PROPHYLACTIC USE OF IV ATROPINE FOR PREVENTION OF SPINAL ANESTHESIA INDUCED HYPOTENSION AND BRADYCARDIA IN ELDERLY; A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT:

Background: Hypotension is common complication of spinal anesthesia (SA) and occurs due to decrease in systemic vascular resistance (SVR) and/or cardiac output (CO). Spinal anesthesia induced hypotension causes activation of the inhibited reflexes of tachycardia and along with atropine helps in prevention of hypotension in elderly. **Methodology:** In this randomized, double-blind, controlled study sixty elder patients planed for inguinal surgeries were included to receive either IV normal saline as placebo or IV atropine 0.6 mg one minute after induction of spinal anesthesia. Heart rate (HR), mean arterial pressure (MAP), were studied intra/postoperatively for 6 hours. **Results:** The patients were comparable against demographic profile, baseline hemodynamic parameters and duration of surgery. When compared to baseline, MAP and mean HR significantly decreased in placebo group in the study ($p<0.05$). Comparing intra group, HR and MAP were also significantly decreased in placebo group. The incidence of hypotension was high in placebo (60%) as compared to atropine group (6.667%). **Conclusion:** Intravenous infusion of atropine 0.6 mg in elderly patients, one min after induction of spinal anesthesia is safe and effective in the prevention of spinal anesthesia induced hypotension and bradycardia.

Key Words: Spinal anesthesia, Atropine, Hypotension, means arterial pressure.

INTRODUCTION:

Hypotension (33%) and bradycardia (33%) are the most prevalant and serious complications of spinal anesthesia. **(1, 2)** .Systemic vasodilation caused by sympathetic inhibition due to spinal anesthesia (SA), resulting in venous pooling of blood and reduction in systemic vascular resistance, is the main mechanism of hypotension. The inhibited reflex tachycardia after hypotension in elderly also play significant role in persistance of hypotension **(3)**. This phenomenon may occur due to blockade of cardioaccelerator sympathetic nerve fibers at T1 to T4, and possibly due to "reversal" of the Bainbridge reflex. Bainbridge reflex is also known as atrial reflex, is increase in heart rate due to distension of large systemic veins or the right atrium. British physiologist Francis Arthur Bainbridge first demonstrated this reflex in 1915

and told that it inhibits the pooling of blood in the venous system. Baroreceptors which are special pressure sensors (or veno-atrial stretch receptors) present in right atrium of the heart they detect increases in the volume and pressure of blood returned to the heart. Central nervous system receives information through vagus nerve (10th cranial nerve). This response activates sympathetic nervous system that increases the strength of contraction of heart muscle and produce tachycardia. Caplan et al. demonstrated that reduced atrial filling and maintaned vagal tone after spinal anaesthesia, produce a sufficient degree of bradycardia and hypotension, leading to cardiac arrest **(4)**. In this study we assumed that the decrease in reflex tachycardia following hypotension is an important factor in the pathogenesis of persistence hypotension in elderly patient, along with venous and arterial dilation.

Reason behind choosing atropine was that elderly patients have blunted cardiac reflexes. The prophylactic use of atropine helps in prevention of inhibition of reflexes, thus, helps in enhancement of heart rate and cardiac output, and ultimately leads to increase in blood pressure. The primary aim of our study is to compare the heart rate and mean arterial pressure and secondary aim is requirement of vasopressor drugs and occurrence of other adverse effects following spinal anesthesia.

MATERIAL AND METHODS

This prospective, randomized, doubleblind controlled study was approved by ethical committee of the institution. Oral and written informed consent was received from each patient to be enrolled in our study. The sample size was obtained from the record of previous years where patients with inguinal abnormality underwent surgeries underspinal anesthesia in the Department of Anesthesiology at Gujarat Adani Institute of Medical Science, Bhuj from July 2014 to March 2015.

In this study total 60 patients were included. The inclusion criteria were, patients of age above 60 years planed for inguinal surgery under spinal anesthesia, with an American Society of Anesthesiologist physical status (ASA PS) I–II. Patients who denied or non-cooperative patient for spinal anesthesia, contraindications for spinal block, arrhythmia like atrial fibrillation, supraventricular tachycardia, heart block more than first degree, left bundle branch block, hypertension (systolic blood pressure more than140 mm Hg or diastolic blood pressure more than 90 mm Hg), unstable angina or cardiomyopathy, ongoing treatment with β-blockers that may change normal response to study drugs are not included in our study. After pre anesthetic evaluation patients were devided in two groups, normal saline (Group N) or atropine 0.6 mg (Group A). All drugs were used in a volume of 2.5 ml in same syringe and drugs were given to patients after one minute from induction of spinal anesthesia as per the group allocation.

