Therapeutic management, delivery, and postpartum risk assessment and screening in gestational diabetes


CRD summary
This review assessed treatment, delivery options and subsequent testing for type-2 diabetes for women with gestational diabetes. The authors concluded that there was insufficient evidence to recommend insulin alternatives or to formulate delivery guidelines and the 75-gm OGTT test should be retained for post-partum testing. This was a well-conducted review. The conclusions reflected the limited evidence accurately and are likely to be reliable.

Authors' objectives
Identified objectives were: to determine the efficacy and safety of oral diabetes agents; to assess the evidence for elective caesarean at term in gestational diabetes compared with attempted vaginal delivery; to assess risk factors for gestational diabetes (not included in this abstract); and to determine the performance characteristics of tests for diagnosing type 2 diabetes following pregnancy in patients with a history of gestational diabetes.

Searching
MEDLINE (from 1950), EMBASE (from 1974), the Cochrane Central Register of Controlled Trials (Issue 1, 2007), and CINAHL (from 1982) were searched to January 2007. Thirteen relevant journals were handsearched from August 2006 to January 2007. References from eligible studies were checked. Search terms were reported in an online appendix. Only studies published in English in peer-reviewed journals were eligible for inclusion in the review.

Study selection
Studies were required to have at least 90 per cent of the sample diagnosed with gestational diabetes or to present a separate analysis of patients with that diagnosis. Diagnosis of gestational diabetes was required to be based on either a three-hour, 100-gm oral glucose tolerance test (OGTT) or a two-hour 75-gm OGTT. A range of maternal and neonatal outcomes were eligible for inclusion for the efficacy and safety review questions, including mode of delivery and mortality and morbidity. The assessment of diagnostic accuracy required that sensitivity, specificity or reproducibility be assessed. Eligibility criteria for the efficacy and safety assessment of oral diabetes agents were randomised controlled trials (RCTs) or observational studies that compared two types of treatment for gestational diabetes. Observational studies that used diet as the comparator were excluded.

Included studies were RCTs and cohort studies for the efficacy and safety questions and cohort studies for the diagnostic question. Different fasting blood glucose (FBG) levels were assessed in diagnostic studies.

Two reviewers independently assessed the studies for inclusion in the review. Differences were resolved through consensus adjudication.

Assessment of study quality
Trials were assessed using criteria based on the Jadad scale, including randomisation, blinding and reporting of withdrawals and dropouts. Observational studies were assessed using elements of the Standards for Reporting of Observational Studies (STROBE) checklist. Diagnostic studies were assessed using elements of the Standards for Reporting of Diagnostic Accuracy (STARD) initiative. Two independent reviewers performed the assessment.

Data extraction
Data were extracted into standard data collection forms by one reviewer, checked and re-entered by a second reviewer. A random sample of data extraction was also assessed by a lead investigator and by other researchers. Meetings were used to resolve differences and problems. Data on variables including infant birth weights were extracted as means and measures of variance.

Methods of synthesis
Meta-analyses using the DerSimonian and Laird random effects model were performed where three or more studies
with sufficient homogeneity were available. Weighted mean differences (WMDs) were calculated for continuous outcomes. Statistical heterogeneity was assessed using $\chi^2$ and the $I^2$ statistic. When meta-analysis was not possible a narrative synthesis was presented.

**Results of the review**

Twenty nine studies were included in the three review questions considered in this abstract: nine RCTs and 20 cohort studies. The quality of the included studies was considered to be generally low.

**Efficacy and safety of diabetes agents** (eight RCTs, five cohort studies and around 2,000 patients): three RCTs found no difference in maternal glucose control or rates of caesarean section between insulin and glyburide groups individually and when pooled showed no significant difference in infant birth weight. One RCT found no difference in the proportions of infants with hypoglycemia, but a second found a significantly higher percentage in the glyburide group compared with the insulin or acarbose groups ($p = 0.006$). Two RCTs compared insulin lispro with insulin and found no differences in caesarean rates or neonatal outcomes between the groups. One RCT found higher levels of hypoglycemia ($p = 0.002$) and hyperbilirubinaemia ($p = 0.002$) in a twice daily insulin group compared with a four times daily group. A final RCT found lower rates of macrosomia ($p = 0.005$) and lower birth weights ($p = 0.002$) in an insulin plus dietary management group compared with a diet alone group. Results of observational studies were also reported.

**Evidence for elective caesarean** (one RCT, seven cohort studies): the single RCT found that induction at 38 weeks gestation reduced birth weight ($p < 0.01$) and rate of macrosomia ($p = 0.05$ or $0.02$ depending on definition) compared to expectant management, but did not alter other outcomes including the caesarean section rate. This finding was replicated in two cohort studies. No firm conclusions could be drawn from the remaining low quality observational studies, which examined a variety of delivery protocols.

**Test for type 2 diabetes performance** (eight cohort studies of 10 test evaluations): six of the eight studies used a reference standard which is no longer recommended for the two-hour 75-gm OGTT (FBG values above 7.0 mmol/L) and all studies had methodological flaws. Sensitivity of the studies was considered to be unpredictable, varying from 46 per cent to 89 per cent (three studies), although the specificity was high with an FBG threshold over 7.0 mmol/L. Results for reproducibility were not reported.

**Authors' conclusions**

There was insufficient evidence to determine the effectiveness of alternatives to insulin for gestational diabetes, but use of such alternatives was unlikely to result in maternal or foetal adverse events. There was insufficient evidence for the development of guidelines for elective induction of labour or caesarean section in women with gestational diabetes. There was insufficient evidence to justify recommending alternatives to the 75-gm OGTT test for detection of type 2 diabetes in women with gestational diabetes.

**CRD commentary**

The review question and the inclusion criteria were clear. The authors searched a number of databases and other relevant sources, but their decision to limit the review to peer-reviewed articles published in English may have led to the introduction of publication and language biases and the omission of some relevant studies. The authors reported using appropriate methods to minimise bias and error in all aspects of the review process. Study validity was appropriately assessed and used in interpreting the results of the review. The decision to use limited meta-analysis combined with narrative synthesis was appropriate in view of the varied nature of the included studies. The authors' cautious conclusions were an accurate reflection of the limited quality of the available evidence and were likely to be reliable.

**Implications of the review for practice and research**

Practice: the authors stated that clinicians should be aware that there was insufficient evidence to determine the effectiveness of alternatives to insulin for either birth weights or maternal glucose control, but use of such alternatives was unlikely to result in maternal or foetal adverse events. They also stated that there was insufficient evidence for the development of guidelines for elective induction of labour or caesarean section in women with gestational diabetes or to justify recommending alternatives to the 75-gm OGTT test for detection of type 2 diabetes in women with gestational diabetes.
Research: the authors stated that well-designed RCTs should be conducted to compare elective induction and caesarean delivery with expectant management in women with gestational diabetes. Observational studies in these areas should use consistent outcome measures and multivariate adjustment for confounders. Longitudinal studies should develop and employ standard protocols to increase follow-up rates and should collect data on relevant covariates which should be accounted for in the analyses. Studies should be undertaken to assess the sensitivity, specificity and reproducibility of screening tests for type 2 diabetes in the gestational diabetes population. In particular, studies should be undertaken in subgroups with a family history of type 2 diabetes or prior gestational diabetes. The impact of varying postpartum intervals on test performance and reproducibility should also be investigated.

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