Carbetocin versus oxytocin for prevention of postpartum haemorrhage: a randomised controlled trial

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Abstract

Background Postpartum haemorrhage (PPH) is the leading cause of maternal death worldwide. Prophylactic uterotonics are effective in reducing PPH, and the drug of choice is oxytocin. Carbetocin, a newer analogue of oxytocin, has a greater biological effect and longer half-life. It is also more heat-stable than oxytocin, which is of crucial importance to resource-poor settings. We compared the efficacy of carbetocin with oxytocin.

Methods In this randomised controlled trial in a tertiary maternity hospital in Mexico, pregnant women with at least one risk factor for PPH were randomly assigned by a central computer-generated list of random numbers in a 1:1 ratio with no masking either to carbetocin 100 µg as a single intravenous bolus or to oxytocin 20 IU as a 6-h infusion, both administered immediately after childbirth. The primary outcome was PPH with blood loss exceeding 500 mL. Secondary outcomes were the volume of blood loss, severe PPH (blood loss >1000 mL), change in haemodynamic and clinical variables within 24 h of childbirth, and the need for additional uterotonic treatment. Comparisons were done by intention-to-treat analysis. This trial is registered with Instituto Mexicano del Seguro Social (IMSS), number R-2011-3606-1.

Findings 1210 women were included with 602 assigned to carbetocin and 608 assigned to oxytocin. Blood loss exceeding 500mL was lower in women assigned to carbetocin than in women assigned to oxytocin (18·4% [111/602] *vs* 25·8 [157/208], relative risk [RR] 0·67, 95% CI 0·54–0·83; number needed to treat [NNT] 14, 95% CI 8–37). Mean blood loss was less with carbetocin than with oxytocin (366 mL [SE 7·8] *vs* 400 [7·6], p<0·001). The frequency of blood transfusion was similar in the two groups (1·7% [10/602] *vs* 2·6% [16/608]; RR 0·67, 95% CI 0·31–1·38). The frequency of severe PPH did not differ between the two groups (1·3% [8/602] *vs* 1·6% [7/608]; 1·15, 0·42–3·16). Fewer participants receiving carbetocin than receiving oxytocin required additional uterotonics (1·5% [9/602] *vs* 5·8% [35/608], adjusted RR 0·3, 95% CI 0·14–0·61), and fluid resuscitation (20·6% [124/602] *vs* 24·2% [147/608]; 0·77, 0·62–0·95). No significant difference in the haemodynamic variables was found.

Interpretation To our knowledge, this is the largest trial comparing carbetocin with oxytocin. An updated meta-analysis, combining the results from six randomised trials, including this study, found that carbetocin was associated with a reduction of PPH compared with oxytocin.

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The **full protocol** is available on request from IMSS

Contributors

SR-O, RPA, RSH, MC, FLC, and MCG conceptualised and designed the trial and data collection tools, monitored data collection for the whole trial, and recruited participants. SR-O and IG cleaned and analysed the data, and drafted and revised the abstract. AC revised the abstract and acts as guarantor.

Conflicts of interest

All authors have received financial support from Ferring Pharmaceuticals. SR-O has received speaking fees from Ferring Pharmaceuticals and has provided lectures and consultancy without funding to Schering-Plough, Ferring Pharmaceuticals, and MSD. AC has received funding from Ferring Pharmaceuticals and other pharmaceutical companies to attend conferences. The remaining authors declare that they have no conflicts of interest.