Prophylactic use of Iv Atropine for Prevention of Spinal Anesthesia Induced Hypotension and Bradycardia in Elderly; a Randomized Controlled Trial

Abstract

Background: Spinal anesthesia induced hypotension is common and hazardous in elderly patients. Reversal of the blunted reflexes of tachycardia following hypotension in elderly with atropine helps in prevention of spinal anesthesia induced hypotension in elderly.

Methodology: In this randomized, double-blind, controlled trial forty ASA PS I to II patients undergoing urological surgeries were assigned to receive either IV normal saline (placebo) or IV atropine 0.6 mg one minute after induction of spinal anesthesia. Heart rate (HR), mean arterial pressure (MAP), requirement mephentermine or phenylepherine and side effects profile were studied intra/postoperatively for 6 h.

Results: The patients were comparable with respect to demographic profile, baseline hemodynamic parameters and duration of surgery. Compared to baseline, mean HR and MAP significantly reduced in placebo group most of the study times (p<0.05). Comparing intra group, HR and MAP were also significantly decreased in placebo group. The incidence of hypotension was high in placebo (60%) compared to atropine group (5%). Thus, requirement of mephentermine for the management of hypotension was significantly high (p<0.001) in placebo (60%) than atropine group (5%).

Conclusion: Intravenous administration of atropine 0.6 mg, one min after induction of spinal anesthesia in elderly patient, is safe and effective method in the prevention of spinal anesthesia induced hypotension and bradycardia.

Keywords: Spinal anesthesia; Hypotension; Atropine

Introduction

The most common and the most serious side effects of spinal anesthesia are hypotension (33%) and bradycardia (13%) [1,2]. Systemic vasodilation induced by sympathetic blockade after spinal anesthesia (SA), resulting in venous pooling of blood and reduction in systemic vascular resistance, has been regarded as the predominant mechanism for hypotension. In addition, the blunted reflex tachycardia following hypotension in elderly also play important role in persistence of hypotension [3]. This phenomenon may result from the blockade of cardioaccelerator sympathetic fibers at T1 to T4, and possibly the “reverse” of the Bainbridge reflex. Bainbridge reflex, also called atrial reflex, is increment of the heart rate resulting from distension of large systemic veins or the right atrium. This reflex was first described by the British physiologist Francis Arthur Bainbridge in 1915 that prevents the pooling of blood in the venous system. Special pressure sensors called baroreceptors (or venoatrial stretch receptors) located in the right atrium of the heart detects increases in the volume and pressure of blood returned to the heart. These receptors transmit information along the vagus nerve.
(10th cranial nerve) to the central nervous system. This response results in the activation of sympathetic nerve pathways that serve to increase the strength of contraction of the heart muscle and to increase heart rate (tachycardia). Caplan et al. postulated that reduced atrial filling and unopposed vagal tone after SA produced a sufficient degree of bradycardia and hypotension, resulting in cardiac arrest [4]. Present study hypothesized that the reduction of reflex tachycardia following hypotension is an important component in the pathogenesis of persistence hypotension in elderly patient, in addition, to the effects of venous and arterial dilation.

Rational of choosing atropine was that elderly have blunted cardiac reflexes. The prophylactic use of atropine helps in preventing the blunted reflexes, thus, helping in increasing heart rate and cardiac output, and finally blood pressure. The primary outcome of the present study was to compare the heart rate and mean arterial pressure and secondary outcome was the requirement of vasopressor, and occurrence of other adverse effects following spinal anesthesia.

Methods

Institutional review board (IRB) at Tribhuvan University Teaching Hospital (TUTH) approved this prospective, randomized, double blind controlled study. Oral and written informed consent was obtained from each patient to enroll in the study. The sample size was derived from the record of previous one-year where patients aged more than 60 years underwent urological surgeries under spinal anesthesia in the Department of Anesthesiology at TUTH. A size of 20 patients per group was required at power of 80% and type I error of 0.05. The inclusion criteria were elderly patient (age more than 60 years) scheduled for urological surgery under spinal anesthesia, with an American Society of Anesthesiologist physical status Physical Status (ASA PS) I–II. Patient refusal or uncooperative patient for spinal anesthesia, contraindications to spinal block, arrhythmia such as atrial fibrillation, supraventricular tachycardia, heart block greater than first degree, left bundle branch block, hypertension (systolic blood pressure more than 140 mm Hg or diastolic blood pressure more than 90 mm Hg), unstable angina or cardiomyopathy, taking β-adrenergic blockers or any drugs that may alter normal response to study drugs are excluded from the study. After pre anesthetic evaluation patients were randomized to one of the two groups, using computer generated random number table to receive either normal saline (Group N) or atropine 0.6 mg (Group A). All drugs were made in total volume of 2.5 ml, was injected intravenously. MAP and HR were recorded at 0 (baseline), 1, 5, 10, 20, 30, 40, 50 and 60 minutes following the administration of study drugs respectively for the study.

