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Investigation the Effects of Phenylephrine on Oxytocin-Induced Hemodynamic Changes in Women Undergoing Cesarean Section

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Pregnancy is considered as one of the most important events in every woman's life, which is not a pleasant event for all women, and in cases where the stages are not managed properly, it can cause a lot of stress on the mother and her family. For this reason, the present study was conducted to investigate the effect of phenylephrine on oxytocin-induced hemodynamic changes. This study was conducted on a group of pregnant women referred to Ayatollah Taleghani Hospital in Ilam and those undergoing cesarean section were included in the study. The objectives of the study explained to the women participating in the study, whether the participation was voluntary or not to participate in the intervention, compliance with the Helsinki and Belmont Declaration, and confidentiality of information. The women included in the study were randomly assigned to experimental and control groups. The checklists of the researchers were completed by observing and asking the patients from the time the patient entered the hospital until the end of the surgery. The variables expected by the researchers were evaluated before the intervention and 2, 4, 6, 8, 10 and 12 minutes after the intervention. In the experimental group, 12 (30%) patients had no nausea, 18 (45%) patients had low nausea, 8 (20%) patients had moderate nausea and 2 (5%) patients had

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severe nausea. While in the control group, 5 (12.5%) patients had no nausea, 13 (32.5%) patients had low nausea, 14 (35%) patients had moderate nausea and 8 (20%) patients had severe nausea. Also, a significant difference was between in the experimental and control groups in terms of nausea (P = 0.02). The study results showed that using phenylephrine can be effective on improving blood pressure, heart rate, nausea and vomiting in patients, which for this reason it is recommended to use this drug to improve the health of women undergoing cesarean section.

Keywords: Phenylephrine; hemodynamic changes; women.

1. INTRODUCTION

Pregnancy is considered as one of the most important events in every woman's life, which is not a pleasant event for all women, and in cases where the stages are not managed properly, it can cause a lot of stress on the mother and her family. So that the fear of labor is an important problem during pregnancy and after labor, and selected as one of the predictors of emergency cesarean section and increasing demand for cesarean section [1, 2]. Cesarean section is one of the most common gynecological surgeries and spinal anesthesia is the most common method of anesthesia in cesarean section, which reduces maternal mortality and has no complication of general anesthesia on the mother and fetus including less likely maternal lung aspiration and fetal respiratory distress [3, 4].

The mechanism of labor is a spontaneous process with no need for intervention and cesarean section is used as a way to save the life of mother and infant in difficult deliveries [5, 6]. For cesarean section, anesthesiologists face various problems, the most important of which are still discussed, are the complications of using anesthetic drugs on the fetus. Anesthetic drugs, because they are mostly fat-soluble and pass easily through cell membranes, pass through the placenta after administration to the mother. After passing through the placenta, these drugs can have various effects on the fetus, including weakening of the central nervous system and respiratory disorders [7].

There are different methods of anesthesia for cesarean section, which divide into two general categories. The first category is general anesthesia in which the patient is intubated using anesthesia drugs and in the second category of cesarean section anesthesia is related to regional anesthesia which includes spinal anesthesia and epidural anesthesia [8,9]. Hemodynamic changes following spinal anesthesia in women undergoing cesarean section will be very important to anesthesiologists in terms of health and comfort of women. In fact, the two main methods of increasing systemic vascular resistance and intravascular fluid volume are important for the treatment of hypotension due to spinal anesthesia [3,10,11].

Ephedrine is the selected vasopressor for the treatment of hypotension during cesarean section anesthesia [5]. Ephedrine is the selected sympathetic mimetic drug for the treatment of hypotension and used in a variety of forms such as continuous infusion, single doses, or intramuscular injection [12]. Ephedrine is a non-catecholamine stimulator of the sympathetic nervous system that stimulates both alpha and beta-adrenergic receptors and exerts its effect by releasing norepinephrine from the autonomic nerve terminals. Phenylephrine is a pure alpha-adrenergic receptor agonist that causes dose-dependent vasoconstriction and has a greater effect on veins than arteries, as well as increasing venous return after sympathetic block [13,14]. Phenylephrine is a stimulant of alpha-adrenergic receptors with minimal beta-adrenergic effects, which can increase blood pressure and reflex bradycardia, and finally reduce cardiac output by constricting peripheral arteries. Phenylephrine and other alpha agonists reduce uterine blood flow by uterine vasoconstriction [15,16].

