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Original Article

Oxytocin Prophylaxis for Prevention of Postpartum Hemorrhage After Cesarean Delivery: Intravenous or Intramyometrial?

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ABSTRACT

Introduction and Aim: Postpartum hemorrhage (PPH) is a significant challenge after cesarean delivery. Oxytocin used to prevent uterine atony and reduce blood loss. However, there is no consensus on the standard route of administration. The current work aimed to investigate the efficacy and safety of intramyometrial versus intravenous route administration of oxytocin for reduction of PPH after cesarean sections.

Patients and methods: The study included 200 women, submitted for elective cesarean delivery from June 2019 through June 2021. They were divided into two equal groups, the intravenous injection of oxytocin (5 IU). The second for intramyometrial injection of 5 IU of oxytocin. Recorded data included blood pressure, heart rate, uterine contractility, before surgery, directly after injection of oxytocin and for 15 minutes. Pre- and post-operative hemoglobin was used as a reflection of blood loss. Finally, operative time and postoperative complications were recorded.

Results: Both groups were comparable regarding obstetric history, CS indications, delivery mode, operative time, uterine contractility and postoperative complications. There was a significant increase of systolic blood pressure at 1, 2 3, and 4 min, and a significant increase of DBP at 2, 3, 4, 5, 6, 8, 11, 12, 13, 14, and 15 min after oxytocin administration, in the intravenous than the intramyometrial group. Heart rate significantly reduced in intravenous than the intramyometrial group at the first minute. The hemoglobin deficit was significantly higher among the intramyometrial group (1.05 ± 0.31 vs 0.87 ± 0.39 g/dl). Postoperative complications were fever (5%), urinary tract infection (7%) and wound infection (6%).

Conclusion: Intramyometrial injection of oxytocin had more transient hypotension and increased blood loss. Thus, it could be said that, the intramyometrial route had no clinical advantages over the intravenous route. However, taking into considerations the possible risk factors for blood loss, the current results could be explained with caution.

Keywords: Oxytocin; Intravenous; Intramyometrial; Postpartum Hemorrhage; Cesarean Delivery.



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INTRODUCTION

Postpartum hemorrhage (PPH) remains a major cause of maternal morbidity and mortality, regardless major advances in the management techniques, specifically after cesarean delivery. The continuous increase of cesarean delivery consequently increases the burden of PPH. However, PPH is a preventable cause of maternal mortality, specifically with provision of proper medical management^(1,2).

PPH is mostly due to uterine atony and usually presented immediately after delivery. Placenta previa and accreta were the two major risk factors for PPH. Other associated factors include multiparity, twin pregnancies, obesity, macrosomia, cesarean delivery, and preeclampsia^(3,4). However, about two thirds of PPH occur without any known predisposing factors⁽⁵⁾.

Oxytocin is normally secreted by the posterior pituitary gland. It contracts the smooth muscle fibers of the uterus. It is the first choice uterotonic used during cesarean deliveries. It is routinely administered by the intravenous route after cesarean delivery to increase the uterine contraction and prevent postpartum hemorrhage^(6,7). However, the direct intramyometrial injection of oxytocin after fetus extraction had been suggested to replace the postoperative intravenous injection. It was suggested to promote uterine contraction and prevent PPH more effectively. However, the topic is not sufficiently addressed^(8,9).

The current work was designed to investigate the efficacy and safety of intramyometrial injection of oxytocin versus intravenous route for prophylaxis of PPH after cesarean sections.

PATIENTS AND METHODS

The present study included 200 females who were presented for elective cesarean section at Damietta General Hospital (Damietta, Egypt). They were recruited from June 2019 through June 2021.

Inclusion and exclusion criteria: Women were included if they were scheduled for elective cesarean delivery under spinal anesthesia, provided that, she had singleton or twin pregnancy, had polyhydramnios or placenta previa. In addition, the delivery was scheduled after full-term pregnancy.

On the other side, those with contraindication to spinal anesthesia, scheduled for emergent cesarean delivery or preterm delivery, had uterine fibroid, hypertension or cardiac diseases, and those who received intravenous ephedrine with 10 minutes of delivery, were excluded from the study.

Patients were randomly allocated to one of two equal groups (each 100 women): the first (the control group) received oxytocin 5 IU by intravenous infusion in 500 ml of saline, and for blinding, an intramyometrial injection of 2 ml saline was administered. The second received 500 ml saline by intravenous infusion, and oxytocin 5 IU (diluted in 2 ml of saline) was received by intramyometrial injection (The study group).

