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Comparative Study of Rectal Misoprostol to Oxytocin Infusion in Preventing Postpartum Haemorrhage After Caesarean Section

Adanikin AI,[1] Orji E,[1] Adanikin PO,[2] Olaniyan O[1]

[1]Department of Obstetrics and Gynaecology, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria

[2] Health Centre, Obafemi Awolowo University, Ile-Ife, Nigeria.

Aims: This comparative study aimed to compare the efficacy of rectal misoprostol to oxytocin infusion in preventing primary postpartum haemorrhage after caesarean section.

Methods: Fifty pregnant women with identifiable risk factors for post-partum haemorrhage who delivered baby by caesarean section were randomized to receive 600 µg rectal misoprostol and a placebo infusion intravenously or placebo rectally and a 20 iu oxytocin infusion. Post-operative blood loss four hours after surgery was estimated by application of pads of known weight.

Results: The mean immediate four hours post-operative blood loss was not significantly different between the rectal misoprostol and oxytocin infusion group (100.08 ± 24.85 ml versus 108.20 ± 29.93 ml; p =0.144) and the change between the pre-operative and post-operative hematocrit was similar.

Conclusions: Post-caesarean section rectal misoprostol has comparative efficacy to oxytocin infusion in preventing post-partum haemorrhage. It is recommended for use as alternative uterotonic in settings where there is low refrigeration capacity.

Keywords: caesarean section, misoprostol, oxytocin infusion, postpartum haemorrhage.

INTRODUCTION

Misoprostol is a synthetic prostaglandin E_1 analogue originally marketed for treatment/prevention of non-steroidal anti-inflammatory drug-induced peptic ulcer.[1] However, due to its uterotonic properties, it has gained wide use for labour induction[2,3] and induction of abortion.[4,5]

Over the years, there has been expanding interest in the use of misoprostol toprevent and manage postpartum haemorrhage.[6-8] With the World Health Organization (WHO) enlisting it as essential medicine for primary postpartum hemorrhage (PPH) in 2011,[9] body of research is growing on the effectiveness and safety for this purpose.

After caesarean section, uterotonic in form of oxytocin infusion (20-40 iu) or rectal misoprostol (200-600 µg) is administered to contract the uterus for the succeeding 4-6 hours post-surgery in patients at risk of PPH.[10-12] Although this practise is popular in our environment, objective comparative assessment of both measures is lacking; this study therefore made the comparison.

METHODS

This study was conducted at the Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria between August 1 and October 31, 2011. The Ethics Review Committee of the hospital approved the study

CORRESPONDENCE
Dr Abiodun Idowu Adanikin
Department of Obstetrics and Gynaecology,
Obafemi Awolowo University Teaching Hospital, Ile-Ife, Osun State, Nigeria.
Email: adanikinbiodun@yahoo.com
Phone: +234 803 4252126

protocol. The primary outcome variable of the study was four-hour post-operative blood loss.

Sample size

In a study by Owonikoko et al[13] comparing sublingual misoprostol with oxytocin infusion in reducing blood loss after caesarean section, they reported a mean 4 hour post-operative blood loss of 58.2 ± 20.7 ml for the misoprostol group and 80.5 ± 26.8 ml for the oxytocin infusion group. These data were used to calculate the study sample size via a formula derived by Kirkwood and Steme.[14] Sample size of 50 (25 in each group) would have 90% power to detect a clinically important difference of 20.7 ml for the misoprostol group versus 26.8 ml for the oxytocin infusion group as observed by Owonikoko et al.[13]

Fifty women who were scheduled to undergo caesarean section with identifiable risk factors for primary postpartum haemorrhage such as prolonged labour, obstructed labour, grand-multiparity, multiple gestations, polyhydraminous were enrolled for the study after written informed consent. Asthmatics or patients with hypersensitivity to prostaglandins were excluded.

