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Comparison of ephedrine and phenylephrine in incidence of headache during spinal anesthesia in cesarean delivery.

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Abstract

Background: Spinal anesthesia is more acceptable method of anesthesia in elective cesarean section, but hypotension is the major limitation of this technique which might trigger to serious complications for both mother and fetus. The use of vasopressors is necessary to control hypotension caused by spinal anesthesia, however, it might be along with side effects like headache.
Methods: In the present study, 105 candidates for elective cesarean delivery were assessed to compare the role of ephedrine and phenylephrine in relation with the incidence of headache. Pearson Chi-square test, Kruskal-Wallis test, Spearman's rho correlation coefficient was performed to analyse the data. P value<0.05 was considered significant. All data were analysed using Stata 12.
Results: The incidence of headache during the surgery was 51.4%, 45.7% and 37.1% in ephedrine, phenylephrine and control groups respectively. Not a significant difference was found between ephedrine and phenylephrine regarding the incidence of headache (P=0.541), also no significant difference were found in the severity of the headache (P=0.277). The severity of the headache was not different 24 h after surgery. The number of doses of vasopressor consumption in ephedrine and phenylephrine recipients was not significantly different (P=0.579). No significant difference was found between the number of doses used and the severity of the headache during surgery (P=0.979). However, the average of systolic blood pressure in ephedrine group was higher than phenylephrine group (P=0.001). Also, the impact of ephedrine and phenylephrine on heart rate was similar and affectless.
Conclusions: In this study, no significant differences were observed in the incidence and severity of headaches during and after surgery, and the number of doses of vasopressor drug consumption between phenylephrine and ephedrine recipients to treat hypotension associated with spinal anesthesia in cesarean section.

Keywords: Anesthesia, Spinal, Cesarean section, Phenylephrine, Ephedrine, Headache.

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Introduction

Spinal anesthesia, recently, has been known as an acceptable anesthesia technique, especially for cesarean section, due to advantageous on epidural anesthesia, such as rapid onset, intensity, symmetric sensory and motor block [1,2]. However, hypotension triggered by spinal anesthesia during cesarean delivery has been known as a common complication that might endanger the lives of both mother and fetus. So, make it necessary to use vasopressors as a treatment of hypotension [3].

Ephedrine and phenylephrine are of common vasoconstrictor drugs which their effect on hypotension during anesthesia have been compared in many studies. Although no definite difference has been observed between two drugs regarding the prevention of hypotension following spinal anesthesia [4], some preferred ephedrine because it does not increase in heart rate of the fetus, and some other preferred phenylephrine to modulate reducing placental perfusion [5-8]. Some studies have shown frequent appearance of fetal tachycardia with use of ephedrine [9], and some demonstrated the effect of phenylephrine on fetal acid base status [10]. Each vasopressor, either ephedrine or phenylephrine, undergoes pros and cons.

The function of a vasopressor is not always in same way of the other; for example, in a comparison among candidate individuals for cesarean section, mean arterial and diastolic blood pressure were only stabilized with phenylephrine, but not with ephedrine [11]. On the other hand, in the study of Loughrey et al. the simultaneous bolus administration of ephedrine and phenylephrine was compared with bolus ephedrine alone. They did not found any superiority for combination therapy than bolus injection of ephedrine in stabilizing hemodynamic subsequences of spinal anesthesia [12]. Also, it has been shown that administration of phenylephrine reduced the frontal lobe oxygenation, while infusion of ephedrine did not significantly affect the level of ScO_2 [13]. Even in some cases of spinal anesthesia in cesarean section, surprisingly, no effect on hypotension was observed

following the administration of either ephedrine or phenylephrine [14].

