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Effect of Pre-Cesarean Section Sublingual or Rectal Misoprostol in Reducing Bleeding in Elective Cesarean Delivery

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ORIGINAL ARTICLE

Effect of Pre-Cesarean Section Sublingual or Rectal Misoprostol in Reducing Bleeding in Elective Cesarean Delivery

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Abstract

Background: ***Preventing postpartum hemorrhage (PPH) has been highlighted as an essential aspect of promoting safe motherhood. Misoprostol is a powerful uterotonic that can be used to prevent and manage preterm labor.***

Aim and objectives: ***To assess the effect of sublingual and rectal misoprostol in reducing blood loss during and after cesarean delivery compared to oxytocin infusion.***

Subjects and methods: ***The research was a prospective randomized controlled trial performed at AL-Zahraa University Hospital and Fayoum General Hospital's Obstetrics and Gynecology departments. The study was applied to 90 women subdivided into three groups (Group A), which included 30 participants received 400μg of misoprostol (two tablets) by sublingual route just before abdominal skin incision, (Group B): included 30 participants received 400μg of misoprostol rectally after induction of anesthesia and (Group C): included 30 participants received oxytocin 20 I.U. (syntocinon) intravenous infusion.***

Results: ***There were highly statistically significant variances among the groups concerning intraoperative blood loss and total blood loss. Oxytocin had the upper hand over misoprostol in controlling blood loss, while rectal misoprostol (Mean ± S.D. 380.20±58.586) was superior to sublingual misoprostol (Mean ± S.D. 432.17±90.036) in reducing intraoperative blood loss with fewer adverse effects.***

Conclusion: ***Oxytocin had the upper hand over misoprostol in controlling blood loss, while rectal misoprostol was superior to sublingual misoprostol. The usage of rectal misoprostol reduces intraoperative blood loss and has fewer adverse effects than sublingual misoprostol.***

Keywords: Cesarean delivery; Misoprostol; Postpartum hemorrhage; Rectal; Sublingual

1. Introduction

Postpartum hemorrhage, also known as PPH, is among the main reasons for maternal mortality, particularly in countries with limited resources. It is responsible for about one-quarter of all maternal fatalities throughout the world and contributes to yearly maternal mortality exceeding 100,000. The inability of the uterus to fully contract after delivery is the most prevalent reason for primary PPH, accounting for roughly 70% of all cases of this type of postpartum bleeding. [1]

Postpartum hemorrhage became increasingly prevalent as the prevalence of cesarean sections increased. This is because the average amount of blood lost following a cesarean section is twice as much as the amount lost with a vaginal birth. [2]

PPH is defined as blood loss from the genital tract of 500 ml after vaginal delivery or 1000 ml following a cesarean section; it occurs within the first twenty-four hours (primary postpartum hemorrhage) or more than 24 hours after delivery (secondary postpartum hemorrhage). [3]

In order to minimize uterine atony and lessen blood loss following cesarean section, intravenous oxytocin is often administered; however, additional uterotonic medicines such as ergot alkaloids and prostaglandins may be necessary for 10-42% of females who receive oxytocin. [4]

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Misoprostol is efficient in preventing postpartum hemorrhage and is an excellent alternative to other oxytocic drugs, particularly in developing countries, due to its safety, thermostability, very rapid absorption found in circulation within two minutes of oral ingestion, and ease of administration through multiple routes absorbed effectively when administered sublingually, orally, and even rectally.[5]

The study aimed to assess the effect of sublingual and rectal misoprostol in reducing blood loss during and after cesarean delivery compared to oxytocin infusion.

2. Patients and methods

A prospective randomized controlled trial was performed between April and October of 2022 at the Obstetrics and gynecology departments of AL-Zahraa University Hospital and Fayoum General Hospital. The cases were selected based on predetermined inclusion-exclusion criteria:

2.1.Inclusion criteria: Females at full-term normal pregnancy for elective Cesarean delivery and pregnant females between twenty and thirty-eight years old.

