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RESEARCH ARTICLE

Comparison of the Mean Minimum Dose of Bolus Oxytocin for Proper Uterine Contraction during Cesarean Section

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Abstract: ***Background*:** Cesarean section is the most common midwifery operation. The aim of this study is to determine the mean minimum dose of bolus oxytocin for proper uterine contraction during cesarean section.

***Methods*:** Patients were divided into two groups: elective cesarean section (n=41) and cesarean section due to difficulty in labor (n=42 patients). Patients underwent spinal anesthesia and oxytocin infusion was begun at 30 drops per minute (20 units of oxytocin per 1000 cc serum), and was also administered as a half-dose in cc to achieve effective contraction of the uterus. Meanwhile, the information of patients including systolic and diastolic blood pressure (SBP and DBP), heart rate and amount of bleeding during the operation was recorded in a questionnaire.

***Results*:** In the elective cesarean section group, the average SBP was about 117.10mmHg, average DBP 70.50 mmHg, the amount of bleeding during surgery was 623.63mL, and heart rate was 88.88bpm. In the cesarean section group due to difficulty in labor progress, SBP was 113.5 mmHg, DBP 62.69 mmHg, and bleeding was 573.81mL. In addition, 9 patients in the elective group and 3 patients in the lack of progress group, did not require bolus oxytocin. In the lack of a progress group, 8 patients needed more than 5 doses of oxytocin. In addition, about 10 (12%) of all patients had no side effects, and hypotension.

***Conclusion*:** Given that, the minimum effective dose of oxytocin in the elective cesarean section was 1IU, and in those in labor progress was 1-1.5IU, less oxytocin administration represents lesser side effects. It is recommended that patients who are candidates of cesarean section should be administered 1.5IU of oxytocin in the form of bolus.

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1. INTRODUCTION

Today, cesarean section is the most common midwifery operation, where studies have shown that 30% of dystocia, 30% of fetal distress and breech pregnancy are responsible for most cases of cesarean section, and progression of labor disorder [1]. The maternal mortality rate in the cesarean section is twice as that of vaginal delivery [2]. One of the causes of maternal mortality is bleeding. Oxytocin, in the form of the drug, is used intravenously on a daily basis all over the world to reduce the rate of postpartum bleeding [3]. It reduces bleeding from the placenta by activating the uterine contraction [4]. IV administration of oxytocin can lead to side effects such as hypotension, nausea, vomiting, chest pain, headache, choking and cardiac muscle infarction [5].

Different doses of oxytocin have been recommended, most of which are concluded from experimental studies, and therefore, the minimum effective dose of oxytocin in cesarean section is yet to be determined. British National Formulary recommends that oxytocin should be given at the dose of 5IU, slowly after delivery [6, 7]. In the United States, the infusion is prescribed at 10-40 units per liter for postpartum hemorrhage [8], but there is no evidence to support the suitability of this dosage [9]. Other proposed protocols include; 10 intramuscular units, 5-10 units of rapid bolus intravenous doses and 0.5-20units / liter infusion at a rate of 100-150 ml / h [10].

On the other hand, the physiological effects of oxytocin can affect the concentration of oxytocin receptors in the uterus and serum oxytocin level [11]. Estrogen can increase the function of the uterine oxytocin receptors during pregnancy, for maximum supply, which is why the uterus is highly susceptible to oxytocin-based side-effects, thereby, some studies suggest a very low dose of oxytocin to be ad-

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ministered [12]. High doses of oxytocin, especially bolus doses, are associated with complications such as hypotension, nausea, vomiting, dysrhythmia, ST-T-segment changes, pulmonary edema, water poisoning and seizures [13, 14]. Thus, a minimal dose of oxytocin needs to be utilized for the purpose [15]. This study was conducted to compare the minimum effective dose of oxytocin needed for effective uterine contraction in women who had been nominated for elective cesarean section in comparison with cesarean section due to lack of labor progression (stalled labor).

2. MATERIALS AND METHODS

This is a cross-sectional study conducted on the patients who were referred to Aslani hospital in Khorramabad in 2016, for childbirth. After the approval of the study plan by the University Research and Ethical committee, patients who were admitted within the 3 months of study were included. Patients were divided into two groups: those with elective cesarean section (n=41) and those with cesarean section due to difficulty in labor (stalled labor, n=42 patients). Written consent was obtained before the initiation of the study from all patients. Inclusion criteria were ASA I or II, age between 18 and 40 years, singleton pregnancies, and elective CD with a Pfannenstiel incision. Patients with active labor pain, multiple gestations, ruptured membrane, preeclampsia and eclampsia, cardiovascular instability, placenta previa, and diabetes mellitus, were excluded from this study.