Some other studies have demonstrated a similar effect of ephedrine and phenylephrine on some other factors. The influence of ephedrine and phenylephrine on systolic blood pressure under spinal anesthesia was found to be equal, for both agents [11]. Furthermore, investigations on the effect of either of ephedrine and phenylephrine on placental vascular resistance did not detect any differences and supported the equal value for both of them [15]. Also, no differences were observed between the effect of ephedrine and phenylephrine on chemical components of umbilical arterial and venous [13].

All of these results demonstrate that the effects of ephedrine and phenylephrine on hemodynamic parameters and post operational condition of patients is not still clear, and superiority of each on the other has been remained controversial.

The present study aimed to compare the influence of each of ephedrine and phenylephrine on headache outcome. In addition, hemodynamic properties were assessed as complementary. For this purpose, 105 candidates for cesarean section were participated in this study to assess the potential relation between the type of vasopressor and post-operational side effects.

Methods

Patients

This clinical trial study was performed on 105 women, candidate for elective cesarean delivery (C-section), presented to Imam Reza Therapeutic Educational Center of Kermanshah in 2016.

Inclusion and exclusion criteria

Patients (candidates) categorized in ASA classes of 1 and 2, age of 18-40, BMI range of 18.5-25, systolic blood pressure of 120 to 140 mmHg were included into the study. Those candidates with any history of migraine, psychiatric diseases, drug using (except authorized pregnancy additives), multiple pregnancy, headache before surgery, contraindications for spinal anesthesia, pregnancy disorders like pre-eclampsia and Umbilical cord anomalies, and those with uncontrolled clinical condition, such as high blood pressure, diabetes, and cardiovascular diseases, were excluded from study. Also, patients who received Atropine, following bradycardia, and those with more than one attempt of spinal anesthesia were excluded.

Performance

Spinal anesthesia was performed in sitting position and using G25 Quincke needles in a location between L3 and L4 spines. After ensuring about Cerebrospinal Fluid (CSF) flow, 12 mg of hyperbaric bupivacaine (Buvanest Spinal 0.5%) was injected into the intrathecal space. Afterward, patient was kept in supine position and vital signs were monitored every 2 min (first 10 min), then continued every 5 min. When patient had a series of two or more episodes of systolic blood pressure decrease below 80% of baseline (hypotension) 15, 10 mg bolus of ephedrine (ephedrine HCL 50 mg/ml, Oterop, Belgium) and 5 μg bolus of phenylephrine (Phenylephrine 10 mg/ml, Nani Pharmaceutical Pvt, India) were administrated to related groups (ephedrine and phenylephrine groups) until systolic blood pressure exceeded baseline values. Patients with normal systolic blood pressure, after spinal anesthesia, were considered as control group. Severity of headache was assessed through Visual Analog Scale (VAS) with scores from 0 to 10 for representing absence and most severe headache, respectively. Sufentanil and Apotel were administered to alleviate headache during and after surgery, respectively.

Ethical consideration

The study was carried out in accordance with the Declaration of Helsinki, and the ethics committee of the University of Kermanshah approved the protocols of the study. All patients' consent was obtained and their records were kept confidential.

Data analysis

Qualitative and quantitative data were analysed and reported as frequency (%) and mean ± standard deviation, respectively. Pearson Chi-square test was performed to compare severity of post-surgical headache between different groups. In addition, Kruskal-Wallis test was exploited to compare headache severity during surgery. Also, Spearman's rho correlation coefficient was performed to assess dependency of vasopressor dose to headache severity. P value<0.05 was considered significant. All data were analysed using Stata 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

Results

The demographic analysis of 105 studied women in this study has been presented in Table 1. The mean value of the age was 29.62 y, and no significant difference was observed in the age value of three different groups. Also, the mean value for weight, height and BMI was 76.9, 1.61, and 29.59, respectively, and there was no significant difference between different three groups, as mentioned for age value.

