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Comparative Study of Prophylactic Vs Conventional Phenylephrine Administration in Preventing Spinal Anaesthesia-Induced Hypotension in Elective caesarean Section Patients: A Quasi Experimental Trial

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Abstract

Objective: To determine the prophylactic effect of phenylephrine in patients undergoing spinal anaesthesia in comparison to the conventional group.

Study design: Quasi experimental trial.

Place and duration of study: HIT Hospital Taxila in the period of 6 months.

Materials and methods: This quasi-experimental trial was conducted in HIT Hospital. Total 68 females were divided into two groups: Control group and Experimental group. Each group consisted of 34 patients aged between 20 to 40 years. The patients were scheduled for elective cesarean section deliveries under spinal anaesthesia. All patients of the experimental group were given prophylactic dose of phenylephrine 100mcg diluted in normal saline after undergoing spinal anaesthesia before the start of procedure. Control group patients were only given normal saline as a placebo after undergoing spinal anaesthesia before the start of procedure. Control group patients were given phenylephrine as conventional treatment only if they experienced hypotension during the procedure.

Results: Among the patients in the experimental group none experienced hypotension. Their blood pressure remained fairly constant in the normal range. In the control group, 4 out of 34 patients (11.7%) had their blood pressure dropped below the cutoff point of 90/60 mmHg.

Conclusion: Our results show that a prophylactic dosage regimen i.e., 100mcg of phenylephrine is effective in controlling spinal -anaesthesia -induced hypotension in patients undergoing Caesarean-section. In comparison with conventional group where hypotension occurs only in few patients.

Keywords: Spinal Anaesthesia -Induced Hypotension, Phenylephrine, Prophylactic Treatment, Blood Pressure

Conflict of Interest: None **Funding Source**: None

Introduction

Elective caesarean sections are one of the most common procedures performed in gynaecology. Most of these procedures (around 80-90%) are performed under spinal anaesthesia because of its rapidity of action, efficacy, and safety. However, a number of undesirable side effects have been reported which include hypotension, post-spinal headache, and failure of anaesthesia induction.[1] Post-spinal hypotension is a worrisome side effect that can affect more than 50% of patients if steps are not taken to prevent it. Furthermore, prolonged maternal hypotension negatively affects fetal well-being by decreasing uteroplacental blood

flow ultimately leading to compromised fetal oxygenation.[2, 24]

A lot of research has been undertaken to prevent this phenomenon of hypotension during spinal anaesthesia. Proposed solutions include intravenous fluid administration for volume expansion as well as the use of sympathomimetic drugs. Intravenous fluids alone have not proven to be of much benefit when used alone for this purpose.[3] Thus, a variety of sympathomimetic drugs like phenylephrine, ephedrine, mephentermine, epinephrine, and dopamine have been used with varied levels of success to counter spinal anaesthesia -induced hypotension.[4-6] However, phenylephrine is superior to other vasopressors due to its high efficacy, being easy to titrate, and ability to use liberal doses to maintain maternal blood pressure near normal without causing fetal acidosis.[7] Furthermore, its usage in combination with ephedrine decreases the incidence of hypotension, need of vasopressors and antiemetics and improves the fetal APGAR scores.[8]

The dosage regimen of phenylephrine has always been a matter of interest among anaesthesiologists. Various studies have proposed different dosage regimens of vasopressors for the treatment of spinal anaesthesia - induced hypotension. Some studies have used bolus dosing during the surgical procedure only in response to hypotension, as conventional treatment [9] while others have proposed a prophylactic dosage regimen before the start of procedure.[10-12] However, the literature regarding prophylactic bolus dosage is scarce because no proper guidelines are available. Thus, we designed this study to check the efficacy of prophylactic bolus dosage regimen of phenylephrine in the prevention of spinal anaesthesia-induced hypotension in pregnant women undergoing Lower Segment Caesarean Section.

Materials and Methods

The sample size was calculated through Openepi software using 95% confidence interval, 99% power of study, and anticipated frequency of hypotension 71.1% in control group and 15.5% in experimental group.[13, 14] In order to reduce the chances of dropout, we inducted 34 patients in each group.[14] Before the start of study ethical permission was taken from IRB committee of HITEC-IMS Taxila.

