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Oxytocin for preventing postpartum haemorrhage (PPH) in non-facility birth settings (Review) Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

# [Intervention Review]

# Oxytocin for preventing postpartum haemorrhage (PPH) in non-facility birth settings

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# ABSTRACT

#### Background

Postpartum haemorrhage (PPH) is the single leading cause of maternal mortality worldwide. Most of the deaths associated with PPH occur in resource-poor settings where effective methods of prevention and treatment - such as oxytocin - are not accessible because many births still occur at home, or in community settings, far from a health facility. Likewise, most of the evidence supporting oxytocin effectiveness comes from hospital settings in high-income countries, mainly because of the need of well-organised care for its administration and monitoring. Easier methods for oxytocin administration have been developed for use in resource-poor settings, but as far as we know, its effectiveness has not been assessed in a systematic review.

#### Objectives

To assess the effectiveness and safety of oxytocin provided in non-facility birth settings by any way in the third stage of labour to prevent PPH.

### Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register, the WHO International Clinical Trials Registry Platform (ICTRP), Clinical Trials.gov (12 November 2015), and reference lists of retrieved reports.

#### **Selection criteria**

All published, unpublished or ongoing randomised or quasi-randomised controlled trials comparing the administration of oxytocin with no intervention, or usual/standard care for the management of the third stage of labour in non-facility birth settings were considered for inclusion.

Quasi-randomised controlled trials and randomised controlled trials published in abstract form only were eligible for inclusion but none were identified. Cross-over trials were not eligible for inclusion in this review.

#### Data collection and analysis

Two review authors independently assessed studies for eligibility, assessed risk of bias and extracted the data using an agreed data extraction form. Data were checked for accuracy.

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# **Main results**

We included one cluster-randomised trial conducted in four rural districts in Ghana that randomised 28 community health officers (CHOs) (serving 2404 potentially eligible pregnant women) to the intervention group and 26 CHOs (serving 3515 potentially eligible pregnant women) to the control group. Overall, the trial had a high risk of bias. CHOs delivered the intervention in the experimental group (injection of 10 IU (international units) of oxytocin in the thigh one minute following birth using a prefilled, auto-disposable syringe). In the control group, CHOs did not provide this prophylactic injection to the women they observed. CHOs had no midwifery skills and did not in any way manage the birth. All other CHO activities (outcome measurement, data collection, and early treatment and referral when necessary) were identical across the control and oxytocin CHOs.

Although only one of the nine cases of **severe PPH (blood loss greater or equal to 1000 mL)** occurred in the oxytocin group, the effect estimate for this outcome was very imprecise and it is uncertain whether the intervention prevents severe PPH (risk ratio (RR) 0.16, 95% confidence interval (CI) 0.02 to 1.30; 1570 women (*very low-quality evidence*)). Similarly, because of the lack of cases of **severe maternal morbidity** (e.g. uterine rupture) and **maternal deaths**, it was not possible to obtain effect estimates for those outcomes (both *very low-quality evidence*).

Oxytocin compared with the control group decreased the **incidence of PPH (> 500 mL)** in both our unadjusted (RR 0.48, 95% CI 0.28 to 0.81; 1569 women) and adjusted (RR 0.49, 95% CI 0.27 to 0.90; 1174 women (both *low-quality evidence*)) analyses. There was little or no difference between the oxytocin and control groups on the rates of **transfer or referral of the mother to a healthcare facility** (RR 0.72, 95% CI 0.34 to 1.56; 1586 women (*low-quality evidence*)), **stillbirths** (RR 1.27, 95% CI 0.67 to 2.40; 2006 infants (*low-quality evidence*)); and **early infant deaths (0 to three days)** (RR 1.03, 95% CI 0.35 to 3.07; 1969 infants (*low-quality evidence*)). There were no cases of needle-stick injury or any other maternal major or minor adverse event or unanticipated harmful event. There were no cases of oxytocin use during labour.

There were no data reported for some of this review's secondary outcomes: manual removal of placenta, maternal anaemia, neonatal death within 28 days, neonatal transfer to health facility for advanced care, breastfeeding rates. Similarly, the women's or the provider's satisfaction with the intervention was not reported.

