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Need of pharmacotherapy to prevent hemodynamic effects after subarachnoid block: A prospective randomized double blind placebo controlled study

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Abstract

Introduction and Objective: The neuraxial anesthesia presents several advantages over general anesthesia, however hypotension and bradycardia are the inevitable consequences of spinal anesthesia (SA). In fear of fall in perfusion of vital organs like kidney, it is a common practice to administer drugs to prevent the hemodynamic changes after SA. Herewith, we have tried to evaluate the need of pharmacotherapy to prevent hemodynamic effects after subarachnoid block.

Materials and Method: Total 120 adult patients of ASA physical status I/II admitted in a tertiary care center for elective surgeries on lower abdomen and lower limb were selected for the study. They were randomly divided into 2 equal groups. Group I (control group) received 1 cc of water for injection while Group II (study group) received 1cc (inj. Atropine 0.3 mg + inj. Ephedrine hydrochloride 5 mg) intravenously 10 min after giving spinal anesthesia. Confounding variables like volume of fluid administered, positioning and sensory level were reduced to minimum.

Hemodynamic variables like heart rate, systolic, diastolic, mean blood pressure, spO2 were recorded at 5 minute intervals up to 2 hrs after commencement of spinal anaesthesia. Urine output was recorded by urometer and the values were noted every 30 min, adverse reactions were noted by a blinded observer.

Observation and Results: The demography and types of surgeries for both the groups were comparable. Heart rates and blood pressures dropped down after giving SA. Though variation between two groups was statistically significant, at the end of 2 hours they resumed baseline levels. There was no adverse effect on urine output and incidence of adverse effects in both the groups was comparable.

Conclusion: It is not necessary to use preventive pharmacotherapy to counterbalance hemodynamic changes occurring after subarachnoid block.

Keywords: Atropine, Ephedrine hydrochloride, Hemodynamic effects, Pharmacotherapy, Subarachnoid block

Introduction

Neuraxial anesthesia (spinal, continuous spinal, epidural, continuous epidural and combined spinal-epidural anesthesia) present several advantages over general anesthesia: like lesser morbidity and mortality, better quality of postoperative analgesia and lesser duration of hospital stay. Though the reported complication rate is low, several complications can result from the neuraxial blockade, such as the infections of the central nervous system, neurological lesions due to spinal or epidural hematomas, toxicity due to the local anesthetics, postdural puncture headache, direct trauma and other less serious, as hypotension and bradycardia, sometimes considered physiological.[1,2] The complications that are noted are: hypoxemia, hypoventilation, arterial hypotension and hypertension, sinus bradycardia and tachycardia, agitation, headache, convulsion, oliguria, vasovagal reaction, blockade failure, accidental perforation of the duramater, ventricular dysrhythmias, cardiac arrest and death. These are correlated with the anesthetic technique, physical state described by the American Society of Anesthesiology (ASA), age, sex and preoperative co-morbidities like arterial hypertension, atrial and ventricular dysrhythmias, obesity, diabetes mellitus, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, asthma, renal failure, thyroid diseases, hepatic failure.[1]

Although somewhat controversial, not every episode of spinal hypotension or bradycardia is clinically significant, but the anesthesiologist's vigilance is challenged to prevent mild aberrations from developing into major hemodynamic compromise.

Hence this study was undertaken to assess whether there is need of pharmacotherapy to prevent hemodynamic effects after subarachnoid block. It is aimed also to evaluate the adverse effects on kidneys, if any, if the preventive pharmacotherapy is not given in healthy adult patients.

Aims and Objectives

To assess hemodynamic changes occurring after spinal anesthesia.

To evaluate the need of pharmacotherapy to prevent hemodynamic effects after subarachnoid block.

Materials and Method

After getting Ethical committee approval, the sample size was determined as 120 by taking 99.5% confidence interval, total 120 adult patients of ASA physical status I/II from both sexes admitted in a tertiary care center for elective surgeries on lower abdomen and

lower limb during February 2016 to November 2016 were selected for the study.

Exclusion criteria: Pregnancy, large intra abdominal mass, high INR, hypovolemia, arterial hypertension, atrial and ventricular dysrhythmias, obesity, diabetes mellitus, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, asthma, renal failure, thyroid diseases, hepatic failure, patients on beta blockers, local infection, deformity of spines, upper abdominal and urological surgeries, surgeries extending more than 2 hrs, patient refusal.

