ORIGINAL ARTICLE

Preload Versus Coload and Vasopressor Requirement for the Prevention of Spinal Anesthesia Induced Hypotension in Non-Obstetric Patients

Mueen Ullah Khan[1], Abdul Saboor Memon[2], Mohammad Ishaq[3] and Mansoor Aqil[1]

ABSTRACT

Objective: To compare the effectiveness of preload and coload for the prevention of Spinal Induced Hypotension (SIH) and vasopressor requirements.

Study Design: Randomized trial.

Place and Duration of Study: Department of Anesthesia, The Aga Khan University Hospital, Karachi, Pakistan, from June 2007 - June 2010.

Methodology: Sixty patients were randomly divided into preload and coload group of 30 each. Patients with ASA 1 - 3, aged 20 - 60 years were included. Patients with history of IHD, COPD, BMI > 30 and surgical procedure TURP were excluded. All patients received crystalloid 10 ml/kg before induction of spinal anesthesia in preload group and at the time of spinal anesthesia in coload group. Blood pressure and heart rate were recorded at different time intervals till 45 minutes. Patients received ephedrine 5 mg when systolic blood pressure dropped below 90 mmHg and heart rate was less than 60 beats/minute and/or phenylephrine 50 micrograms when systolic blood pressure dropped below 90 mmHg and heart rate was more than 60 beats/minute.

Results: There was no statistically significant difference at different time intervals in heart rate, systolic and mean arterial pressure between the groups. Diastolic blood pressure was significantly different in both groups at 6 - 15 minutes after spinal anesthesia. SIH occurred (21) 70% and (15) 50% in preload and coload groups, respectively ($p=0.187$). Ephedrine requirement for SIH was significantly high in preload group ($p=0.017$). Phenylephrine requirement for SIH was high in preload group which was statistically non-significant ($p=0.285$).

Conclusion: Coload group has lower incidence of spinal induced hypotension and significantly less vasopressor requirement than the preload group.

Key Words: *Spinal anesthesia. Hypotension. Crytalloid. Preload. Coload.*

INTRODUCTION

Hypotension is the most common cardiovascular response to spinal anesthesia which occurred due to increase in venous capacitance and a reduction in systemic vascular resistance.[1] Seventy to eighty percent of the patients, undergoing spinal anesthesia, develop intraoperative spinal induced hypotension.[2,3] This is common practice to administer large volumes of crystalloids 15 - 20 minutes before spinal anesthesia in order to prevent spinal induced hypotension.[4]

Efficacy of crystalloid administration before spinal block has been tested mostly in obstetric patients and found to be less beneficial.[5,6] Administrations of intravenous crystalloids are having the risk of development of pulmonary edema in susceptible individuals and it may also lead to postoperative urinary retention in non-catheterized patients.[7] The goal of administering fluids before spinal block is to increase the venous return in order to preserve central blood volume and cardiac output.

It has been shown that crystalloid administration, before spinal block (preload) in general and other surgical specialty patients, does not reduce the incidence of spinal induced hypotension.[8] It may partly be explained by short intra-vascular half-life of crystalloids. However, rapid administration of crystalloids just after induction of spinal anesthesia (coload) was found to have beneficial effect in preventing cardiovascular side effects in general and other surgical specialty patients.[4] Administration of intravenous fluids just after induction of spinal anesthesia provides additional intravascular fluid. The arterial pressure is better maintained in the period of increased risk of cardiovascular side effects.[9] Worldwide, most of the work was done on obstetric patients. Research work on this subject in non-obstetric patients is lacking.

[1] *Department of Anesthesia, College of Medicine, King Saud University, Riyadh, Saudi Arabia.*
[2] *Department of Anesthesia, Northern Area Armed Forces Hospital, King Khalid Military City, Hafr Al Batin, Saudi Arabia.*
[3] *Department of Anesthesia, Shalamar Hospital, Shalamar Road, Lahore, Pakistan.*

Correspondence: Dr. Mueen Ullah Khan, Department of Anesthesia, College of Medicine, King Saud University, P.O. Box 7805 (41), Riyadh-74800, Saudi Arabia.
E-mail: mueenullahpk@hotmail.com

Received: September 20, 2013; Accepted: September 22, 2015.

