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The Effect of Metformin in Gestational Diabetes

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Abstract

Gestational diabetes is glucose intolerance identified in the second trimester of pregnancy. This occurs mainly due to the diabetogenic effects of placental hormones and is associated with certain critical fetal and maternal consequences.¹

If maternal normoglycaemia cannot be achieved by diet and lifestyle changes, medication will be needed. The standard treatment for achieving adequate glucose levels is insulin therapy. However, the disadvantages of insulin for the mother include the need for injections, risk of hypoglycaemia, increased appetite and weight gain. Furthermore, this treatment requires modification based on the patient's body mass index, glucose levels and lifestyle.²

Metformin appears to be a viable option for use in GDM. This medication with a different mode of action from insulin is an antihyperglycemic agent. Its primary mechanism of action is in reducing hepatic glucose production. Secondly, it decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization and does not cause either hypoglycemia or hyperinsulinemia.³

Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. It is observed in 7–18% of pregnancies and is associated with an increased risk of a variety of maternal and perinatal complications, including preeclampsia, Caesarean section, shoulder dystocia, birth injuries, hypoglycaemia and respiratory distress syndrome (RDS).⁴

Metformin is an anti-hyperglycaemic agent that reduces hyperglycaemia by suppressing hepatic glucose output (hepatic gluconeogenesis), increasing insulin sensitivity and enhancing peripheral glucose uptake. Implementation of metformin should be in conjunction with diet and exercise for glycemic control. The U.S. Food and Drug Administration categorizes this medication as a class B drug in pregnancy; however, it cautions that metformin can cross the placenta and should not be used during pregnancy unless clearly needed. Despite these concerns, metformin appears to be an alternative option for the treatment of GDM.³

Discussion

The study by Rowan et al., suggests no increase in perinatal complications in women treated with metformin. Other study from Moore et al and Hyer et al shows no big differences between women treated with metformin and those treated with insulin.

In the insulin group, severe neonatal hypoglycemia (i.e., blood glucose levels < 28.8 mg/dl) was seen more often than in those exposed to metformin. However, preterm births were different in the metformin group. Also the secondary neonatal outcomes did not differ significantly between groups in terms of birth weight, birth length, circumference (head, abdominal, and chest), and skin thickness. Approximately 46% of women using metformin at the maximum dose used in the trial (2,500 mg/day) required supplemental insulin. Overall, neonatal and maternal complications were similar in the two groups, indicating that metformin is an acceptable alternative treatment to insulin in GDM.⁴

The study by Goh et al. reinforces the MiG trial finding that metformin in GDM is associated with fewer adverse complications and better glycemic control than insulin. This study differs from the earlier studies by Rowan et al. in its design (a prospective analysis from a single center) and its treatment groups (diet alone, insulin, and metformin). A small, randomized study by Ijas et al. showed that mean birth weight of newborns did not differ significantly between metformin and insulin groups . another small, prospective observational study by Rai et al. shows that metformin is not associated with fetal anomalies when used during the first trimester of pregnancy. In addition, metformin appears to be safe in the second and third trimesters of pregnancy.²

Study of Terti et al found that the average 2-h postprandial glucose levels in the first week after randomization were significantly lower in the metformin group, which is consistent with the result of the previous review . This finding indicates that in the metformin group, glucose targets might be reached sooner, possibly because metformin reduces hyperglycaemia by suppressing hepatic glucose output, increasing insulin sensitivity and enhancing peripheral glucose uptake . These effects are potentially useful during pregnancy, when glucose control deteriorates with changes to insulin resistance. Furthermore, for insulin, it takes time for participants to master the usage and dose computation. The glycaemic control outcomes were not worse in metformin-treated women; however, a large proportion of women randomized to the metformin group required the addition of insulin to achieve adequate glycaemic control.³

Conclusion

DM is growing in prevalence and if left untreated, is associated with poor maternal and fetal outcomes. For this reason, prenatal testing of pregnant women at high risk for GDM is recommended at the first prenatal visit.

Evidence from many studies suggest potential advantages of metformin over insulin in GDM in maternal complication in terms of less maternal weight gain and caesarian delivery. Although insulin remains the mainstay of therapy for GDM, the use of metformin is a safe alternative supported by clinical research showing no change or even improved outcomes with the use of metformin compared to insulin.

References

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