Table 1. *Demography of 105 women candidate for cesarean section.*

	N	Median	Value*
Age (y)			
Control	35	27	28.54 ± 6.670
Ephedrine	35	29	29.89 ± 7.194
Phenylephrine	35	30	30.43 ± 4.654
Total	105	29	29.62 ± 6.269

Weight, Kg			
Control	35	75	77.700 ± 12.2668
Ephedrine	35	75	76.375 ± 9.8622
Phenylephrine	35	74	76.657 ± 10.9871
Total	105	75	76.906 ± 10.9801
Height, m			
Control	35	1.62	1.6203 ± 0.04687
Ephedrine	35	1.62	1.6119 ± 0.05835
Phenylephrine	35	1.63	1.6083 ± 0.06939
Total	105	1.62	1.6135 ± 0.05857
BMI			
Control	35	29.21	29.580 ± 4.2826
Ephedrine	35	29.172	29.441 ± 3.9916
Phenylephrine	35	27.789	29.777 ± 4.8664
Total	105	28.995	29.598 ± 4.3517

*Data are presented as mean ± SD.

As presented in Table 2, the doses of phenylephrine were more than ephedrine; however, this difference was not statistically significant. Also, severity of headache during surgery in groups receiving either ephedrine or phenylephrine was higher than control group, but there was no significant difference between two groups that received vasopressor.

Table 2. *Vasopressors dosage and headache severity during surgery among three different groups.*

	N	Median	Value
Dosage			
Ephedrine	35	1	1.61 ± 0.72
Phenylephrine	35	2	2.31 ± 1.62
Total	70	2	1.95 ± 1.29
Headache severity			
Control	35	0.0000	0.3714 ± 0.49024
Ephedrine	35	0.5000	0.5000 ± 0.50709
Phenylephrine	35	0.0000	0.4571 ± 0.50543
Total	105	0.0000	0.4434 ± 0.49915

*Data are presented as mean ± SD.

Systolic blood pressure (mean value) during the surgery for ephedrine group was higher that phenylephrine group (P=0.001) (Table 3). Also, the difference of systolic pressure between control and phenylephrine groups was significant (P<0.001), but not for control and ephedrine groups. In addition, respecting to the diastolic pressure, this value was lower in phenylephrine group compare with control (P<0.001), however, no significant differences were observed between ephedrine and phenylephrine groups (P=0.112) or between ephedrine and control groups (P=0.97). Moreover, assessment of heart rate did not demonstrate any significant difference between all three groups.

Table 3. *Hemodynamic stability parameters in relation with vasopressors.*

	Mean	Std. error	df	95% confidence interval	
				Upper Bound	Lower Bound
Systolic blood pressure					
Ephedrine	116.011[b]	1.007	261.332	114.028	117.993
Phenylephrine	110.697[b]	1.023	261.332	108.681	112.712
Control	118.958[b]	1.026	261.332	116.938	120.977
Diastolic blood pressure					
Ephedrine	66.886[b]	0.901	244.2	68.661	65.112
Phenylephrine	64.200[b]	0.916	244.2	66.004	62.396
Control	69.657[b]	0.918	244.2	71.465	67.85
Heart rate					
Ephedrine	96.906[b]	1.569	189.651	100.001	93.811
Phenylephrine	95.589[b]	1.594	189.52	98.732	92.445
Control	97.618[b]	1.597	189.563	100.769	94.467

The assessment of headache incidence after surgery has been presented in Table 4. Comparing all the groups with each other in a binary manner shows that there was no significant difference between all groups regarding the incidence of headache.

Table 4. *Headache-vasopressor cross tabulation analysis*[*]*.*

	Headache			
	Negative	Positive	P value	PR
Control	22 (62.9)	13 (37.1)	0.466	0.812
Phenylephrine	19 (54.3)	16 (45.7)		
Ephedrine	17 (48.6)	18 (51.4)	0.632	1.125
Phenylephrine	19 (54.3)	16 (45.7)		
Control	22 (62.9)	13 (37.1)	0.228	0.722
Ephedrine	17 (48.6)	18 (51.4)		

*Data are presented as no. (%).