The aim of this study was to evaluate the superiority of crystalloids preload or coload in preventing the spinal induced hypotension, and the vasopressor requirements for the treatment of spinal induced hypotension in non-obstetric patients undergoing spinal anesthesia.

METHODOLOGY

This trial was conducted at the Department of Anesthesia, The Aga Khan University Hospital, Karachi, Pakistan, from June 2007 - June 2010.

After approval from the University IRB and written informed consent, a total of 60 adult patients of either sex, aged 20 - 60 years and with ASA physical status 1 - 3 scheduled for surgical procedure under spinal anesthesia were included in the study. Patients with diabetes mellitus, cardiovascular or crebrovascular disease on medications, extremes of weight (< 40 or > 100 kg) and height (< 140 cm or > 180 cm), any contra-indications to neuraxial anesthesia, surgical procedure transurethral resection of prostate and patients requiring pain medications were excluded from the study.

Patients were randomly divided into two groups of 30 each, named Group-P (preload) and Group-C (coload). Patient in both groups were kept nil per oral for 6 hours before surgery and pre-meditated with tablet midazolam 7.5 mg 1-hour before operation. A 16-gauge intravenous (IV) catheter was inserted under local anesthesia in left hand. One litter ringers, lactate solution was attached with IV catheter. Standard monitors of electro-cardiography and pulse oximetry (SpO_2) were applied. The non-invasive blood pressure was applied on the right arm. Base Line (BL) and just after induction of spinal anesthesia, Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Blood Pressure (MAP) were recorded. The same hemodynamic parameters were recorded at 1, 3, 6, 9, 12, 15, 20, 25, 30, 35, 40 and 45 minutes after spinal anesthesia. Spinal anesthesia was induced with 2.5 cc of isobaric 0.5% bupivacaine and 25 µg fentanyl. Group-P patients received crystalloids 10 ml/kg during 20 minutes before induction of spinal anesthesia. Group-C patients received crystalloid 10 ml/kg within 20 minutes when drug was injected in the subarachnoid space. In this study hypotension was defined as systolic blood pressure less than 20% of the calculated baseline value or less than 90 mmHg. Intravenous ephedrine 5 mg was administered when systolic blood pressure was decreased below 90 mmHg and heart rate was less than 60 beats/minute. Intravenous phenylephrine 50 µg was given when systolic blood pressure was decreased below 90 mmHg and heart rate was above 60 beats/minute. The consumptions of ephedrine in milligrams and phenylephrine in micrograms were recorded.

Sample size was determined by power analysis based on pilot data (desired power = 0.8, alpha = 0.05, hypotension incidence 80% and significant if 50% decrease in incidence) and a minimum of 28 patients per group was required. Patients were divided into two groups (preload (P)- group and coload (C)- group) of 30 each. Randomization was performed using sealed envelope method. These envelopes were prepared using computer generated random number table. A Statistical Package for Social Sciences (SPSS) version 21 was used for data entry and analysis. Mean and standard deviation were computed for quantitative variables like age, weight, height, heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure for preload and coload groups. Independent-sample t-test was applied for quantitative variables like age, weight, height, BMI and vasopressor ephedrine and phenylephrine requirements. Chi-square was applied for qualitative variables like gender, ASA physical status, surgical procedure, spinal induced hypotension, height of sensory block between preload and coload groups. Repeated measures were applied for hemodynamic at different time intervals for HR, SBP, DBP and MAP. Means of HR, SBP, DBP and MAP were compared and significance at different time intervals were verified with independent-sample t-test. A p-value of less than 0.05 ($p < 0.05$) was taken as significant.

