

## **NZSSD EXPERT OPINION**

### **Comment on the MiG Trial**

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Until recently, oral hypoglycaemic agents were not used in pregnancy for the management of gestational diabetes (GDM) because of concerns about their safety and efficacy. A randomized controlled trial published in 2000 demonstrated that glibenclamide could be safely used in pregnancy<sup>1</sup>. Although it possesses some theoretical advantages over glibenclamide, there was no similar trial evidence for metformin. The MiG Trial (Metformin in Gestational Diabetes)<sup>2</sup> examined whether metformin treatment for GDM could provide equivalent outcomes to insulin treatment.

751 women with GDM at 20-33 weeks gestation were randomized to open label treatment with metformin (titrated up to 2.5g/day - with supplemental insulin, if required, to reach glycaemia goals) or to insulin treatment alone. The primary outcome measure was a composite score of a number of neonatal morbidities: hypoglycaemia (<2.6mmol/l), respiratory distress, need for phototherapy, birth trauma, 5 min Apgar score <5, or premature delivery (<37 weeks). The study was led from Auckland, where most of the patients were recruited.

Metformin was well tolerated and adherence to treatment was good. The two groups achieved similar glycaemic control. There was no difference in the main outcome measure between subjects allocated to metformin and those allocated to insulin, and there were similar numbers of adverse events in the two groups. Women using metformin gained an average 1.6kg less weight from enrolment to term, and a questionnaire assessing the acceptability of treatment indicated that most women would be happy to take metformin again in subsequent pregnancies.

46% of women allocated to metformin needed supplemental insulin. Not unexpectedly, those needing supplemental insulin tended to be fatter and more hyperglycaemic at presentation. Metformin treatment, which was continued in patients needing supplementary insulin, appeared to have a modest sparing effect on insulin dose requirements.

The results of the MiG study indicate that metformin can be safely used in the management of GDM, but that it is less likely to be successful as monotherapy in women with higher blood glucose levels. It would be useful to see additional data on the probability of needing supplementary insulin in relation to particular levels of glycaemia at presentation. This would enable clinicians and patients to assess soon after diagnosis the likelihood of any individual women needing insulin. Although the proportion of women allocated to oral hypoglycaemic agents that needed supplementary insulin was significantly greater in the MiG trial than in the glibenclamide trial<sup>1</sup> (46% vs 4%), the women in the MiG study had higher average fasting blood glucose levels and were recruited later in pregnancy than in the latter study.

1. Langer O, Conway DL, Berkus MD, Xenakis EM, Gonzales O. A comparison of glyburide and insulin in women with gestational diabetes. *N Engl J Med* 2000; 343: 1134-1138.
2. Rowan JA, Hague WM, Gao W, Battin MR, Moore MP; MiG Trial Investigators. Metformin versus insulin for the treatment of gestational diabetes. *N Engl J Med* 2008; 358: 2003-2015.