Original Research Article

A comparative study of the haemodynamic effects in patients undergoing lower abdominal surgeries under sub-arachnoid block by using prophylactic intravenous low doses of ephedrine

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Abstract

Background: Despiteintravenous fluid preloadsub-arachnoid block induced hypotension often need the use of vasopressors, to prevent this condition prophylactic intravenous ephedrine in doses of 5mg and above has been used successfully. Use of doses lower than 5mg of intravenous ephedrine prophylactically has limited data. This study compared the efficacy of prophylactic intravenous ephedrine 3mg with 6mg ephedrine in the prevention of sub-arachnoid block induced hypotension in patients undergoing lower abdominal surgeries. **Materials and methods:** Sixty nine ASAI and II patients scheduled for elective lower abdominal surgeries were randomly allocated into 3 groups (A, B and C). Spinal anaesthesia was induced in all the patients using 3.0mls of 0.5% plainbupivacaine after a preload with 10ml/kg of 0.9% Normal saline. Patients in group A received 2mls of Normal salineintravenously, while those in groups B and C received 3mg and 6mg intravenous ephedrine respectively, diluted in 2mlsof normal saline, all within 2 minutes of intrathecal injection of bupivacaine. The incidence and severity of hypotensionand also the intraoperative ephedrine use were compared. **Results:** Results showed no significant difference in incidence of post-spinal hypotension between patients in groups B and C, p= 0.69. There was no significant difference in intra-operative ephedrine consumption by patients in groups B and C, p= 0.38. **Conclusion:** Intravenous ephedrine given prophylactically in dose of 3mg is as effective as ephedrine 6mg in reducing the incidence and severity of sub-arachnoid block induced hypotension during lower abdominal surgeries.

Key Word: Intravenouspreload with 10ml/kg of 0.9% Normal saline, sub-arachnoid blockinduced hypotension, prophylaxis, Intravenous low-dose ephedrine.

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INTRODUCTION

Sub-arachnoid block commonly used for lower abdominal surgeries is often complicated by hypotension[1]. The incidence of hypotension following sub-arachnoid blockcan be as high as 70%-80% when pharmacological prophylaxis is not used.[2,3] Hypotension is associated with nausea and vomiting. In severe cases, respiratory depression and cardiac arrest may occur[4]. Because volume expansion alone with intravenous fluids (preload) does not always prevent spinal anaesthesia-induced hypotension,

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administration of vasopressors becomes necessary[5,6,7]. A study by Desalu and Kushimo[5] confirmed the effectiveness of prophylactic ephedrine given by standard intravenous infusion for the prevention of hypotension during spinal anaesthesia for elective caesarean section. Eroglu *et al*[8]. successfully treated spinal anaesthesia-induced hypotension using intravenous bolus doses of ephedrine 3mg. Although, intravenous bolus ephedrine 5mg and above have been shown to prevent hypotension following spinal anaesthesia (especially amongst parturients)[9], there is limited data on the use of doses lower than 5mg as prophylaxis. This study therefore compared the efficacy of prophylactic intravenous ephedrine 3mg and 6mg in prevention of spinal anaesthesia-induced hypotension in lower abdominal surgeries.

MATERIALS AND METHODS

After the study protocol had been approved by the Institutional review committee, informed and written consent to participate in the study was obtained from all the patients. A randomized, double-blind, comparative study was done in Department of Anaesthesiology GEMS and Hospital, Srikakulam from October 2018 to February 2019.

Inclusion criteria: Patients between ages 18 and 64 years scheduled for elective lower abdominal surgeries
American Society of Anesthesiologists (ASA) physical status I and II.