RESULTS

A total of 60 patients (30 in each group) underwent the trial. The male to female ratio in preload and coload group were 14:16 and 21:9, respectively. There was no statistically significant difference found with regard to age, gender, height, weight, BMI, ASA physical status and surgical specialty procedure between preload and coload groups (Table I and II). Hemodynamic variables heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure were measured at different time intervals (base line, after drug injection for spinal anesthesia and then at 1, 3, 6, 9, 15, 20, 25, 30, 35, 40 and 45 minutes) after spinal anesthesia injection. Heart Rate (HR), Mean Blood Pressure (MAP) and Systolic Blood Pressure (SBP) were compared in both study groups with no statistical difference. However, mean heart rate gradually decreased in both groups and maximum decline was observed at 6 minutes 61.20 ±5.92 vs. 61.46 ±7.75 ($p = 0.88$) beats per minute after induction of spinal anesthesia. Maximum drop in mean SBP (> 20%) from base line occurred in preload and coload groups at 6-minute 94.56 ±7.55 vs. 94.60 ±6.93 mmHg ($p= 0.47$), 9-minute 96.10 ± 10.61 vs. 94.36 ±8.05 mmHg ($p= 0.47$) and 12-minute 96.33 ±9.64 vs. 96.53 ±6.58 mmHg ($p= 0.70$) after induction of spinal anesthesia. The decrease in mean DBP after spinal anesthesia in preload and coload groups at 6-minute was 54.53 ±4.27 vs. 61.33 ±4.80 mmHg ($p=0.0005$), at

Table I: Patient characteristics in preload and coload group. The data is presented as means ±SD and percentages as required. A p-value of less than 0.05 (p=<0.05) was considered as significant.

Patient characteristics	Preload group N = 30	Coload Group N= 30	p-value	Statistical test applied
Age (years) Mean ± SD	48.83 ± 11.59	47.14 +11.72	0.567	Independent samples t-test
Height (cm) Mean ± SD	165.13 ± 6.45	165.20+ 6.75	0.969	Independent samples t-test
Weight (kg) Mean ± SD	63.93 ± 4.90	65.43+ 4.33	0.215	Independent samples t-test
BMI (kg/m^2) Mean ± SD	23.80 ± 2.14	23.41+2.14	0.868	Independent samples t-test
Gender Male/Female	14 /16 (47% / 53%)	21/9 (70% / 30%)	0.058	Chi-square
Surgical procedure Orthopedic/ urology/general	15/2/13 (50% /7%/43%)	17 /3 /10 (57% /10% /33%)	0.699	Chi-square
ASA 1/2/3	9/6/15 (30% / 53% /15%)	10/16/4 (33% / 53% /14%)	0.921	Chi-square

Table II: Comparison of surgical specialty, height of block, hypotension, ephedrine and phenylephrine requirements in preload and coload group. The data is presented as means ± SD and percentages as required. A p-value of less than 0.05 (p=<0.05) was considered as significant.

Patient characteristics	Preload Group N= 30	Coload Group N= 30	p-value	Statistical test applied
Surgical specialty				
Orthopedics	15 (50%)	17 (56.66%)	0.604	Chi-square
General surgery	13 (43.33%)	10 (33.33%)	0.4251	Chi-square
Urology	2 (6.66%)	3 (10%)	00	Fisher's exact-test
Height of block T4/T5/T6/T7/T8	5/6/6/1/12 17% /20% /20% / 3%/40%	4/9/12/0/5 13% /30% /40% /0% / 17%	0.159	Chi-square
Hypotension Yes/No	21/9 17% /30%	15/15 50% /50%	0.094	Fisher's exact-test
Ephidrine requirement (mg)	15.2 ±4.99	7.0 ± 2.73	0.002	Independent samples t-test
Phenylephrine requirement (µg)	64.70 ±23.48	75.0 ± 26.35	0.303	Independent samples t-test

9-minute 57.50 ±5.90 vs. 64.13 ±5.49 mmHg (p=0.0005), at 12-minute 59.63 ±6.56 vs. 65.03 ±5.84 mmHg (p=0.001) and at 15-minute 59.60 ±6.85 vs. 69.80 ±8.56 mmHg (p=0.005). These were statistically significant.

