

A comparative study on infusion of usual dose of oxytocin and 80 units dose of oxytocin in the prevention of postpartum hemorrhage in cesarean section

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J. Adv. Pharm. Technol. Res.

ABSTRACT

Postpartum hemorrhage is one of the main causes of mothers' death mostly in developing country. The frequency of postpartum hemorrhage after natural pregnancy and cesarean are reported 2%–4% and 6%, respectively. The main goal of this study is to compare two regimens of oxytocine: One with high dose and the other with normal one to prevent uterine atony. The study has been done via a clinical trial method on 150 pregnant women in Zahedan, Iran. The society is randomly divided into two groups. The patients having risk factors of uterine atony and postpartum hemorrhage were omitted from the list. Oxytocin with 80 and 30 dose was, respectively, infused in 500 cc Ringer serum for control and witness group immediately after infant emersion during a period of 30 min. Decline of hemoglobin 6 and 24 h after cesarean section, uterine atony, blood infusion, and extra uterotonic drug needs after oxytocin infusion have been measured for both groups. The data have been analyzed using Chi-square via SPSS software. The result indicates that there exist meaningful differences between control and witness group in uterine atony and extra utertonic drug need while and after surgery (0 as compared with 22.6% and $P = 0$); whereas there is no significant difference between control and trial group in decline of hemoglobin 6 and 24 h after cesarean section ($P = 0.714$ and 0.231 , respectively). It means that oxytocin infusion with 80 dose has a good impact on the above four variances. It is recommended that oxytocin infusion with 80 dose during a period of 30 min could be a good substitution for oxytocin infusion with 30 dose for the prevention of uterine atony during and after cesarean delivery, especially when utertonic drug is not accessible and in the case of counterindication of other drugs' use.

Key words: Cesarean section, oxytocin, postpartum hemorrhage, uterine atony

INTRODUCTION

Neatly 600,000 women around the world die from postpartum hemorrhage annually. Postpartum hemorrhage

is the third leading cause of maternal death after pulmonary embolism and high blood pressure in developed countries and the first cause of maternal death in Iran. Postpartum hemorrhage is defined as bleeding >500–1000 cc after the third stage of delivery, and if it is not treated, it can lead to maternal complications.^[1-3] Severe hemorrhage refers to reduction of over 10% postpartum hematocrit or need for blood transfusion, which is seen in 6% of cases of cesarean

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How to cite this article: Ahmadi F. A comparative study on infusion of usual dose of oxytocin and 80 units dose of oxytocin in the prevention of postpartum hemorrhage in cesarean section. *J Adv Pharm Technol Res* 2018;9:102-6.

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Access this article online

Quick Response Code:



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DOI:

10.4103/japtr.JAPTR_297_18

section and 4% of normal delivery.^[1,2] About 75% of postpartum hemorrhage is associated with uterus atony.^[4] Although risk factors of uterus atony are well known, it is impossible to recognize women with atony individually. It has been reported that half of women with atony have been affected without any risk factor. The uterus that is excessively dilated is at the risk of postpartum atony. Thus, coarse embryos, twin pregnancy, and polyhydramnios are at risk of uterus atony, and women whose labor is associated with severe or almost ineffective uterus activity are at the risk of uterine atony. High parity and labor stimulation with oxytocin increase the probability of uterus atony and postpartum hemorrhage.

Another risk factor is the previous history of postpartum hemorrhage, as well as attempt to accelerate delivery by hand.^[6] Oxytocin, ergot alkaloids, and prostaglandins are the drugs used to stimulate uterine contractions in cases of postpartum hemorrhage.^[5] Oxytocin is a peptide hormone produced in the hypothalamus and secreted from the posterior pituitary. During pregnancy, its value does not change significantly and increases slightly before delivery but begins to increase during delivery and reaches its peak in the second stage.^[6] Its synthetic form is octapeptide with nine amino acids, of which six amino acids of it form a ring and the other three amino acids form a tail. One milligram of it is equivalent to 500 units of usp, and each cc of it is equivalent to 10 units of usp. Oxytocin is injected intravenously and intramuscularly and is also prepared as a spray. This drug is in the inactive edible form and does not bound to proteins in blood. This drug is broken down in the liver and kidneys with a half-life of 5 min. The pregnant uterus sensitivity to oxytocin is high and causes severe uterus contraction. The contractile power of this drug is reduced by the anesthetics of beta-adrenergic antagonists and magnesium sulfate.^[7] The onset of the effect after intramuscular injection is 2½ min. This effect is severe for 15 min and ends after ½ h.^[7] It contracts the uterus quickly in the uterus atony.^[6] Complications of oxytocin are very rare and include cardiovascular complications (hypotension and erythema), water poisoning, and nausea and vomiting. These complications are resolved by diluting in normal saline and Ringer's lactate solution.^[8] Oxytocin has been discovered and produced more than 50 years ago and is now widely used in delivery in developed countries.^[9] In fact, oxytocin is the only drug used to treat and prevent postpartum hemorrhage, and it is not associated with serious complication.^[8] Ergometrine is a kind of alkaloid derived from ergot.