Exclusion criteria: Patient refusal, Emergency surgeries, known hypersensitivity to bupivacaine, Infection at the proposed site of intrathecal injection, Bleeding disorder, neurological disease, Conversion to general anaesthesia and BMI $\geq$ 30 kg/m^2. A formula used to determine the appropriate sample size for the study showed that a minimum of 63 participants, comprising of 21 patients for each of three groups were required [10]. This was adjusted to 69 patients to accommodate for 10% attrition. All the patients were seen preoperatively at least one day before surgery during which they were clinically assessed and fitness for the study verified. All the patients gave written, informed consent, and were fasted overnight. They were also pre-medicated with oral diazepam 10mg the night before surgery and 5mg on the morning of surgery (about two hours before surgery). Randomization: Using a balloting technique, with coded papers inside an envelope, the patients were randomly allocated into 3 groups (A, B and C). Patients in group A received 2ml Normal saline intravenously while patients in groups B and C received 3mg and 6mg boluses of intravenous ephedrine respectively, diluted in 2ml of normal saline, all within 2 minutes of induction of spinal anaesthesia. In the operating theatre, baseline vital signs: heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) mean arterial pressure (MAP), oxygen saturation (SpO_2), electrocardiogram and temperature were recorded. A 18 gauge cannula was inserted into a forearm vein and 10ml/kg of 0.9% saline was infused over the 15 minutes preceding the block. The block was performed under aseptic conditions at the interspace between the 3rd and 4th lumbar vertebrae by an anaesthetist who was blinded to the study drugs. With the patient in the sitting position, 3ml of 0.5% plain bupivacaine was injected through a 25-gauge quincke needle into the intrathecal space over 15 seconds. The patient was immediately returned to the supine position. Solution A, B or C was injected intravenously, within 2 minutes of induction of spinal anaesthesia. At this point, a second anaesthetist (in a room outside the operating theatre), unaware of the patients group, came in and was responsible for intraoperative data collection. Haemodynamic parameters such as SBP, DBP, MAP, and HR were recorded every 3 minutes for the first 15 minutes and at 5 minutes intervals until the end of the procedure. Moderate hypotension was defined as a fall in SBP greater than 25% of baseline value or less than 90mmHg and, severe hypotension as a fall in SBP greater than 30% of baseline value or less than 80mmHg[9]. Hypertension was defined as increase in SBP greater than 30% of baseline value[9]. Bolus intravenous ephedrine 5mg was given intermittently to manage episodes of hypotension that did not respond to rapid infusion of 250mls of 0.9% saline. Bradycardia was defined as HR less than 60 beats per minute and tachycardia as HR greater than 100 beats per minute [9]. Cold sensation was used to assess sensory level of the regional block before surgery and was repeated every 3 minutes after induction of spinal anaesthesia. The level at 15 minutes after induction was noted and taken as the upper sensory level of block. Loss of cold sensation up to 6ththoracic dermatomal level was considered adequate for surgery. When the block failed to reach this level 15 minutes after intrathecal injection, general anaesthesia was administered and the patient was excluded from the study. Supplemental doses of ephedrine used and duration of surgery were also recorded. Complications that occurred (nausea, vomiting, shivering, tachycardia, and reactive hypertension) were recorded and appropriately treated. Primary outcome was the effect on blood pressure (SBP, MAP, and DBP) and incidence of hypotension. Secondary outcomes were total amount of ephedrine used after induction of spinal anaesthesia and incidence of complications (nausea, vomiting, reactive hypertension, tachycardia and shivering). All data collected were analysed using the statistical package for social sciences (SPSS) 20.0 software (SPSS, Chicago, IL, USA) for windows. A p- value < 0.05 was considered statistically significant.

RESULTS

There was no difference in demographic characteristics and intra-operative variables between the groups as shown in Table I. Also there was no difference between the 3 groups with regard to distribution of surgical procedures performed. The baseline SBP (mmHg) of the patients in groups A, B and C in Table II were comparable p= 0.56. Also, baseline MAP (mmHg) of the patients in the three groups were not significantly different, p= 0.21. In Table II, the difference in the overall incidence of spinal anaesthesia-induced hypotension between the three groups was not significant (p=0.21). Similarly, no significant difference in the overall incidence of hypotension was noticed between groups A and B (p=0.39), groups A and C (p=0.18) and, groups B and C(p= 0.69)respectively. There was no significant difference in the incidence of moderate hypotension between patients in group A and those in groups B and C (p=0.49). Conversely, there was significant difference in the incidence of severe hypotension between patients in group A and those in groups B and C (p= 0.043). There was also a significantly higher consumption of rescue doses of ephedrine among patients in group A (35.00+04mg) compared to groups B and C (5.0 mg), respectively, p= 0.018. Nausea and vomiting were the most common complications observed in the study as shown in Table III. These occurred more frequently in the control group although the difference was not statistically significant from the test groups (B and C). The incidences of post spinal shivering were similar in the groups (A, B and C), p=0.91. There was no significant difference with regard to the incidence of tachycardia between the 3 groups, p= 0.44. Reactive hypertension was noticed in 2 patients in group C after administration of prophylactic ephedrine. Patients in groups A and B experienced no such complication. There was no incidence of bradycardia, respiratory depression or dizziness in this study.

Table 1: Socio-Demographic characteristics, Surgical procedures and Intra-operative variables

Parameter	Group A (n=23)	Group B (n=23)	Group C (n=23)	P-value
Age (years)	30.13±9.67	34.35±10.22	31.09±7.20	0.25
Weight (kg)	71.5 2±9.11	70.91±8.65	70.56±10.71	0.79
Height (m)	1.69±0.07	1.70±0.07	1.68±0.09	0.43
BMI (kg/m2)	25.08±1.79	24.61±2.15	25.03±2.09	0.80
ASA I:II	23:0	23:0	23:0	
Upper sensory level at 15min	T4(T3-7)	T4(T3-7)	T4(T4-7)	0.54
Surgical procedures				
Inguinal herniorhaphy	15(65.2)	14(60.9)	14(60.9)	0.94
Hydrocoelectomy	1(4.3)	3(13.0)	4(17.4)	0.38
Appendicectomy	6(26.1)	4(17.4)	3(13)	0.52
Paraumbilical hernia repair	1(4.3)	1(4.3)	1(4.3)	1.00
Incisional hernia	0	1(4.3)	1(4.3)	0.60
Duration of Surgery (min)	54.48±13.58	57.04±15.10	46.52±7.99	0.81
Estimated blood loss (mls)	<100	<100	<100	1.00

