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Umbilical Vein Injection of Misoprostol Versus Oxytocin for Managing Retained Placenta After Parturition: A Randomized Clinical Trial

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Abstract

Objectives: Retained placenta in the third stage of labor causes complications that may threaten a mother's life. In this clinical trial, we compared umbilical vein injection of misoprostol and oxytocin for managing the retained placenta in the women who had referred to Moheb-Yass and Shariati hospitals in Tehran and Bandar Abbas cities, Iran.

Materials and Methods: Between 2012 and 2015, 44 women with a long third stage of labor (retained placenta for more than 30 minutes) were chosen for this study. They were randomly divided into 2 groups: oxytocin and misoprostol groups (22 women in each group). In oxytocin group, oxytocin was injected into the umbilical vein with 50-unit concentration in 30 mL of normal saline. In misoprostol group, 800 µg of misoprostol was injected into the umbilical vein in 30 mL of normal saline. Placenta delivery time, bleeding after parturition, and hemoglobin drop were compared between the 2 groups.

Results: There was no significant difference between umbilical vein injection of misoprostol or oxytocin regarding spontaneous placental delivery in the mothers younger than 30 years old. Totally, spontaneous placental delivery was significantly more in the misoprostol group. This was magnified among women who were pregnant for more than 30 weeks.

Conclusions: Umbilical vein injection of misoprostol is more effective than that of oxytocin in managing the retained placenta in the third stage of labor.

Keywords: Retained placenta, Misoprostol, Oxytocin, Umbilical vein

Introduction

Parturition process consists of three stages: 1) from parturition pain onset to complete cervical dilatation; 2) from complete cervical dilatation to child delivery; and 3) from complete fetus delivery to placental delivery. Retained placenta means that the placenta is remained in the mother's uterine for a certain period after fetus delivery. This period is reported to be between 30-60 minutes in different countries (1,2).

The prevalence of retained placenta is different between various countries and it has been 0.01% to 6.3% in different studies (3). Parturition is a prevalent complication caused by a long third stage bleeding. It is a common cause of death in the developing and even developed countries (4).

Risk factors for the retained placenta can be gestational age (especially less than 26 weeks), preeclampsia, abortion history, old age, high polarity, use of parturition medicines such as oxytocin, being of non-Asian race and also other factors such as small placenta, too much bleeding and vaginal damage history (5). Furthermore, studies have revealed that taking intra-vein ergometrine can be a risk factor for the retained placenta (5-7). Likewise, taking methyl ergometrine rather than oxytocin is more associated with retained placenta (8). Many treatments have been proposed for the retained placenta, however, there are a few reports on using prostaglandins and umbilical vein injection of oxytocin (9). Moreover, different administration methods of oxytocin and misoprostol (oral, vaginal, or intravenous injection) have had different results (10,11).

We undertook this investigation because this treatment can prevent dangerous consequences for a mother's life. Few studies have compared the effects of umbilical vein injection of oxytocin and misoprostol. Therefore, this study compared the umbilical vein injection of misoprostol and oxytocin to manage retained placenta in the women who had referred to Moheb-Yass and Shariati hospitals in Tehran and Bandar Abbas cities, Iran.

Materials and Methods

This randomized clinical trial was done on 44 women suffering from a long third stage parturition (retained placenta after 30 minutes) who had referred to the hospital between 2012 and 2015. They were randomly divided into 2 groups: oxytocin and misoprostol groups. The inclusion criteria were: 1) successful first and second parturition stages and 2) having a retained placenta 30 minutes after fetus delivery. The exclusion criteria were: 1) instability

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of mother's homodynamic situation and 2) the patients request to be excluded. Written informed consent was obtained from the participants before their participation in the study. The participants were selected for each group based on tetra blocking method (Figure 1).

For the oxytocin group, 50 units of oxytocin was dissolved in 30 mL of normal saline and for the misoprostol group, 800 µg of the compound was dissolved in 30 mL of normal saline. Then they were injected into the umbilical veins of the participants. This method was based on the study of Harara et al (12). Vein oxytocin was not injected unless the placenta was delivered completely.

The data were obtained from a researcher-made questionnaire which was validated by a group of obstetricians and gynecologists. The study consequences, final time of placenta delivery and hemoglobin drop were recorded after the injections. The participants and physicians were unaware of the used medicines (the study was double-blinded). The following formula was used to calculate the sample size:

$n=Z^2 P(1-P)/d^2$

In this formula: as in previous studies (17), P= prevalence of retained placenta, 3% = 0.03; d = sample volume estimation accuracy, 0.1; Z= 95% confidence interval (α=5%), 1.96.

Considering the significance level of 0.05, at least 22 samples were required in each group. The considered variables were as follows: mother's age, gestational age, parturition and pregnancy frequencies, abortion, retained placenta, curettage and caesarian history, taking misoprostol or oxytocin, placental delivery time and hemoglobin.

The data were analyzed using statistical package for social sciences (SPSS) software version 16.0 (Chicago, IL, USA). Frequency and percentage were calculated for the qualitative variables and mean and standard deviation for the quantitative variables. Chi-square, Fisher's exact test and McNemar test were used to analyze qualitative data. Quantitative data were analyzed by T-test and Mann-Whitney U test.