Clinically significant hypotension was defined as systolic blood pressure of <90 mm Hg and if developed treated with inj mephentermine 6 mg IV. Inj phenylepherine 50 mcg IV was administered as a rescue drug if more than 30 mg of inj. mephentermine was required. Bradycardia (HR<50 bpm) was treated with atropine 0.6 mg. Tachycardia (HR>140/min) was treated with bolus IV esmolol 10 mg. Hypertension (SBP more than 160 mmHg or DBP more than 100 mmHg) was treated with bolus IV esmolol 10 mg and repeated till corrected.

Amount of vasopressor (mephentermine or phenylephrine) required, sensory level achieved at 15 min of Spinal anesthesia, presence of intraoperative angina and intra/postoperative confusion and other side effects were recorded till 6 h postoperative.

Data were collected as per the proforma. For the analysis of the data Statistical Package for the Social Sciences (SPSS) 17 was used. P values <0.05 were considered as statistically significant.

Results

All forty patients enrolled completed the study. Demographic data (Age, Weight, ASA PS and Diagnosis) in both groups were comparable as shown in Table 1. There were no differences regarding demographics and type of surgeries in both groups. The types of surgeries were transurethral resection of prostate under spinal anesthesia for prosthetic enlargement (BEP) or Carcinoma of Urinary bladder.

As compared to the baseline, mean heart rate was increased in Group A at 1, 5, 10, 15, 20 and 30 minutes (Table 2). Maximum heart rate in Group A was 89.30± ± 14.62 bpm at 5 minutes at 5 minute. In contrast, HR significantly decreased in Group N at 30, 40, 50 and 60 minutes with minimum mean HR was 65.40 ± 11.34 bpm. In-group N, 40% of the patient required atropine for the treatment of bradycardia, which was statistically significant (p=0.01) (Table 3).

As compared to baseline, MAP didn’t change significantly in Group A except at one minute (Table 3). However, in-group N, MAP significantly decreased all the times (Table 4) and treatment is required in 40% cases (Table 3).

Intragroup comparison, heart rate was significantly high in atropine group as compared to placebo group at 1, 5, 10 and 15 minutes following the administration of study drugs (p<0.05).

Table 1 Demographic data.

| Age (yrs.) | Group A (n=20) | Group N (n=20) | p  |
|-----------|---------------|---------------|----|
| 70.00 ± 7.90 | 69.85 ± 8.09 | 0.79 |
| Weight (Kg) | 60.00 ± 10.31 | 59.50 ± 6.62 | 0.91 |
| Baseline (HR) | 73.60 ± 10.30 | 71.35 ± 7.70 | 0.75 |
| Baseline MAP | 97.88 ± 6.70 | 92.38 ± 9.23 | 0.10 |
| Duration (Min) | 70.85 ± 7.92 | 72.55 ± 6.45 | 0.46 |

Data described as mean ± SD, *p<0.05 considered statistically significant. MAP- means arterial pressure, SD standard deviation.
Whereas at 20, 40, 50 and 60 minutes HR was significantly lower as compared to other groups in placebo group (Figure 1).

Intra group comparison, MAP was significantly high in atropine group as compared to placebo group at 1 minute. Whereas at 5, 10, 15, 30, 40, 50, and 60 minute MAP was lower in placebo as compared to atropine (Figure 2).

Intraoperatively, 60% patient developed hypotension (p=0.01) and 40% developed bradycardia (p=0.01) in placebo group who required treatment, which was statistically significant as compared to other group (Table 3). None of the patients in both group developed side effects like intra operative angina and intra/postoperative confusion till 6 h postoperatively. No other side effects were detected in any of the groups.