After obtaining informed written consent from the selected patients, they were randomly divided into 2 groups by lottery method, 60 patients in each group. Baseline values of heart rate, blood pressure, SpO2 were recorded and a drip of 500ml Normal saline was started through a peripheral vein secured with 20G intracath. Spinal anesthesia was given by injecting 0.5% hyperbaric Bupivacaine in a dose of 3.5cc by Quincke needle in sitting position at L4-L5 space to all the patients by an anesthesiologist.

All the patients were given supine position immediately after SA. Sensory level up to T9 was achieved irrespective of type of surgery and confirmed by pinprick method. Group I (control group) received 1 cc of water for injection while Group II(study group) received 1cc (inj. Atropine 0.3 mg +inj. Ephedrine hydrochloride 5mg)intravenously 10 min after giving spinal anesthesia. All surgeries ended within 90-120 min. All patients received 500ml Normal saline and 500ml Ringer lactate (5ml/kg/hr) during the surgery. The intra-operative fluid loss was also replaced.

Hemodynamic variables like heart rate, systolic, diastolic, mean blood pressure, SpO2 were recorded at 5 minute intervals up to 2 hrs after commencement of spinal anaesthesia. Urine output was recorded by urometer and the values were noted every 30 min. Adverse reactions were noted by a blinded observer. The reduction in heart rate (HR) > 30% of baseline and reduction in Systolic blood pressure (SBP)> 30% of baseline at any point of time was considered clinically undesirable; which is in concordance with most of studies in the literature. If such readings were noted, the patients were treated with intravenous atropine 0.6 mg and ephedrine HCl in increments of 5 mg respectively as rescue drugs.

Statistical Analysis: The data was tabulated in excel sheet. Taking confidence interval as .95, p value <0.05 was considered significant. Descriptive statistics in the form of frequencies, means, standard deviations and percentages were calculated. Statistical analysis was done by using Chi square test, paired t test using SSPE version 22. For our study, we included larger number of patients to decrease the β error. Taking an α error of 0.05, post-hoc analysis to compare the episodes of hypotension and bradycardia for the sample size of 120 revealed that power of the study (1−β) to be >90%.

Observation and Results

As revealed in Table 1 & 2, demography, types and duration of surgeries were comparable in both the groups.

Table 1: Distribution according to demography of patients between two groups

Characteristics		Group I (n=60)	Group II (n=60)
Mean age (years)		33.00 ± 7.59	33.40 ± 7.56
Sex	Male	30	34
	Female	30	26
ASA	I	49	51
	II	11	9
Weight	Kg	59.81± 6.29	61.43 ± 6.88
Height	cm	160.0 ± 5.0	161.05 ± 5.05
Duration of surgery	min	90± 21.2	87±22.77

Characteristics expressed as **Mean ± SD**

Table 2: Distribution according to type of surgeryof patients between two groups

Type of surgery	Group I (n=60)	Group II (n=60)
Vaginal Hysterectomy	16	14
Tibia/ Femur surgeries	8	10
Appendicectomy	9	7
Ovarian cystectomy	5	4
Hernia repair	13	15
Arthroscopic knee surgeries	6	8
Varicose veins repair	3	2

Table 3: Heart rate variation between two groups at different time intervals

Groups (n=60)	Baseline	After supine	2 mins	5 min	10 mins	15 mins	20 mins	25 mins	30 mins	35 mins	40 mins	45 mins	50 mins	60 mins	2 hrs
I	80.15± 12.10	79.5± 11.78	78.18± 11.79	77.23± 12.39	76.31± 10.37	75.31±1 1.10	75.28±1 1.36	75.15±1 0.28	76.2± 10.2	76.45± 9.30	75.98± 8.93	75.78± 8.23	76.9± 7.08	77.45± 7.13	79.76± 6.85
II	81±13	81±12	79±12	77± 13	77.6± 12.2	77±12	77±12	77±12	77±12	78±10	77±9.8	76±8.3	76± 7.9	78±7.9	80±8.4
p value	0.7115	0.4909	0.7064	0.9211	0.5338	0.4248	0.4217	0.3663	0.6047	0.3811	0.5524	0.8843	0.5124	0.6896	0.8641

It is evident from the table that mean heart rates dropped more in control group, though statistically not significant. They dropped >30% in 2 patients 25-30 min after giving SA which was treated by giving 0.6 mg atropine intravenously. In spite of receiving preventive pharmacotherapy, heart rate in one patient from study group also dropped>30% but after 50 min post block. This was also treated with 0.6 mg Atropine as per protocol.

