PROPHYLACTIC PHENYLEPHRINE INFUSION VERSUS RESCUE BOLUSES: EFFECT ON THE PHYSICIAN INTERVENTION AND FLUID ADMINISTRATION

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ABSTRACT

**Objective:** To compare the effect of prophylactic phenylephrine infusion on the fluid management and physician intervention as compared with rescue boluses of phenylephrine alone.

**Study Design:** Randomized controlled trial.

**Place and Duration of Study:** Anesthesiology department, Combined Military Hospital, Rawalpindi; from Feb to Jul 2016.

**Material and Methods:** A total of 70 patients were randomly divided into two groups, 35 in each. After a preload of 10ml/kg of ringer lactate; spinal anesthesia was given with 12 mg 0.75% hyperbaric bupivacaine. Group A given prophylactic phenylephrine infusion at the rate of 0.75ug/kg/minute for 5 minutes after initiation of spinal anesthesia. Group B was given 50ug rescue bolus of phenylephrine when hypotension occurred.

**Results:** The two groups did not differ in their demographic profile and mean fluid preload. The mean preload was 691.4ml (±110.1) in group A versus 721.4ml (±89.3) in group B, p-value 0.215. The total fluid administered in group A was lower than group B, 1634.2ml (±232.5) versus 1777.1ml (±328.1); p-value 0.039. An average of 0.23 (±0.49) number of physician interventions were done in hypotensive patients in group A versus 1.26 (±1.29 in group B; p-value 0.06, which is statistically insignificant. The group A received a much higher dose of phenylephrine, mean dose 287.2ug ± 48.8 versus 64.2ug ± 64.8; p-value<0.001. The mean rescue phenylephrine bolus dose in group A was 15.7ug (±31.5) in group A versus 64.2 ± 64.8ug, p-value<0.001; which is statistically insignificant.

**Conclusion:** Prophylactic phenylephrine infusion with crystalloid preload was found associated with reduced number of rescue boluses and rescue phenylephrine dose and lesser total intraoperative fluid administration, when compared to preload with rescue boluses.

**Keywords:** Elective cesarean section, Fluid preload, Prophylactic phenylephrine infusion, Rescue boluses, Spinal anesthesia.

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**INTRODUCTION**

Maternal hypotension is one of the most common complication of spinal anesthesia for cesarean section. The incidence is as high as 70-80% when pharmacological prophylaxis is not used. Various techniques have been used for prevention and treatment of hypotension. These include IV crystalloid and colloid fluid pre-load and co-load, lateral uterine displacement, gravity (Trendelenburg or leg raising), compression devices on the legs and prophylactic vasopressors. No single method has been shown to completely prevent maternal hypotension. Jacob et al showed that the incidence of hypotension (60 versus 46%, p-value 0.1607) was similar whether crystalloid preload or co-load was done. Recent research has shown that phenylephrine is as effective as ephedrine in prevention of maternal hypotension, nausea and vomiting and it is associated with higher umbilical blood pH with no difference in APGAR scores or neonatal outcome. Prophylactic phenylephrine given as infusion provides better hemodynamic stability than rescue boluses. In normal pregnancy, the overall venous tone is low and spinal anesthesia further reduces venous tone, often unmasking the effects of caval compression, by blocking the compensatory sympathetic response. Increasing the venous...
tone with an alpha agonist can be effective at countering the effects of spinal anesthesia and caval compression. Alkaissi et al reported lower number of patients that required rescue boluses when preventative phenylephrine was used as compared to ephedrine. However, the total fluid given, total blood loss and anesthesia were comparable in both groups. According to the authors’ knowledge, limited data is available on the intraoperative fluid therapy, the dose administered for effectively preventing maternal hypotension or the number of rescue boluses required when prophylactic phenylephrine infusion is used. The aim of our study was to compare the effect of prophylactic phenylephrine infusion and rescue boluses on the fluid management, rescue bolus and physician intervention to maintain hemodynamic stability.