Randomization was performed using the closed envelope method, with a single number included and indicated the group.

The envelope was opened by a nurse in the surgical theatre.

Spinal anesthesia was induced in the sitting position at the L₂₋₃ or L₃₋₄ interspaces using a 27-gauge spinal needle. Intra-operative monitoring included ECG, pulse oximetry and automated non-invasive blood pressure monitoring. All parturients received 3 L/minute of oxygen by nasal cannula or nasal mask until delivery of the infant.

The patient was positioned supine with left uterine displacement with a standard device immediately after intrathecal injection.

Ephedrine was administered in 5 mg increments by intravenous injection before delivery if systolic blood pressure (SBP) decreased to <100 mmHg. The researcher – with help of a pharmacist- prepared the syringes containing the study solutions under aseptic conditions according to the random table and delivered them to the delivery room in a plastic bag. A 3 ml syringe with a 22-needle contained 2 ml of the study solution for intramyometrial administration. The second 1.0 ml syringe contained 0.5 ml of study solution for intravenous injection.

All parturients were given two simultaneous injections. The injections were conducted in a double-blind fashion where neither the attending anesthetist nor obstetrician had knowledge of the content of the syringes.

Patients in the intramyometrial group received intramyometrial 2 ml oxytocin (5 IU/ml) in the uterine fundus and 0.5 ml intravenous sterile saline. Conversely, women in the intravenous oxytocin group received 2 ml sterile saline into the myometrium and 2 ml (5 IU/ml) oxytocin.

Intramyometrial and intravenous injections of study solutions were given immediately after the expulsion of the placenta. The obstetrician assessed uterine tone on a 10-point linear analog scale s (0 = flaccid, 10 = maximum contraction)

The following data were recorded: 1) Baseline blood pressure, 2) heart rate before delivery and at one-minute interval for fifteen minutes after injection of oxytocin; 3) uterine contractility at 1,2,4,6,8,10 and 15 minutes after oxytocin injection; 4) hemoglobin before surgery and on the first post-operative day; 5) the total volume of crystalloid solutions infused during operation and total operative time.

Statistical data analysis:

The data analysis was performed by the statistical package for social sciences, version 16 (SPSS Inc., Chicago, Illinois, USA). Data were anonymized and coded before entrance to SPSS. Categorical data were presented in the form of relative frequency and percentages, while quantitative data were presented in their means and standard deviations (SD). Minimum and maximum values were also calculated for quantitative data. Two means were compared by independent sample's student test "t-Test", while categorical parameters were compared by Chi square or equivalent tests according to the data situation. P value < 0.05 was considered significant.

RESULTS

Table (1) showed patients demographics, obstetric history, mode of delivery, CS indications and total operative time. There was no statistically significant difference between both groups regarding any variables.

Systolic blood pressure showed non-significant difference between IV and IMY groups at all times, except the significant increase in IV than IMY groups at 1, 2 3, and 4 minutes after oxytocin administration (Table 2). In addition, there was a significant increase of diastolic blood pressure in IV than IMY group at 2, 3, 4, 5, 6, 8, 11, 12, 13,1 14, and 15 minutes after oxytocin administration (Table 2).

Heart rate however, showed non-significant difference between IV and IMY groups at different points of time, except a significant decrease of heart rate in the intravenous than the intramyometrial group at the first minute after oxytocin

administration (Table 3).

Regarding contractility, there was no significant difference between IV and IMY groups at any time after oxytocin injection (Table 4).

Preoperative and postoperative hemoglobin were comparable between both groups. However, the hemoglobin deficit (preoperative-postoperative values) was a significantly higher among the IMY than IV group (1.05±0.31 vs 0.87±0.39 g/dl, respectively). The intraoperative fluid administration also did not differ significantly between both groups (Table 5).

Regarding postoperative complications, it was in the form of fever in 5% of cases, urinary tract infection (UTI) in 7% and wound infection in 6% and there were no complications in 82% of cases; with statistically insignificant difference between groups (Table 6).

