

Uterotonic drugs to prevent postpartum haemorrhage: a network meta-analysis

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Declared competing interests of authors: Ioannis Gallos, Metin Gülmezoglu, Justus Hofmeyr and Arri Coomarasamy have been involved in one or more previous or ongoing trials related to the use of uterotonics for the prevention of postpartum haemorrhage that were considered for inclusion in this review. Ferring Pharmaceuticals (Saint-Prex, Switzerland) and Novartis Pharmaceuticals UK Ltd (Surrey, UK) have supplied carbetocin and oxytocin to these studies. Ioannis Gallos, Metin Gülmezoglu, Justus Hofmeyr and Arri Coomarasamy have not participated in decisions regarding inclusion of these trials in this review or any tasks related to them such as data extraction or quality assessment. Arri Coomarasamy is involved in a World Health Organization-sponsored randomised controlled trial of carbetocin versus oxytocin, supported by Merck for Mothers (Merck & Co., Inc., Kenilworth, NJ, USA). Metin Gülmezoglu was involved in a large multicentre trial included in the review as part of the central co-ordination unit. As part of the central co-ordination unit, he is also involved in an ongoing World Health Organization-sponsored randomised controlled trial of carbetocin versus oxytocin supported by Merck for Mothers. Abi Merriel is part-funded by Ammalife (a UK-registered charity 1120236) and the Birmingham Women's NHS Foundation Trust. Harry Gee and Arri Coomarasamy are trustees of Ammalife. Jonathan Deeks is a member of the Health Technology Assessment (HTA) Commissioning Board and the HTA Efficient Study and Designs Board.

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Plain English summary

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Postpartum haemorrhage (PPH) is the most common reason why mothers die in childbirth worldwide. Although most healthy women can cope well with blood loss after birth, some do not, and this can pose a serious risk to their health and even life. To reduce blood loss after birth, the routine administration of a drug to contract the uterus (uterotonic) has become standard practice across the world. This research seeks to identify which is the most effective and cost-effective drug.

Different drugs have been used for reducing the occurrence of PPH. They include oxytocin, misoprostol, ergometrine, carbetocin, and combinations of these drugs, each with different effectiveness and side effects. The study synthesised the available evidence to compare all of these drugs and combinations thereof. After putting the results of all available comparisons together in a network, a ranking among them was calculated, and provided robust effectiveness and side-effect profiles for each drug and their associated costs.

The study included 137 randomised trials, involving a total of 87,466 women. The results suggested that ergometrine plus oxytocin, carbetocin and misoprostol plus oxytocin are the most effective strategies for preventing PPH and are more effective than the currently recommended drug, oxytocin. Each of these three strategies had almost 100% probability of being ranked first, second or third most effective. Oxytocin was ranked fourth with an almost 0% probability of being ranked in the top three. Ergometrine plus oxytocin and misoprostol plus oxytocin were the worst drug combinations for side effects, with carbetocin having the most favourable side-effect profile. Carbetocin could prevent approximately one further event of PPH out of three in comparison with oxytocin. However, existing carbetocin studies were small and of poor quality. There is need for a large high-quality study comparing carbetocin with the current standard treatment of oxytocin for the prevention of PPH. The cost analyses of the alternative drug strategies remain inconclusive.

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