This quasi-experimental trial was conducted at HIT Hospital Taxila over a period of 6 months, from February 2021 to August 2021. All the patients aged between 20-40 years and were scheduled to undergo elective C-section under spinal anaesthesia were included in the trial. These patients were made to go through pre-anaesthesia checkups from specialist anaesthetists and were declared fit for surgery. The drug bupivacaine (administered via central neuraxial anaesthesia /subarachnoid block) at dose of 0.3 mg/kg of body weight was given to patients for spinal anaesthesia. Patients who were hypertensive or already taking anti-hypertensive medications were excluded from the study. During the process of taking patient consent, they were briefed about the treatment and possible outcomes of the study and were divided into experimental and control groups. All patients in the experimental group were given a prophylactic 100 mcg bolus dose of phenylephrine diluted in normal saline after undergoing spinal anaesthesia before the start of procedure. Control group patients were given normal saline as a placebo after undergoing spinal anaesthesia before the start of procedure and were given 100-200 mcg of phenylephrine as conventional treatment only if they experienced hypotension during the procedure. The acceptable cut-off for hypotension, below which conventional treatment would be required was set at 90/60 mmHg. Upon arrival to the operation theatre, patients were given 5 minutes to stabilize after which three blood pressure and pulse readings were taken 1 minute apart and their mean recorded as the baseline pulse and blood pressure. The monitoring was done by 3-lead electrocardiogram. Pulse, systolic, and diastolic pressure were measured every 2-3 minutes after anaesthesia.

Measurements were repeated and recorded at 5, 8, 12, and 15 minutes during the surgery. The strategy was made that if the bradycardia occurred below 50 beats per minute along with hypotension, atropine will be administered as required dose i.e., 0.5-1mg bolus (with repeat doses every 3-5 minutes up to 3 mg if necessary). If there was still no response, then dopamine infusion will be given to manage this condition.[4] This management of the complication is explained in the guidelines of American Heart Association. The data was analyzed using SPSS version 22. Independent sample t-test was used to compare the baseline mean blood pressure and pulse at different time intervals of both experimental and control group after administering spinal anaesthesia. *P* value of <0.05 was considered as significant

Results

The mean values of age, pulse, blood pressure are given in table 1. (Mean value for the normal parameters)

Table 1: Comparison of Baseline parameters including Age (years), Pulse(bpm), Blood Pressure Systolic and Diastolic(mmHg) in both groups

Parameters	Experimental Group (Mean±SD)	Control Group (Mean±SD)
Age (years)	28±8.56	28.76±9.70
Pulse(bpm)	90.00±12.46	83.147±8.95
Blood Pressure Systolic	122.2±11.33	120.08±5.85

Blood Pressure Diastolic	76.12±9.05	75.88±6.88

Among the patients in experimental group who received prophylactic dosage of 100 mcg of phenylephrine, none experienced hypotension or bradycardia. Their blood pressure and pulse remained fairly constant in the normal range. On the flip side, 4 out of 34 patients (11.7%) in the control group had their blood pressure dropped below the cutoff point of 90/60 mmHg where they had to receive rescue bolus of phenylephrine to counter it as conventional therapy. The blood pressure of these four patients 1,2,3 and 4 on 3 min of reading was 75/55 mmHg, 80/58 mmHg, 85/50 mmHg and 85/50 mmHg respectively. Bradycardia was observed in few of the patients in control group but not severe that required atropine or dopamine.

From our data, two patients from the experimental group experienced bradycardia. The first patient had a pulse of 56 at 3 minutes and 55 at 5 minutes. The other patient had the pulse of 59 at 5 minutes. The first patient had a pulse of 65 at 8 minutes that is why she did not receive atropine. The second patient who experienced bradycardia had a pulse of 75 at 8 minutes that is why she also did not receive atropine because normal physiological functions restored it to the point where no treatment was required. None of the other patients in the group required bolus dose of phenylephrine.