2.2.Exclusion criteria: All women for emergency cesarean section, overdistended uterus as polyhydramnios, fetal macrosomia, and multifetal pregnancy, women with medical conditions or complications such as hemoglobinopathy, preeclampsia, asthma, heart, lung, or liver disease, allergy to misoprostol and contraindication to spinal anesthesia.

2.3.Sample Size(n):

This study is based on a study carried out by Leduc D. The sample size was measured utilizing Epi Info STATCALC, taking into account the following assumptions: The study was done utilizing a 95% two-sided confidence level and a power of 80%, with a margin of error of 5%—the ultimate maximum sample size extracted from the Epi-Info output was82. Therefore, the sample size was augmented to include 90 cases to account for any dropout throughout the follow-up period. [6]

$$\left(\frac{Z_{a/2} + Z_B}{P_1 - P_2}\right)^2 (p_1q_1 + p_2q_2)$$

Takazawa& Morita. [7]

n = sample size

Z a/2 (The crucial number that demarcates the center 95% of the Z distribution)

ZB (The crucial number that demarcates the center 20% of the Z distribution)

p1 = prevalence in case group

p2 = prevalence in control group.

q = 1-p

The 90 participants were separated into 3 categories based on method of randomization: Group A: 30 participants received 400µg of misoprostol (two tablets) (Misotac®, Sigma Pharmaceuticals) by sublingual route just before abdominal skin incision, Group B: 30 participants received 400µg of misoprostol rectally after induction of anesthesia, and Group C: 30 participants received oxytocin 20 I.U. (syntocinon) intravenous infusion soon following the birth of the infant in 1000 ml saline or ringer solutions for 8 hours after the operation, at frequency of 125 ml per hour.

2.4.Statistical Analysis

SPSS version 23 was used for data processing, during which time the data were validated, inputted, and analyzed. For qualitative variables, their values were reported as numbers and percentages, while for quantitative variables, their values were stated as means + standard deviations (SD). In order to do the comparison, we used the student t-test, which is designed for parametric data. The Mann–Whitney test is used for analyzing data that is not parametric. Test using the chi square. The Z test. A probability level equal to P value that is greater than 0.05 indicates that the findings are not significant, but a P value that is less than 0.05 indicates that the outcomes are significant.

3. Results

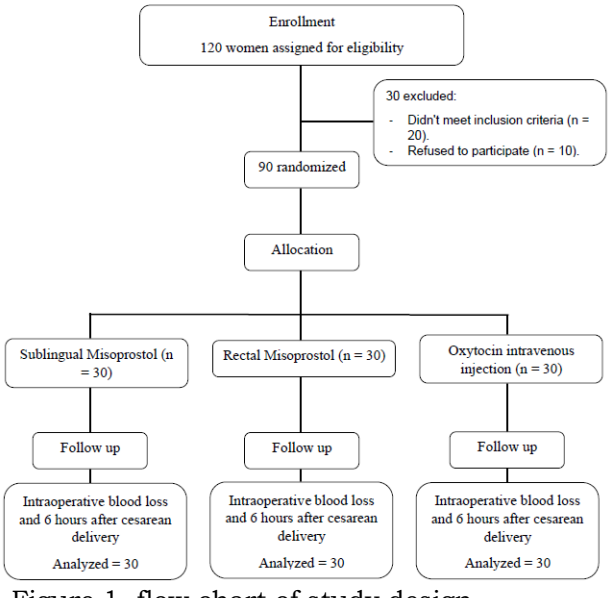

Figure 1. flow chart of study design

Out of 120 women assessed for eligibility; 30 cases were not counted because they either did not satisfy the inclusion requirements or they declined to participate. The 90 participants were allocation at random between the three categories, none of the patients required conversion to general anaesthesia.

Table 1. Comparison among the studied groups as regard to patient's demographic data.

