Safety of insulin glargine use in pregnancy: a systematic review and meta-analysis
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CRD summary
The review concluded there was no documented evidence for increased adverse foetal outcomes from insulin glargine in pregnancy when compared to NPH insulin and that the results increased the choices for women who required basal insulin therapy in pregnancy. These conclusions appear to be over-optimistic as they are based on results from cohort studies which may not be reliable.

Authors' objectives
To determine the foetal safety of insulin glargine use compared with NPH (neutral protamine Hagedorn) insulin therapy in the treatment of diabetes in pregnancy.

Searching
MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science were searched from 1980 to June 2010 for studies in English; search terms were reported. Reference lists of review articles were searched. Authors of abstracts were contacted to obtain full study reports.

Study selection
Eligible studies had to compare insulin glargine with another form of insulin in pregnant women with either gestational or pre-gestational diabetes. Case-control, cohort and randomised controlled trials (RCTs) were the eligible study designs. Studies had to report foetal outcomes for both groups and clearly specify initiation or duration of treatment.

Where reported, most women had pre-gestational diabetes and most had type 1 diabetes (a small proportion had type 2). Group mean maternal ages ranged from 22 to 35 years. Mean pre-gestational duration of diabetes ranged from 4.5 to 16.8 years. All studies compared insulin glargine with NPH insulin; doses varied in studies that reported dose.

It appeared that two reviewers independently selected studies. Disagreements were resolved by discussion.

Assessment of study quality
Study quality was assessed by two reviewers using the Strengthening of the Reporting of Observational Studies in Epidemiology Criteria assessment tool.

Data extraction
Data were extracted to calculate risk ratios and mean differences with 95% confidence intervals.

Two reviewers independently extracted data. Disagreements were resolved by discussion.

Methods of synthesis
Meta-analyses were performed to calculate pooled risk ratios or weighted mean differences using a random-effects model. Heterogeneity was assessed using the Cochran Q test and the I² statistic.

Results of the review
Eight cohort studies reported on 702 women. Seven studies were retrospective and one was prospective. Results of study quality assessment were not reported.

There were no statistically significant differences in occurrence of foetal outcomes studied when comparing insulin glargine with NPH insulin. The foetal outcomes analysed were: large for gestational age infants, macrosomia, neonatal hypoglycaemia, neonatal intensive care unit (NICU) admissions, shoulder dystocia, congenital anomalies, preterm delivery, perinatal mortality, hyperbilirubinaemia, respiratory distress, infant birth weight and gestational age at birth.

Heterogeneity was not observed except for mean difference in gestational age at birth (no further details provided).
Authors' conclusions
No evidence was documented for increased adverse foetal outcomes with the use of insulin glargine in pregnancy compared to use of NPH insulin. These results increased the choices for women who required basal insulin therapy in pregnancy.

CRD commentary
The review addressed a clear question and was supported by reproducible inclusion criteria. Attempts to identify relevant studies were made by searching electronic databases and checking references. The restriction to studies in English meant that relevant studies may have been missed and the review may have been subject language bias. It appeared that suitable methods were used during the review to minimise risks of reviewer error and bias affecting the results.

Sufficient study details were provided. Appropriate methods were used to pool data and assess heterogeneity. The authors reported that study quality was assessed but no results were presented; they acknowledged the considerable limitations of using data from retrospective cohort studies.

The authors' overall conclusions appear to be over-optimistic as their reliability is uncertain.

Implications of the review for practice and research
Practice: The authors stated that their results will potentially improve the options for women with diabetes in pregnancy who wish to achieve excellent control of their glucose levels without fear of adverse foetal complications.

Research: The authors stated a need for future studies to adopt a randomised controlled trial design.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.