

Metformin in pregnancy

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Metformin is a biguanide oral hypoglycaemic agent whose place in the management of type II diabetes mellitus is well established. Its use for type II diabetes in pregnancy and gestational diabetes (GDM) has been controversial.

It seems a logical treatment option, but it does cross the placenta and there have been concerns about possible adverse fetal outcomes. The mainstay of management of GDM remains diet, exercise and insulin therapy. However, metformin is a valid addition/alternative

to insulin therapy and may offer some advantages in terms of avoiding maternal weight gain and hypoglycaemia.

Metformin acts by reducing insulin resistance through various mechanisms. These include a reduction in hepatic glucose production, decreased absorption of glucose and increased peripheral uptake and utilisation of glucose. Serious side effects are rare. Common side effects include abdominal bloating, diarrhoea, indigestion and nausea. However, metformin is generally well tolerated.

The first prospective randomised controlled trial, *Metformin Versus Insulin for the Treatment of Diabetes in Pregnancy* published in 2008¹, showed that metformin was not associated with increased perinatal complications compared to insulin. This study included 751 women with gestational diabetes and used doses of up to 2500mg daily. Metformin was found to be safe for mother and infant and follow-up studies in the offspring are awaited. Metformin had the obvious advantage of being in tablet form rather than injections and women preferred metformin over insulin. In the last few years, the use of metformin in pregnancy has become more widespread with positive outcomes.²

The Australasian Diabetes in Pregnancy Society currently does not recommend the use of metformin in pregnancy. However, their position statement is up for review later in 2010. British guidelines do include metformin as an adjunct or alternative to insulin.³ We believe that there is a definite role for metformin in the management of gestational diabetes and the following scenarios are provided as examples.

A 32-year-old woman with polycystic ovarian syndrome (PCOS) and impaired glucose tolerance has been trying to conceive for three years. She recently started metformin 500mg bd and then finds out she is six weeks pregnant. She wonders what to do now with this medication.

- Metformin has been extensively studied in the PCOS population, where there is a wealth of safety data showing no increased teratogenic effects.⁴
- Metformin decreases the rate of miscarriage in PCOS.
- Metformin in PCOS reduces insulin resistance and can return the patient to ovulatory status.
- Good blood sugar control in early pregnancy is vital in order to reduce the risk of fetal anomaly.
- In this case, metformin should be continued.

A 25-year-old woman is screened for gestational diabetes at 28 weeks gestation and her two-hour blood sugar level (BSL) is 10mmol/L. She monitors her BSLs for one week and they are all slightly over target. She is advised to take insulin, however, is very

reluctant to do so as she has a needle phobia. She asks if there is any alternative. Is metformin a reasonable option?

- Metformin is a reasonable option if the patient refuses insulin.
- The patient must be counselled that up to 50 per cent of women will require insulin as well to achieve good control.¹
- The patient can be reassured that there is now data showing that metformin is safe in pregnancy.¹
- The only contraindication for use of metformin is presence of fetal growth restriction.²

A 38-year-old type 2 diabetic woman falls pregnant unexpectedly. She is taking metformin 1g bd, perindopril 5mg daily, atorvastatin 40mg daily and gliclazide MR 60mg daily. Her GP tells her to stop taking all of her medication immediately. Is this appropriate?

- Metformin should be continued while awaiting specialist review.⁵
- It is important that any change in therapy occurs without deterioration in glycaemic control in early pregnancy. Stopping metformin may result in greater teratogenic risk by exposing the fetus to high blood sugar levels.⁵
- ACE inhibitors/statins/sulphonylureas should be ceased.

A 29-year-old woman with type 2 diabetes and obesity has been taking insulin and metformin during pregnancy and delivers a healthy baby boy at 38 weeks. She wants to breastfeed but is concerned about the risk of breastfeeding with metformin.

- The dose of metformin in breast milk is much less than the usual ten per cent level of concern and women can be reassured that it is unlikely to have any effect on their baby.^{6,7}
- In particular, because of the mechanism of action of metformin, there is no risk of hypoglycaemia as opposed to drugs which stimulate insulin secretion, such as sulphonylureas.
- Maintenance of normal blood sugar while breastfeeding is important to reduce the risk of obesity in the child.

A 32-year-old woman has gestational diabetes and is told that this means she will have to be induced at 38 weeks if she needs insulin. Her sugars are high, the baby is macrosomic and her insulin requirements are now several hundred units a day despite maximum efforts.

- Metformin reduces insulin resistance and may help to control this patient's blood sugar and reduce her insulin requirements.
- Induction prior to 38 weeks may be necessary in this patient.

Although not a first-line drug, metformin has a definite role to play in the management of gestational and type II diabetes in pregnancy.

References

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