Discussion

Spinal anesthesia is known as a standard technique for elective C-section due to its cost effectiveness and less amount of surgical hemorrhage [16,17]. However, the incidence of

hypotension is major complication of spinal anesthesia, it can be lowered by several ways among which vasopressor are more reliable [18]. In the present study, the severity of incidence of headache between ephedrine and phenylephrine was compared. Following, the effectiveness of each vasopressor on modulation of hypotension was investigated.

As the demographic results of the present study shows, the total mean values of age, weight and height for all the participants were 29.62, 76.9 and 161, respectively. These values were consistent with the demographic results obtained in other studies [19,20] and confirmed the validity of the selected sample. As mentioned in Table 1, the demographic differences between three groups of control, ephedrine and phenylephrine were negligible which implies the similar distribution between all groups, and the independency of vasopressors influence from demographic variables.

Foss et al. studied the effect of phenylephrine and ephedrine on frontal lobe oxygenation during caesarean section with spinal anesthesia, and the results of this study demonstrated the equal effect of both of ephedrine and phenylephrine to maintain the systolic, diastolic and mean arterial blood pressure [13]. Also, in the study conducted by Lundorff et al. comparing two different anesthesia method, ephedrine was used to treat hypotension. In this study, ephedrine did not significantly influenced hemodynamic stability as no differences were observed in the mean arterial pressure [21]. Alkaissi et al. study reinforces the practicality of phenylephrine for the retainment of blood pressure during administration of anesthesia in the spine for optional surgical delivery [22]. On the other hand, the results of our study demonstrated the remarkable effect of ephedrine on systolic and diastolic pressure than phenylephrine. Our findings were in consistent with the study of Aziz et al. which introduced ephedrine as a more effective agent than phenylephrine along with lower side effects [18]. In Kulkarni et al. study ephedrine with spinal injection was more effective in maintaining maternal hemodynamic stability and better neonatal outcome as compared to crystalloid preloading during cesarean delivery [23]. In another study, both of the ephedrine and phenylephrine significantly increased the value of systolic pressure compare with control group, however, in contrast with our results, the influence of phenylephrine was greater than ephedrine [20].

In the study performed by Foss et al. maternal heart rate was not impressed by ephedrine, but it decreased as a result of phenylephrine infusion [13]. The same result was observed regarding the effect of phenylephrine and ephedrine on fetal heart rate [13]. In contrast, the results of our study did not show any significant influence of both ephedrine and phenylephrine on heart rate. In a same way, study of Lundroff et al. did not find any impact on heart rate resulted by ephedrine or phenylephrine [21].

Headache is a complication which has commonly observed in many anesthesia treatments, such as atropin, ondansetron, ephedrine and phenylephrine, and its incidence with respect to different techniques of infusion and different dosage of drug has been studied [19,24]. Some studies did not report any incident of headache, even in different anesthesia methods, after using ephedrine to prevent hypotension [21]. According to the results of the present study, although the incidence of headache during surgery in groups of ephedrine and phenylephrine was equal and more than control group, no significant difference was found in three groups with respect to the incidence of drug induced headache. In consistent with our results, the study of Thiangtham and Asampinwat indicated to the similar impact of ephedrine and phenylephrine on the incidence of headache [25]. In contrast with our results, some studies indicated to the higher incidence of headache in ephedrine groups compare with phenylephrine which it might be due to the method or dosage of ephedrine [26,27].

In conclusion, the results of the present study demonstrated that there was no significant difference between ephedrine and phenylephrine with respect to the incidence of headache, neither during nor after surgery. However, the impact of ephedrine on systolic pressure compare with phenylephrine was significant. Thus, regardless the critical alteration in hemodynamic indices, ephedrine and phenylephrine are similar in the term of headache incidence. Finally, we propose a larger sample of candidates to obtain more reliable results.

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