The incidence of hypotension was 70% (21/30) in preload group and 50% (15/30) in coload group which was statistically non-significant (p=0.187). Overall the vasopressor requirement for hemodynamic instability was significantly high (p=0.017) in preload group as compared to coload group (mean 15.2 mg vs. 7 mg). Phenylephrine requirement was higher in preload group as compared to coload group (mean 64.7 vs. 75 µg) which was statistically non-significant (p=0.415). In preload group (21/30), 13 patients required both the vasopressors (ephedrine and phenylephrine) and 4 patients required either ephedrine or phenylephrine respectively. In coload group 5 patients required ephedrine, 10 patients required phenylephrine and none of the patients required both vasopressors (Table II).

Level of sensory block and its relation to spinal induced hypotension was also studied. It has been observed that with the increase in height of block there was increase in the incidence of hypotension. However, in both groups the difference in height of block was statistically non-significant (p=0.159, Table II).

DISCUSSION

Spinal anesthesia is most commonly used technique for lower abdominal and lower limb surgeries. Spinal induced hypotension as a consequence of sympathetic blockade is most common and most important physiologic derangement that occurs due to peripheral vasodilatation.[10] Peripheral vasodilatation causes decrease in venous return to heart, that leads to low cardiac output and hypotension. Simultaneously, vagal responses to decreased preload or venous return and increase height of sympathetic block also contribute to hypotension.[11] Intraoperative hypotension is considered to be one of the predictors of postoperative morbidity and prolonged hospital stay.[12] Spinal induced hypotension, if left untreated, can lead to cardiovascular collapse. Different methods have been used for the prevention of SIH, such as intravenous fluid preloading,[13] infusing fluids at the time of drug injection,[7] restriction of block to one side (unilateral spinal anesthesia), low dose spinal anesthesia[10] and use of vasoactive agent like ephedrine and phenylephrine.[14]

Physical methods such as leg elevation and compression stockings[15] are also used for the prevention of spinal induced hypotension. Preload is the most commonly used method for the prevention of hypotension. The aim of administration of fluids before spinal anesthesia is to fill the intravascular compartment and to prevent the occurrence of hypotension due to sympathetic blockade. Crystalloid and colloid are both used as preload. Crystalloid is the preferred solution but as the half life of crystalloid is 15 - 20 minutes so its effectiveness for prevention of hypotension is questionable. Colloids have an advantage of having long half life so can effectively maintain intravascular volume and prevent hypotension. However, colloids are expensive, not easily available and associated with allergic reactions. Different studies revealed that larger volume of colloid is required to sustain intravascular volume longer than thirty minutes.[16]

To evaluate the hemodynamic effects of preload and coload, most of the studies were done on obstetrical patients.[17,18] This study was conducted on non-obstetrical patients as very limited data is available in specialties other than obstetrics.

In this study, the hemodynamic effects of preload and coload on SIH were compared. There was no significant difference in heart rate, systolic blood pressure and mean arterial pressure changes in both groups. These results are comparable with the Bose study,[19] who demonstrated insignificant difference between preload and coload regarding heart rate and mean arterial pressure. Dyer *et al*. noticed in obstetric patients an increase in heart rate in both groups but heart rate returned to baseline more rapidly in coload group.[7] In this study, the trends of decrease in heart rate were different from the Dyer's study. The difference may be due to different patient population, difference in height of block, drug effect, difference in height and weight, age, pre-medication and parasympathetic over activity. Rout *et al*. has also reported significant decline in systolic blood pressure at 4 - 6 minutes after induction of spinal anesthesia in obstetric patients.[20] He compared crystalloid preload (20 ml/kg) over either 20 minutes or 10 minutes before spinal anesthesia. These results are comparable with Rout's study showing more than 20% drop in SBP between 6 and 12 minutes after induction of spinal anesthesia. Mojica *et al*. showed significant increase in systolic blood pressure after induction of spinal anesthesia in preload group,[9] which contradicts with this study. This difference may be due to fact that small volume 10 ml/kg versus 20 ml/kg of crystalloid was infused in this study.