1.1 Objectives

Women's health, especially pregnant ones, is very important and one of the most important factors affecting the health of society. Given that the health of this group affects the health status of the whole society, for this reason, it is important to conduct studies on the factors that contribute to maternal health. For this reason, the present study was conducted to investigate the effect of phenylephrine on oxytocin-induced hemodynamic changes.

2. METHODS

2.1 Study Design

This study is a double-blind clinical trial.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion criteria

1. Informed consent to participate in the study
2. Age between 18 and 45 years
3. Living in Ilam

2.2.2 Exclusion criteria

1. Patient's desire to leave the study at any time of the research
2. History of *cardiovascular* diseases, diabetes, brain diseases, hypertension, and etc. in pregnant mothers
3. Any contraindication to spinal anesthesia,
4. Beginning of labor phase for mothers,
5. High-risk pregnancies,
6. History of allergy to anesthetic drugs

2.3 Data Gathering

Demographic information checklist including information on age, gender, height, weight, gestational age, blood pressure (systolic and diastolic), heart rate, and Apgar score (first and fifth minutes) was used. The patients' nausea was also divided into 4 categories without nausea (score zero), low nausea (score one), high nausea (score 2) and vomiting [17].

2.4 Method of Research

This study was conducted on a group of pregnant women referred to Ayatollah Taleghani Hospital in Ilam and those undergoing cesarean section were included in the study. The objectives of the study explained to the women participating in the study, whether the participation was voluntary or not to participate in the intervention, compliance with the Helsinki and Belmont Declaration, and confidentiality of information. The women included in the study were randomly assigned to experimental and control groups.

After entering the operating room, patients underwent cardiorespiratory monitoring and their vital signs including blood pressure, basal heart rate and spo2 status were recorded. The patients' treatments and drugs were all performed at the discretion of the gynecologist and anesthesiologist. Spinal anesthesia of pregnant women was with oxygen therapy (at the discretion of the specialist), in a sitting position from L4-L3 or L4-L5 with needle No. 25 and 12 mg of 0.5% bupivacaine hyperbar 0.5% and after completed anesthesia, pregnant women were placed on their backs [18,19]. 50 µg of phenylephrine or 3 ml of bolus of either saline (3 U over 15 s) was injected to the patients by an anesthetist who was not present in the study [20].

The checklists of the researchers were completed by observing and asking the patients from the time the patient entered the hospital until the end of the surgery. The variables expected by the researchers were evaluated before the intervention and 2, 4, 6, 8, 10 and 12 minutes after the intervention.

2.5 Data Analysis

The data obtained from the completed checklists were introduced into SPSS software version 16 and the data were analyzed by descriptive and analytical tests.

3. RESULTS

According to the results of the Table, no statistically significant difference was observed in any of the demographic information such as maternal age, maternal weight, and gestational age (P> 0.05). Also, age M (SD) of patients in the experimental group was 34.87 (3.59) and 35.07 (4.21) in the control group (P = 0.82). Also, weight M (SD) of the experimental group was 80.30 (10.50) and 83.75 (9.83) in the control group that no difference was between these two groups (P = 0.13). It should be noted that gestational age (week) M (SD) in the experimental group was 37.4 (0.49) and 37.5 (0.50) in the control group (P = 0.37).

In the experimental group, 12 (30%) patients had no nausea, 18 (45%) patients had low nausea, 8 (20%) patients had moderate nausea and 2 (5%) patients had severe nausea. While in the control group, 5 (12.5%) patients had no nausea, 13 (32.5%) patients had low nausea, 14 (35%) patients had moderate nausea and 8 (20%) patients had severe nausea. Also, a significant difference was between in the experimental and control groups in terms of nausea (P = 0.02).