Results

The participants' mean age was 30 ± 5 years old (ranging between 18 and 48 years old). The mean of gestational age was 35± 5 weeks (ranging between 24 and 42 weeks). There were 22 participants in each group (Table 1).

There was no significant difference between injecting misoprostol or oxytocin in spontaneous placental delivery in the mothers younger than 30 years old (P=0.08). However, there was a significant difference between injecting misoprostol and oxytocin in the mothers older than 30 years old. Totally, spontaneous placental

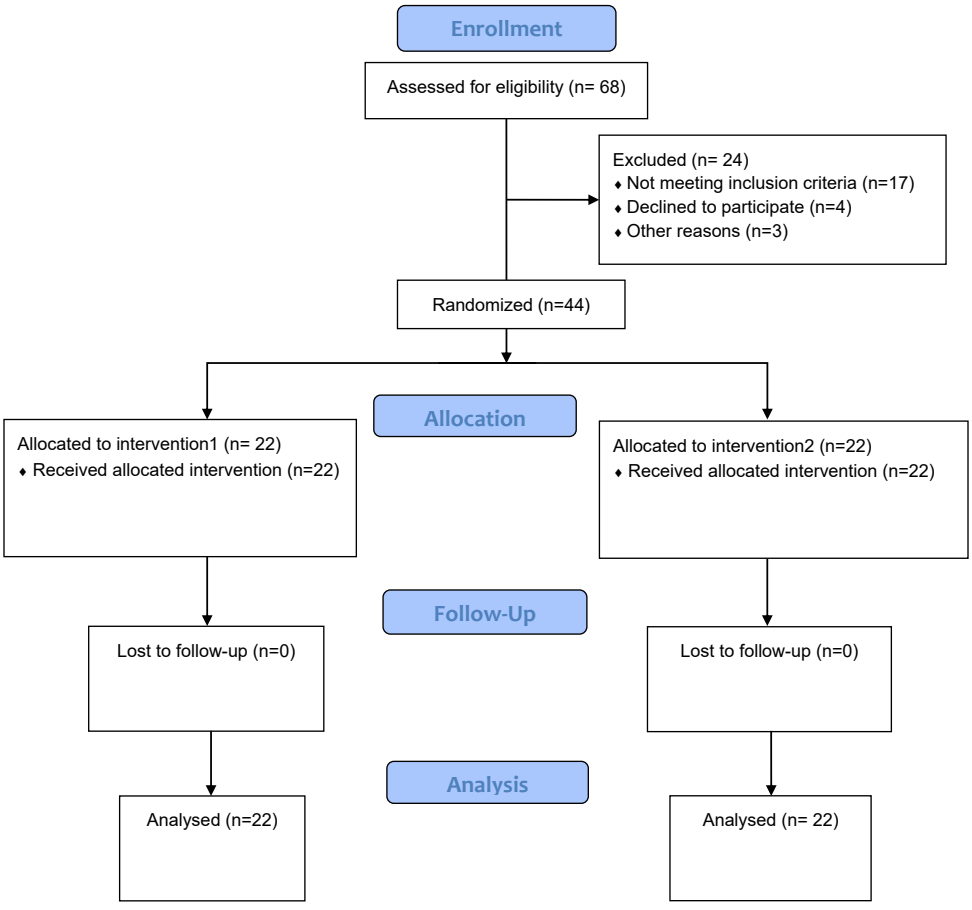

Figure 1. Flowchart of the Study.

Table 1. Previous Complications of the Participants

Variable	Group		*P* Value
	Misoprostol Group	Oxytocin Group	
Mean age	30.27 ± 5.95	29.90 ± 6.18	0.83
Mean gestational age	34.09 ± 6.10	36.32 ± 5.20	0.36
Number of previous abortions	10 (45.5%)	13 (60%)	0.37
History of retained placenta	7 (32%)	6 (27%)	0.74
Curettage history	11 (50%)	14 (64%)	0.36
Caesarian history	2 (9%)	2 (9%)	1
Blood pressure history in previous pregnancy	4 (18%)	7 (32%)	0.29
Blood pressure history in recent pregnancy	11 (50%)	15 (68%)	0.22
Hemoglobin amount before parturition	11.79 ± 1.47	11.8 ± 1.32	1

P value less than 0.05 was significant.

Table 2. Intervention of Mother's Age in Placental Delivery

Group of intervention			Placental Delivery		Total
			Spontaneous	Not Spontaneous	
Mother's Age	<30 years old	Misoprostol	6 (66.7%)	3 (33.3%)	9 (100%)
		Oxytocine	3 (27.3%)	8 (72.7%)	11 (100.0%)
		Total	9 (45.0%)	11 (55.0%)	20 (100.0%)
	≥30 years old	Misoprostol	10 (83.3%)	2 (16.7%)	12 (100.0%)
		Oxytocine	4 (40.0%)	6 (60.0%)	10 (100.0%)
		Total	14 (63.6%)	8 (36.4%)	22 (100.0%)

delivery was more in the misoprostol group than that in the oxytocin group ($P=0.03$; Table 2). There was no significant difference in placental delivery time between the 2 groups ($P=0.28$) (Table 3).