VARIABLE	GROUP (A) (N=30)		GROUP (B) (N=30)		GROUP (C) (N=30)		P VALUE	TEST OF SIG. BETWEEN GROUPS
	No.	%	No.	%	No.	%		
AGE (YEARS)								
RANGE	20-34		19-34		19-32		0.891	A vs B =0.974
MEAN ± S. D	25.37±3.557		25.40±4.190		24.97±3.864			A vs C =0.691
								B vs C =0.666
GRAVIDITY (NO. OF PREGNANCY)								
PRIMIGRAVIDA	0	0	3	10.0	3	10.0	0.200	A vs B =0.237
MULTIGRAVIDA	30	100	27	90.0	27	90.0		A vs C =0.237
								B vs C =1.000
PARITY								
NULLIPAROUS	0	0	3	10.0	3	10.0	0.356	A vs B =0.161
PRIMIPAROUS	15	50.0	16	53.3	12	40.0		A vs C =0.189
MULTIPAROUS	15	50.0	11	36.7	15	50.0		B vs C =0.552
GESTATIONAL AGE (WEEKS)								
MIN.- MAX.	37-39		27-39		37-40		0.263	A vs B =0.499
MEAN ± S. D	37.70±0.596		37.40±2.799		37.97±0.765			A vs C =0.547
								B vs C =0.203

Table 1 showed that all groups were demographically homogeneous with no statistically significant variances among them with regard to age, gravidity, parity & gestational age.

Table 2. Comparison among the studied groups as regard to patient's duration of operation and hospital stay.

VARIABLE	GROUP (A) (N=30)	GROUP (B) (N=30)	GROUP (C) (N=30)	P VALUE	TEST OF SIG. BETWEEN GROUPS
PATIENT'S DURATION OF OPERATION (MINUTES)					
RANGE	35-45	35-43	36-42	0.021*	A vs B =0.073
MEAN ± S. D	40.03±2.059	39.20±1.769	38.70±1.466		A vs C =0.005
					B vs C =0.280
PATIENT'S DURATION OF HOSPITAL STAYS (HOURS)					
RANGE	24	24	24	1	A vs B =1
MEAN ± S. D	24	24	24		A vs C =1
					B vs C =1

Table 2 demonstrated that there was statistically significant variance among the groups concerning the duration of operations as sublingual misoprostol (A) consumed more operation time than oxytocin group (C).

Table 3. Comparison among the studied groups as regard to patient's mean arterial pressure & heart rate.

VARIABLE	GROUP (A) (N=30)	GROUP (B) (N=30)	GROUP (C) (N=30)	P VALUE	TEST OF SIG. BETWEEN GROUPS
MAP (MMHG)*					
PREOPERATIVE: -					
RANGE	70.6-99.7	70.8-98.9	71.0-97.2	0.677	A vs B =0.424 A vs C =0.470 B vs C =0.938
MEAN ± S. D	87.01±9.630	85.11±9.140	85.29±8.694		
POSTOPERATIVE: -					
RANGE	63.6-94.5	64.8-93.9	62.0-87.3	0.063	A vs B =0.387 A vs C =0.020* B vs C =0.139
MEAN ± S. D	81.11±9.766	79.04±9.304	75.49±8.533		
HEART RATE (BEAT/MIN.)					
PREOPERATIVE: -					
RANGE	79-106	79-103	80-104	0.190	A vs B =0.337 A vs C =0.384 B vs C =0.069
MEAN ± S. D	92.57±9.016	90.43±9.413	94.50±7.070		
POSTOPERATIVE: -					
RANGE	82.0-112	97-126	99-125	<0.001*	A vs B <0.001* A vs C <0.001* B vs C = 0.046*
MEAN ± S. D	97.30±9.158	109.30±9.322	113.77±6.981		

*MAP= mean arterial pressure

Table 3 The mean arterial pressure & heart rate preoperative show no statistically significant variances among the groups. While there were statistically significant variances between them at postoperative time regarding the heart rate which increased with oxytocin group C than sublingual, and rectal misoprostol groups. Also, postoperative mean arterial pressure was lesser in oxytocin group C than sublingual group A.

Table 4, Showed no statistically significant variance among the groups concerning Hb level & HCT percent preoperative & postoperative.

