Carbetocin for the prevention of postpartum hemorrhage: a systematic review

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CRD summary
This review evaluated the efficacy and safety of carbetocin for prophylactic management of the third stage of labour and concluded that it was probably as effective as oxytocin or syntometrine, but that further research is needed. Due to limitations in the review methods a cautious interpretation of the results is recommended.

Authors' objectives
To evaluate the efficacy and safety of carbetocin for preventing postpartum haemorrhage.

Searching
MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), DARE and Cochrane Review Methodology Database were searched up to April 2008 for studies in English, French, German and Dutch. Search terms were reported. References of eligible studies were searched.

Study selection
Clinical trials that compared carbetocin administered intravenously or intramuscularly as part of active management of the third stage of labour with placebo, oxytocin or a mixture of oxytocin and ergometrine were eligible for inclusion. Outcomes of interest were blood loss, uterine tone, amount and type of lochia, fundal position, adverse effects, vital signs, haemoglobin or haemocrit levels before delivery compared with 24 to 48 hours after delivery, need for additional uterotonic therapy and/or uterine massage and duration of the third stage of labour. Postpartum haemorrhage (PPH) was defined as blood loss 500mL or more and severe PPH as a loss of 1,000mL or more.

Included studies were of women who underwent vaginal deliveries (mostly singleton pregnancies) or scheduled caesarean sections under epidural or regional anaesthetic. Carbetocin was delivered intravenously as a 100μg bolus preceded or followed by saline solution and compared with a 2.5, 5 or 10 IU oxytocin bolus followed by a higher dose or saline infusion.

The authors did not report how many reviewers performed study selection.

Assessment of study quality
Study validity was not formally assessed, but studies were rated using levels of evidence from Oxford Centre for Evidence Based Medicine.

The authors did not report how many reviewers performed level of evidence rating.

Data extraction
Results for primary and secondary outcome measures were extracted.

The authors did not report how many reviewers performed data extraction.

Methods of synthesis
Results were presented as a narrative synthesis.

Results of the review
Five studies (n=1,163) were included: four randomised double-blind trials (n=1,045) and one retrospective cohort study (n=118). Four studies were classed as level 1b evidence (RCT with narrow confidence interval) and one as 2b (cohort study or low-quality RCT).
Carbetocin versus oxytocin (three studies): Two studies assessed women who underwent a scheduled caesarean section and found no statistically significant differences for blood loss, amount of lochia, uterine tone, vital signs, postpartum chemistry, fundal position, blood cell count, haemoglobin levels or adverse events. One study (n=635) reported a statistically significant reduction in need for additional uterotonic therapy (4.7% versus 10.1%, p<0.05) and a shorter delay between drug administration and adequate uterine contractions or additional uterotonic therapy (11 versus 120 minutes, p<0.001), but the other study (n=57) found no significant difference in additional uterotonic therapy. One study of vaginal delivery (n=160) reported a statistically significant reduction in the need for uterine massage (p=0.02), but no significant differences for any other outcomes. There were no significant differences for adverse events.

Carbetocin versus syntometrine (two studies): A retrospective cohort study (n=118) reported statistically significantly lower blood loss (mean loss 388mL versus 551mL), fewer women with a blood loss of 500mL or more (21.4% versus 43.5%) and lower haemocrit levels for carbetocin compared with syntometrine. The RCT (n=300) reported significantly fewer adverse events for carbetocin (nausea 1.3% versus 7.3%; vomiting 0.7% versus 6.7%; hypertension 0% versus 5.3% after 20 minutes), but an increase in tachycardia in the carbetocin group (32% versus 19%). The cohort study found fewer adverse events in the carbetocin group (numbers not reported).

Authors' conclusions
Carbetocin was probably as effective as oxytocin or syntometrine for prophylactic management of the third stage of labour, but more research was needed.

CRD commentary
This review had a clear question and specified inclusion criteria for interventions, participants and outcomes. Only two databases of primary research were searched and inclusion was restricted to studies reported in four languages, so publication and language biases were likely problems. It was unclear whether adequate systematic review methods were followed (such as more than one person performing study selection, validity assessment and data extraction) so error or bias may have occurred during the review. Studies were rated using levels of evidence that provided some indication of their quality, but a full validity assessment was not performed. Some of the reporting of the study results was limited and did not include relevant effect sizes. Due to limitations in the review methods a cautious interpretation of the results is recommended.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future studies should be large, have PPH reduction as the primary outcome and address potential cardiac side-effects.

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