Study procedure

By 1:1 computer-generated randomization, participants were assigned to their group while the pharmacy department provided the study drugs and placebos in unidentifiable form. The numbered medications contained 600 µg tablets of misoprostol to be used rectally plus a pre-filled syringe with normal saline solution, or identical placebo tablets to be used rectally plus a pre-filled syringe with 20 iu of oxytocin. A resident doctor was responsible for the patient's allocation according to randomisation table. The patients and the outcome assessor were blinded to the study medications. In accordance to the randomisation, after cord clamping participants received either 600 µg of rectal misoprostol plus an infusion of 500 ml of 5% dextrose saline solution supplemented with placebo over 4 hours, or a rectal placebo plus an infusion of 500 ml of 5% dextrose saline solution supplemented with 20 iu of oxytocin over four hours. Additional administration of uterotonics was allowed in cases of bleeding in excess of 500 ml within the four-hour period, but no patient needed it.

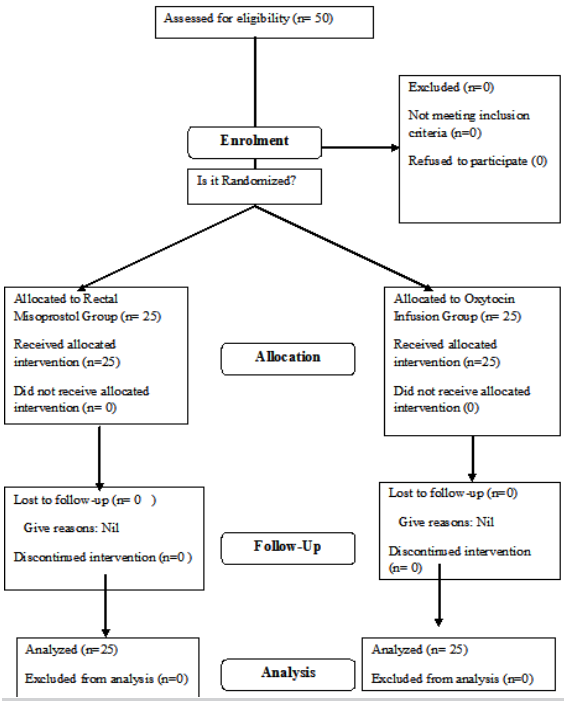

Figure 1. Diagram of detailed study design.

Calculation of blood loss

Immediate blood loss up till four hours post-partum was measured by the application of pads of known weight to the perineum. These pads were weighed four hours post-partum, and the blood loss estimated from the pads' weight gain as: 1g ≈1ml.[15,16] The instrument used to weigh the pads was a *MettlerPB153* weighing scale, which had a sensitivity of 0.001 gm. The scale was calibrated prior to weighing as well as during weighing of large numbers of products. The instrument was evaluated as stable; inter-weigher reliability was 0.98. The used pads were weighed in triplicate and the mean of the three weights were entered into the database. Haematocrit was checked before and two days after surgery.

Statistical analysis

Data were analyzed using the computer soft ware SPSS version 15. Frequency tables were generated. Association between continuous variables was tested using the student t-test while Chi square or Fisher's exact test was used to test association between categorical variables. Level of significance (α) was set at 0.05.

RESULTS

Fifty women who met the inclusion criteria were enrolled and randomized into either misoprostol or oxytocin infusion group (Figure 1).

Table 1. Baseline characteristics of participants (n=50).