Midwifery data including, the duration of the second stage of labor, dilation of the cervix at the time of labor progress, and the duration intravenous oxytocin administration was recorded. Infusion of oxytocin was halted in the cesarean section in stalled labor group, 30 minutes before the surgery.

In each patient, blood pressure and heart rate were checked and 18G cannula peripheral intravenous line was inserted where 10 ml/kg of Ringer Lactate solution was preloaded, 30 minutes before spinal anesthesia, 1.5 to 2 cc of 5% xylocaine, administered at L2-L3 or L3-L4 levels, with needle number 25. In supine positions, the patient received supplemented oxygen through a mask. Surgery proceeded after achieving a T6 sensory level to pinprick. The anesthetist and obstetrician involved in each case were blinded in the study to the oxytocin dose.

Monitoring includes TB, T4, non-invasive baseline blood pressure after every 2 minutes; systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and pulse oximetry, recorded before administering spinal anesthesia. If the SBP was reduced by more than 20%, 5 mg ephedrine was administered. Immediately after the surgery, oxytocin was first prescribed as a bolus. The initial dose of bolus was 1IU. Oxytocin was administered from a syringe containing 1IU/mL, within 5 seconds. The obstetrician was told to allow assisted placenta spontaneous delivery, without massage of the uterine, and to keep the uterus inside the abdominal cavity until the spontaneous uterine contraction was achieved.

Once the delivery of the accomplished, uterine incision was closed. The obstetrician rated the degree of uterine contraction as either satisfactory or unsatisfactory.

In this study, we define the minimum effective dose as the dose at which satisfactory response was achieved in 90% of patients (*i.e.*, ED90). The surgeon then pushed out the uterus out of the uterine cavity with the exit of the placenta without massaging the womb to begin to close the lining. At the same time, oxytocin infusion was initiated at 40 mU/min, which was 20IU oxytocin per 1000 cc serum at a rate of 30 drops/min. After 2 minutes, the interval between bolus and the initial dose was observed by the surgeon to determine the satisfaction level of the contraction. In the case of inadequacy, another 0.5IU of oxytocin was injected into the bolus, and this procedure was repeated every minute to provide a satisfactory uterine contraction, determined by the surgeon.

Oxytocin was recovered with the same infusion rate, upon induction of satisfactory uterine contraction. The response time is the time interval between the administration of the first dose of oxytocin and satisfactory uterine contraction. The amount of bleeding during cesarean section was estimated based on the count of blood-stained gases and the amount of blood in the suction in cc. Complications recorded before and after the cesarean section included; hypotension, arrhythmia, nausea, vomit, chest pain, shortness of breath, and headache, using Apgar score 1-5min. Uterine responses to venous bolus oxytocin administration were recorded, every 1 minute.

Finally, the dose of bolus oxytocin was calculated and compared between the two groups. The information was recorded in the questionnaire and entered in the computer. In this study, patients within the 3 months of the study were eligible and were entered in the consecutively in the study, the random probability sampling method was used. T-test, covariance analysis, or parametric equations were used for statistical analysis of the recorded data.

3. RESULTS

The present study aimed to determine the mean minimum dose of bolus oxytocin for proper uterine contraction during cesarean section. Patients were divided into two groups: those with elective cesarean section and those with cesarean section due to difficulty in labor (Table **1**). The effect of cesarean section on the total dose of oxytocin: before the measurement of systolic blood pressure (SBP), the results from one-variable covariance analysis showed that, by eliminating the effect of spinal confounding variables and spinal anesthesia, the cause of cesarean section had an effect

Table 1. Demographic data.

Measures	Values Elective Lack of Progress	
Number of patients	41	42
Age (y)	33.09±3.2	33.12±3.4
Weight (Kg)	77.5±11.25	77.40±12.51
Height (cm)	163.8±8.25	162.95±12.27
BMI	28	29

Values are mean±standard deviation.

Table 2. The frequency of patients' side effects.

Type of Side Effects	n	Elective	Lack of Progress	Percent
No Complications	10	6	4	12
Hypotension	14	6	8	16.9
Hypotension and nausea	14	5	9	16.9
Hypotension, nausea, vomiting	6	2	4	7.2
Hypotension, nausea, chest pain	16	8	8	19.3
Hypotension, nausea, headache	2	1	1	2.4
Hypotension, chest pain	4	1	3	4.8
Hypotension, difficulty in breathing	3	1	2	3.6
Hypotension, difficulty in breathing, headache	2	1	1	2.4
Hypotension, difficulty in breathing, BeriCardi	1	0	1	1.2
Hypotension, headache	1	0	1	1.2
Hypotension, ventricardia	1	0	1	1.2
Nausea	5	2	3	6
Nausea, chest pain	2	1	1	2.4
Nausea, difficulty in breathing	1	0	1	1.2
Aspiration in breathing	1	0	1	1.2
Total sum	83	34	49	100

on the total received dose of oxytocin before heart rate (HR) Spinal (P=0.280) (Table **2**).