All patients were loaded with 1,000 mg acetaminophen and anxious patients were loaded with either 7.5 mg midazolam or 10 mg oxazepam orally 2 hours before surgery. Normal saline (NS) at a rate of 10 ml/kg for 20 minutes was infused to every patient before the induction of spinal anesthesia. Every patient was monitored for baseline heart rate, blood pressure, arterial oxygen saturation and electrocardiogram till completion of surgery in operation theatre. A

27 gauge pencil-point needle was inserted in the subarachnoidspace at the L2-3 or L3-4 interspace. Sub arachnoid block was induced with 2.5 ml of 0.5% hyperbaric bupivacaine in sittingposition and were immediately made to lie in supine position. One minute after spinal anesthesia, first study drug, was injected intravenously in total volume of 2.5 ml. MAP and HR were recorded at 0 (baseline), 1, 5, 10, 20, 30, 40, 50 and 60 minutes followed by administration of second drug for the study. When systolic blood pressure is below than 90 mm Hg it is called clinically significant and if developed managed with inj-mephentermine 6 mg IV. Inj-phenylepherine 50 mcg IV was used as a rescue drug if more than 30 mg of inj.mephentermine was given. Bradycardia (HR<50 bpm) was managed with atropine 0.6 mg. Hypertension (SBP more than 160 mmHg or DBP more than 100 mmHg) and Tachycardia (HR>140/min) were treated with bolus IV esmolol 10 mg and repeated till controlled. Dose of vasopressor agents (mephentermine or phenylephrine) used, presence of intraoperative angina and intra/postoperative confusion and other side effects were recorded till 6 hpostoperative. Data were arranged according to the proforma. Data were analysed by Statistical Package for the Social Sciences (SPSS) 17th version. P values <0.05 were considered as statistically significant.

RESULTS

All sixty enrolled patients completed the study. Demographicdata (Age, Weight, ASA PS and Diagnosis) in both groups werecomparable as shown below:

Table 1 Demographic data.

	Group A (n=30)	Group N (n=30)	p
Age (yrs)	70.00 ± 7.90	69.85 ± 8.09	0.79
Weight (Kg)	60.00 ± 10.31	59.50 ± 6.62	0.91
Baseline (HR)	73.63 ± 10.32	71.37 ± 7.72	0.76
Baseline MAP	97.87 ± 6.70	92.38 ± 9.23	0.10
Duration (Min)	70.86 ± 7.93	72.55 ± 6.46	0.46

No differences were present regarding demographics and type of surgeries in both groups. The types of surgeries were hernioplasty under spinal anesthesia for inguinal hernia.

Table 2 Comparison of mean HR with baseline in every group.

	Group A (n=30) Mean±SD	P	Group N (n=30) Mean±SD	P
HR	73.60 ± 10.30		71.35 ± 7.70	
HR1	83.35 ± 14.13	0.00*	71.45 ± 9.74	0.88
HR5	89.94 ± 14.62	0.00*	68.95 ± 10.07	0.15
HR10	85.40 ± 13.18	0.00*	67.60 ± 9.95	0.08
HR15	83.81 ± 14.35	0.00*	68.06 ± 9.82	0.11
HR20	82.31 ± 13.57	0.00*	69.01 ± 13.95	0.25
HR30	80.95 ± 13.53	0.01*	65.95 ± 11.04	0.01*
HR40	76.21 ± 13.32	0.47	65.40 ± 11.35	0.01*
HR50	76.30 ± 9.57	0.25	65.80 ± 10.67	0.04*
HR60	76.21 ± 12.91	0.50	66.26 ± 10.47	0.02*

*p<0.05 considered statistically significant

As compared to the baseline, mean heart rate was increased in Group A at 1, 5, 10, 15, 20 and 30 minutes .Maximum heart rate in-Group A was 89.94 ± 14.62 bpm at 5 minutes. In contrast, HR significantly lowered in Group N at 30, 40, 50 and 60 minutes with minimum mean HR was 65.40 ± 11.35bpm at 40 minutes.

Table 3 Intra operative events.

	Group A (n=30)	Group N (n=30)	p
Mephentermine used	2 (6.667%)	18 (60%)	0.01*
Bradycardia	0	12 (40%)	0.01*
Tachycardia	2 (6.667%)	0 (0%)	0.48
adverse effects	0	0	

In-group N, atropine was used for 40% of total patients for the treatment of bradycardia, which was statistically significant (p=0.01*)

Table 4 : Comparison of mean MAP with baseline in every group.

