Treatment of gestational diabetes: oral hypoglycemic agents or insulin?

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Summary

Our report aims to verify whether perinatal maternal glycemic control in gestational diabetes can only be achieved with insulin or with oral hypoglycemic agents. Then we want to evaluate the efficacy and safety of oral hypoglycemic agents in the treatment of gestational diabetes and then to compare these results with those associated with the use of insulin.

Key Words: Gestational diabetes; Fetal hyperinsulinemia; Fetal macrosomia; Insulin; Oral hypoglycemic.

Introduction

Gestational diabetes (GDM) is one of the most common medical conditions complicating pregnancy and its prevalence increases proportional to woman obesity in the childbearing age (1). In pregnant women suffering from gestational diabetes, despite a significant reduction in perinatal mortality observed in the last decade, the morbidity remained essentially unchanged (10-50%) (2).
Fetal hyperinsulinemia and achieving macrosomia, accompanied by the increase of operative deliveries, shoulder dystocia and birth trauma, are a clear marker of the degree of metabolic control achieved during pregnancy (3) because we find them in approximately 40% of the children of untreated mothers suffering from this pregnancy disease (4). If the diet, which is the first-line therapy, fails (glycemia is higher than 130 mg / dl one hour after eating and 120 mg / dl two hours after eating and / or on an empty stomach glycemia is higher than 95 mg / dl) it is indicated application of insulin therapy that is used approximately 30% of pregnant women suffering from GDM.
Subcutaneous insulin therapy has been the mainstay of treatment of women with gestational diabetes not controlled by modification diet.
In reality the use of insulin is often associated with hypoglycemia and increased weight. Moreover, this treatment is inconvenient and expensive because it requires refrigerated storage and skilled handling, which are not always available in low-resource countries (5).
The use of oral hypoglycemic agents in pregnancy has been so controversial because case reports and small-sample studies have reported adverse effects as the potential risks of neonatal hypoglycemia and teratogenicity associated with placental transfer to the fetus (6, 7).
In fact, several studies with glyburide and metformin showed similar or even better neonatal outcomes if compared to treatment with insulin (8-12).

Material and Methods

We reviewed several studies that have compared the oral hypoglycemic agents and insulin in the management of gestational diabetes. Among the oral agents, in particular, several studies have investigated the action of Glyburide and Metformin, and then comparing them. Glyburide and metformin, in fact, work differently. Glyburide binds to pancreatic -cell receptors to increase insulin secretion, with the effect of increasing the insulin sensitivity of peripheral tissues (13). Metformin inhibits hepatic gluconeogenesis and glucose absorption and stimulates glucose uptake in peripheral tissues, with the effect of reducing weight gain.The studies measured one or more of the following maternal glycemic control, neonatal hypoglycemia, birthweight, macrosomia, birth injuries, neonatal intensive care unit (NICU) admissions, small for gestational age (SGA) and preterm births, intrauterine fetal deaths (IUFD), congenital anomalies, maternal hypoglycemia or ketoacidosis, hypertensive complications, incidence of cesarean section, side

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effects of treatment, and maternal satisfaction/ quality of life.

Results

In all the studies we reviewed, the results were almost overlapping. In particular, the amount of sugar in the blood was kept lower in women treated with insulin compared to those treated with oral hypoglycemic agents, and in this group no difference was found between metformin and glyburide. However, the differences were not statistically significant between both groups. The birth weight of children was slightly lower in cases in which metformin was administered compared to insulin or glyburide. There was no difference in neonatal outcomes: neonatal respiratory distress, incidence of birth injuries, incidence of SGA, incidence of preterm births, congenital anomalies and incidence of IUFD. Patients with gestational diabetes receive oral hypoglycemic agents only after organogenesis and the rate of congenital anomalies are similar to the group treated with insulin. The rate of maternal hypoglycemia was higher in women treated with insulin than those treated with hypoglycemic. There was not significant difference in the rate of caesarean sections.

Discussion

Gestational diabetes mellitus affects millions of women around the world, from 15% to 60% of these women need insulin treatment (14). Insulin is effective for glucose control, but its cost and the fact that it requires skilled handling may bar it from use in many places. The assurance that low-cost, oral, user-friendly medications are safe and effective for glucose control would therefore welcome them. However, we found that there was no significant difference in postprandial glucose control between insulin and OHAs. This is reflected in similar rates of fetal macrosomia and mean birthweights in those women receiving insulin or oral hypoglycemic agents as a first line therapy. In addition it was shown that women treated with metformin had a greater weight loss than women in the group insulin. Then the oral hypoglycemic gives good control of maternal glycemia and good perinatal outcomes entirely comparable with those offered by the treatment with insulin. In the light of short-term outcomes reported metformin and glyburide should be considered as credible and safe alternative to insulin, that should be reserved as a second-line agent for patients in which glycemic control is not achieved by oral treatment. Further follow-up data are needed to establish long-term safety.

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