Methylergometrine and ergometrine are derived from lysergic acid, and their effect is similar. These alkaloids are prepared as maleate (methergine) in the form of an injectable solution or tablet for oral use. This drug is a potent stimulant of uterine contraction, whose contractile effect on uterus is effective in controlling postpartum hemorrhage. Ergometrine maleate is

injected at a dose of 0.2–1 mg. This drug should be injected after the removal of placenta. Its side effects include diarrhea, nausea and vomiting, long-term vasospasm, insomnia, illusion, and a temporary increase in blood pressure.^[6] The α -F2 prostaglandins are prescribed intramuscularly. However, it is expensive and not available everywhere. Its prescription is associated with high risk. Recently, 20 mg prostaglandin E2 rectal suppositories have been used in the treatment of uterus atony, which can cause hypotension. Reports suggest that prostaglandin E1 (misoprostol) is effective in the treatment of uterus atony. However, it was concluded that the use of misoprostol is not more effective than oxytocin in preventing postpartum hemorrhage.^[10] Given the importance of the proper management of the third and fourth stages of labor in preventing postpartum hemorrhage and uterus atony (as one of its major causes) and the results of studies, comparison of two doses of oxytocin, one with usual dose of 30 units and the other with high dose of 80 units, can be effective in reducing postpartum hemorrhage resulting from uterus atony. It also reduces the need for other drugs, such as methylergometrine and prostaglandins, which are more complicated. In addition, oxytocin is also cheaper and more accessible. In recent studies, injecting high dose of oxytocin in vaginal delivery was associated with reduced hematocrit. The recent study may provide information on whether this reduction is also true in delivery.

METHODOLOGY

This study was a clinical trial and nonrandomized and convenient sampling method was used in this study. Research sample size was calculated to be 75 subjects in each group, and the subjects were randomly assigned to each group. Women with parity 0>7 (number of delivery), high blood pressure, preeclampsia, high parity, polyhydramnios, and elongated labor, women with hemoglobin less than 10 and systolic blood pressure less than 100 mmHg, those who had placenta previa were not included from the beginning of the study, and those who had prolonged surgery for any reason or needed blood transfusions were excluded from the study. Women with single pregnancy and the pregnancy number of less than seven times, without the above-mentioned criteria, were included in study. The research tool to collect the data was a questionnaire containing five demographic questionnaires, and a checklist for each patient on initial examinations and initial tests, atony and hemorrhage during and 1 h after the surgery, need for more uterotonic drug, hemoglobin drop 6 and 24 h after surgery, need for blood transfusion, and duration of operation was provided. To confirm the scientific validity of the questionnaire and the checklist, content validity was used, and to confirm the scientific reliability of the questionnaire and the checklist, simultaneous observation was used. Informed consent was first taken from all people who met the inclusion criteria. Then, information on blood pressure and routine tests such as hemoglobin check and other required information were taken from subjects. The subjects were

randomly assigned into two groups, in which the first group received 80 units of oxytocin and the second group received 30 units of oxytocin in the 500 cc Ringer serum immediately after the removal of placenta. The oxytocin used in this study was manufactured by Tamin Rasht Pharmaceutical Company. The incidence of atony and hemorrhage during the 1st h after surgery, need for additional uterotonic drug, blood transfusion, and duration of operation were recorded, and hemoglobin 6 and 24 h after operation was also recorded. Data were analyzed by SPSS 21 software (Uterotonic drug- oxytocin made by Caspian company, Tehran, Iran).

RESULTS

There was no significant difference between two groups in terms of age and number of pregnancies ($P=0.612$ and 0.535 , respectively). In this study, there were 17 atony cases in two groups, which each of 17 cases needed an additional drug. In the first group, no uterus atony was seen, and all 17 cases of uterus atony were seen in the second group. There was a significant difference between the two groups in terms of uterus atony and the need for other uterus contractile drugs ($P < 0.001$).

Table 1 shows the frequency of uterus atony in two groups and comparison of two groups (Chi-square test and Fisher's exact test).

There was no significant difference between two groups in terms of in terms of hemoglobin drop after 6 h ($P = 0.714$), although the hemoglobin drop was lower in the first group.

Table 2 provides the comparison of two groups in terms of hemoglobin drop 6 h after operation groups (Chi-square test).

Table 1: Frequency of uterus atony in two groups and comparison of two groups (Chi-square test and Fisher's exact test)

Uterus atony	Oxytocin dose (unit usp)				P
	80 units		30 units		
	Frequency	Percentage	Frequency	Percentage	
Yes	0	0	17	22.6	<0.001
No	75	100	58	77.33	
Total	75	100	75	100	

Table 2: Comparison of two groups in terms of hemoglobin drop 6 h after operation groups (Chi-square test)

Hemoglobin drop	Oxytocin dose (unit USP)						P
	30 units		80 units		Total		
	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	
2/1-3	5	6/66	6	8	11	7/3	>0/0.001
1/1-2	29	38/66	33	44	62	41/33	
≤1	41	54/66	36	48	77	51/33	

There was no significant difference between the two groups in terms of hemoglobin drop 24 h after surgery.