VARIABLE	GROUP (A) (N=30)	GROUP (B) (N=30)	GROUP (C) (N=30)	P VALUE	TEST OF SIG. BETWEEN GROUPS
HB (MG/DL) *					
PREOPERATIVE:					
RANGE	10.0-12.9	9.70-12.7	10.0-12.5	0.937	A vs B =0.587 A vs C =0.875 B vs C =0.700
MEAN ± S. D	11.57±0.753	11.46±0.752	11.54±0.697		
POSTOPERATIVE:					
RANGE	9.2-12.0	9.2-12.4	9.6-12.2	0.398	A vs B =0.749 A vs C =0.320 B vs C =0.190
MEAN ± S. D	10.91±0.656	10.86±0.707	11.09±0.688		
HCT (%) **					
PREOPERATIVE:					
RANGE	24.0-40.7	28.6-38.6	29.0-36.8	0.867	A vs B =0.344 A vs C =0.783 B vs C =0.501
MEAN ± S. D	33.26±2.866	33.83±2.072	33.43±1.799		
POSTOPERATIVE:					
RANGE	23.0-38.0	27.0-37.0	28.5-36.0	0.918	A vs B =0.659 A vs C =0.596 B vs C =0.929

MEAN ± S. D	32.18±2.854	32.45±2.092	32.50±1.840	

* Hb = hemoglobin, ** Hct = hematocrite.

Table 4 Comparison among the studied groups as regard to patient's Hemoglobin & Hematocrit value.

Table 5. Comparison among the studied groups as regard to patient's blood loss (ml) intraoperative, postoperative & total blood loss.

VARIABLE	GROUP (A) (N=30)	GROUP (B) (N=30)	GROUP (C) (N=30)	P VALUE	TEST OF SIG. BETWEEN GROUPS
INTRAOPERATIVE: -					
RANGE (ML)	244-584	214-470	240-430	<0.001*	A vs B =0.003 A vs C <0.001* B vs C =0.118
MEAN ± S. D	432.17±90.036	380.20±58.586	352.90±43.883		
POSTOPERATIVE: -					
RANGE (ML)	70-150	70-160	60-140	0.021*	A vs B =0.312 A vs C =0.062 B vs C =0.005*
MEAN ± S. D	106.57±20.193	111.87±22.132	96.70±18.056		
TOTAL BLOOD LOSS: -					
RANGE (ML)	344-704	304-600	380-540	<0.001*	A vs B =0.012* A vs C <0.001* B vs C =0.023*
MEAN ± S. D	539.40±97.179	492.07±60.196	449.63±45.950		

Table 5 Demonstrated that there were statistically significant variances among the groups concerning intraoperative & total blood loss which were more significant in sublingual group A than rectal group B, also they were lower with oxytocin group C than others. While postoperative blood loss was more in rectal group than oxytocin group.

Table 6. Comparison among the studied groups as regard to the need for additional oxytocin.

VARIABLE (ADDITIONAL OXYTOCIN)	GROUP (A) (N=30)		GROUP (B) (N=30)		GROUP (C) (N=30)		P VALUE	TEST OF SIG. BETWEEN GROUPS
	No.	%	No.	%	No.	%		
NO	24	80.0	27	90.0	30	100	0.036*	A vs B =0.472 A vs C =0.024* B vs C =0.237
YES	6	20.0	3	10.0	0	0		

Table 6 Demonstrated that, there was highly statistically significant variance among the studied groups indicating superiority of oxytocin over misoprostol in uterine involution.

Table 7. Comparison among the studied groups as regard to patient's drug side effects.

