High-dose vs low-dose oxytocin for labor augmentation: a systematic review
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CRD summary
The authors concluded that high-dose oxytocin for labour augmentation was associated with a decrease in caesarean section, shortened labour and a small increase in spontaneous vaginal delivery. As acknowledged by the authors, there were some issues over the quality of the included studies. High levels of variability across studies for some outcomes should be borne in mind.

Authors' objectives
To estimate the efficacy and safety of high-dose versus low-dose oxytocin for labour augmentation on the risk of caesarean section and on indicators of maternal and neonatal morbidity.

Searching
PubMed, EMBASE and The Cochrane Library were searched without language restrictions to January 2010. Search terms were reported. References of relevant articles were searched manually for additional studies.

Study selection
Randomised controlled trials (RCTs) that compared high-dose and low-dose oxytocin in pregnant women in spontaneous labour (without prior use of oxytocin) were eligible for inclusion. High dose was defined as an initial dose of at least 4mU/min and dose increments of at least 4mU/min. Low-dose protocols were defined as those with an initial dose ranging between 1mU/min to 4mU/min with increments of 1mU/min to 2mU/min. Eligible studies measured at least one of caesarean section, spontaneous vaginal delivery, operative vaginal delivery, duration of labour, hyperstimulation, postpartum haemorrhage, use of epidural analgesia, maternal blood transfusion, Apgar score and neonatal complications.

In half of the included studies active management of labour was compared with a more conservative approach to care, such as early administration of high-dose oxytocin compared to a delayed low-dose oxytocin regimen. In the other studies, contrast consisted of a simple comparison of high-dose to low-dose oxytocin for labour augmentation. High-dose regimens varied across trials with starting doses that ranged from 4mU/min to 10mU/min and maximum rates that ranged from 4mU/min to 90mU/min. Low-dose regimens commenced infusion at from 1mU/min to 4mU/min and maximum rates that ranged from 1mU/min to 31.7mU/min. Seven trials enrolled women who were in normal spontaneous labour at the time of randomisation and three trials enrolled women with established delays in labour progress. At randomisation mean cervical dilation ranged from to 2.9cm to 6.2cm. Half of the studies were conducted in USA and single studies were undertaken in Nigeria, New Zealand, Zimbabwe, Iran and UK.

Two reviewers independently selected studies for the review.

Assessment of study quality
Two reviewers independently assessed study quality based on Cochrane Handbook criteria (selection bias, performance bias, detection bias and attrition bias). Disagreements were resolved through discussion with a third reviewer.

Data extraction
Events for dichotomous outcomes were extracted to enable calculation of risk ratio (RR) and 95% confidence interval (CI); mean difference (MD) and 95% CIs were calculated for continuous outcomes.

Two reviewers independently performed the data extraction.

Methods of synthesis
Risk ratio or weighted mean difference (WMD), and 95% confidence intervals, were pooled in a meta-analysis using a Mantel-Haenszel fixed-effect model. Statistical heterogeneity between trials was assessed with $I^2$ and $X^2$. When $I^2$
exceeded 50%, random-effects models were used to pool outcomes. The number needed to treat (NNT) was calculated and results were stratified by type of comparison.

Results of the review
Ten RCTs (n=5,423 participants, range 40 to 1,915) were included. Most trials were conducted without blinding; oxytocin dosage was double-blinded in one trial.

High-dose oxytocin was associated with a moderate decrease in the risk of caesarean section (RR 0.85, 95% CI 0.75 to 0.97, NNT=50, I²=47%; 10 studies), a small increase in spontaneous vaginal delivery (RR 1.07, 95% CI 1.02 to 1.12, I²=58%; seven studies), a decrease in labour intervals (WMD -1.54 hours, 95% CI -2.44 to -0.64, I²=96%; five studies) and less chance of labour duration exceeding 12 hours (RR 0.46, 95% CI 0.30 to 0.70, I²=53%; three studies).

High-dose oxytocin was associated with increased hyperstimulation (RR, 1.91, 95% CI 1.49 to 2.45, I²=35%; five studies), but did not result in increased maternal or neonatal morbidity.

Cost information
The average reduction in labour and delivery costs was estimated at US $210/patient (one study) for intravenous oxytocin administration with standard maternal and foetal monitoring and assuming that labour was shortened by 1.5 hours with high-dose oxytocin augmentation

Authors' conclusions
High-dose oxytocin for labour augmentation was associated with a decrease in caesarean section, shortened labour and a small increase in spontaneous vaginal delivery.

CRD commentary
The review question and supporting inclusion criteria were clearly stated. The literature search was adequate. There were no language restrictions. There were some attempts to identify unpublished data, which minimised the possibility of publication bias. All parts of the review were undertaken in duplicate, which minimised potential for reviewer error and bias. Study quality was assessed using appropriate criteria, but the results for each study were not fully reported. There was variability among studies and evidence of statistical heterogeneity for some comparisons, so statistical pooling of the studies may not have been appropriate. For some outcomes a fixed-effect model was used despite statistical heterogeneity.

This was generally a well-conducted review and the conclusions reflect the available data. As acknowledged by the authors, there were some issues over the quality of the included studies. High levels of variability across studies for some outcomes should be borne in mind.

Implications of the review for practice and research
Practice: The authors stated that women should be made aware of the potential beneficial effects of high-dose oxytocin augmentation on mode of delivery as well as its possible effects on comfort. Practitioners should consider maternal and foetal characteristics including medical history, parity and indicators of maternal and foetal well-being when planning oxytocin augmentation for labour management.

Research: The authors stated that large, simple double-masked trials were required to determine the safety, effectiveness, acceptability and cost implications of oxytocin augmentation.

Funding
Canada Research Chair from the Canadian Institutes of Health Research (CIHR); CIHR Strategic Training Initiative in Research in Reproductive Health Sciences; Fonds de Recherche en Sante du Quebec.

Bibliographic details
Wei SQ, Luo ZC, Qi HP, Xu H, Fraser WD. High-dose vs low-dose oxytocin for labor augmentation: a systematic
PubMedID
20451894

DOI
10.1016/j.ajog.2010.03.007

Original Paper URL
http://dx.doi.org/10.1016/j.ajog.2010.03.007

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Delivery, Obstetric; Dose-Response Relationship, Drug; Female; Humans; Labor, Induced; Labor, Obstetric; Oxytocics /administration & dosage; Oxytocin /administration & dosage; Pregnancy; Pregnancy Outcome: Randomized Controlled Trials as Topic; Time Factors

AccessionNumber
12010007375

Date bibliographic record published
26/01/2011

Date abstract record published
27/07/2011

Record Status
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.