Table (1): Comparison between IV and IMY groups regarding patient demographics, obstetrics history, delivery, indication of CS and total operative time

Variables		IV group	IMY group	Test	P
Age (years)	Mean±SD; Min.-Max.	27.76±2.13; 22-31	28.30±1.99; 21-32	1.85	0.07
Gravidity	Mean±SD; Min. – Max.	3.10±0.78; 1-4	3.22±0.50; 2-4	1.28	0.20
Parity	Mean±SD; Min. Max.	2.10±0.79; 0-3	2.20±0.53; 1-3	1.05	0.29
Previous abortion (n, %)	None	76(76.0%)	78 (78.0%)	0.69	0.71
	Previous one	20 (20.0%)	20 (20.0%)		
	Previous Two	4 (4.0%)	2 (2.0%)		
GA at delivery	Mean±SD;	38.1±0.91; 37- 40	37.9±0.75; 37 - 39	1.69	0.09
Mode of last delivery	CS	44 (44.0%)	52 (52.0%)	1.28	0.26
	NVD	56 (56.0%)	48 (48.0%)		
CS indications	Previous CS	36 (36.0%)	42 (42.0%)	2.46	0.78
	Malpresentation	12 (12.0%)	8 (8.0%)		
	Twin pregnancy	10(10.0%)	12 (12.0%)		
	Placenta previa	4 (4.0%)	6 (6.0%)		
	Polyhydramnios	32 (32.0%)	26 (26.0%)		
	Accidental hemorrhage	12 (12.0%)	6 (6.0%)		
Operative time (minute)	Mean±SD; Min. – Max.	46.16±11.39; 30-69	47.22±11.69; 31- 70	0.65	0.51

Table (2): Comparison between study groups regarding systolic blood pressure at different time intervals

		Group 1(IV)		Group 2 (IMY)		Statistics	
		Mean	S. D	Mean	S. D	t	p
Systolic BP	Preoperative	122.30	5.73	122.10	7.22	0.21	0.82
	Basal	117.26	5.58	117.76	6.08	0.60	0.54
	At 1 min.	106.20	4.69	102.70	5.17	5.03	<0.001*
	At 2 min.	109.00	4.73	104.46	4.33	7.10	< 0.001*
	At 3 min.	109.50	4.87	105.80	4.08	5.84	< 0.001*
	At 4 min.	108.30	4.69	104.90	3.97	5.55	< 0.001*
	At 5 min.	106.60	4.21	105.80	3.69	1.43	0.15
	At 6 min.	105.20	4.51	104.40	3.86	1.35	0.17
	At 7 min.	104.20	4.20	103.60	4.04	1.03	0.30
	At 8 min.	103.40	4.78	103.00	4.28	0.62	0.53
	At 9 min.	102.58	4.44	102.40	4.19	0.29	0.76
	At 10 min.	102.20	4.31	102.30	4.06	0.17	0.86
	At 11 min.	101.58	4.08	99.42	13.21	1.57	0.12
	At 12 min.	101.08	3.93	100.70	2.85	0.78	0.43
	At 13 min.	100.68	4.02	100.30	2.74	0.78	0.43
At 14 min.	100.58	3.97	99.70	2.75	1.83	0.08	
At 15 min.	100.08	4.55	99.40	2.60	1.30	0.19	
Diastolic BP	Preoperative	82.40	5.07	82.70	6.71	0.35	0.72

		Group 1(IV)		Group 2 (IMY)		Statistics	
		Mean	S. D	Mean	S. D	t	p
	Basal	77.34	5.02	77.86	6.07	0.66	0.50
	At 1 min.	66.50	4.65	65.40	3.89	1.82	0.07
	At 2 min.	69.20	4.66	65.10	3.73	6.89	< 0.001*
	At 3 min.	74.40	4.47	70.80	4.32	5.81	< 0.001*
	At 4 min.	68.80	4.23	65.50	3.67	5.91	< 0.001*
	At 5 min.	67.10	3.92	66.00	3.91	1.99	0.0047*
	At 6 min.	65.90	4.36	64.50	3.67	2.46	0.015*
	At 7 min.	64.80	3.90	63.80	3.71	1.86	0.064
	At 8 min.	64.60	3.89	63.50	3.67	2.06	0.040*
	At 9 min.	63.82	3.69	62.90	3.65	1.78	0.08
	At 10 min.	63.28	3.72	62.50	3.81	1.47	0.13
	At 11 min.	62.68	3.51	61.50	3.23	2.48	0.014*
	At 12 min.	62.88	3.03	61.00	2.67	4.67	<0.001*
	At 13 min.	62.18	2.48	60.50	2.52	4.76	<0.001*
	At 14 min.	61.78	2.40	59.90	2.57	5.36	< 0.001*
	At 15 min.	61.58	2.73	59.60	2.44	5.43	< 0.001*