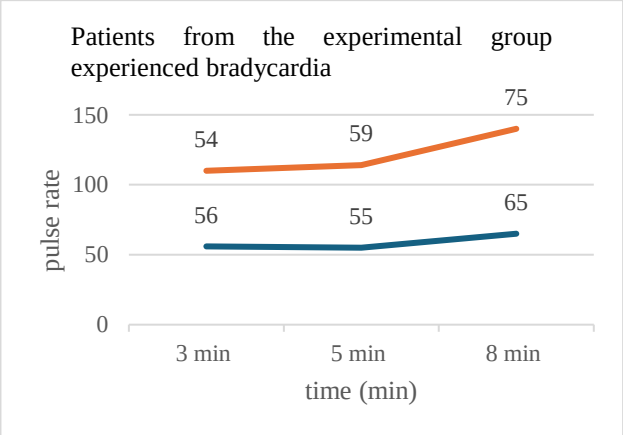

Figure 1: Patients from the experimental group experienced.

From the above-mentioned Table 2, it is visible that the patients in experimental group who received phenylephrine prophylactically did not appear to be hypotensive however there was a mild decrease in the pulse that is considered insignificant During the BP monitoring at 5- and 12-minutes interval, a significant difference was observed in the blood pressure readings between the control and experimental group (Table 2).

Discussion

Different techniques have been proposed to counter maternal hypotension post-spinal anesthesia. Some studies have shown that intravenous (IV) fluids [15, 16, 22] are effective while others suggest using various kinds of vasopressors.[7-9, 14, 17]

According to the International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anesthesia', alpha agonist drugs are the most appropriate agents in treating or controlling hypotension, and among all the different types of alpha-agonist drugs, phenylephrine is currently the recommendation of choice due to the amount of supporting data that is present. [18]

Table 2: Comparison of Pulse (bpm), Blood Pressure (mmHg) Systolic and Diastolic at 3,5, 8, 12, and 15 minutes in both groups.

Parameters	Experimental Group (Mean±SD)	Control Group (Mean±SD)	Statistics *p*-value
Blood Pressure Systolic 3 min	118.65±14.11	115.09±15.01	0.363
Blood Pressure Diastolic 3 min	72.11±12.83	72.70±9.71	0.832
Blood Pressure Systolic 5 min	121.62±8.47	115.85±11.61	0.037
Blood Pressure Diastolic 5 min	78.38±8.29	72.26±9.47	0.003
Blood Pressure systolic 8 min	120.38±9.32	117.76±10.57	0.283
Blood pressure diastolic 8 min	80.71±6.38	73.24±7.77	0
Blood pressure systolic 12 min	120.41±8.64	117.00±8.16	0.199
Blood pressure diastolic 12 min	79.73±6.45	74.00±6.45	0
Blood pressure systolic 15min	120.85±6.5	119.53±7.4	0.501
Blood pressure diastolic 15 min	81.26±6.86	76.00±7.27	0.003
Pulse 3 min	91.35±14.7	83.32±8.7	0.086
Pulse 5 min	90.47±14.0	83.70±7.44	0.022
Pulse 8 min	87.94±12.0	82.38±6.8	0.018
Pulse 12 min	84.62±16.21	111.68±15.5	0.317
Pulse 15 min	85.03±9.01	85.82±7.8	0.646

A healthy fetus can withstand the changes in blood circulation but an already compromised fetus can suffer from devastating effects.[19, 20] For many years, it has been known that the use of vasopressors during pregnancy could harm the fetus as they can decrease the uteroplacental blood flow or they may have direct effects on the fetus.[20] But different drugs can have variable effects on the fetus, some can be beneficial for the fetus i.e. a study showed that Phenylephrine is associated with a lower incidence of fetal acidosis and maternal nausea and vomiting as compared to ephedrine. The reason for fetal acidosis associated with ephedrine could be due to decreased uteroplacental blood flow caused by either decreased maternal artery pressure, uteroplacental vasoconstriction or by a direct fetal effect of ephedrine.[19]