**Discussion**

The most common serious side effects from spinal anesthesia are hypotension and bradycardia and closed claims surveys of 40,000-550,000 spinal anesthetics indicate an incidence of cardiac arrest from 0.04–1/10,000 [1,2,5,6]. Risk factors for hypotension block are height T5 or greater, age 40 yrs or greater, baseline systolic blood pressure less than 120 mmHg, and spinal puncture above L3–L4. Risk factors for development of bradycardia include baseline heart rate less than 60 bpm, ASA PS I, use of β-adrenergic blockers, prolonged PR interval on electrocardiogram, and block height T5 or greater [1,7].

Currently various techniques are been using for the prevention of hypotension and bradycardia which include pre or co-loading of IV fluid, vasopressors, and physical methods such as table tilt, leg binders, and compression devices [8-14]. However, a Cochrane review concluded that none of these techniques alone is effective and suggested that the future research be directed towards a combination of interventions [11]. This study aimed to prevent the spinal anesthesia induced hypotension with combination of preloading with normal saline 10 ml/kg and pretreatment with either IV atropine.

Atropine is esters of an aromatic acid combined with an organic base. It competitively blocks acetylcholine binding to its

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**Table 2** Comparison of mean HR with baseline in each group.

|                | Group A (n=20) | p    | Group N (n=20) | p    |
|----------------|---------------|------|----------------|------|
| HR            | 73.60 ± 10.30 |      | 71.35 ± 7.70   |      |
| HR1           | 83.35 ± 14.13 |  0.00* | 71.45 ± 9.74   |  0.88 |
| HR5           | 88.95 ± 14.62 |  0.00* | 68.95 ± 10.07  |  0.15 |
| HR10          | 85.40 ± 13.18 |  0.00* | 67.60 ± 9.95   |  0.08 |
| HR15          | 83.80 ± 14.35 |  0.00* | 68.05 ± 9.82   |  0.11 |
| HR20          | 82.30 ± 13.56 |  0.00* | 69.00 ± 13.95  |  0.25 |
| HR30          | 80.95 ± 13.53 |  0.01* | 65.95 ± 11.03  |  0.01*|
| HR40          | 76.20 ± 13.31 |  0.47  | 65.40 ± 11.34  |  0.01*|
| HR50          | 76.30 ± 9.56  |  0.25  | 65.80 ± 10.66  |  0.04*|
| HR60          | 76.20 ± 12.91 |  0.5   | 66.25 ± 10.47  |  0.02*|

Data described as mean ± SD, *p<0.05 considered statistically significant. MAP- means arterial pressure, SD standard deviation.

**Table 3** Intra operative events.

|                        | Group A (n=20) | Group N (n=20) | p    |
|------------------------|---------------|----------------|------|
| Mephentermine used     | 1 (5%)        | 12 (60%)       |  0.01*|
| Bradycardia            | 0             | 8 (40%)        |  0.01*|
| Tachycardia            | 1 (5%)        | 0 (0%)         |  0.48 |
| Other adverse effects  | 0             | 0              |      |

Data described as number (percentage), *p<0.05 considered statistically significant.

15 minutes. Whereas at 20, 40, 50 and 60 minutes HR was significantly lower as compared to other groups in placebo group (Figure 1).

Intra group comparison, MAP was significantly high in atropine group as compared to placebo group at 1 minute. Whereas at 5, 10, 15, 30, 40, 50, and 60 minute MAP was lower in placebo as compared to atropine (Figure 2).

Intraoperatively, 60% patient developed hypotension (p=0.01) and 40% developed bradycardia (p=0.01) in placebo group who required treatment, which was statistically significant as compared to other group (Table 3). None of the patients in both group developed side effects like intra operative angina and intra/postoperative confusion till 6 h postoperatively. No other side effects were detected in any of the groups.

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receptor and prevents receptor activation thus cellular effects of acetylcholine are inhibited. In general, atropine lowers the parasympathetic activity of all muscles and glands regulated by the parasympathetic nervous system and increase heart rate via abolishing the vagal tone acting on M2 receptor at heart.

