Expectant management of severe preeclampsia remote from term: a structured systematic review

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CRD summary
This review concluded that observational evidence suggested that expectant management of early severe pre-eclampsia prolonged pregnancy by one to two weeks, had low maternal risk and improved neonatal outcomes compared with interventionist management. The findings supported the limited randomised data available. Due to the authors’ limited search and biases associated with observational evidence these conclusions require some caution in interpretation.

Authors’ objectives
To evaluate observational evidence on clinical outcomes associated with expectant versus interventionist care of severe pre-eclampsia remote from term.

Searching
MEDLINE was searched from 1980 to July 2007. Search terms were reported. The reviewers checked personal files and reference lists of retrieved articles, reviews in the Cochrane Database of Systematic Reviews, other review articles and guidelines. The search was limited to articles published in English or French. Abstracts were excluded.

Study selection
Observational studies that comprised at least six women with severe pre-eclampsia remote from term (<34 weeks at presentation or delivery) who received expectant or interventionist care were eligible for inclusion; relevant maternal or perinatal clinical outcomes had to be reported. Randomised controlled trials, case reports and surveys were excluded.

Most participants in the included studies had severe pre-eclampsia or HELLP syndrome (haemolysis, elevated liver enzyme levels and a low platelet count) at less than 34 or less than 28 weeks; gestational age at recruitment ranged from 20 to 36 weeks. In most cases women were recruited for expectant care only after a successful stabilisation period. Expectant care was described in half the studies as good. It usually involved management of blood pressure and use of magnesium sulphate and/or antenatal corticosteroids; indications for delivery varied (see review for details). Interventionist care usually involved antihypertensives, magnesium sulphate, corticosteroids and planned delivery within 48 hours. The review included all relevant clinical outcomes reported by the primary studies, with the exception of subjectively defined outcomes (worsening maternal condition, renal failure and oliguria). Potential predictors of adverse outcomes were reported. Most studies were conducted in single tertiary care centres in developed countries.

The authors did not state how the papers were selected for the review.

Assessment of study quality
Study validity was assessed using a modified version of the Newcastle-Ottawa Quality Assessment Scales for case-control and cohort studies. No details of items assessed were reported.

The authors did not state how many reviewers performed the assessment.

Data extraction
Event rates were extracted for dichotomous outcomes and mean or median values for continuous outcomes, with interquartile ranges (IQR: 25th and 75th percentiles). For some outcomes the upper limit of the range was reported. Where studies included more than one study arm that received expectant care, the arms were included as separate cohorts.

Two reviewers extracted data independently. Disagreements were resolved by consensus. Study authors were contacted for more information on cohorts that potentially overlapped.
**Methods of synthesis**

Studies were combined by calculating the median event rate for dichotomous outcomes and the median of reported medians or means for continuous outcomes, both with the IQR. Multivariate analysis of methodological and clinical differences between studies was planned, but not conducted due to insufficient data on specific variables. The effect of study setting was investigated by subgroup analyses, which compared developed world studies versus Dutch and versus developing world studies (where the gestational age for foetal viability was generally higher).

**Results of the review**

Seventy-two studies were included in the review \((n=5,672, \text{range six to 975})\). Within these were 19 RCTs and 20 prospective and 19 retrospective cohort studies and one study of unknown design which reported on clinical outcomes in 63 distinct cohorts of women. The median quality score ranged from 5 to 6.5 out of 9 points. Thirteen studies examined prognostic factors.

In women with severe pre-eclampsia at less than 34 weeks, expectant care \((39\text{ cohorts, } n=4,650)\) prolonged pregnancy by one to two weeks. Serious maternal complications were uncommon, apart from hypotension \((\text{upper limit 30\%})\) and recurrent severe hypertension \((\text{upper limit 38\%})\) associated with blood pressure management.

In women with HELLP, expectant care \((12\text{ cohorts, } n=438)\) prolonged pregnancy by about five days. Severe complications were relatively common, especially recurrent severe hypertension. There were few data on maternal morbidity in interventionist cohorts for women with either severe pre-eclampsia or HELLP at less than 34 weeks. In women with severe pre-eclampsia at less than 28 weeks, expectant care \((6\text{ cohorts, } n=305)\) prolonged pregnancy by almost two weeks. Rates of maternal morbidity were similar in expectant and interventionist cohorts, although limited data suggested that rates of recurrent severe hypertension were more common with interventionist care.

No predictors of adverse outcomes were identified \((13\text{ studies})\).

Detailed results for these and other outcomes were reported in the review.

**Authors’ conclusions**

Observational evidence suggests that expectant management of early severe pre-eclampsia prolonged pregnancy by one to two weeks, had low maternal risk and improved neonatal outcomes compared with interventionist management. These findings supported the limited randomised data available.

**CRD commentary**

The objectives and inclusion criteria of the review were clear. The search was limited to two databases and was subject to limitations by language and publication status, so it was possible that some studies were missed. Data extraction was undertaken by two reviewers working independently; it was unclear whether similar steps were taken to minimise the risk of reviewer bias and error in the processes of study selection and validity assessment. An appropriate quality assessment tool was used, but the results of the assessment were not fully presented. The statistical techniques used to combine the studies were of questionable reliability because they gave equal weighting to each study and failed to allow for the differences in design and sample size across the various cohorts. The overall comparisons between expectant and interventionist care were indirect and highly prone to bias, since the cohorts that were compared may have differed in their risk of adverse outcomes. However, the review was well conducted in many respects and the review findings were supported by the randomised evidence cited by the authors. Due to the limited search and the biases associated with observational evidence the authors’ conclusions require cautious interpretation.

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

**Practice**: The authors stated that in developed countries women who presented with pre-eclampsia at least 34 weeks were not at increased maternal risk and had less risk of neonatal complications with expectant care than with interventionist care, particularly in the absence of HELLP syndrome. Women with HELLP should be offered antenatal corticosteroids and stabilised for 48 hours, which may facilitate delivery using regional rather than general anaesthesia. Pregnancy prolongation beyond 48 hours may not be beneficial. These findings should not be applied to women with pre-eclampsia at or near term.
Research: The authors stated that an adequately powered RCT was required to definitively establish whether expectant or interventionist care had the best maternal and neonatal outcomes for women with early severe pre-eclampsia.

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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.