To determine the effect of the cause of cesarean on the dose of oxytocin at different times: The results of the combined test of repeated measurements and analysis of covariance in two distinct parts was presented. The first part of the test is a case study that evaluates the difference in the dose of oxytocin at different times. Before the spinal anesthesia, SBP and diastolic blood pressure (DBP) (taking into account the age-appropriate effect, the level of spinal anesthesia and the amount of bleeding during the operation), HR, and parity were checked (Table **3**).

With a confidence level of about 90%, it was seen that duration of the surgery had significant relation with the dose of oxytocin, that is, between the second to sixth minutes in terms of dose timings (P <0.106).

Table 3. Tests of Between-Subjects Effects for repeated measures analysis.

Effective Factor	P-Value
Causes of cesarean section	535/0
Age	698/0
G.A (42-37 weeks)	421/0
Parity	791/0
SBP Before the spinal	126/0
DBP Before the spinal	788/0
HR Before the spinal	384/0
(T4 – T6) Anesthesia level	279/0
(cc) The amount of bleeding	846/0

Table 4. Distribution of patients in each dose of ephedrine.

-	n	Percent
Less than 5 mg	14	17.2
5 to 10 mg	10	12.5
10 to 15 mg	8	9.4
More than 15 mg	51	60.9
Total sum	83	100

Meanwhile, under $\alpha = 0.1$, it can be stated that there is a significant difference between the time of oxytocin dose during the pre-spinal, and the amount of hemorrhage during the operation. SBP, as well as variables such as age, parity, DBP, GA, had an inverse relationship with the time taken to receive oxytocin dose during the operation. The HR before

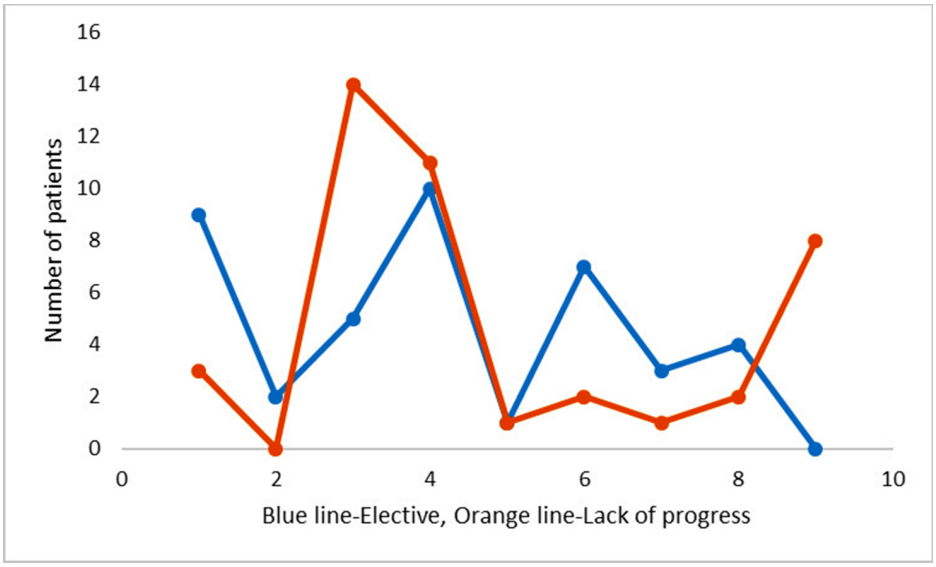

Fig. (1). The distribution of patients according to the reason for cesarean section and uterine contractions. Where: TS- Totally satisfaction, S4D- Satisfy up to the fourth dose, SUS- Satisfy, unsatisfied and then satisfy, S2D- Satisfy from the second dose to the next, USUS- Unsatisfied, satisfy, unsatisfied, and then satisfy, S3D- Satisfy of the third dose afterwards, S4DN- Satisfy from the fourth dose to the next, S5D- Satisfy of the fifth dose, and TU- Totally unsatisfied.

spinal anesthesia also showed an overall effect of cesarean section on the average dose of oxytocin (taking into account the effect of all confounding variables).

During this study, it was found that 10 patients were without any complications among all the groups, and 73 patients had complications. The most commonly observed hypotensive condition was in 64 patients who required ephedrine injection. The results of ephedrine administration are shown in Table **4**. This finding can be due to oxytocin-induced complications or because of regional anesthesia, whose symptoms were temporarily seen in patients.