Table (3): Comparison between studied groups as regard heart rate at different time intervals

Heart rate	Intravenous		Intramyometrial		Statistics	
	Mean	SD	Mean	SD	t	p
Preoperative	89.66	5.19	88.28	8.10	1.47	0.14
Basal	80.68	7.00	80.78	8.57	0.18	0.84
At 1 min.	92.12	5.00	96.30	5.33	7.24	<0.001*
At 2 min.	90.40	5.04	89.90	7.08	0.55	0.58
At 3 min.	90.74	5.09	89.70	6.51	1.37	0.17
At 4 min.	85.24	5.22	85.70	8.31	0.67	0.50
At 5 min.	88.40	4.52	88.10	5.41	0.36	0.72
At 6 min.	87.90	5.52	86.70	5.04	1.76	0.08
At 7 min.	85.70	4.75	84.90	5.07	1.26	0.20
At 8 min.	84.90	5.53	84.30	5.35	0.97	0.33
At 9 min.	84.14	5.16	83.80	5.53	0.39	0.69
At 10 min.	83.70	5.18	82.81	5.42	0.17	0.86
At 11 min.	82.98	4.89	82.70	5.99	0.50	0.61
At 12 min.	82.58	4.80	82.10	5.54	0.73	0.46
At 13 min.	82.18	4.90	81.70	5.50	0.72	0.47
At 14 min.	81.99	4.90	81.10	5.57	1.67	0.10
At 15 min.	81.80	5.26	80.80	5.49	1.66	0.09

Table (4): Comparison between the study groups as regard uterine contractility at different time intervals

Uterine contractility	Intravenous		Intramyometrial		Statistics	
	Mean	SD	Mean	SD	t	p
At the first minute	8.07	0.79	8.17	0.75	0.91	0.36
At the second minute	8.34	0.55	8.24	0.59	1.23	0.21
At the 4 th minute	8.34	0.55	8.26	0.56	1.01	0.31
At the 6 th minute	8.35	0.59	8.28	0.53	0.87	0.38
At the 8 th minute	8.06	0.55	8.00	0.53	0.78	0.43
At the 10 th minute	7.90	0.54	7.88	0.59	0.25	0.80
At the 15 th minute	8.55	6.93	7.82	0.52	1.05	0.29

Table (5): Comparison between the study groups regarding hemoglobin concentration and total intraoperative crystalloids

		Mean	S. D	Minimum	Maximum	t	p
Preoperative Hemoglobin	Group 1	11.66	0.56	10.10	12.60	1.58	0.12(NS)
	Group 2	11.71	0.46	10.30	12.40		
Postoperative Hemoglobin	Group 1	10.79	0.70	8.50	11.80	1.04	0.30(NS)
	Group 2	10.66	0.53	9.00	11.70		
Hemoglobin deficit	Group 1	0.87	0.39	0.40	1.70	3.99	<0.001*
	Group 2	1.05	0.31	0.40	1.90		
Total intra-operative crystalloids	Group 1	2070.00	298.975	1500.00	2500.00	1.51	0.13(NS)
	Group 2	2165.00	325.806	1500.00	2500.00		

Table (6): Comparison between the study groups as postoperative complications

	Group 1 (n=100)		Group 2 (n=100)		Total (n=200)	
	n	%	n	%	n	%
None	42	84.0%	40	80.0%	82	82.0%
Fever	3	6.0%	2	4.0%	5	5.0%
UTI	3	6.0%	4	8.0%	7	7.0%
Wound infection	2	4.0%	4	8.0%	6	6.0%
Statistics	X ² =1.06, p = 0.78					

DISCUSSION

Cesarean delivery increased continuously during the last years. With the subsequent increase of associated morbidity and mortality. Hemorrhage, anemia, and the need for blood transfusion are the main complications of CS delivery. The CS-associated intra or post-partum hemorrhage is a major challenge, and prophylaxis and proper management are of utmost importance. However, the active management of the third stage at CS received little attention⁽¹⁰⁾.