Table 3 shows the comparison of two groups in terms of hemoglobin drop 24 h after operation (Chi-square test).

There was a significant difference between the two groups in terms of the need for other uterus contracting drugs so that 17 subjects in the group receiving the usual dose needed for other drugs, and in the group received higher dose, none of the subjects needed other drugs.

Table 4 shows the comparison of two groups in terms of need for more uterotonic drug during and after cesarean section.

DISCUSSION AND CONCLUSION

Based on this study, the use of a dose of 80 units of oxytocin in prevention of uterus atony after cesarean section compared to a dose of 30 units of oxytocin leads to reduction in uterus atony and reduced need for an additional uterotonic drug. However, it has no significant effect on the rate of hemoglobin drop 6 and 24 h after surgery.

In a study conducted by Munn *et al.* (2001), two doses of 30 units and 80 units immediately after umbilical cord clamp were compared in cesarean section. It was found that need for an additional uterotonic drug in the group of 80 units was significantly lower compared to that in the group of 30 units and there was no significant difference between the two groups in terms of blood pressure drop. Our results were also in line with these results.^[11] In a study conducted by Alan *et al.*, three regimens of 80 units, 40 units, and 10 units in preventing uterus atony after vaginal delivery showed that the blood loss rate was not significantly different in

Table 3: Comparison of two groups in terms of hemoglobin drop 24 h after operation (Chi-square test)

Hemoglobin drop	Oxytocin dose (unit USP)						P
	30 units		80 units		Total		
	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	
2/1-3	14	18/66	9	12	23	15/33	>0/0.001
1/1-2	31	41/33	41	54/66	72	48	
≤1	30	40	25	33/33	55	36/66	

Table 4: Comparison of two groups in terms of need for more uterotonic drug during and after cesarean section

	The group needed for more drugs				P
	80 units		30 units		
	Frequency	Percentage	Frequency	Percentage	
Yes	0	0	17	22.6	<0.001
No	75	100	58	77.33	
Total	75	100	75	100	

two groups of high dose (80 units) and low dose (40 units and 40 units). In addition, in the group with higher dose, hemoglobin drop rate was more, which was different from the results of our study. Only the need for additional uterotonic drug was lower in the group with high dose, as our study.^[12] In a study conducted by Mojibian *et al.* (2005) in Yazd, the doses of 20 units and 100 units of oxytocin after the complete removal of embryo were compared, while type of delivery (cesarean section or vaginal delivery) was not accurately separated in this study. Based on the study conducted by Mojibian *et al.* in Yazd, the results showed that the rate of uterus atony cases and postpartum hematocrit loss was lower in the high-dose group and there was no significant between the two groups in terms of rate of blood pressure drop.^[13] In a study conducted by Dyer *et al.* to compare the doses of 80 units and 10 units, it was found that there was no difference between groups in terms of the need for more uterotonic drug and uterus atony, which this result was in contrast to our study result.^[14] The study conducted by Lee *et al.* (2014) compared the dose of 10 units and 30 units of oxytocin in the third stage of delivery in elective cesarean sections. There was no significant difference between the groups in terms of lost blood volume and the need for more uterotonic drug, which, in contrast to our results, lower doses of oxytocin were compared.^[15] In a study conducted by Gibbins *et al.* (2013) to compare the 40 units of oxytocin for 15 min per liter of normal saline serum with 800 µg sublingual misoprostol in the treatment of postpartum hemorrhage in elective cesarean section, the results showed that the volume of blood lost and the need for more uterotonic drug were significantly lower in the group receiving oxytocin than that in the group receiving misoprostol. In line with the results of this study, infusion of 40 units of oxytocin during 15 min indicated a better effect of oxytocin infusion with higher dose compared to other drugs. In addition, the rate of incidence of complications

was more in the misoprostol group.^[16] In a study conducted by Chaudhuri *et al.* (2012) to compare infusion of 10 units of oxytocin and 400 µg sublingual misoprostol in prevention of postpartum hemorrhage, it was found that postpartum hemoglobin drop and the volume of blood lost were equal in the two groups, and these results were in line with our results, but the complication of fever was >40°C in the misoprostol group, indicating a lower complication of oxytocin.^[17]

Given the above results and studies conducted in this area, it is recommended:

More studies are needed to identify the complications of higher doses to use the dose of 80 oxytocin units with more confidence to prevent and reduce postpartum hemorrhage. Due to the short half-life duration of oxytocin, studies are recommended on the duration of the effect of oxytocin on keeping the uterus contracted and serum levels of oxytocin at different postpartum hours. Given the cost-effectiveness and availability of oxytocin compared to other uterotonic drugs and lower complication of this drug compared to other drugs (ergot and misoprostol products), it is recommended that higher doses of oxytocin to be used, rather than using other drugs, to prevent postpartum hemorrhage.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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