Table 4: Systolic blood pressure variation between two groups at different time intervals

Groups (n=60)	Baseline	After supine	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	35 mins	40 mins	45 mins	50 mins	60 mins	2 hrs
I	127±11	124± 12	123± 15	118.61± 12.10	118± 13	117± 12	117.1± 12.17	116± 12.7	117.5± 13.53	119± 12.1	120± 11.6	120± 11.4	120.6± 10.8	121± 10.5	123.5± 10.61
II	127.13± 10.10	124.23± 10.81	122.91± 11.31	119.65± 12.74	119.411 2.76±	118± 12.49	119.05± 12.12	118.68± 11.11	119.38± 10.71	119.35± 12.17	120.71± 10.90	120.85± 10.57	120.91± 10.35	122.11± 9.88	122.83± 11.19
p value	0.9464	0.9124	0.9705	0.6575	0.5499	0.6555	0.3810	0.2210	0.4004	0.8747	0.7303	0.6727	0.8768	0.5521	0.7371

Table 5: Mean of MAP variation between two groups at different time intervals

Groups	Baseline	After supine	2 min	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	35 mins	40 mins	45 mins	50 mins	60 mins	2 hrs
I	90± 10	89±10	88.6± 10.6	86± 11	85± 12	84.8± 11.3	83.7± 10.81	84.1± 11.5	84.4± 11.2	85.7± 10.5	87.2± 10.3	87± 10	88.58± 9.91	88.53± 10.04	89.77± 9.80
II	91.91± 7.90	91.26± 8.09	91.18± 9.72	90.26± 10.70	88.26± 10.63	88.95± 10.79	88.5± 10.15	89.13± 10.52	89.26± 10.26	89.51±1 0.05	89.55± 9.17	91.26± 9.72	91.4± 9.40	91.1± 9.65	91.9± 9.09
p value	0.2480	0.1761	0.1673	0.0336	0.1179	0.0418	0.0135	0.0138	0.0146	0.0446	0.1894	0.0196	0.1124	0.1555	0.2195

It is evident from the tables that SBP (systolic blood pressure) and MAP (Mean arterial pressure) dropped more in control group maximally at 20-25 min post SA.9 patients in group I and 6 patients in group II,SBP dropped more than20% & less than 30% of baseline. Though the intergroup difference was statistically significant, the drop in BP was not clinically significant that is drop in SBP > 30% and reverted back spontaneously without administration of rescue medications. There was no significant variation in oxygen saturation as well as urine output between two groups throughout the surgical period.

Table 6: Adverse events

Complications	Group I (n =60)	Group II (n=60)
Fall in SBP >20% & <30%	9(15.0%)	6(10.0%)
Fall in MAP/SBP>30% of baseline	-	-
Fall in HR > 30% of baseline	2(3.33 %)	1(1.66 %)
Nausea/ vomiting	1 (1.66 %)	1 (1.66 %)
Shivering	3 (5.00 %)	2 (3.33 %)
Dysrhythmias	-	-
Fall in urine output <0.5 ml/kg/hr	-	-
Respiratory depression (fall in SpO2)	-	-

The rate of complications was low in both the groups. However, 2 patients in Group I and one patient in Group II developed clinically significant bradycardia (HR>30%) which was treated successfully with inj. Atropine 0.6 mg intravenously.

Discussion

Bupivacaine, an amide local anesthetic, is one of the most widely used local anesthetics for spinal anesthesia and provides adequate anesthesia and analgesia for intermediate to long duration surgeries. It has an onset time of 5 to 8 min with a duration time of 210 to 240 min, the suggested dose is 8-10 mg for perineal and lower extremity surgeries and 15-20mg for abdominal surgeries.[2,3]In the present study, spinal anesthesia was given by injecting 0.5% hyperbaric Bupivacaine in a dose of 3.5 cc.

The sympathectomy produced by spinal anesthesia induces hemodynamic changes. Hypotension and bradycardia are the most common side effects seen with sympathetic denervation.[1,4,5,6]The incidence of hypotension reported by various researchers ranges from 33- 80% of the non-obstetric population.[2,7] Hypotension that occurs after neuraxial anesthesia is one of the most important etiological factors for intraoperative nausea and vomiting. The factors responsible for hypotension being the presence of a systolic blood pressure (SBP) greater than 140 mmHg, an advanced age (>50 yrs), a high body mass index(BMI), an increased foetal weight, a puncture level above L2-L3,chronic alcohol consumption, emergency surgery and a high blockade.[6]

