneously. All 137 women in this study had a confirmed diagnosis of PCOS (Rotterdam criteria). These women were followed up during their course of pregnancy; data forms were completed once they had delivered. Cases were divided into three groups: group A, 40 women who stopped metformin between 4-16 weeks of pregnancy; group B, 20 women who received metformin up until 32 weeks of gestation; and group C; 45 women who continued metformin throughout pregnancy. All the groups were matched by age, height and weight. Comparison was in terms of early and late pregnancy complications, intrauterine growth restriction and live birth rates. In groups A, B and C the rate of pregnancy-induced hypertension/pre-eclampsia was 43.7%, 33% and 13.9% respectively (P<0.020). Rates of gestational diabetes requiring insulin treatment in groups A and B were 18.7% and 33.3% compared to 2.5% in group C (P<0.004). The rate of intrauterine growth restriction was significantly low in group C: 2.5% compared to 19.2% and 16.6% in groups A and B respectively (P<0.046). Frequency of preterm labor and live birth rate was significantly better in group C compared to groups A and B. Overall rate of miscarriages was 7.8%. Controls were comparable to group A in terms of early and late pregnancy complications. **In women with PCOS, continuous use of metformin during pregnancy significantly reduced the rate of miscarriage, gestational diabetes requiring insulin treatment and fetal growth restriction. No congenital anomaly, intrauterine death or stillbirth was reported in this study.**

Source: Medline

Full Text:
Available from *John Wiley and Sons* in Journal of Obstetrics and Gynaecology Research
Available from *John Wiley and Sons* in Journal of Obstetrics and Gynaecology Research

---

Title: Metformin versus insulin for the treatment of gestational diabetes

Citation: New England Journal of Medicine, May 2008, vol./is. 358/19(2003-2015), 0028-4793;1533-4406 (08 May 2008)

Author(s): Rowan J.A., Hague W.M., Gao W., Battin M.R., Moore M.P.

Language: English

Abstract: Background: Metformin is a logical treatment for women with gestational diabetes mellitus, but randomized trials to assess the efficacy and safety of its use for this condition are lacking. Methods: We randomly assigned 751 women with gestational

diabetes mellitus at 20 to 33 weeks of gestation to open treatment with metformin (with supplemental insulin if required) or insulin. The primary outcome was a composite of neonatal hypoglycemia, respiratory distress, need for phototherapy, birth trauma, 5-minute Apgar score less than 7, or prematurity. The trial was designed to rule out a 33% increase (from 30% to 40%) in this composite outcome in infants of women treated with metformin as compared with those treated with insulin. Secondary outcomes included neonatal anthropometric measurements, maternal glycemic control, maternal hypertensive complications, postpartum glucose tolerance, and acceptability of treatment. Results: Of the 363 women assigned to metformin, 92.6% continued to receive metformin until delivery and 46.3% received supplemental insulin. The rate of the primary composite outcome was 32.0% in the group assigned to metformin and 32.2% in the insulin group (relative risk, 1.00; 95% confidence interval, 0.90 to 1.10). More women in the metformin group than in the insulin group stated that they would choose to receive their assigned treatment again (76.6% vs. 27.2%, P<0.001). The rates of other secondary outcomes did not differ significantly between the groups. There were no serious adverse events associated with the use of metformin. **Conclusions: In women with gestational diabetes mellitus, metformin (alone or with supplemental insulin) is not associated with increased perinatal complications as compared with insulin. The women preferred metformin to insulin treatment**. (Australian New Zealand Clinical Trials Registry number, 12605000311651.)

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *New England Journal of Medicine* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *Free Access Content* in New England Journal of Medicine
Available from *Massachusetts Medical Society* in New England Journal of Medicine; Note: ; Notes: Please select 'Login via Athens or your institution' and enter your OpenAthens username and password.
Available from *ProQuest* in New England Journal of Medicine, The