Oxytocin is widely used to restore uterine tone and reduce postpartum blood loss after cesarean delivery. At least, more than 38 different oxytocin infusion protocols exist, with the lack of consensus^(11,12).

The bolus dose of 5 units of intravenous oxytocin was recommended due to reported deaths after oxytocin administration⁽¹³⁾. However, side effects still reported after rapid IV injection⁽⁹⁾.

Oxytocin is routinely used by intravenous injection after CS to promote uterine contractions. Thus, decreasing blood loss from the placental site. However, IV bolus injection is associated with a transient hypotension, with hypovolemia or cardiac disease. Uterine atony could also be prevented by direct intramyometrial injection of oxytocin⁽⁸⁾.

It is hypothesized that, intramyometrial oxytocin injection during CS will result in a significant reduction of side effects associated with direct IV injection. Thus, the present work was designed to compare intravenous versus intramyometrial injection of similar doses of oxytocin. The present study included 200 women presented for elective cesarean section at Damietta General Hospital, Damietta, Egypt. Patients were randomly allocated to one of two equal groups, *The first* received intravenous oxytocin 5 IU. *The second* received Intramyometrial oxytocin in a dose of 5 IU. Hemodynamics and side effects were recorded.

We can summarize the main findings of our study as the following: no significant differences were found between both groups regarding age, obstetric history, indications of CS, uterine contractility or complications after CS. These results are in agreement with that reported by Dennehy *et al.*⁽¹⁴⁾ who reported that, there was no difference between groups in demographic data. There was also no difference between groups in the volume of Ringer's lactate infused before injection of oxytocin or the recorded timelines during surgery. They added, there was no difference between groups in uterine tone after oxytocin injection.

On the other hand, in the present study, Systolic blood pressure showed non-significant difference between IV and IMY groups at all times, except the significant increase in IV than IMY groups at 1, 2 3, and 4 minutes after oxytocin administration. In addition, there was a significant increase of diastolic blood pressure in IV than IMY group at 2, 3, 4, 5, 6, 8, 11, 12, 13, 14, and 15 minutes after oxytocin administration. Finally, there was a significant increase of heart rate in the intramyometrial injection group at the first minute after injection. These data can be explained by the short half-life of intravenous injection oxytocin (4-10 minutes)⁽¹⁵⁾.

Our results indicated that, both routes of oxytocin administration have nearly an equal safety profile. These results are in agreement with Dennehy *et al.*⁽¹⁴⁾ who reported that, systolic blood pressure was also lower in the intramyometrial group than the intravenous group at the three- and four-minute intervals after oxytocin injection. Heart rate increased one minute after oxytocin administration in both groups, but the increase in heart rate was higher in patients in the intramyometrial group. The most likely explanation for decreased blood pressure in the intramyometrial than the intravenous group, is that intramyometrial oxytocin injection results in extensive, rapid absorption of oxytocin from the myometrium into the systemic circulation.

Furthermore, unexpectedly, the results of the present study showed significantly increased hemoglobin deficit in the intramyometrial than the intravenous group. This reflects increased blood loss with intramyometrial injection in comparison to intravenous injection, but it cannot be completely explained by the administration route, as many other factors may contribute to increased blood loss, such as the indication of CS.

These results are in contradiction to that reported by Dennehy *et al.*⁽¹⁴⁾ who reported that, there was no difference between study groups in hemoglobin concentration 24 h after CS, indicating that there was no difference between the groups in the amount of blood lost during surgery. The explanation for this contradiction may be related to different indications for CS between both studies. In addition, they did not attempt to estimate blood loss, as this is notoriously difficult considering admixture of amniotic fluid in suction apparatus and bleeding from sources other than the placental site, where we indirectly estimated blood loss by measuring hemoglobin deficit. Confirming this explanation, it was reported that, increasing parity order, induction of labor, and labor arrest may be related to uterus atony⁽¹⁶⁾ and thus explain the association with severe blood loss. In addition, bleeding episodes during pregnancy and

low hemoglobin levels were not associated with severe blood loss in elective cesarean delivery.

Also, bleeding episodes combined with low hemoglobin level was a stronger predictor than low hemoglobin level only, whereas bleeding episodes not followed by a low hemoglobin value was marginally associated with severe blood loss. This indicates that there are maternal- and/or delivery-related conditions that trigger severe bleeding in this particular patient group that cannot be attributed to placenta previa or placental abruption (no interaction/ small numbers) ⁽¹⁷⁾.