There was no significant difference in placental delivery between the participants with less than 30 gestational age in both groups. But there was a significant difference in the women more than 30 gestational age. The probability of placental delivery was more in the use of misoprostol compared to the use of oxytocin ($P=0.002$; Table 4).

There was a significant difference between the participants with less than three times of pregnancies in both groups in placental delivery ($P=0.006$). The probability of placental delivery was 14 times more in the misoprostol group (confidence interval: 1.5-147). However, there was no significant difference in placental delivery in both groups between the participants with less than three times of pregnancies ($P=0.05$; Table 5).

There was no significant difference between both groups regarding the placental delivery in the participants that had an abortion history, retained placenta, curettage, caesarian and pregnancy more than three times. However, among those who did not have these histories and had less than three pregnancies, the significant difference in placental delivery was nine times more in the misoprostol group compared to the oxytocin group ($P=0.02$). A significant difference was observed in hemoglobin level before and after the intervention in both groups, but there was less hemoglobin drop in the misoprostol group.

Table 3. Time of Placental Delivery

	Placental Delivery Time (min)		Total
	<5	>5	
Misoprosol group	3 (13.6)	19 (86.4)	22 (100.0)
Oxytocine group	1 (4.5)	21 (95.5)	22 (100.0)
Total	4 (9.1)	40 (90.9)	44 (100.0)

Data are shown as No. (%).

Discussion

Our results about the association of mother's age with the 2 treatments are similar to the results of Rogers and colleagues in which the spontaneous placental delivery with the umbilical vein injection of misoprostol was more than that with the umbilical vein injection of oxytocin (13). In the studies of Rajab et al (14) and Harara et al (12), spontaneous placental delivery was more in misoprostol group compared to placebo group. However, in these studies the differences were not significant. In the study of van Stralen et al, spontaneous placental delivery was also not significantly different between misoprostol and placebo groups. This might be because of oral administration of misoprostol or considering retained placenta for 60 minutes (15).

Regarding placental delivery time, there was no significant difference in our study which is inconsistent with the results of Harara et al. In their study, this time was shorter for the misoprostol group. This might be because of the difference in the concentration of injected oxytocin in the 2 studies. In a study by Eldaly, it was revealed that the placental delivery time had decreased efficiently when umbilical vein injection of oxytocin was associated with rectal use of misoprostol (16).

Table 4. Intervention of Gestational Age in Placental Delivery

Group of Intervention			Placental delivery		Total
			Spontaneous	Not Spontaneous	
Gestational age	<30 weeks	Misoprostol	2 (40.0)	3 (60.0)	5 (100.0)
		Oxytocine	0 (0.0)	3 (100.0)	3 (100.0)
		Total	2 (25.0)	6 (75.0)	8 (100.0)
	≥ 30 weeks	Misoprostol	14 (87.5)	2 (12.5)	16 (100.0)
		Oxytocine	7 (36.8)	12 (63.2)	19 (100.0)
		Total	21 (60.0)	14 (40.0)	35 (100.0)

Data are shown as No. (%).

Table 5. Intervention of Number of Pregnancies in Placental Delivery

Group of Intervention			Placental Delivery		Total
			Spontaneous	Not Spontaneous	
Pregnancy times	<3 times	Misoprostol	8 (72.7)	3 (27.3)	11 (100.0)
		Oxytocine	1 (20.0)	4 (80.0)	5 (100.0)
		Total	9 (56.3)	7 (43.8)	16 (100.0)
	≥3 times	Misoprostol	3 (60.0)	2 (40.0)	5 (100.0)
		Oxytocine	4 (30.8)	9 (69.2)	13 (100.0)
		Total	7 (38.9)	11 (61.1)	18 (100.0)

Data are shown as No. (%).

These differences in results can also be because of the number of participants. Non-significant difference in the effect of used medicines between the participants who had an abortion, retained placenta, curettage, caesarian and pregnancy more than three times could be because of vaginal scars caused by previous traumas. This might increase placenta adherence and interfere in the applied medicines. However, the effect of misoprostol is more than that of oxytocin in the cases who have no trauma history and therefore placenta adherence to the uterine wall is normal.

Less hemoglobin drop among misoprostol group in our results was similar to the results of Bellad et al (10), but different from those of Atukunda et al and Rajaei et al (11,17). In these 2 studies, hemoglobin drop was not significantly different between their study groups. But the concentration of medicine and method of administration were different in our study which can be the reason for the differences of the results.

Conclusions

Umbilical vein injection of misoprostol is more effective in treating elongated third stage labor (retained placenta for more than 30 minutes) and also in decreasing bleeding, especially in the cases without vaginal trauma history, compared to umbilical vein injection of oxytocin. Therefore, the use of this medicine is strongly recommended.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

The Ethics Committee of Tehran University of Medical Sciences, Iran, approved the study protocol and the study was registered in the Iranian Registry of Clinical Trials.

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