MATERIAL AND METHODS

This randomized controlled trial was conducted at Anesthesiology department, Combined Military Hospital, Rawalpindi from Feb to Jul 2016. WHO sample size calculator was used to calculate a sample size of 70 (n=35 in each group) with power of test 80% and level of significance 5%. The anticipated population proportion was 20% and 90% hypotension in the two groups. The patients were divided into two equal groups (n=35 in each group) randomly by battery method. After the approval of hospital ethical committee, the preanesthesia assessment was done as per institute protocol. Patients with American Society of Anesthesiology physical status I, II, age 18-35 years with full term, singleton pregnancy undergoing elective lower segment cesarean delivery were included in our study by non-probability, consecutive sampling. Patients with pre-existing or pregnancy induced hypertension, gestational or pre-existing diabetes mellitus, cardio respiratory or peripheral vascular disease; and any contraindication to spinal anesthesia were excluded from the study. On the day of surgery, 18 G intravenous cannula was inserted. All the patients were premedicated with intravenous metoclopramide 10mg and dexamethasone 8mg. Patient were preload with 10ml/kg Ringers lactate over 20 minutes, and same fluid was used for maintenance during surgery. Under complete aseptic measures, spinal anesthesia was initiated with 12 mg bupivacaine (0.75% hyperbaric) was given by using 25 G Quincke needle at L3-4 level. Surgery was allowed when sensory block level of T4 was achieved and at least 10 minutes after initiation of subarachnoid block. If spinal block failed completely general anesthesia or re-injection were offered and patient were excluded from study and more females were included to complete the sample size. Group A received phenylephrine infusion at 0.75ug/kg/min for five minutes once intrathecal bupivacaine was given; whereas group B received phenylephrine rescue boluses if maternal hypotension occurred. The infusion was made in syringe pump with a strength of 50microgram/ml and weight dependent dose was calculated according to measured weight in kilograms. The number of physician interventions was recorded; 50microgram phenylephrine rescue bolus in case of maternal hypotension (maternal systolic blood pressure less than 100 mm Hg). The fluid given as preload and total intraoperative fluid were also recorded.

All collected data was analyzed using SPSS version 25. Descriptive statistics were calculated for both quantitative and qualitative variables. Mean and standard deviation were calculated for quantitative variables like age, weight, fluid administered. Independent t-test was used for normal quantitative values (pre-load, total fluid and weight) and Mann Whitney U test for non-normal quantitative values (number of bolus, bolus dose and total phenylephrine dose). Chi square test and Fisher’s exact test to compare the qualitative values (ASA status) between the two groups. A p-value of less than or equal to 0.05 was considered as statistically significant.

RESULTS

A total of 70 parturient were included in my study. The demographic profile is tabulated as table. The mean preload was 691.4ml (±110.1) in group A versus 721.4ml (±89.3) in group B,
Phenylephrine Infusion Versus Rescue Boluses

Phenylephrine Infusion

VERSUS RESCUE BOLUSES


p-value 0.215. The total fluid administered in group A was lower than group B, 1634.2ml (±232.5) versus 1777.1 ml (±328.1); p-value 0.039. An average of 0.23 (±0.49) number of physician interventions were done in hypotensive patients in group A versus 1.26 (±1.29 in group B; p-value 0.06, which is statistically insignificant. The group A received a much higher dose of phenylephrine, mean dose 287.2ug ± 48.8 versus 64.2ug ± 64.8; p-value<0.001. The mean rescue phenylephrine bolus dose in group A was 15.7ug (±31.5) in group A versus 64.2 ± 64.8 ug, p-value<0.001; which is statistically significant.

