PICO Search Assignment Worksheet **Name Jay Kolasinac**

A 34F, G3P101, who is 37w1d with a multigestational pregnancy, has a PMH of PPH. Misoprostol [Cytotec] and Oxytocin [Pitocin] are commonly used to ripen the cervix and induce contractions, however, can be used to prevent PPH and in fact treat it.

Search Question: Is there a difference in efficacy between misoprostol and oxytocin for prevention/decrease of post partum hemorrhage?

Question Type: What kind of question is this? (boxes now checkable in Word)

☐Prevalence ☐Screening ☐Diagnosis

☒Prognosis ☐Treatment ☐Harms

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)?
Please explain your choices.

Along with meta-analyses and systemic reviews, RCTs would also be sources of evidence where my question is in fact regarding efficacy related to the drugs being used. I would consider studies such as Cohort Studies. Cohort studies are prospective studies that follow individuals over time where data is collected as circumstances change.

PICO search terms:

P	**I**	**C**	**O**
Pregnant patients	Misoprostol	Oxytocin	Prevention of PPH
High risk pregnancies			Decreased bleeding

Search tools and strategy used:

Database	Terms	Filter	# of Articles
PubMed	Misoprostol vs oxytocin AND post partum hemorrhage AND prevention	Medline, last 10 years	12
ScienceDirect	Misoprostol vs oxytocin AND post partum hemorrhage AND prevention	Research articles, last 10 years	71

Results found:

Article 1

Citation

Chaudhuri, P., Mandi, S., & Mazumdar, A. (2014). *Rectally administrated misoprostol as an alternative to intravenous oxytocin infusion for preventing post-partum hemorrhage after cesarean delivery. Journal of Obstetrics and Gynaecology Research, 40(9), 2023–2030.* doi:10.1111/jog.12464 **https://sci-hub.se/https://doi.org/10.1111/jog.12464**

Article Type

Randomized Control Study

Abstract

Aim: With the increasing rate of cesarean delivery (CD) worldwide, there is a need for a revision of practices to prevent post-partum hemorrhage (PPH) after CD. In search of a safe, cheap and effective alternative to oxytocin for prevention of PPH during the postoperative period of CD, the present study aimed to compare rectally administrated misoprostol with i.v. oxytocin infusion.

Methods: A randomized, placebo-controlled, double-blind prospective trial was undertaken on 192 women who did not have risk factors for PPH and who had an uneventful emergency CD under spinal anesthesia. They were randomly allocated to receive either 800 mg of rectal misoprostol or an i.v. infusion of oxytocin at the end of operation. Primary outcome measures were the amount of postoperative (24 h) blood loss and incidence of PPH during the postoperative period. The secondary outcome measures were the postoperative drop in hemoglobin concentration after 24 h, need for additional uterotonic and blood transfusion, and side-effects/complications during the 24-h observation period.

Results: There was a significant reduction of blood loss in the misoprostol group compared with the oxytocin group (144.5 ± 100.1 vs 191.7 ± 117.1, $P < 0.0001$). The two groups were similar in terms of the secondary outcome parameters.

Conclusion: Rectally administrated 800-mg misoprostol may be an effective alternative to oxytocin infusion to prevent PPH after CD.

Key Points

- Significant reduction of blood loss in the misoprostol group compared to the oxytocin group
- Rectal administration of misoprostol can be an effective alternative to oxytocin
- Secondary measures were very similar compared to the two groups

Reason for choosing:

I chose this article since it was published within the last 10 years. I also chose it because it is a randomized control trials which is a high level of evidence only second to meta analyses and systematic reviews. I used 500 patients which is a decent sample size to conduct the study as well.

Article 2

Citation

Al-Sawaf, A., El-Mazny, A., & Shohayeb, A. (2013). *A randomised controlled trial of sublingual misoprostol and intramuscular oxytocin for prevention of postpartum haemorrhage. Journal of Obstetrics and Gynaecology, 33(3), 277–279.* doi:10.3109/01443615.2012.755503
sci-hub.se/10.3109/01443615.2012.755503

Article Type

Randomized Control Trial

Abstract

This study aims to evaluate the efficacy and side-effects of 200 μg sublingual misoprostol vs 5 IU i.m. oxytocin, administered immediately following cord clamping in normal non-augmented vaginal delivery, in prevention of postpartum haemorrhage (PPH).

A total of 104 women were randomised into three groups: misoprostol group (28 patients); oxytocin group (37 patients) and control group (39 patients). Misoprostol and oxytocin significantly minimised the blood loss during the third stage of labour and reduced the need for additional treatments for PPH as compared with the control group. Oxytocin was more effective than misoprostol in minimising blood loss and the need for additional uterotonic treatments. However, a significant decrease in systolic and diastolic blood pressure, associated with tachycardia was observed in the oxytocin group.

In conclusion, sublingual misoprostol appears to be less effective than i.m. oxytocin in the prevention of PPH; however, it has the potential advantages of being easily used, cost-effective and stable at room temperature. Therefore, sublingual misoprostol is still a feasible drug for routine management of third stage, especially in areas with limited medical facilities.

Key Points

- Both misoprostol and oxytocin minimized the blood loss seen in post partum hemorrhage.
- Reduced the need for additional services compared to the control group
- Decrease in BP and tachycardia was seen in oxytocin group.

- Seems that oxytocin is more efficacious compared to misoprostol, however, in facilities with limited resources, sublingual misoprostol can be seen as the optimal drug.

