Gestational diabetes affects an estimated 20% of pregnant women during the third trimester. Untreated, this condition is associated with fetal macrosomia and increased rates of perinatal death and complications. The hallmark of therapy for gestational diabetes is a low-carbohydrate diet and, when needed, injectable insulin.

Studies have shown that tight control of maternal glucose levels is associated with favourable pregnancy outcomes. Tight control, however, is hampered by poor compliance due to both the high level of discipline demanded from patients and the prohibitive cost of insulin and injection paraphernalia. It is fair to assume that women in developing countries and poor women in developed countries can rarely afford such a regimen.

The main objection to using oral hypoglycemics for gestational diabetes is that they cross the human placenta and can cause hyperinsulinism in unborn babies and subsequently life-threatening neonatal hypoglycemia. This has led to sweeping avoidance of this class of drugs during the third trimester.

Two studies by Elliott and associates and Langer and colleagues, however, changed people’s minds on this issue. Ten years ago, these researchers conducted placental perfusion studies that showed that the oral hypoglycemic glyburide does not cross the human placenta in clinically relevant amounts. Subsequently, they conducted a trial in which they randomized more than 400 women with gestational diabetes to receive either injectable insulin or oral glyburide. The two regimens were similarly effective in treating the condition, had similar rates of birth defects and neonatal morbidity, and resulted in similar birth weights. Glyburide did not cause
neonatal hypoglycemia. Umbilical cord levels of the drug were undetectable, and maternal levels were within the therapeutic range, further confirming results of the in vitro perfusion studies.

Although it is now 3 years later, I am unaware of any study that has repeated this protocol. Motherisk callers report that, while glyburide is not yet offered in most academic centres, more and more community practitioners are using it. Moreover, postmarketing registries in Europe and South America have not revealed higher fetal or neonatal risks. Glyburide is a cheap oral medication that circumvents the problems of patient compliance with insulin.

The mechanisms preventing glyburide from crossing the human placenta are not completely understood. A combination of very high protein binding (more than 99.8%) and a short elimination half-life might partially explain it. Motherisk is now investigating the hypothesis that glyburide, being a substrate for the placental p-glycoprotein carrier system, might be actively pumped from baby to mother.

It is also important to note that a study just completed by the Motherisk Program showed that glyburide, when used at the recommended dose, did not to cross into breast milk.

References