According to the results, in the control group after 3, 8 and 9 minutes, changes in heart rate were not significant (P> 0.05) but at other times these changes were significant (P <0.05). While in the control group after 3, 4, 8 and 10 minutes no significant difference was observed in changes in heart rate (P> 0.05) but at other times these changes were significant (P = 0.000). For systolic blood pressure, the results showed that no statistically significant change was observed in the control group, but in the experimental group, except after 4, 8 and 10 minutes, the changes in systolic blood pressure were significant (P <0.05).

Table 1. Comparison of vital signs of patients in the experimental and control groups before and after the intervention

Variable	Time		Group	
			Intervention M(SD)	Control M(SD)
Systolic blood pressure	Before		113.10(14.32)	119.67(12.25)
		1 minutes	114.22(13.00)	112.65(13.92)
		2 minutes	114.15(12.46)	100.77(21.19)
		3 minutes	114.25(12.50)	92.55(12.07)
		4 minutes	115.42(12.21)	89.17(10.99)
	After	5 minutes	113.07(13.44)	90.45(14.20)
		6 minutes	114.50(12.43)	90.80(9.93)
		7 minutes	112.57(11.97)	92.62(14.48)
		8 minutes	114.00(14.08)	90.32(14.34)
		9 minutes	112.70(12.50)	90.15(13.99)
		10 minutes	113.15(12.22)	87.97(11.99)
Diastolic blood pressure	Before		75.42(4.16)	70.87(12.61)
		1 minutes	75.97(3.94)	63.82(11.16)
		2 minutes	77.77(4.87)	59.67(4.69)
		3 minutes	76.55(5.50)	58.35(5.64)
		4 minutes	75.52(5.12)	57.52(4.87)
	After	5 minutes	76.52(5.41)	55.50(5.07)
		6 minutes	76.20(5.33)	57.45(5.14)
		7 minutes	74.95(5.50)	55.52(6.34)
		8 minutes	72.20(5.47)	54.95(5.08)
		9 minutes	73.45(5.69)	58.27(5.36)
		10 minutes	71.92(6.02)	58.72(5.25)
Heart rate	Before		78.40(4.97)	98.85(5.71)
		1 minutes	82.40(4.97)	104.55(6.03)
		2 minutes	79.37(5.02)	99.85(5.47)
		3 minutes	79.45(4.94)	97.35(16.70)
		4 minutes	80.70(5.21)	100.10(5.45)
	After	5 minutes	81.37(4.98)	98.90(5.81)
		6 minutes	82.05(5.18)	101.05(5.67)
		7 minutes	82.57(4.92)	98.32(5.68)
		8 minutes	82.35(4.99)	98.15(5.50)
		9 minutes	82.52(4.83)	99.82(5.69)
		10 minutes	83.20(5.20)	100.02(5.61)
Mean arterial blood pressure	Before		91.90(4.13)	77.92(5.86)
		1 minutes	82.67(3.64)	65.20(5.52)
		2 minutes	87.77(3.84)	69.55(5.85)
		3 minutes	88.47(3.76)	70.25(5.86)
		4 minutes	88.42(3.55)	68.55(5.50)
	After	5 minutes	87.70(3.74)	67.55(5.65)
		6 minutes	86.32(3.70)	69.57(5.66)
		7 minutes	87.47(3.52)	67.20(11.89)
		8 minutes	85.60(3.54)	67.40(5.93)
		9 minutes	85.50(3.55)	69.77(6.00)
		10 minutes	86.45(3.56)	69.60(5.85)