Variables	Misoprostol group (n=25)	Oxytocin group (n=25)	Odd ratio	95% Confidence	P-value
Age (years)	30.6 ± 6.33	30.84 ± 5.69			0.671
GA (weeks)	39.03 ± 1.62	39.07 ± 1.26			0.853
Parity	1.88 ± 1.42	1.76 ± 1.09			0.726
Indications for C/S, n(%):					
Prolonged labour	8 (32)	7 (28)	1.00		
Obstructed labour	1 (4)	4 (8)	4.57	0.51- 40.90	0.194
Multiple pregnancy	4 (16)	2 (8)	0.57	0.09- 3.57	0.577
Grand multiparity	4 (16)	2 (8)	0.57	0.09- 3.57	0.577
Fetal macrosomia	5 (20)	3 (12)	0.69	0.13- 3.60	0.673
Failed Induction	2 (8)	4 (16)	2.29	0.37-14.30	0.407
Others	1 (4)	3 (12)	3.43	0.38- 30.68	0.313
Type of Anaesthesia, n (%):					
Spinal	20 (80)	22 (88)	1.00		
General	5 (20)	3 (12)	0.55	0.13-2.36	0.440
Duration of surgery (mins)	54.72±9.51	54.80 ± 8.77			0.974

Data presented as: mean ± standard deviation; n (%).
C/S: Caesarean section.

Table 1 shows that the participants in both groups did not differ significantly in mean age, gestational age at delivery, parity, indication for caesarean section, type of anaesthesia and mean duration of surgery.

Table 2. Operative outcome in both groups (n=50).

Variables	Misoprostol group	Oxytocin infusion	P-value
Pre-operative hematocrit (%)	34.68 ± 3.67	34.24± 3.09	0.577
Post operative hematocrit (%)	33.12 ± 3.77	32.52± 3.54	0.436
4 hours post operative EBL (ml)	100.8 ±24.8	108.20± 29.93	0.144
Side effects:			
Shivering, n (%)	1(4)	2(8)	>0.999
Pyrexia, n (%)	4(16)	2(8)	0.667
Nausea, n (%)	2(8)	1(4)	>0.999
Vomiting, n (%)	2(8)	2(8)	>0.999

Data presented as: mean ± standard deviation; n (%). Abbreviations: EBL, estimated blood loss.

From Table 2, the studied groups had no significant difference in pre-operative and post-operative hematocrit. The mean four hours post-operative blood loss was also not significantly different in the two groups (100.08 ± 24.85 ml versus108.20 ± 29.93 ml; p =0.144).

There was no difference in occurrence of shivering (p = 0.999), pyrexia (P= 0.667), nausea (p =0.999) and vomiting (p =0.999).

DISCUSSION

The mean immediate four hours post-operative blood loss was not significantly different in the two groups studied. No patient had bleeding in excess of 500 ml to warrant additional uterotonic. This outcome indicated the efficacy of both drugs in preventing PPH. The finding is in synchrony with earlier conclusion by Nasr et al[6] that rectal misoprostol was effective in reducing blood loss after delivery. Lapaire et al[17] who compared oral misoprostol with oxytocin infusion post-caesarean section and found similar efficacy of both drugs, though misoprostol had higher side effects profile. Also, Owinikoko et al[13] found comparative efficacy of sublingual misoprostol to oxytocin infusion after caesarean section but with significant misoprostol side effect.

Side effect of misoprostol was not prominent in this study. Rectal misoprostol is known to have a steady serum rise with lower peak serum concentration and longer half life.[18,19] This may account for the low side effect profile. The longer half-life of rectally administered misoprostol equally has a beneficial effect of prolonging uterine contraction and preventing a delayed haemorrhage.[19,20]

Post-surgery, other routes of administration of

misoprostol may not be favoured. There is likelihood that the surgeon may want patient to avoid immediate oral intake while lochia flow after delivery may wash away vaginal misoprostol. Rectal administration is therefore an appropriate route. In tropical developing countries, tendency of oxytocin losing potency is high as proper refrigeration capability is low. Because of this, there are occasions where post-partum haemorrhage ensues despite the use of oxytocin. Misoprostol on the other hand, is stable in tropical climate while still maintaining its potency.[21]

CONCLUSIONS

This study showed that misoprostol was as effective as oxytocin infusion in preventing PPH. Misoprostol can serve as alternative to oxytocin in tropical climates with little capability for refrigeration for prevention of post-partum haemorrhage. Authors recommend further studies on this subject.

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