A statistically significant decline in DBP was observed in preload group at 6 - 15 minutes period after induction of spinal anesthesia. This contradicts an earlier study, which demonstrated no difference in DBP among study groups.[9] This difference may be due to the different methodology, different type of population, use of hyperbaric marcaine and difference in height of sympathetic block.

Vasopressors are used for the prevention and treatment of hemodynamic instability. Most commonly used vasopressors are ephedrine and phenylephrine.[14] Epinephrine is used when blood pressure and heart rate do not respond to ephedrine and phenylephrine. Ephedrine is indirect acting sympathomimetic agent with effect on both alpha and beta receptors resulting in increase in heart rate and blood pressure. Phenylephrine is a pure alpha agonist resulting in increase in blood pressure and reflex bradycardia. These drugs are usually used alone or in combination to acquire the desired hemodynamic stability. Recently, prophylactic administration of phenylephrine infusion has been advocated to be more effective in reducing intraoperative nausea, vomiting and incidence of hypotension.[21] Cause of hypotension after spinal anesthesia depends on patient volume status, comorbids as well as on the height of block and drug effect etc. Vasopressor can be used for the prevention and treatment of spinal induced hypotension when different techniques for prevention of hemodynamic instability are coupled. In this study vasopressor requirement in preload group was high as compared to coload group and results are comparable to the recent study done by Khan.[22] It has been postulated that cohydration promotes better circulation of vasopressors and coincides with the peak effect of spinal anesthesia.[23] This may be due to the fact that at the time of pre-hydration and institution of spinal anesthesia, the fluid might have been distributed in the body compartments. The distributed fluid might not have contributed much in increasing the intravascular volume and might not be enough to satisfy the increased intravascular capacity.[9] In coload method, the intra-vascular fluid is available which may be responsible for better distribution of injected vasopressors. This may be the reason for decrease in requirement of vasopressors.

Hartmann[3] and Ewaldsson *et al*.[24] have demonstrated the positive relation between hypotension and height of block which correlates with our results. However, in this study, the achieved height of block was comparable in both groups.

The limitations of this study are lack of a control group or placebo group precluded determination of an absolute reduction in the incidence of hypotension. The authors chose to omit it as withholding fluids would not have been in keeping with their clinical practice. Blinding was not done because it was technically difficult and fixed dose of isobaric bupivacaine was used. However, the judgment of hypotension or ephedrine/ phenylephrine administration was done under clear-cut standard and the effect of this unblinded method on these results might be small.

CONCLUSION

Both preload and coload methods were unable to prevent the spinal induced hypotension in non-obstetric patients. However, the coload group had a lower incidence of spinal induced hypotension and significantly less vasopressors requirements than the preload group.

Acknowledgement: This work / study was supported by the College of Medicine Research Centre, Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia.