Reason for choosing:

Article directly answers my PICO question. Published within the last 10 years which is good. The method of study was a RCT which is very good. I do wish the sample size was a little bit larger. The secondary parameter [HgB/HCT] differences were all statistically insignificant just like the other study which was very interesting.

Article 3

Citation

Esther C Atukunda, Mark J Siedner, Celestino Obua, Godfrey R Mugyenyi, Marc Twagirumukiza, Amon G Agaba,
Sublingual misoprostol versus intramuscular oxytocin for prevention of post-partum haemorrhage in Uganda: a randomised, controlled, non-inferiority trial, The Lancet, Volume 384, Supplement 1, 2014, Page S3, ISSN 0140-6736,
https://doi.org/10.1016/S0140-6736(14)61866-3.
https://www-sciencedirect-com.york.ezproxy.cuny.edu/science/article/abs/pii/S0140673614618663

Article Type

Randomized Control Trial

Abstract

Background

Postpartum haemorrhage is a leading cause of maternal death in sub-Saharan Africa. Although WHO recommends use of oxytocin for prevention of postpartum haemorrhage, misoprostol is increasingly used owing to advantages in shelf life, ease of use, storage, and potential for sublingual administration. We assessed the comparative efficacy of oxytocin and sublingual misoprostol for prevention of postpartum haemorrhage during labour.

Methods

We did a double-dummy, non-inferiority, randomised, controlled trial from September 2012, to September 2013, at Mbarara Regional Referral Hospital in Uganda. We randomly assigned (1:1) women to receive misoprostol 600 μg sublingually or oxytocin 10 IU along with matching placebos. Patients and investigators giving treatment were both masked to treatment assignment. The primary outcome was postpartum haemorrhage (measured blood loss ≥500 mL within 24 h postpartum) with a non-inferiority margin of 6%. Secondary outcomes included measured blood loss of more than 1000 mL, mean blood loss at 1 h, 2 h, and 24 h postpartum, death, requirement of blood transfusion, haemoglobin change, and use of additional uterotonic drugs. We did the analyses in the intention-to-treat population. The trial was registered with ClinicalTrials.gov, number NCT01866241.

Findings

We included 1140 women: 570 (50%) assigned to misoprostol and 570 (50%) assigned to oxycotin. The primary outcome occurred in 163 (28·6%) participants in the misoprostol group versus 99 (17·4%) participants in the oxytocin group (relative risk [RR] 1·64, 95% CI 1·32–2·05, p<0·001. The lower

95% CI for the absolute difference was 6·44%, greater than our non-inferiority margin limit. Blood loss of more than 1000 mL occurred in 20 (3·6%) versus 15 (2·7%) participants (RR 1·33, 95% CI 0·69–2·58, p=0·391). 11 (1·9%) versus ten (1·8%) participants had severe postpartum haemorrhage at 1 h postpartum (RR 1·10, 95% CI 0·47–2·57, p=0·826). Mean measured blood loss was 341·5 mL (SD 206·2) versus 304·2 mL (SD 190·8; p=0·002) at 2 h postpartum and 484·7 mL (SD 213·3) versus 432·8 mL (SD 203·5; p<0·001) at 24 h. There were no significant differences between the groups for any other secondary outcomes. Participants in the misoprostol group more commonly had shivering (321 [56·4%] *vs* 168 [26·5%]; RR 1·91, 95% CI 1·65–2·21, p<0·001) and fever (53 [9·3%] *vs* 12 [2·1%]; RR 4·42, 95% CI 2·39–8·18, p<0·001). No maternal deaths or postpartum surgical interventions occurred in either group.

Interpretation

Misoprostol 600 μg is not non-inferior to oxytocin 10 IU for prevention of postpartum haemorrhage in active management of labour, supporting the preferential use of oxytocin when feasible. However—although our study was not powered to assess differences—similar rates of severe postpartum haemorrhage, haemoglobin change, and other clinically significant secondary outcomes seem to suggest that sublingual misoprostol might have a role for prevention of severe postpartum haemorrhage and other complications of postpartum haemorrhage in settings where oxytocin use is not feasible. Further research should focus on clarifying if and which subpopulations benefit most from use of oxytocin.

Key Points

- More patients in the misoprostol group had prevention of PPH compared to the oxytocin group
- No difference between the groups in regards to secondary outcomes
- Misoprostol should not be considered inferior to oxytocin for prevention of postpartum hemorrhage
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Reason for choosing:

This article was a randomized control trial which is really good. I like the larger population size of 1100+ patients. It answered my PICO question directly as well as other secondary parameters were tracked.

What is the clinical "bottom line" derived from these articles in answer to your question?

Misoprostol and Oxytocin are pharmaceutical agents used for the prevention of postpartum hemorrhage in pregnant patients. Taking into consideration all of the studies, it is safe to say that Misoprostol is just as effective as Oxytocin in the prevention of postpartum hemorrhage. However, we must take into consideration that the FDA has not approved Misoprostol as an agent for prevention of postpartum hemorrhage even though it seems that studies show it is worth the use. As a clinician, would you consider off label usage of a drug vs an FDA approved drug for the prevention of postpartum hemorrhage? Personally, I believe more studies should be done with larger sample sizes directly comparing one particular method of administration compared to another. Lots of these studies different in administration of the drug and that could play a role. Personally, I would stick to the Oxytocin [Pitocin] as the go to agent for prevention of PPH until more concrete evidence suggests otherwise. As mentioned

in article 2, if facilities do not have the available resources for the usage of oxytocin, Misoprostol could be an alternative.