Arterial and venodilatation both occur in spinal anesthesia and combine to produce hypotension. Arterial vasodilatation is not maximal after spinal blockade, and vascular smooth muscle continues to retain some autonomic tone after sympathetic denervation. Due to retention of autonomic tone, total peripheral vascular resistance (TPVR) decreases only by 15% to 18%, thus MAP decreases by 15% to 18% if cardiac output is not decreased. If a patient is asymptomatic, decreases in blood pressure up to 33% need not be treated. Venous return to the heart, or preload, depends on patient positioning during spinal anesthesia.[2,4,5]The block height determines the level of sympathetic blockade, which determines the degree of change in cardiovascular parameters.[1,2,4,8] A block with sensory level not extending beyond T10 does not modify peripheral resistance since there is compensatory vasoconstriction above it.[6]

Spinal puncture level and volume of drug are the most important factors determining the height of analgesia. To avoid confounding variables, we punctured dura at L4-L5 space and kept the dose constant in all study subjects. The patients likely to have raised intra abdominal pressure modifying spread of drugs were excluded from the study. We kept all the patients in supine position after confirming the desired sensory level (T9) irrespective of the surgery.

The extent of reduction in cardiac output after central neuraxial blockage depends upon magnitude of vasodilatory changes determined by baseline sympathetic tone of the patient and height of the block (sympathectomy).[9] If normal cardiac output is maintained, systemic vascular resistance (SVR) should decrease by 15-18% in healthy normovolemic patients even with near total sympathectomy.[9]

Pregnancy considerably modifies the spread of local anesthetics injected in spinal, epidural or subdural spaces.[6] Hypotension is further compounded in pregnancy by aortocaval compression. Robert A. Dyer et al[10]while studying hemodynamic changes associated with spinal anesthesia for cesarean delivery in pre-eclamptic patients concluded that cardiac output does not deviate by more than 20% from the baseline value in this subset of high risk patients.

Hypotension caused by a reduction in systemic vascular resistance (SVR) is physiologically compensated by an increase in cardiac output (CO). However, a high level of spinal block can inhibit the cardio accelerator fibers leading to a fall in the heart rate, and hence the CO, thus, instead of a compensatory increase, CO usually decreases. The combined effect of reduced CO and decreased systemic vascular resistance accounts for the high incidence of hypotension after spinal anesthesia.[7]

Sancetta et. al[4] while studying hemodynamic changes in humans following induction of low and high spinal anesthesia found that the low spinal group showed an average reduction of systolic blood pressure by 21per cent, and that in high spinal group by 44 per cent from the basal level. In the low spinal group the maximal average reduction in the cardiac output was16.2 per cent, and in the high spinal group it was 31 per cent from the basal level. There was an average maximal decrease of 8 beats in the low and 10.8 beats in the high spinal group. The changes in the stroke volume reflected those of the cardiac output. They observed that the peripheral arterial pressures reached a maximal reduction within 15 minutes, which was maintained for about an hour, and then a gradually came back to basal levels within two or two and half hours. The administration of vasopressors is seldom indicated.

The two opposing responses namely uninhibited parasympathetic tone below the block compensated by sympathetic response on baroreceptors above the block maintain heart rate within lower side of normal range when the block height does not exceed level T4.[9] The heart rate may decrease during neuraxial block higher than T4 as a result of blockage of cardioaccelarator fibers originating from T1-T4.[5,6,9] Reduction in heart rate may be precipitous in presence of extensive peripheral sympathectomy from T5-L2.[9]

The incidence of bradycardia in the non-pregnant population is about 13%.[8] Decreased venous return may also cause bradycardia, due to a fall in filling pressures. This triggers the intra-cardiac stretch receptors to lower the heart rate. Even though both of these mechanisms are proposed to cause bradycardia, other as yet undetermined factors may contribute to the bradycardia seen with spinal anesthesia. However, in patients with coronary artery disease, asystole and second- and third-degree heart block can occur, so it is wise to treat hypotension and bradycardia promptly so that the myocardium and brain remain perfused after spinal anesthesia.[5] Fluid bolus given as treatment should be carefully monitored as excess fluid may cause patients to go into congestive heart failure, pulmonary edema, or both, and also may necessitate bladder catheterization after surgery which has its own set of set of problems, including urinary tract infections.[5,11,12] Bradycardia is a consequence from blocking heart-accelerating fibres (T1-T4) or from a decreased venous return. There are certain risk factors for the appearance of bradycardia: baseline heart rate less than 60 /min, ASA I, use of beta-blockers, block level above T6, younger age (< 50 yrs) and longer PR interval.[6]

Schmidt and Bittner et al[13] studied incidence, contributing factors and consequences of postoperative hemodynamic severe adverse events after spinal anesthesia on 232 patients. They observed that severe hypotension and bradycardia occur in about 5% of patients recovering from spinal anesthesia. The events were associated with administration of spinal anesthesia in the lateral compared with sitting position, and with postoperative opioid administration. The adverse events were noticed up to 6 hrs in the postoperative period leading to increased length of stay in post anesthesia care units (PACUs). Singh et al[14] conducted a comparative study of two preventive regimens on post spinal hypotension in 100 elderly patients undergoing orthopedic surgery. They observed greater hemodynamic stability with preemptive injection ephedrine 30 mg (i.m.), given 10 min before subarachnoid block compared with an infusion of a colloid injection polygeline 3.5% 500 ml.

