

Medicine by the Numbers

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➤ Metformin for Improving Maternal and Infant Outcomes in Pregnant Women Who Are Obese

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Details for This Review

Study Population: Pregnant women who are obese (defined as first trimester or prepregnancy body mass index [BMI] of at least 30 kg per m²) who do not have preexisting diabetes mellitus or polycystic ovary syndrome

Efficacy End Points: Decrease in the risk that infants will be large for gestational age, defined as greater than 90th percentile for gestational age and sex

Harm End Points: Adverse events associated with medication, most notably diarrhea

Narrative: More than one-half of pregnant women in the United States are overweight or obese. Infants born to these women are at increased risk of prematurity, hypoglycemia, respiratory distress at birth, admission to the neonatal intensive care unit, stillbirth, congenital anomalies, macrosomia with possible birth injury, and childhood obesity. Overweight and obese women are also at increased risk of complications during pregnancy.¹ Metformin, an inexpensive medication used to treat type 2 and gestational diabetes, improves insulin sensitivity by decreasing hepatic glucose production and increasing peripheral uptake and use of glucose. Women who are overweight or obese have increased insulin resistance, which exposes the developing fetus to higher levels of blood glucose over time and contributes to excessive fetal growth. Diet and lifestyle modifications have shown only modest effects in this population. Metformin use during pregnancy may increase insulin sensitivity, thereby decreasing the risk of maternal and fetal complications.²

A Cochrane review of three randomized controlled trials including 1,099 pregnant women in the United Kingdom and Alexandria, Egypt,

METFORMIN USE IN PREGNANT WOMEN WHO ARE OBESE

Benefits

No infants were prevented from being born large for gestational age

Harms

1 in 6 women experienced diarrhea

compared metformin (initiation between 10 and 20 weeks' gestation and continuing until birth) with placebo. The studies looked only at women who were obese (one study, BMI of at least 30 kg per m²; two studies, BMI greater than 35 kg per m²) and not those who were overweight. Out of 831 infants, there was no difference in the incidence of large for gestational age (primary outcome) between the metformin and placebo groups (risk ratio [RR] = 0.95; 95% confidence interval [CI], 0.70 to 1.30).²

This lack of benefit was also reflected in little to no difference in the incidence of secondary infant outcomes between the treatment and placebo groups. Secondary infant outcomes included birth weight (mean difference [MD] = 6.39 g; 95% CI, -81.15 g to 93.92 g), hypoglycemia/hyperbilirubinemia requiring treatment, birth trauma, Apgar score less than 7 at five minutes, admission to the neonatal intensive care unit, stillbirth after 20 weeks' gestation, and neonatal death within 28 days of birth.²

Among secondary maternal outcomes, there was little to no difference in incidence of gestational hypertension, preeclampsia, or preterm birth despite a high level of heterogeneity between the included trials. Women who received metformin did not have significantly different gestational weight gain (MD = -2.60 kg [-5.73 lb]; 95% CI, -5.29 to 0.10 kg [-11.66 to 0.22 lb]), and there was no difference in rates of gestational diabetes (RR = 0.85; 95% CI, 0.61 to 1.19).²

Women receiving metformin were more likely to experience at least one

The NNT Group Rating System

Green	Benefits greater than harms
Yellow	Unclear benefits
Red	No benefits
Black	Harms greater than benefits

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adverse effect, namely diarrhea (RR = 2.34; 95% CI, 1.74 to 3.14).² The differences for other adverse effects were not statistically significant between the two groups.

Caveats: This meta-analysis of three high-quality, randomized controlled trials using metformin ranging from 500 mg to 3,000 mg per day in pregnant women who are obese from the United Kingdom and Egypt showed no clear benefit for metformin in reducing the risk of large for gestational age infants. The number needed to harm to cause diarrhea is 6. Additionally, there was no difference in important secondary outcomes such as gestational diabetes, hypertensive disease in pregnancy, shoulder dystocia, advanced perineal lacerations, need for cesarean delivery or induction of labor, preterm birth, or postpartum hemorrhage. Additional studies may be needed with higher numbers of participants to reflect possible changes in these secondary outcomes.¹

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