



# Pharmacotherapy for gestational diabetes mellitus: still insulin, or what about sulfonylureas?

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Risk factors of gestational diabetes mellitus (GDM) include overweight, hormonal changes, previous GDM, a family history of type 2 diabetes mellitus (T2DM), and polycystic ovarian syndrome (1,2). In approximately 90% of women, metabolic perturbations are transient (1,2). However, some women progress to T2DM post-partum, with ongoing endothelial inflammation, early atherosclerosis, increased coagulation, insulin resistance, central adiposity, metabolic syndrome (MetS), atherogenic dyslipidaemia and cardiovascular (CV) complications (3-7).

During pregnancy, maternal hyperglycaemia must be avoided by all means (8-10). Thus, pharmacotherapy of GDM for tight glycaemic control is needed to reduce foetal adverse outcomes (11-13). Among oral antidiabetic agents, biguanides and sulfonylureas (SUs) have been used in GDM, but they have never gained wide acceptance (13). The most used SU in GDM is glyburide (12), but insulin is the mainstay of treatment (13,14). SUs are more effective for post-prandial hyperglycaemia and their plasma concentrations are approximately 50% lower in pregnant women than in non-pregnant patients (15). Second-generation SUs pass through the placenta, but it is not clear if placental transfer increase risk of foetal hypoglycaemia and macrosomia (16,17).

In this context, the multicentre study by Sénat *et al.* (18) has compared glyburide with subcutaneous insulin in GDM in terms of perinatal complications. No significant between-group differences were found in the rates of macrosomia,

hyperbilirubinaemia, admission to the neonatal intensive care unit, or respiratory distress syndrome (18). However, the glyburide group exhibited increased rates of neonatal hypoglycaemia (18). This is in agreement with the latest meta-analysis (19), as well as other recent studies (20,21).

Based on this new study (18), it appears that glyburide is non-inferior to insulin in preventing perinatal complications, should an oral agent be needed. Nevertheless, there are some limitations to consider (18). First, there was no cross-over design, which would have increased the impact of findings. Secondly, this study used a neonatal criterion as the primary outcome, which was different from other works (19-21), rendering comparisons more difficult.

In conclusion, interesting though the new data may be (18), they do not overall encourage preferring SUs over insulin in GDM. Thus, insulin remains the first-line treatment (13). However, given the easiness of using oral agents, additional trials with SUs in GDM are warranted.

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