REFERENCES

1. Morgan PJ, Halpern SH, Tarshis J. The effects of an increase of central blood volume before spinal anesthesia for cesarean delivery: a qualitative systematic review. *Anesth Analg* 2001; **92**:997-1005.
2. Klöhr S, Roth R, Hofmann T, Rossaint R, Heesen M. Definitions of hypotension after spinal anaesthesia for caesarean section: literature search and application to parturients. *Acta Anaesthesiol Scand* 2010; **54**:909-21.
3. Hartmann B, Junger A, Klasen J, Benson M, Jost A, Banzhaf A, *et al.* The incidence and risk factors for hypotension after spinal anesthesia induction: an analysis with automated data collection. *Anesth Analg* 2002; **94**:1521-9.
4. Ah-Young OH, Jung-Won Hwang, In-Ae Song, Mi-Hyun Kim, Jung-Hee Ryu, Hee-Pyoung Park, *et al.* Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: preload versus coload. *BMC Anesthesiol* 2014; **14**:36.
5. Lotfy ME, Moustafa AM, El Feky EME, Mowafy IA. Colloid versus crystalloid coload with spinal anesthesia during emergent cesarean section and their effect on hemodynamic changes. *J Am Sci* 2014; **10**:158-63.
6. Langesater E, Dyer RA. Maternal haemodynamic changes during spinal anaesthesia for caesarean section. Current Opinion in Anaesthesiology. 2011.
7. Dyer RA, Farina Z, Joubert IA, DU-Toit P, Meyer M, Torr G, *et al.* Crystalloid preload versus rapid crystalloid administration after induction of spinal anaesthesia (coload) for elective caesarean section. *Anaesth Intensive Care* 2004; **32**:351-7.
8. Tawfik MM, Hayes SM, Jacoub FY, Badran BA, Gohar FM, Shabana AM, *et al.* Comparison between colloid preload and crystalloid coload in cesarean section under spinal anesthesia: a randomized controlled trial. *Int J Obstet Anesth* 2014; **23**: 317-23.
9. Mojica JL, Melendez HJ, Bautista LE. Timing of intravenous crystalloid administration and incidence of cardiovascular side effects during spinal anesthesia: the results from a randomized control trial. *Anesth Analg* 2002; **94**:432-7.
10. Varshney R, Jain G. Comparison of colloid preload versus coload under low dose spinal anesthesia for cesarean delivery. *Anesth Essays Res* 2013; **7**: 376-80.
11. Seyedhejazi M, Madarek E. The effect of small dose bupivacaine-fentanyl in spinal anesthesia on hemodynamic nausea and vomiting in cesarean section. *Pak J Med Sci* 2007; **23**:747-50.
12. Weiniger CF, Ivri S, Ioscovich A, Grimberg L, Evron S, Ginosar Y. Obstetric anesthesia units in Israel: a national questionnaire-based survey. *Int J Obstet Anesth* 2010; **19**:410-6.
13. Wollman SB, Marx GF. Acute hydration for prevention of hypotension of spinal anesthesia in parturients. *Anesthesiology* 1968; **29**:374-80.
14. Simin A, Zahra F, Pouya HM, Reza T. Comparison the effect of ephedrine and phenylephrine in treatment of hypotension after spinal anesthesia during cesarean section. *OJOG* 2012; **2**:192-6.
15. Rout CC, Rocke DA, Gouws E. Leg elevation and wrapping in the prevention of hypotension following spinal anaesthesia for elective caesarean section. *Anaesthesia* 1993; **48**:304-8.
16. Ueyama H, He YL, Tanigami H, Mashimo T, Yoshiya I. Effects of crystalloids and colloid preload on blood volume in the parturients undergoing spinal anesthesia for elective cesarean section. *Anesthesiology* 1999; **91**:1571-76.
17. Rout CC, Akoojee SS, Rocke DA, Gouws E. Rapid administration of crystalloid does not decrease the incidence of hypotension after spinal anaesthesia for elective caesarean section. *Br J Anaesth* 1992; **68**:394-7.
18. Riaz A, Munzar Z. Preloading before spinal anesthesia for Cesarean section. A comparison between colloid and crystalloid preload. *Anesth Pain Intens Care* 2006; **10**:9-12.
19. Bose M, Kini G, Krishna HM. Comparison of crystalloid preloading versus crystalloid coloading to preventing hypotension and bradycardia following spinal anesthesia. *J Anaesth Clin Pharmacol* 2008; **24**:53-6.
20. Rout CC, Rocke DA, Levin J, Gows B, Reddy D. A re-evaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. *Anesthesiology* 1993; **79**:262-9.
21. Habib AS. A review of the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. *Anesth Analg* 2012; **114**:377-90.
22. Khan M, Waqar-ul-Nisai, Farooqi A, Ahmad N, Qaz S. Crystalloid co-load: a better option than crystalloid pre-load for prevention of postspinal hypotension in elective caesarean section. *Internet J Anesthesiol* 2013; **32**:1
23. Ngan Kee WD, Khaw KS, Ng FF. Comparison of phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for caesarean section. *Br J Anaesth* 2004; **92**:469-74.
24. Ewaldsson CA, Hahn RG. Bolus injection of ringer's solution and dextran 1 kDa during induction of spinal anesthesia. *Acta Anaesthesiol Scand* 2005; **49**:152-9.