Pharmacologic treatment of hypotension by combined α- and β-adrenergic agonists may be better than pure α-agonists, and ephedrine is currently the drug of choice. Cardiac output and peripheral vascular resistance are increased by ephedrine, which restores blood pressure.[2,6] Ephedrine is a sympathomimetic amine which can cross the blood-brain barrier, producing CNS stimulation by increasing the activity of norepinephrine (noradrenaline) on postsynaptic α and β adrenergic receptors. It can decrease urination due to vasoconstriction of renal arteries; it also constricts the internal urethral sphincter, mimicking the effects of sympathetic nervous system stimulation.[2]

Spinal anesthesia does not alter autoregulation of renal blood flow. The kidneys remain perfused when the MAP remains within the range 50- 150 mm Hg. Importantly, urine output is not auto regulated, but is linearly related to MAP values above 50 mm Hg.[3] Transient decreases in renal blood flow may occur when MAP is less than 50 mm Hg, but even after long decreases in MAP, renal function returns to normal when blood pressure returns to normal. If mean blood pressure is maintained after placing a spinal anesthetic, neither hepatic nor renal blood flow will decrease. In patients with liver disease either regional or general anesthesia can be given, as long as the MAP is kept close to baseline.[3] A study by Gamulin on effects of renal sympathetic blockade on renal hemodynamics in patients undergoing major aortic abdominal surgery found no difference in creatinine changes following regional anesthesia[5] Though there is a predictable reduction in renal blood flow after central neuraxial blockade, this has negligible physiological significance.[9]

It is exceedingly difficult to administer 'rational fluid management' because there are very few well designed trials evaluating fluid management protocols in terms of renal response and the potential for renal failure. It is rational to expect that decreased cardiac output secondary to insufficient preload can lead to end-organ (including renal) failure.[11] We advocated around 1litreof crystalloid (5ml/kg/hr)[8] to each patient plus replacement of intraoperative blood loss by administration of crystalloids.

Bashir et al while comparing preloading with crystalloids and no preloading, for assessment of

hemodynamic changes following spinal anesthesia in patients undergoing transurethral resection of prostrate (TURP); concluded that there is no role of pre-emptive hydration before spinal anesthesia, especially in elderly patients undergoing elective surgeries and if hypotension occurs should be treated with boluses of vasopressors.[8]

Increased vagal activity after sympathetic block causes increased peristalsis of the gastrointestinal tract, which leads to nausea. Atropine is useful for treating nausea after high spinal blockade. Nausea and vomiting occur after spinal anesthesia approximately 20% of the time, and risk factors include blocks higher than T5, hypotension, opioid administration, and a history of motion sickness.[2,4,7]

In the present study we tried to test the hypothesis that pharmacotherapy is necessary to avoid untoward renal and hepatic complications caused by hypotension and bradycardia secondary to spinal anesthesia. Our observations and results were in line with the previous studies.[2,3,4,8,10] There was no statistically significant difference in intraoperative urine output between both the groups. The incidence of side effects was low and also comparable.

Evidence given in favor of prophylactic volume loading or vasopressor administration is generally unsupportive, not every episode of spinal hypotension or bradycardia is clinically significant.[15] Controlling sensory block height, being alert to downward trends in heart rate and blood pressure, and reacting quickly and decisively to these changes are the key steps toward preventing major hemodynamic compromise.[15]

Limitations

The study was done on healthy adult patients and extrapolation of these results in ASA III/IV patients or in group of patients deliberately excluded from the study needs further study with large sample size.

Conclusion

The hemodynamic changes after giving spinal anesthesia return to baseline spontaneously within 2 hrs without causing adverse effects on kidneys. Based on our results, we conclude that it is not necessary to use preventive pharmacotherapy to counterbalance hemodynamic changes occurring after subarachnoid block. However, one should be prepared to treat severe hypotension and bradycardia occurring as a consequence of subarachnoid block. Further work is required to determine the optimal therapy for hypotension in high-risk patients.

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