Data expressed as mean ± standard deviation or numbers (%) or median (range)

Table 2: Blood pressure changes and rescue ephedrine use

Parameter	Group A(n=23)	Group B(n=23)	Group C(n=23)	p-value
Baseline SBP (mmHg)	124.16±2.10	119.08±4.87	121.62±5.30	0.56
Baseline MAP (mmHg)	86.78±7.19	89.52±7.92	93.05±6.97	0.21
Incidence of hypotension(overall)	10(43.5)	4(17.4)	4(17.4)	0.21*
Incidence of moderate hypotension	5(21.7)	0.49	0.49	0.49
Incidence of severe hypotension	5(21.7)	1(4.4)	1(4.4)	0.043
Total rescue ephedrine use(mg)	35.00±0.04	5±0.00	5±0.00	0.018

Data is expressed as mean ± standard deviation and number (%); *p=0.39 for group A versus group B; *p=0.18 for group A versus group C; *p=0.69 for group B versus group C

Table 3: Incidence of Complications

Parameter	Group A (n=23)	Group B (n=23)	Group C (n=23)	P-value
Nausea/Vomiting	8(34.8)	5(21.7)	7(30.43)	0.61
Shivering	4(17.4)	4(17.4)	5(21.7)	0.91
Tachycardia	2(8.7)	3(13.0)	5(21.7)	0.44
Reactive Hypertension	0	0	2(8.7)	0.13

Data expressed as number (%)

DISCUSSION

Prophylactic use of intravenous ephedrine in a low dose of 3mg is as effective as 6mg in reducing the occurrence of spinal anaesthesia-induced hypotension. It also showed that both low doses of ephedrine provided significant reduction in occurrence of severe hypotension and ephedrine requirement compared to the control. Nineteen (27.5%) out of the 69 patients who participated in this study developed hypotension. This is made up of nine (19.6%) patients in the ephedrine groups (B and C), and 10 (43.5%) patients in the control group (group A). Therefore, the incidence of hypotension in the ephedrine groups (B and C), during this study was 19.6%, while it was 43.5% in the control group (group A). In a study involving 60 male and female patients of ASA classes 1 and 2 who received spinal anaesthesia for lower abdominal and lower limb surgical procedures, Tiwari, etal[11], reported a similar incidence of hypotension (23.33%)following prophylactic 1Omg single intravenous dose of ephedrine compared to 80% with crystalloid preload alone ($p<0.05$).Similarly, Eroglu *et al*[8] also noticed that oral ephedrine halved the incidence of spinal induced-hypotension (23.33%) compared to control (50%),$p=0.003$. The greater margin of difference in incidences of post spinal hypotension between the control andephedrine groups found in the Tiwari *et al*[11] study may be attributable to the larger dose of ephedrine (10mg) infused, compared to 3mg and 6mg respectively used in our own study. While Desalu and Kushimo[5] reported a higher incidence (70% with crystalloid preload versus 40% using ephedrine infusion), Tsen *et al*[12] found no difference in incidence of hypotension between use of intravenous ephedrine prophylaxis and crystalloid preload alone (70% respectively). One possible explanation for the low incidence of hypotension in this 5study compared with findings by Desalu and Kushimo[5] and Tsen *et al*[12] is the effect of gravid uterus in those studies. Aorto-caval compression by gravid uterus when parturients are placed supine, leads to supinehypotension. This supine hypotension is present in all pregnant women to some degree; it is incompletely relieved by 15-20 degrees left lateral tilt[13]. It is a major factor which increases the incidence of spinal-induced hypotension amongst parturients[4,13]. Also, regarding the insignificant effect of ephedrine noticed by Tsen *et al*[12], it is likely that the dose of intravenous ephedrine (10mg) used, may have been insufficient to counteract the haemodynamic fluctuations encountered by parturients during spinal anaesthesia in that study. Alater randomised controlled trial by Iqbal *et al*[14] showed intravenous ephedrine 15mg to be the optimal prophylactic dose required to minimize the incidence of post-spinal hypotension during caesarean section. In this study, significantly less incidence of severe post spinal hypotension was observed using 3mg and 6mg ephedrine (4.4%, respectively) compared to the control (21.7%), $p= 0.043$. Desalu and Kushimo[5]also reported a significant reduction in incidence of severe hypotension with ephedrine infusion (13.3%) compared to control (40%), $p= 0.039$. One challenge in comparison of the studies above is the employment of different definitions of maternal hypotension. Whereas some authors defined maternal hypotension as a fall in systolic blood pressure or mean arterial pressure greater than 20% of baseline values, others used fall in blood pressures greater than [15] 25% or more. Klohr *et al*[5] demonstrated that even minor changes in the definition of hypotension can cause significant differences in the incidence of hypotension. There was significantly higher consumption of rescue doses of ephedrine in the control group compared to the ephedrine groups, $p= 0.018$. Many studies on haemodynamic changes following spinal anaesthesia, consistently reported a reduction in total intraoperative ephedrine consumption with use of ephedrineprophyl axis compared to control[6,7,9,16]. While Vercauteren *et al*[9] reported a reduction in proportion of patients requiring rescue doses of ephedrine in spinal anaesthesia for lower abdominal surgeries from 75% (control group) to 33% (using prophylactic IV ephedrine 5mg), $p<0.05$; Kafle *et al*[16] found a reduction from 83% (control) to 55% (prophylactic oral ephedrine) $p<0.01$. These two studies employed rescue doses of ephedrine as first response at onset of hypotension. This partly explains their reported use of higher rescue doses of ephedrine. In this study, only hypotensive episodes unresponsive to initial fluid therapy received rescue doses of ephedrine. The use of oral ephedrine 30mg in the Kafle *et al*[16] study and effects of postural and physiological changes in pregnancy in the Vercauteren *et al*[9] study provide additional reasons for the higher rates of ephedrine consumption in these studies. Administration of vasopressors before spinal anaesthesia may be associated with risk of reactive hypertension in the event of failure of subarachnoidblock[7]. To avoid this risk, intravenous ephedrine was administered, always after successful injection of bupivacaine into the subarachnoid space (evidenced by free backflow of CSF before injection). Although the incidence of reactive hypertension (8.7%) in the group of patients(group C) that received 6mg prophylactic ephedrine was not significantly different from what was observed in groups A and B, this complication was noticed only in group C. In this study, 30% of participants had nausea and vomiting. Desalu and Kushimo[5]found a higher incidence of nausea/ vomiting (41%) which was promptly resolved by restoration of maternal blood pressure. This suggests a direct relationship between post-spinal hypotension and incidence of nausea and vomiting. Other studies have also related its incidence