However, use of phenylephrine is not completely risk-free as there is a possibility of dose-dependent maternal bradycardia while using this drug. A comparative study is conducted using different infusion rates of phenylephrine showed that patients receiving 50µg/min had significantly less bradycardia as compared to patients receiving 100µg/min 13. Some of our patients also witnessed a decrease in pulse levels only at some times during the procedure but the pulse did not drop below 50bpm and a decrease in pulse rate was not associated with any complications, so they did not require any intervention. Nevertheless, use of vasopressors during any surgical procedure should be done with caution as there are chances of organ damage like acute kidney injury.[21]

Referring to the question that which dosage regimen is the most effective, a double-blind trial comparing the effects of bolus vs continuous infusion regimen did not find any difference in outcome in regard to hemodynamic effects.[17] Another study showed that in patients receiving spinal anesthesia for elective cesarean delivery, a prophylactic phenylephrine infusion decreased the incidence and level of hypotension but with no change in neonatal outcome in comparison with a patient in control group which received IV bolus phenylephrine on requirement.[14] This control/conventional group was basically made to limit the use of drug to only those patients undergoing fall in blood pressure. We also compared the use of prophylactic vs conventional phenylephrine administration in preventing post spinal anesthesia hypotension in elective caesarean section patients. Our study showed that prophylactic regimen of phenylephrine is better in controlling blood pressure than rescue boluses alone without causing any significant adverse effects because that can risk very low blood pressure in conventional group where only conventionally used

Another popular method is to administer IV fluids either before or during the administration of spinal anesthesia. Administration of colloids has been observed to be more effective against spinal anesthesia-induced hypotension when used before giving the anesthesia as they have a longer half-life in the intravascular compartment while crystalloids are considered better than colloids when given during the administration of anesthesia.[16, 22] Excessive and unchecked fluid resuscitation can lead to terrible effects like edema of various vital organs 15.

Recent consensus demands that a multimodal approach should be used to counter this problem. Although volume therapy alone is hardly effective in controlling hypotension during spinal anesthesia, simultaneous volume therapy decreases the amount of vasopressor required to achieve therapeutic goals. A review stated that rapid pre-loading with a colloid is effective in combating hypotension, and it also causes less vasopressor to be administered.[23]

From this discussion, it is evident that maternal hypotension during spinal anesthesia is a preventable problem. Of all the drugs phenylephrine has the best results to prevent post-spinal anesthesia hypotension when used prophylactically. Also, the dose of vasopressor being used can be decreased by simultaneously using a volume expander.

In our study, patients who were hypertensive or those who were already taking any anti-hypertensive medications were excluded from the study. All those patients undergoing this C-section were under close monitoring and blood pressure was being maintained at the normal limits. An exception occurred in only a few patients where blood pressure was falling below the mentioned limit of 90/60 mmHg that was then maintained by bolus of phenylephrine vasopressor along with IV infusions during procedure in the control group. While the experimental group was already administered the drug mentioned before the start of procedure according to methodology. A study can be done to compare the use of phenylephrine administration in hypertensive and normotensive patients undergoing spinal anesthesia during elective cesarean sections. In the future research can be done to compare the simultaneous use of multiple vasopressors along with volume expanders while monitoring maternal and fetal well-being. Long-term fetal follow-ups should be done to observe any prolonged side effects.

Conclusion

According to our results, it has been shown that prophylactic dosage regimen of phenylephrine is more effective in controlling spinal anesthesia-induced hypotension in patients undergoing C-section. While in comparison of conventional therapy there is still a risk of fall in blood pressure that required thorough monitoring along with rescue doses of phenylephrine. As it was a quasi-experimental study, next randomized clinical

studies in Pakistani setup are required in this regard to explore the concomitant usage of volume expansion methods and their effect on hypotension during spinal anesthesia.

Conflict of Interest

The authors declare that there is no conflict of interest.

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5. Dr. Hassam Nasir Khan Alizai (Drafting)
6. Prof. Naila Abrar (Final approval of the version)
7. Prof. Amanat Ali Khan (Final approval of the version)
8. Prof. Munir Ahmad (Final approval of the version)