4. DISCUSSION

The present study was conducted aimed to evaluate the effect of phenylephrine on oxytocin-induced hemodynamic changes in cesarean section in Ilam. According to the study results, a statistically significant difference was in patients' blood pressure, heart rate, nausea and vomiting. In a study by Rumboll et al. on 40 pregnant women undergoing cesarean section, 20 women were placed in the phenylephrine group and another 20 women were in the saline group. The study results showed that phenylephrine compared to saline had no effect on patients' hypotension and tachycardia, but had a significant effect on patients' heart rate [20], which is consistent with the results of this study. In a study by Shafeinia et al. on 116 patients in the phenylephrine and normal saline control groups, it was shown that phenylephrine reduced some of the complications of pregnant women undergoing cesarean section, such as hypotension (systolic and diastolic), arterial hypertension, nausea and vomiting [17]. Also in a study by Nikooseresht et al., 120 patients undergoing cesarean section were divided into 3 groups: Therapeutic Bolus, Prophylactic Bolus and Prophylactic Infusion. The results showed a statistically significant difference in blood pressure, nausea, vomiting, Apgar score and bradycardia. It should be noted that systolic blood pressure 1 and 7 minutes after spinal block was significantly different [21].

In a study by Pouranjafian et al., 74 pregnant women undergoing cesarean section were divided into phenylephrine and ephedrine groups. The patients' diastolic blood pressure during surgery and 5, 10, 15, 20, 25, 25 and 30 minutes after neonatal departure was lower in the phenylephrine group and neonatal Apgar score was higher after a minute, which were significant. It should also be noted that no significant difference was observed between systolic blood pressure and neonatal Apgar score after 5 minutes and neonatal pH in patients of the two groups [15]. While a study by Atashkhoi et al. showed that in women undergoing cesarean section, 100 micrograms of phenylephrine compared to 5 mg of ephedrine in terms of heart rate only after 2 and 4 minutes, a significant difference was observed between the two groups. At other times, no significant difference was found that using both drugs in cesarean section patients was mentioned as the conclusion of this study [22]. A study by Manouchehrian et al. on 80 women undergoing cesarean section with randomly spinal anesthesia in ephedrine experimental and control groups, 10 mg of ephedrine in the experimental group and 100 µg of phenylephrine in the control group, found that no difference was between the studied variables in the two groups. According to the study results of Manouchehri et al., no difference was between the mean arterial pressure, blood pressure (systolic and diastolic), nausea and vomiting in patients [23].

Other studies have been conducted in different groups of patients on the effect of ephedrine on patients' vital signs. In a study by Farsani et al. on 110 patients undergoing orthopedic lower limb surgery, in general, no significant difference was observed between ephedrine and phenylephrine groups in terms of systolic and diastolic low blood pressure, and only 2 and 4 min after vasopressor administration a difference was observed [14].

5. CONCLUSION

The study results showed that using phenylephrine can be effective on improving blood pressure, heart rate, nausea and vomiting in patients, which for this reason it is recommended to use this drug to improve the health of women undergoing cesarean section.

CONSENT

As per international standard or university standard, respondents' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The Ethics Committee of the Ilam University of Medical Sciences approved (IR.MEDILAM.REC.1400.059).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Alipour Z, Lamyian M, Hajizadeh E, Vafaei MAJIjon, research m. The association