to the occurrence of hypotension[4,6,14]. Multiple factors can cause nausea and vomiting during spinal anaesthesia. Hypotension can cause brain stem hypo-perfusion thus triggering emesis[17]. Traction on viscera, concomitant opioid administration and patient's mental status could also be responsible for intraoperative emetic symptoms during abdominal surgery under regional anaesthesia. A similar number of patients in each group of this study experienced postspinal shivering, constituting an average of 18.8% of the total participants. Sule *et al*[1] reported a similar incidence (15.0%) in their study. Similarity in the incidence of post-spinal shivering in this study was probably due to the same factors which affected the participants such as temperature of the operating room and the intravenous fluids used. Reactive hypertension was observed in group C only, affecting only 2 patients that received prophylactic ephedrine. Also tachycardia was observed mostly in group C (21.7%), this was followed by group B (13.0%). Although, fewer patients in the control group (8.7%) experienced tachycardia intra-operatively, there was no statistically significant difference from the ephedrine groups. Desalu and Kushimo[5] also reported no significant difference in the incidence of tachycardia in patients who received intravenous ephedrine during spinal anaesthesia for caesarean section. Occurrence of tachycardia in the control group suggests additional sources such as catecholamine release due to apprehension and anxiety. Bradycardia could be a complication of spinal anaesthesia due to blockade of the sympathetic cardiac accelerator fibres that emerge from T1 to T4 leading to a fall in heart rate and hence a fall in cardiac output[18]. However, none of the patients in this study developed bradycardia. A limitation is that temperature of the isobaric bupivacaine was not specified in this study. At or near body temperature, plain bupivacaine becomes slightly hypobaric. This can influence intra-thecal drug spread. Also, there was a dearth of literature comparing the effect of prophylactic intravenous doses of ephedrine less than5mg in spinal anaesthesia for surgical interventions. This limits comparison of the outcomes of the study.

CONCLUSION

This study showed that prophylactic ephedrine 3mg is safe and is as effective as ephedrine 6mg in prevention of spinal-induced hypotension in patients undergoing lower abdominal surgeries. Although, side effects such as reactive hypertension, tachycardia, nausea and vomiting were fewer with the use of 3mg than the use of 6mg, this was not significant. Prophylactic intravenous ephedrine 3mg may be used instead of ephedrine 6mg to reduce the incidence of spinal anaesthesia-induced hypotension during lower abdominal general surgeries due to similar efficacy.

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