It is well known that intravenous bolus injection of oxytocin may result in short-lived hypotension in non-pregnant patients, during pregnancy and after Caesarean delivery. The cause of the observed hemodynamic changes is controversial and most likely multi-factorial ⁽¹⁴⁾.

These data were confirmed by who Yamaguchi *et al.* ⁽¹⁸⁾ reported that, besides the contraction of the uterine smooth muscle and myoepithelium that surrounds the alveolar ramifications in the breast, oxytocin has systemic effects, such as relaxation of the smooth muscle of the vessels, promoting vasodilation; this leads to a reduction in systolic blood pressure and, especially, of the diastolic blood pressure, besides reflex tachycardia. This vasodilation, usually temporary, can be clinically significant when oxytocin is administered in bolus, and may lead to a reduction in coronary perfusion and cardiac collapse; these effects are more prominent in the presence of general anesthesia. It was demonstrated that the association of the bolus administration of oxytocin with general anesthesia could reduce mean arterial pressure by up to 30% to 40 seconds after the injection, lasting up to 210 seconds.

Initially, it was believed that this cardiac effect was due to maternal self-transfusion after detachment of the placenta, but it has been shown that the cardiac output also increases when a bolus of oxytocin is administered at the beginning of the pregnancy (in uterine curettage, for example). It was then suggested that pure synthetic oxytocin had a β -stimulating action, increasing chronotropism and inotropism, and promoting peripheral vasodilation. Since this has not been proven yet and the cardiac changes appear from 10 to 20 seconds after vasodilation, it is more probable that this is a reflex phenomenon. More importantly, the cardiovascular effects seem a consequence of the excessive administration of oxytocin and not of its preservative. Thus, it should be clear that parturients that do not have cardiac disorders tolerate the vasodilation, and its cardiovascular consequences, after the administration of bolus or excessive doses of oxytocin. However, this can be fatal in parturients under anesthesia who present hypovolemia or with preexisting disorders of the cardiovascular system, such as valvulopathy, hypertension, fixed cardiac output, or disease of the myocardium ⁽⁹⁾.

Previous studies in intact animals indicate that administration of oxytocin results in peripheral vasodilatation, resulting in a decreased mean arterial pressure with an associated increase in heart rate and cardiac output). Some investigators have observed a biphasic change in blood

pressure; an initial decrease followed by an increase in mean arterial pressure. However, these effects may be attributed to preservatives added to general anesthetics used such as chlorobutanol ⁽¹⁹⁾.

Pure oxytocin has been shown to have positive chronotropic and inotropic effects in amphibians, reptiles and mammals. These studies indicate that the observed increase in heart rate and cardiac output may also be the result of a direct cardiac effect, not merely a reflex response to peripheral vasodilatation. Pure oxytocin is an arteriolar vasoconstrictor in animals, and also causes constriction of the human umbilical and cerebral vasculature ⁽²⁰⁾.

In addition, oxytocin plays a role in the central control of cardiovascular function. Wsol *et al.* ⁽²¹⁾ determined that oxytocin decreased the sensitivity of the baroreflex in conscious rats. Furthermore, oxytocin may play a role in modulating autonomic control of the heart. Thus, it can be said that, there is no evidence that oxytocin per se is a direct negative inotropic drug or causes peripheral vasodilatation. Rather, the temporary hypotensive effect observed after intramyometrial or intravenous bolus administration of commercial oxytocin solution may largely be due to the negative inotropic and vasodilatory effect of the preservative ⁽²¹⁾.

In summary, the results of the present study revealed that, intramyometrial oxytocin results in more severe transient hypotension than does intravenous injection after elective Cesarean delivery. In addition, intravenous and intramyometrial injections of oxytocin result in similar, effective uterine contraction after Cesarean delivery. However, blood loss is more extended with intramyometrial injection. Thus, it can be concluded that, there is no clinical advantage associated with administration of oxytocin by the intramyometrial route rather than by conventional intravenous injection. Additionally, intramyometrial injection had a drawback of increased blood loss, but, taking into consideration the possible risk factors increased blood loss as incision, uterine atony, indication for cesarean, this result needs to be reevaluated and validated.

Declaration of Financial and Non-Financial Relationships and Activities of Interest:

None to be declared

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