# **Authors' conclusions**

It is uncertain if oxytocin administered by CHO in non-facility settings compared with a control group reduces the incidence of severe PPH (>1000 mL), severe maternal morbidity or maternal deaths. However, the intervention probably decreases the incidence of PPH (> 500 mL).

The quality of the one trial included in this review was limited because of the risk of attrition and recruitment biases related to limitations in the follow-up of pregnant women in both arms of the trials and some baseline imbalance on the size of babies at birth. Additionally, there was serious imprecision of the effect estimates for most of the primary outcomes mainly because of the size of the trial, very few or no events and CIs around both relative and absolute estimates of effect that include both appreciable benefit and appreciable harm.

Although the trial presented data both for primary and secondary outcomes, it seemed to be underpowered to detect differences in the primary outcomes that are the ones more relevant for making judgments about the potential applicability of the intervention in other settings (especially severe PPH).

Therefore, taking into account the extreme setting where the intervention was implemented, the limited role of the CHO in the trial and the lack of power for detecting effects on primary (relevant) outcomes, the applicability of the evidence found seems to be rather limited.

Further well-executed and adequately-powered randomised controlled trials assessing the effects of using oxytocin in pre-filled injection devices or other new delivery systems (spray-dried ultrafine formulation of oxytocin) on severe PPH are urgently needed. Likewise, other important outcomes like possible adverse events and acceptability of the intervention by mothers and other community stakeholders should also be assessed.

# PLAIN LANGUAGE SUMMARY

# Oxytocin for preventing postpartum haemorrhage in non-facility birth settings

#### What is the issue?

Postpartum haemorrhage (PPH) - excessive blood loss (of more than half a litre) following a vaginal birth - is the single leading cause of maternal mortality worldwide. Most of the deaths associated with PPH occur in low-income settings where effective methods of prevention and treatment are not easily accessible.

# Why is this important?

Oxytocin is a drug widely used for preventing and treating PPH, but most of the evidence supporting its effectiveness comes from hospital settings in high-income countries. Easier methods of oxytocin administration have been developed for use in low-income settings, such as pre-filled auto-disposable intramuscular injection syringes or a spray-dried ultrafine formulation of oxytocin. The effectiveness of these methods has not been assessed in a systematic review.

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#### What evidence did we find?

On 12 November 2015 we searched for evidence from randomised controlled trials and found a single trial conducted across four rural districts in Ghana. The trial randomised 28 community health officers (serving 2404 potentially eligible pregnant women) to the intervention group and 26 community health officers (3515 potentially eligible pregnant women) to the control group.

It was uncertain from this trial whether the intervention prevented loss of more than one litre of blood (severe PPH) as the results were variable and suggested anything between a 98% decrease to a 30% increase in blood loss (*very low-quality evidence*). Because there were no cases of severe maternal illness (for example, because of uterine rupture), or maternal deaths, it was not possible to fully assess the effect of the intervention on those outcomes (the*quality of the evidence was very low*).

The women receiving oxytocin had half the incidence of PPH (> 500 mL) compared with the control group (*low-quality evidence*). There was little or no difference between the oxytocin and control groups on the rates for transfer or referral of women to a healthcare facility (*low-quality evidence*), stillbirths (*low-quality evidence*), or the numbers of babies that died within three days of being born (*low-quality evidence*).

There were no cases of oxytocin use during labour, needle-stick injury or any other major or minor adverse events or unanticipated harmful event.

Overall, the quality of the evidence was low/very low because of methodological limitations in the trial and imprecision in the effect estimates for all the important outcomes.

#### What does this mean?

It is uncertain if the administration of oxytocin by community health officers without midwifery skills administered in non-health facility settings compared with a control group reduces the incidence of severe PPH, severe maternal illness or maternal deaths when compared with a control group. However, oxytocin probably decreases the incidence of PPH (> 500 mL).

Considering the very specific setting where the trial was conducted and the limited role played by the community health officer in the trial, the applicability of the evidence is rather limited.

Further high-quality randomised controlled trials are urgently needed to assess the effects of using oxytocin in pre-filled injection devices or other new delivery systems on severe PPH. Similarly, future studies should consider other important outcomes like possible adverse events and the acceptability of the intervention for mothers and other community stakeholders.