VARIABLE	GROUP (A) (N=30)		GROUP (B) (N=30)		GROUP (C) (N=30)		P VALUE	TEST OF SIG. BETWEEN GROUPS
	No.	%	No.	%	No.	%		
NAUSEA							0.008*	A vs B =0.103 A vs C =0.024* B vs C =1.000
NO	24	80.0	29	96.7	30	100.0		
YES	6	20.0	1	3.3	0	0		
VOMITING							0.015*	A vs B =0.112 A vs C =0.112 B vs C =------
NO	26	86.7	30	100.0	30	100.0		
YES	4	13.3	0	0	0	0		
SHIVERING							0.770	A vs B =1.000 A vs C =1.000 B vs C =1.000
NO	28	93.3	29	96.7	29	96.7		
YES	2	6.7	1	3.3	1	3.3		

HYPERPYREXIA							0.355	A vs B =0.492 A vs C =1.000 B vs C =1.000
NO	30	100.0	28	93.3	29	96.7		
YES	0	0	2	6.7	1	3.3		
RESPIRATORY DISTRESS							0.364	A vs B =------- A vs C =1.000 B vs C =1.000
NO	30	100.0	30	100.0	29	96.7		
YES	0	0	0	0	1	3.3		
UTERINE ATONY							0.053	A vs B =0.424 A vs C =0.052 B vs C =0.492
NO	25	83.3	28	93.3	30	100.0		
YES	5	16.7	2	6.7	0	0		

Table 7 shown a statistically significant variance in the incidence of vomiting & nausea among the groups, which were more in sublingual group A than rectal group B. Shivering and uterine atony noticed more with group A, while respiratory distress noticed with oxytocin group C, so the table indicated fewer side effects with oxytocin group C, than misoprostol groups A and B.

4. Discussion

One of the leading causes of maternal death is PPH. The inability of the uterus to contract is typically the leading reason for PPH, accounting for around 70% of all cases. [8]

Our research aims to compare the efficacy of oxytocin infusion with that of sublingual and rectal misoprostol in preventing and treating excessive blood loss before, during, and after cesarean delivery.

Regarding demographic data of the studied patients, our results demonstrated no significant variances among the studied groups concerning patients' age, gravidity, parity, or gestational age. This is in line with Bagheri et al., who researched to investigate the influence of misoprostol on avoidance and treatment of PPH during Cesarean delivery in 180 pregnant females, which were divided into three groups, group A = sublingual misoprostol, group B = rectal misoprostol, and group C = oxytocin. They reported that there was no significant variance among participants in the studies concerning the mean age (years) 28.3±6.3, 28.6±6.6, and 29.3±6.2 in groups A, B & C, respectively, and gestational age (weeks) means were 37.7±3.1, 37.8± 0.9, and 38.2±1.1 in groups A, B & C. [9]

These results were supported by Sweed et al., who aimed to assess the efficacy of rectal vs. sublingual misoprostol prior to cesarean delivery in decreasing intra-operative blood loss in cesarean delivery. All groups in this study were demographically homogenous with no statistical significance. [10]

Statistically significant differences among the groups were observed in this investigation concerning the duration of operations, as the sublingual misoprostol group consumed more operation time (40.03±2.059 min.) than the oxytocin group (38.70±1.466 min.).

This conformed with Bagheri et al., who stated that the sublingual misoprostol group consumed more operation time than the rectal group and oxytocin group (62.2±14.4, 49.5±13.7, and 55.2±18.3 min.) respectively. However, the rectal misoprostol group had a shorter duration of surgery than others. 9 But this disagreed with Gavilanes et al. as they reported that no difference was found in surgery duration between sublingual and oxytocin groups (p>0.05). [11]

There were no statistically significant variations among the groups in this investigation regarding mean arterial pressure and heart rate preoperative. However, there was a statistically significant difference among the groups at postoperative time concerning cases's heart rate (P less than 0,001), which increased with the oxytocin group than others. At the same time, postoperative mean arterial pressure showed a slight drop with the oxytocin group (75.49±8.533mmHg) than with sublingual and rectal misoprostol groups (81.11±9.766 and 79.04±9.304mmHg), respectively.

