Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

GLIBENCLAMIDE AND METFORMIN VERSUS STANDARD CARE IN GESTATIONAL DIABETES (GRACES) – A FEASIBILITY OPEN LABEL RANDOMISED TRIAL

Researchers

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Aim

Metformin is widely used to treat gestational diabetes (new onset diabetes in pregnancy), but a significant proportion of women still have high blood sugar levels and require additional drug treatment. We aimed to determine recruitment rate and participant throughput in a randomised trial of glibenclamide compared with standard therapy insulin (both in addition to maximum tolerated metformin) for the treatment of gestational diabetes.

Project Outline/Methodology

We carried out an open label feasibility study in five antenatal clinics in Scotland. Pregnant women ≥ 16 weeks or ≤ 36 weeks' gestation with gestational diabetes and failing to achieve adequate blood sugar control on metformin monotherapy were randomised to additional glibenclamide or insulin therapy. The primary outcome was the recruitment rate. We also explored feasibility with uptake, retention, adherence, safety, glycaemic control, participant satisfaction and clinical outcomes.

Key Results

Records of 197 women with gestational diabetes were screened and 23 women were randomised to glibenclamide (n=13) or insulin (n=10).

Mean (SD) recruitment rate was 0·39 (0·62) women/centre/month. From this we estimate that a large randomised trial of glibenclamide compared with insulin (assuming a sample size of between 500 and 800) would require 30-60 centres recruiting for 3 years.

9/13 (69·2%, 95% CI 38·6-90·9%) women adhered to glibenclamide and all provided outcome data (100% retention). We showed significantly greater frequencies of excursions in blood glucose below 3·5 mmol/L in the glibenclamide group compared to the insulin group. Women's preference for oral therapy was not universal, with 45% of all participants either expressing no preference or preferring insulin.

Conclusions

A large randomised controlled trial comparing glibenclamide or insulin in combination with metformin, in women with GDM who are failing to achieve adequate glycaemic control would be feasible, but may not show equivalence of glycaemic control compared with current treatment with metformin and insulin. The combination of metformin and glibenclamide should be reserved for women with GDM with true needle phobia or inability to use insulin therapy.

What does this study add to the field?

Both metformin and glibenclamide are widely used as monotherapy for treatment of gestational diabetes and their use is endorsed by national guidelines including NICE and SIGN. The two drugs are commonly taken in combination in people with type 2 diabetes who are not pregnant. This is the first study to use the two drugs taken in combination in pregnancy.

Implications for Practice or Policy

With increasing numbers of women being diagnosed with GDM in Scotland it is important to identify cost-effective strategies to optimise care. Our study suggests that the current therapeutic pathway of adding insulin to metformin if metformin therapy is failing to achieve adequate glycaemic control should continue. The lack of adverse effects in our study suggests that the combination of metformin and glibenclamide may be considered as treatment option for individual women with GDM who are failing metformin monotherapy, if there is careful monitoring of glycaemic control. Such an option may be useful for women with a needle phobia, women with an inability to use insulin therapy or where insulin is unavailable.

Where to next?

The research team has formed a strong collaboration through working on this project and plan to work together on a new study in the field of diabetes and pregnancy with a focus on early diagnosis and treatment of gestational diabetes.

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