	Group A (n=30) Mean±SD	P	Group N (n=30) Mean±SD	P
MAP BL	97.89 ± 6.70		92.38 ± 9.23	
MAP1	103.17 ± 8.87	0.01*	91.10 ± 11.30	0.24
MAP5	99.81 ± 10.74	0.31	76.93 ± 11.60	0.00*
MAP10	98.80 ± 8.27	0.81	81.43 ± 13.68	0.00*
MAP15	97.00 ± 8.16	0.56	85.00 ± 10.79	0.00*
MAP20	95.74 ± 11.68	0.37	82.41 ± 10.48	0.00*
MAP30	94.89 ± 10.70	0.12	82.93 ± 10.30	0.00*
MAP40	96.31 ± 9.51	0.48	82.61 ± 10.81	0.00*
MAP50	94.40 ± 9.41	0.09	84.42 ± 9.84	0.00*
MAP60	95.10 ± 9.36	0.13	83.20 ± 9.40	0.00*

*p<0.05 considered statistically significant

When we compare with baseline, MAP didn't change significantly in Group A except at one minute. However, in group N, MAP significantly decreases at all the times. Side effects like intra operative angina and intra/postoperative confusion did not developed in patients of both group till six hours postoperatively. No other side effects were present in both groups.

DISCUSSION

Blood pressure reduced up to a significant level after onset of spinal anaesthesia. Hypotension and bradycardia are the most prevalent serious adverse effects of spinal anesthesia. 40,000-550,000 spinal anesthetics demonstrated in their Closed claimed surveys that the incidence of cardiac arrest were from 0.04–1/10,000 cases **(1, 2, 5, 6)**. Height of anaesthesia is T5 or above, age 40 yrs or more, baseline systolic blood pressure is less than 120 mmHg, and spinal puncture above L3–L4 are the risk factors for hypotension. Baseline heart rate less than 60 bpm, use of β-blocker drugs, ASA PS I. prolonged PR on interval on electrocardiogram, and block height T5 or greater are the risk factors for development of bradycardia (1,7). In this study, this was occurred due to decrease in CO and not by adecrease in SVR. Several mechanisms are explained for the development of hypotensive response after SA. First, sympathetic blockage from T1 to L2 followed by arteriolar vasodilation produce reduction in SVR, contributing to intra-operative hypotension. This decrease in SVR is often thought to be the chief cause of hypotension after SA. Second, a reduction in venous vasomotor tone increases venous pooling and consequently reduced venous return, there by reducing CO. physiological hemodynamic reserve capacity decreases with age, and limited

cardiovascular compensation mechanisms contribute to decrease in CO and blood pressure in response to SA.**(8)**

Now a days many techniques are used to prevent hypotension and bradycardia induced by spinal anaesthesia which include pre or co-loading of IV fluids, infusion of vasopressor agents, and physical procedures like table tilt, leg binders, and compression devices **(9-15)**. Our study aimed to prevent hypotension induced after spinal anesthesia through combination of preloading with normal saline 10 ml/kg and pre treatment with IV atropine. Atropine is an ester of an aromatic acid combined with an organic base. It competitively blocks binding of acetylcholine to its receptor and prevents activation of receptor and biological effects of acetylcholine are inhibited. Generally atropine reduces parasympathetic activity of all muscles and glands controlled by parasympathetic nervous system and increase heart rate via inhibition of vagal tone acting on M2 receptor on heart. The present study showed that incidence of brady cardia was significantly more at various times in placebo group compared to atropine groups and require treatment with atropine (p=0.01). Compared with baseline, heart rate was high 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. MAP was also lower in placebo group as compared to atropine group. In our study, 60% patients of placebo group and 5% patients of atropine group required mephentermine for treatment of hypotension. Use of mephentermine was significant (p=0.01*) in placebo group as compared with atropine group.This indicates that both incidence and severity of hypotension are more in placebo group as compared to atropine group. These findings are similar to various other studies. crystalloid infusion of IV atropine in patients undergoing spinal anaesthesia could increase HR very quickly in a dose-dependent manner and decrease the incidence of significant hypotension also in a dose-dependent manner **(16)**. PUN Nze demonstrated that the incidence and severity of hypotension were decreased in parturients undergoing ceesarian section under spinal anesthesia with use of prophylacticintravenous bolus of atropine **(17)**. Thus intravenous atropine may be a useful supplement to the existing procedures in preventing hypotension following spinal anaesthesia.

Hirabayashi et al. demonstrated no beneficial effect in hemodynamic stability during SA when IM atropine was infused, because the absorption of IM atropine may be unpredictable, and the onset may have been too slow in comparison to the onset of hypotension following SA **(18)**. Though our study didn't show any significant side effect during intra/post-operative period, many clinicians hesitate with use of atropine because it can cross blood brain barrier and concerned about effects of atropine on CNS. Glycopyrrolate also have similar effect in preventing spinal anaesthesia induced hypotension and brady cardia but it cannot be concluded from our study and further investigation is required.

CONCLUSIONS

Hypotension and bradycardia just after spinal anesthesia are very common in elderly patients. Use of IV atropine is beneficial one minute after the induction of spinal anesthesia in elderly patients to maintain hemodynamic stability and

decrease the incidence and severity of the spinal anesthesia induced hypotension and bradycardia. The need of vasopressor agents also decreases significantly.

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