In Said's study, S. K. reported no significant differences among the groups concerning mean arterial blood pressure preoperative postoperative (P equal 0.22) after administration of rectal misoprostol. At the same time, there was a statistically significant drop preoperative and postoperative after oxytocin infusion (82.3±12.2 mmHg and 72.1±10.5 mmHg, respectively). Also, the heart rate in cases with the oxytocin group increased significantly from 102±17 beats/min. To 123±22 beat/min. (P=0.005). Which was in line with our study. [4]

Rahbar et al. noticed that within one hour following Cesarean section, the hypotension in the oxytocin group was 18% and none in the other group. In contrast, no tachycardia was noticed in either sublingual misoprostol or oxytocin groups. [12]

Our results indicated no statistically significant

variations among the groups concerning preoperative and postoperative mean hemoglobin levels among groups A, B, and C, which were in line with Sayed et al., who aimed to evaluate the effectiveness of sublingual versus rectal misoprostol on intraoperative postoperative blood loss & the consequent influence on hemoglobin levels. [13]

There were highly statistically significant variances among the studied groups, with the mean bleeding in the oxytocin group intraoperative (352.90±43.883 ml) lower than other groups. However, rectal misoprostol has better results in decreasing intraoperative blood loss (380.20±58.586 ml) than sublingual misoprostol (432.17±90.036 ml). At the same time, postoperative blood loss was less in sublingual (106.57±20.193 ml) than in rectal misoprostol (111.87±22.132 ml). Hence, there were highly statistically significant variances among the studied groups, with total blood loss lower in the oxytocin group contrasted with other groups and more with sublingual than rectal misoprostol.

This was in agreement with Yaliwal et al., which aimed to compare sublingual misoprostol versus intravenous oxytocin (10IU) in avoidance of postpartum hemorrhage during Cesarean delivery. It was claimed that more blood was lost in the misoprostol group than in the oxytocin group as the delayed effect of misoprostol caused blood to pool in the surgical area due to uterine atony, which hampered the surgeon's ability to close the uterine walls. Because of this, blood loss may have been higher.[14] Since oxytocin's activity was quicker than misoprostol, the research concludes it is more effective than misoprostol during cesarean delivery.

In contrast, Bagheri et al. Comparing three groups of rectal and sublingual oxytocin revealed that the groups differed in the mean amount of hemorrhage. Compared to other groups, the average amount of hemorrhage in the misoprostol group was 118.9 ml. The average blood loss in the sublingual misoprostol group was 138.9 ml, while the oxytocin group experienced 225.4 ml. Misoprostol administered rectally during surgery has a more significant effect on reducing hemorrhage than sublingual misoprostol and intravenous oxytocin, according to the researchers. [9]

The present study demonstrated that there was statistically significant variance among the studied groups concerning the need for additional oxytocin in the sublingual group, which was 6 cases. In the rectal group, there were 3 cases, while there were no cases in the oxytocin group.

These findings corroborated those of Yaliwal et al., who reported that misoprostol caused more significant blood loss than oxytocin and that eight misoprostol women needed extra oxytocics, whereas none of the oxytocin women did.[14] Contrary to our research, Bagheri et al. stated a significantly higher need for excess oxytocin in the oxytocin group than in the rectal and sublingual misoprostol group (p=0.001). [9]

In the current study, shivering and uterine atony were noticed more in the sublingual misoprostol group than others, and the rectal misoprostol group showed hyperpyrexia in more cases. At the same time, the oxytocin group showed respiratory distress apart from the other groups.

Higher rates of pyrexia and chills were seen with misoprostol usage compared to placebo, and this effect was shown more so with the sublingual than the rectal route, as demonstrated by Sweed et al. [10]

Our study disagrees with Albazee et al., who reported that The number of shivering females was significantly higher in the rectal misoprostol group than in the oxytocin group (p=0.004). Concerning postoperative pyrexia, nausea, and vomiting, no significant variance was identified among the two groups. [15]

Therefore, we recommend the addition of misoprostol with intravenous oxytocin as a uterotonic agent after cesarean or vaginal delivery to prevent postpartum hemorrhage.

4. Conclusion

This study showed that oxytocin had the upper hand over misoprostol in controlling blood loss, while rectal misoprostol was superior to sublingual misoprostol. As the use of rectal misoprostol not only reduces intraoperative blood loss but also has fewer adverse effects compared to sublingual Misoprostol..

Disclosure

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Authorship

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