DISCUSSION

Prophylactic phenylephrine has been shown to reduce the incidence of maternal hypotension by various authors8-11. It is considered as vasopressor of choice by many obstetric anesthetists. Phenylephrine infusion has been shown to maintain the blood pressure near the baseline without potentially harmful extremes of hypotension or hypertension that may be associated with phenylephrine boluses. According to the authors’ knowledge, limited data is available regarding the effect of phenylephrine infusion on the physician intervention. In our study, the prophylactic phenylephrine infusion was associated with reduced number of rescue bolus number as well as rescue dose; total fluid administered intraoperatively as compared to phenylephrine rescue boluses alone. Sayyid et al compared variable rate phenylephrine infusion with rescue boluses with crystalloid co-load. They reported a reduced number of physician intervention in the infusion group, median 0 vs 3 in either group; difference in median=3, 95% confidence interval. They also reported the number to treat was 1.4 women to prevent hypotension8. A study by Allen et al reported reduction in the number of physician intervention when 25 and 50 microgram/ minutes were compared with 100 microgram/ minutes infusion p=0.004 and p=0.02 respectively. However, there was no difference in number of physician intervention when the prophylactic infusion was compared with placebo15. Although the number of physician interventions required to maintain maternal hemodynamics may not matter in institute with 1:1 anesthetist to patient ratio or where the obstetric workload is comparatively light. Our institute caters to ten surgical specialties, including obstetrics with upto 150 cases in 18 operation theaters every day. When the physician intervention are reduced in addition to providing better hemodynamics, the workload on the anesthetist may be reduced with improved patient care. We studied a weight based infusion which may not always be the most appropriate dose for all the hospital. Further study is required to prove the safety of fixed dose, weight independent prophylactic phenylephrine infusion and the optimal dose in Asian population. According to authors knowledge, no single method has been shown to completely prevent maternal hypotension. Some studies have shown superiority of colloids over crystalloids2,4,14. Intravenous crystalloid combination with vasopressor has been shown to reduce the frequency of maternal hypotension15,16. A study by Loubert et al reported the minimum effective fluid volume of hydroxyethyl starch to be 733ml (95% CI, 388-917ml) for prevention of maternal hypotension in 50% of the parturient17. Limited research has been done regarding the fluid administered intraoperatively when phenylephrine prophylactic infusion is used. Ngan et al studied a combination of phenylephrine infusion with crystalloid co-

Table: Demographic profile of study population.

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<tr>
<th></th>
<th>Group-A (n=35)</th>
<th>Group-B (n=35)</th>
<th>p-value</th>
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<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>27.2 ± 3.43</td>
<td>28.7 ± 3.33</td>
<td>0.09</td>
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<tr>
<td>ASA I</td>
<td>n=30 (85.7%)</td>
<td>n=34 (97.1%)</td>
<td>0.198</td>
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<tr>
<td>Weight (kg)</td>
<td>73.6 ± 7.24</td>
<td>74.8 ± 11.4</td>
<td>0.605</td>
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Phenylephrine Infusion Versus Rescue Boluses


hydration. They infused phenylephrine infusion at 100ug/minute with one group receiving maintenance dose of crystalloid versus high flow of crystalloid. They reported a much higher crystalloid infusion rate in second group; 63.5ml/minute versus 1.7ml/minutes, p-value <0.00115,10. In our study the fluid was given as weight calculated preload over 20 minutes. The preload given was comparable, whereas the total intraoperative fluid was significantly lower in prophylactic phenylephrine group. In healthy parturient, the total fluid administration may not make a difference in their outcome; however, patients with limited cardiac reserve may be better managed with fluid restriction. The safety of phenylephrine infusion has not been proven in parturient suffering from cardiovascular disease and its use is not recommended at present. In our study, the total phenylephrine given as rescue bolus was significantly higher in the prophylactic infusion group. Similar results have been reported by Doherty et al who reported increased phenylephrine administration in infusion group; 1740 versus 964 microgram in bolus group, p-value <0.00118. They had used a much higher infusion rate of 120ug/min post initiation of spinal anesthesia versus 0.75ug/kg/min for 05 minutes in our study. Ngan et al also reported a higher dose of 1260microgram in infusion group versus 450ug in rescue bolus group. They used an infusion of 100ug/min for 03 minutes after spinal anesthesia and bolus of 100ug; while we used a prophylactic infusion for 05 minures and rescue bolus of 50 ug. We have safely given a prophylactic phenylephrine infusion in our study with reduced number of physician interventions required to maintain hemodynamic stability.

CONCLUSION

Prophylactic phenylephrine infusion with crystalloid preload was found associated with reduced number of rescue boluses and rescue phenylephrine dose and lesser total intraoperative fluid administration, when compared to preload with rescue boluses. The weight based phenylephrine infusion can be safely given for prevention of maternal hypotension during cesarean section under spinal anesthesia. It can not only improve patient outcome by improving hemodynamics but also reduces anesthetist workload.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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Phenylephrine Infusion Versus Rescue Boluses