between antenatal anxiety and fear of childbirth in nulliparous women: a prospective study. 2011;16(2):169.
2. Taheri Z, Khorsandi M, Amiri M, Hasanzade AJJoRUoMS. Investigating the causes of fear of childbirth in Shahrekord pregnant women, in 2013: A short report. 2015;14(4):345-50.
3. Macarthur A, Riley ETJIac. Obstetric anesthesia controversies: vasopressor choice for postspinal hypotension during cesarean delivery. 2007;45(1):115-32.
4. Lord Lasemi S, Delavar P, Hadavand SJTIJoO, Gynecology, Infertility. Prevalence of pruritus following Intrathecal fentanyl and sufentanil after spinal anesthesia in cesarean section. 2021;24(3):33-41.
5. Alereza Amiri H, Banihashem N, Naziri F, Rabiee M, Ghasemi A, Shirkhani Z, et al. The effects of phenylephrine and ephedrine on maternal hemodynamic changes and neonatal acid-base Status during spinal anesthesia for cesarean delivery. 2013;23(107):117-24.
6. Hassanzadeh H, Faraji Lamouki H, Khatty Dizabadi F, Yazdani Charati JJJoMUoMS. Comparing the factors associated with selecting normal vaginal delivery or caesarian section in nulliparous women. 2019;29(174):53-63.
7. Habibi MR, Zamani A, Moslemizadeh N, Rezaei M, Shahmohammadi S, Peyvandi S. Comparing the Effect of Two Different Doses of Remifentanil Infusion on Apgar Score of the Neonates and the Mothers' Awareness During General Anesthesia Under Elective Cesarean Section %J Journal of Mazandaran University of Medical Sciences. 2011;21(83):17-23.
8. Chestnut DH, Wong CA, Tsen LC, Kee WDN, Beilin Y, Mhyre J. Chestnut's obstetric anesthesia: principles and practice e-book: Elsevier Health Sciences; 2014.
9. Rollins M, Lucero JJBmb. Overview of anesthetic considerations for Cesarean delivery. 2012;101(1).
10. Noorian C, Kheire SJJoGUoMS. Pharmacutical effects of ephedrine, atropine and mucosal phenilephrin on hemodynamic alterations of women during spinal anesthesia in cesarean section. 2012;13(4):27-34.
11. Dyer RA, Reed AR, van Dyk D, Arcache MJ, Hodges O, Lombard CJ, et al. Hemodynamic effects of ephedrine, phenylephrine, and the coadministration of phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. 2009;111(4):753-65.
12. Simon L, Provenchère S, de Saint Blanquat L, Boulay G, Hamza JJJoca. Dose of prophylactic intravenous ephedrine during spinal anesthesia for cesarean section. 2001;13(5):366-9.
13. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kokri MSJTJotASoA. Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. 2002;97(6):1582-90.
14. Moradi D, Naghibi K, Alikiaii B, Mashayekhi ZJJoBUoMS. Comparison of the effects of intravenous phenylephrine and ephedrine in treatment of hypotension after spinal anesthesia in orthopedic surgery. 2016;18(6):21-7.
15. Pournajafian A, Rokhtabnak F, Ghodrati M, Kholdebarin A, Hassani A, Dayani AJTIJoO, Gynecology, et al. Comparison of the effect of phenylephrine and ephedrine on the neonate in treatment of hypotension due to spinal anesthesia in pregnant women candidate for cesarean section. 2020;23(1):7-18.
16. Collins VJJL, Philadelphia F. General and regional anesthesia. 1993;573.
17. Shafeinia A, Ghaed MA, Nikoubakht NJA, medicine p. The effect of phenylephrine infusion on maternal hemodynamic changes during spinal anesthesia for cesarean delivery. 2020;10(1).
18. Alereza Amiri H, Banihashem N, Naziri F, Rabiee M, Ghasemi A, Shirkhani Z, et al. The Effects of Phenylephrine and Ephedrine on Maternal Hemodynamic Changes and Neonatal Acid-Base Status During Spinal Anesthesia for Cesarean Delivery %J Journal of Mazandaran University of Medical Sciences. 2013;23(107):117-24.
19. Brinbach DJM. Anesthesia for obstetrics; 2005.
20. Rumboll C, Dyer R, Lombard CJIjooa. The use of phenylephrine to obtund oxytocin-induced hypotension and tachycardia during caesarean section. 2015;24(4): 297-302.
21. Nikooseresht M, Seifrabiei MA, Hajian P, Khamooshi SJA, Medicine P. A clinical trial on the effects of different regimens of phenylephrine on maternal hemodynamic

after spinal anesthesia for cesarean section. 2020;10(4).
22. Simin A, Zahra F, Pouya HM, Reza TJOJOG. Comparison the effect of ephedrine and phenylephrine in treatment of hypotension after spinal anesthesia during cesarean section. 2012;2(03):192-6.
23. Manouchehrian N, Tarbiat M, Yaghobi MJJ oGUoMS. Comparison of Intravenous bolus Phenylephrine and Ephedrine in the Prevention of Post-spinal Hypotension during Cesarean Section. 2020;29(1): 76-84.

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