The results show that there is a 87% confidence interval with a slight margin of error. The pre-treatment SBP had an effect on the average dose of oxytocin-administered patients (as a confounding factor). However, it did not have any significant effect on the means dose of oxytocin (Fig. **1**).

4. DISCUSSION

The aim of this study was to determine the minimum effective dose of oxytocin in patients with elective cesarean section and cesarean section due to lack of progress (stalled labor). To determine the minimum effective dose of oxytocin in each group, McNemar's double-blind comparison was conducted [16]. The results of the double-blind comparison of McNemar showed that in the elective cesarean section, the doses used can be divided into two distinct categories: the first and second dose, and the third, fourth and fifth doses, where the first batch was ineffective and the second batch was effective [17] that is effectiveness threshold was achieved between the second and third dose (1-1.5 units). The results of this McNemar double-blind comparative study in the cesarean section confirmed the lack of labor progress from the previous results. With differences, the uncertainty in the group of patients is slightly lower [18]. However, with a slight margin of error, the threshold of effect can be seen in the time between the second and third dose, or, in other words, between 1 and 1.5 unit, which is close to one unit [19].

It is seen that the cause of cesarean section and determination of the minimum effective dose had no significant effect [20]. Nevertheless, it can be stated that the difference in average doses received every minute among the two groups was of no statistical significance [21].

Physiological effects of oxytocin can be affected by the concentration of oxytocin receptors in the uterus and oxytocin serum levels [22]. Estrogen can increase the expression of uterine oxytocin receptors during pregnancy so that they reach a maximum level during the delivery, which is why the uterus is highly susceptible to oxytocin-related effects [23]. Similarly, in other studies, such as the study by Carvalho *et al*., using randomized one-way blinded study, 40 pregnant women were nominated for elective cesarean section under spinal anesthesia [24]. In these individuals, oxytocin was injected at a dose of 0.5 IU andthe satisfactory and unsatisfactory uterine tone was either repeated or not. Finally, after an evaluation, the minimum effective dose in these patients was 0.35 IU. In our research, we used McNemar's two-to-two comparisons to determine the minimum effective dose of oxytocin in the group of patients undergoing a cesarean section. The results of the comparison showed that in the elective cesarean section, the doses used can be divided into two distinct categories: the "first dose" and "the third, fourth, and fifth dose". The first one was ineffective and the later ones were all effective [25]. That is, the threshold of the effect was seen to be the time between injections of second and third, 1-1.5 units. Therefore, in our study, the minimum effective dose was high than other studies, which may be due to the difference in Estrogen Levels.

The response to oxytocin in cesarean section due to lack of labor progress induced by oxytocin is likely to be different

from an elective cesarean section. In a similar study conducted by Balki *et al*., [26] among patients with cesarean section with failure to develop appropriate uterine contraction, initial dose of 2.5-3.5 units was required for 3 minutes, while patients who received a dose lesser than 2 IU, failed to respond well within 3 minutes, and needed higher doses. Patients receiving 3.5 IU responded within 1-2 minutes.

In addition, in this study, the complications of oxytocin administration in patients were using hemodynamic data during the surgery [27]. Our findings indicate hypotension related complications in the patients which might be because of oxytocin, regional anesthesia or were temporary symptoms [28].

In a study by Weis Jr. *et al*., [29] young women undergoing elective cesarean section had an arterial blood pressure of 30% and an overall environmental resistance of 50%, 40 seconds after injection of 5-10 units of bolus oxytocin. The heart rate increased by 30%, whereas, when impact volume increased by 25% and the heart rate rose by 50%. Therefore, they recommended that oxytocin should be infused in the form of a diluted solution.

CONCLUSION

Since the minimum effective dose of oxytocin in the elective cesarean section was 1 IU, and in those in labor progress was 1-1.5IU, less oxytocin administration represents lesser side effects for the patients. It is recommended that patients who are candidates for the cesarean section should be administered with about 1.5IU of oxytocin in bolus form.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was supported by the ethical committee of Lorestan University of Medical Sciences, Khorramabad, A81, Iran with registration number: (LUMS /125401-10).

HUMAN AND ANIMAL RIGHTS

No animals were used in the study all reported human were experimented in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the *Helsinki Declaration* of 1975, as revised in 2008 (http://www.wma.net/en/20activities/10ethics/10helsinki/).

CONSENT FOR PUBLICATION

All participants provided informed consent

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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CONFLICT OF INTEREST

The authors deny any conflict of interest in any terms or by any means during the study.

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