Effects of treatment in women with gestational diabetes mellitus: systematic review and meta-analysis

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CRD summary
This well-conducted systematic review aimed to determine the benefits and harms of specific treatments for women with gestational diabetes mellitus. The authors concluded that treatment appeared to lower the risk of some perinatal or neonatal complications, but that insufficient data were available to draw conclusions on possible long-term effects of treatment. These conclusions are likely to be reliable.

Authors' objectives
To determine the benefits and harms of specific treatments for women with gestational diabetes mellitus.

Searching
MEDLINE, EMBASE, AMED, BIOSIS Previews, CCMed (Current Contents Medicine), CINAHL, CDMS, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, DARE, HTA, NHS EED, HECLINET (Health Care Literature Information Network), Journals@Ovid Full Text, SciSearch, publishers' databases and the reference lists of relevant secondary literature were searched up to October 2009. Further details of the search strategy were reported to be available via the Institute for Quality and Efficiency in Health Care website.

Study selection
Randomised controlled trials (RCTs) that compared specific treatment for gestational diabetes with usual care, or compared 'intensified' specific treatment with 'less intensified' specific treatment, for pregnant women with an impairment of their glucose tolerance (based on the results of an oral glucose tolerance test), were eligible for inclusion in the review. Trials had to assess at least one outcome from a list of several efficacy and safety outcomes, including mortality, complications and adverse events.

Participants in the included trial groups had an average age ranging from 26 to 33 years; the average gestation at trial entry was between 26 and 32 weeks, where stated. The average body mass index of participants ranged from 21 to 38, where stated. Ethnicity of participants varied.

Interventions that were compared with usual care in the included trials were diet, insulin, or diet plus insulin. Interventions assessed at different intensities included one or more of the following: insulin, metformin, glyburide, diet, physical activity, blood glucose self-monitoring, intensive counselling and monitoring, foetal monitoring, blood glucose self-control, blood glucose control at visits, and telemonitoring. All trials comparing interventions with usual care used a two-step approach for selecting participants (glucose challenge test/screening for risk factors and oral glucose tolerance test).

Two reviewers independently selected the studies and disagreements were resolved by discussion or a third reviewer.

Assessment of study quality
Trial quality was assessed based on the adequacy of randomisation, allocation concealment, blinding of outcome assessors, comparability of participants between groups at baseline, and handling of missing data, such as withdrawals or drop-outs.

Two reviewers independently assessed quality and disagreements were resolved by discussion or a third reviewer.

Data extraction
Two reviewers independently extracted data on the number of events in the intervention and control groups, and odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.
Methods of synthesis
Trials were divided into two groups: those that compared specific treatment with usual care; and those that compared different intensities of specific treatment. Odd ratios were combined for outcomes within each group using the DerSimonian and Laird random-effects model, except in the case of rare events (less than 1%), when the Peto one step method was used. Heterogeneity between trials was assessed using the $X^2$ test and I² statistic; when heterogeneity was significant ($P<0.2$), the pooled estimate was not reported.

Results of the review
Nineteen RCTs were eligible for inclusion in the review, but one RCT was excluded because of discrepancies between publications, preventing data interpretation. Therefore, 18 RCTs were included in the review, five that compared specific treatment with usual care (n=2,999 participants) and 13 that compared different intensities of specific treatment (n=1,934 participants). Only two trials in each group were classed as having a low potential for study bias.

Specific treatment versus usual care (five RCTs): Shoulder dystocia was significantly less common in the intervention group than the usual care group (OR 0.40, 95% CI 0.21 to 0.75; two RCTs), as was pre-eclampsia ($p=0.02$; one RCT). Macrosomia was also significantly less common in the intervention group (OR 0.38, 95% CI 0.30 to 0.49; four RCTs), as was the number of 'large for gestational age' infants (OR 0.48, 95% CI 0.38 to 0.62; four RCTs). There were no statistically significant differences between the intervention and usual care groups in the rate of caesarean sections, birth trauma, development of type 2 diabetes in the mother, perinatal or neonatal mortality, number of small for gestational age infants, or number of newborn infants requiring admission to a neonatal intensive care unit. None of the RCTs reported on maternal deaths or long-term effects on the children. No adverse effects from treatment were reported.

Intensive versus less intensive specific treatment (13 RCTs): Shoulder dystocia was significantly less common in patients receiving more intensive treatment (OR 0.31, 95% CI 0.14 to 0.70; five RCTs). For other reported outcomes, either no significant differences were found or trial heterogeneity precluded meta-analysis.

Authors' conclusions
Specific treatment for gestational diabetes, mostly consisting of treatment to lower blood glucose concentration alone or with special obstetric care, appeared to lower the risk of some perinatal or neonatal complications. Insufficient data were available to draw conclusions on possible long-term effects for mothers or their children.

CRD commentary
The review addressed a clear question and was supported by well defined inclusion criteria. A large number of databases were searched in order to identify relevant studies. The reviewers used appropriate methods to reduce the potential for reviewer error and bias in selecting studies, performing validity assessment and data extraction.

Validity of the included trials was assessed using appropriate criteria and the results were presented. The majority of included trials had a high potential for study bias. However, the two better quality trials, comparing treatment with usual care, accounted for almost two thirds of all participants, and were included in all of the meta-analyses for which significant results were found.

Adequate details of the included trials were presented. Appropriate methods appear to have been used to combine the results of trials and investigate statistical heterogeneity, which was taken into account when deciding whether to present pooled results.

This was a well-conducted systematic review and the authors' conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that decisions regarding treatment for gestational diabetes should take into account that the evidence of benefit is derived from trials for which women were selected with a two step strategy (glucose challenge test/screening for risk factors and oral glucose tolerance test). They also recommended that pregnant women should be informed about the possible benefits of gestational diabetes screening, as well as the uncertainties concerning
Research: The authors stated that studies comparing different screening strategies for gestational diabetes are required, in order to allow a proper assessment of the balance of benefits and harms of screening.

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