The present study showed that the incidence of bradycardia was significantly high at various time (Table 1) in placebo group and require treatment with atropine (p=0.01) compared to atropine groups. Compared to baseline, heart rate was high in in atropine group at 5 minutes, which corresponds to the peak effect of the IV atropine. The increase in HR is statistically significant but only one patient required treatment for tachycardia. Similarly, MAP was also lower in placebo group at most of the time compared to atropine group. In present study, 60% patient in placebo group and 5% patient in atropine group required mephentermine for the treatment of hypotension. Use of mephentermine was significant (p=0.01) in placebo group as compared atropine group. This indicates that both incidence and severity of hypotension are greater in placebo group as compared to the atropine group. The findings are similar to various other studies. IV atropine after a crystalloid infusion in patients undergoing SA could increase HR very quickly in a dose-dependent manner and decrease the incidence of significant hypotension also in a dose-dependent manner [15]. PUN Nze demonstrated the incidence and severity of hypotension were reduced in parturients undergoing cesarian section under spinal anesthesia with use of prophylactic intravenous bolus of atropine [16]. Thus intravenous atropine may be a useful supplement to the existing methods in preventing hypotension induced by spinal anaesthesia. However, when IM atropine was used, Hirabayashi et al. did not demonstrate any beneficial effect in hemodynamic stability during SA because the absorption of IM atropine may be unpredictable, and the onset may have been too slow in comparison to the onset of hypotension after SA [17]. Another anticholinergic agent, glycopyrrolate, when administered IV after SA increased HR and reduced the severity of hypotension in women presenting for elective cesarian section and concluded that glycopyrrolate reduce the severity of hypotension after SA, evidenced by reduced ephedrine requirements (p=0.002) [18]. Though, the present study didn’t show any significant side effect in intra/ post-operative period (Table 3) many practitioners hesitate to administer atropine as it cross blood brain barrier and concerned about the central CNS effects of atropine. Glycopyrrolate may have similar effect in preventing spinal induced hypotension and bradycardia but it cannot be concluded from present study and further investigation is required. All patients were observed for 6 h in postoperative ward for the study and no untoward effects were noted.

In summary, hypotension and bradycardia after induction of spinal anesthesia were common in elderly patients. The use of IV atropine one minute after the induction of spinal anesthesia in elderly patient was beneficial in maintaining hemodynamic stability. Although, the incidence of tachycardia was high in atropine group the incidence of clinically significant tachycardia (HR>140 bpm) were comparable among all the three groups. None of the patients in both groups developed other side effects. So, the study suggests prophylactic IV atropine can be safely used in elderly patient for the prevention of spinal anesthesia induced hypotension.

**Limitations**

Amount of blood loss, which can influence the hemodynamic parameters, was not recorded in our study. For the measurement of blood pressure oscillatory noninvasive blood pressure methods was used, invasive blood pressure monitoring method would have been used to monitor real time blood pressure. Only urological surgeries (TURP, CA UB) were taken for the study, which require only lower thoracic block for surgery. This population may not be the actual representative of the SA induced hypotension associated with higher blocks more than T8.

**Conclusions**

The use of prophylactic IV atropine after one minute of induction of spinal anesthesia reduces the incidence and severity of the spinal anesthesia induced hypotension as well as the incidence of bradycardia in elderly patients. The need of vasopressors also decreases significantly.

### Table 4 Comparison of mean MAP with baseline in each group.

|          | Group A (n=20) | p    | Group N (n=20) | p    |
|----------|----------------|------|----------------|------|
| MAP BL   | 97.88 ± 6.70   | 0.01*| 92.38 ± 9.23   | 0.24 |
| MAP 1    | 103.17 ± 8.87  | 0.31 | 91.10 ± 11.30  | 0.00*|
| MAP 5    | 99.80 ± 10.74  | 0.81 | 76.92 ± 11.60  | 0.00*|
| MAP 10   | 98.80 ± 8.27   | 0.56 | 81.43 ± 13.68  | 0.00*|
| MAP 15   | 97.00 ± 8.16   | 0.37 | 85.00 ± 10.79  | 0.00*|
| MAP 20   | 95.73 ± 11.68  | 0.12 | 82.40 ± 10.48  | 0.00*|
| MAP 30   | 94.88 ± 10.70  | 0.48 | 82.92 ± 10.30  | 0.00*|
| MAP 40   | 96.30 ± 9.51   | 0.09 | 82.60 ± 10.81  | 0.00*|
| MAP 50   | 94.40 ± 9.41   | 0.13 | 84.42 ± 9.84   | 0.00*|
| MAP 60   | 95.10 ± 9.36   | 0.01*| 83.20 ± 9.40   | 0.00*|

Data described as mean ± SD, *p<0.05 considered statistically significant. MAP- means arterial pressure, SD standard deviation.
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