Research Article

Comparison between oral ephedrine and control (without oral ephedrine) in reducing the incidence of hypotension after subarachanoid block- a randomized placebo controlled trial

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Abstract

Background: Spinal anaesthesia enjoys being the most popular anaesthetic technique for elective surgical procedures involving the lower abdomen or lower limbs as it provides rapid, reliable and profound symmetrical sensory and motor block. However, despite crystalloid or colloid preloading, hypotension remains a common complication. Vasopressors are required to treat the spinal induced hypotension among most of these patients. Studies involving prophylactic Ephedrine as an intravenous infusion, bolus or intramuscular routes are in plenty but studies pertaining to prophylactic oral administration are sparse. **Objectives:** This study was conducted to evaluate the safety and efficacy of prophylactic oral Ephedrine (30mg given 30minutes before spinal anaesthesia) in preventing spinal anaesthesia induced hypotension. **Method:** This is a prospective randomized placebo controlled comparative study conducted in hundred patients aged between 20 to 40 years belonging to ASA grade I/II, scheduled for caeserean section under spinal anesthesia were randomly allocated into one of the two groups. Group A (n=50) received prophylactic Oral Ephedrine 30mg 30minute before spinal anaesthesia while Group B (n=50) received a placebo 30minutes before spinal anaesthesia. **Results:** The study showed no significant changes in respiratory rate and oxygen saturation levels in any of the patients in both the groups. The incidence of hypotension is 8% and 40% in Group A and Group B patients respectively. This hypotension developed within the first 20minutes after intrathecal block. In our study 18% of patients in Group B required vasoprcssor supplementation intraoperatively and none in Group A. **Statistical analysis**: It was done using Unpaired "t" and Chi-square tests. The values of $p<0.05$ were considered statistically significant. **Conclusion:** This study demonstrates that prophylactic Oral Ephedrine 30mg when given 30minutes before spinal anaesthesia is a simple, easy, economical, effective and a reliable method in reducing the incidence of spinal induced hypotension without any deleterious effects.

Keywords: Oral Ephedrine; Subarachnoid Block; Bupivacaine; Hypotension.

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INTRODUCTION

Spinal anaesthesia was introduced into clinical practice by August Bier in 1898 even before the break-through of orotracheal intubation by Franz Kuhn in 1901. Regional techniques are the preferred anaesthetic procedure for surgeries involving abdomen and lower extremities. The various advantages include blunting of stress response to surgery, avoidance of intubation, decrease in intraoperative blood loss, earlier return of gastrointestinal function and lower incidence of postoperative thromboembolic events. The unavoidable sequence of spinal anaesthesia is blockade of sympathetic preganglionic efferents leading to peripheral venous pooling causing hypotension. Especially in pregnancy because of gravid uterus, patients are more prone for hypotension. Therapies are primarily aimed at reducing the severity of hypotension. They include prophylactic leg elevation and wrapping, use of inflatable boots, preloading of the patient with crystalloids and colloids and lateral uterine displacement in obstetric patients. Exaggerated lumbar lordosis in pregnancy and vasopressors used as last resort. Ephedrine is the most commonly used drug among vasopressors to treat spinal induced hypotension[1,2]. Studies in relation to prophylactic

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parenteral Ephedrine have been described earlier in plenty compared to oral Ephedrine studies which are sparse. So this prospective randomized study is performed in caesarean section to determine the efficacy of prophylactic oral Ephedrine in preventing spinal hypotension following subarachnoid block. Bupivacaine[3,4,5] is 1 -n-butyl-DL-piperidine-2-carboxylicacid-2, 6 dimethylanilide hydrochloride. It has probably had the greatest influence on the practice of regional anaesthesia due to the combined properties of an acceptable onset, long duration of action, profound conduction blockade, and significant separation of sensory to motor block. The primary action of local anesthetics is on the cell membrane of the axon. The large transient increase in the permeability to sodium ions, necessary for propagation of impulses is prevented. Thus the resting membrane potential is maintained and depolarization in response to stimulation is inhibited. Onset of action is between 3 to 4 minutes and complete spinal anaesthesia ensues by 6 to 8 minutes. The duration of spinal anaesthesia varies from 75 to 150 minutes. Ephedrine [6,7,8] is an alkaloid initially extracted from the Chinese herb Ma-Huang. Now it is synthetically prepared. It is a colourless white crystalline powder or granules with a bitter taste. It is odourless or may have a slight aromatic odour. It acts directly as a nonselective sympathomimetic agent acting on both alpha and beta receptors and indirectly on peripheral postsympathetic norepinephrine release, central nervous stimulation and inhibition of norepinephrine reuptake.

MATERIALS AND METHODS

After institutional Ethical committee approval and informed consent from each patient, the study was conducted on one hundred pregnant females of ASA grade 1 and of age group between 20-40yrs posted for caesereansection under spinal anaesthesia. Patient who refused for spinal anesthesia, any other comorbid disease, patients on MAO- inhibitor, antidepressants and β-blockers, patients with haemorrhagic disorders or patients who are on anticoagulant therapy, disease and deformities of spinal cord or vertebral column and patients with haemoglobin less than l0gm/dl were excluded from the study. Patients were explained in their own language the anaesthetic procedure they are going to undergo. Pre-anesthetic examination was done on the day of surgery which included patient's height and weight, general examination, systemic examination of cardio vascular system, respiratory system, CNS and examination of spine. Basic investigations like heamoglobin percentage, total blood count, differential blood count, urine routine, bleeding and clotting time, blood sugars (if urine sugar positive). On the day of surgery, drugs and resuscitation equipments were kept ready. The baseline Heart rates (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) were recorded for all patients using the L and T. monitor. Patients then were randomly allocated into two groups. Group A (n=50) were given Tab. Ephedrine 30mg orally with a sip of water 30 minutes before surgery. Group B (n=50) were given a placebo to be taken orally with a sip of water 30 minute before surgery. Patients were shifted to the operation theatre in left lateral position and intravenous access was obtained using a 18 gauge cannula, an infusion of ringer lactate was started. The pre subarachnoid block Heart rates (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) were recorded for all patients and continuous monitoring done with L. and T. monitor. Under strict aseptic precaution lumbar puncture was performed in left lateral position using 25-gauge disposable Quincke type of spinal needle at L_3-L_4 spinal intervertebral space by midline approach. After the free flow of cerebrospinal fluid, 2ml of 0.5% heavy Bupivacaine Hydrochloride was injected intrathecally irrespective of weight and height of the patients and the time noted. The patients were repositioned with wedge of 10 cm, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) were recorded in all patients at every 2 minutes interval for 10 minutes, then at every 10 minutes interval up to 45minutes and then at every 15 minutes till the end of surgery. Level of sensory blockade was checked using a 23G hypodermic needle. Success of the block was defined as pinprick analgesia extending cranially at least to the T_6 dermatome. Following subarachnoid block the following vitals were monitored during peri-operative period. They included hypotension, nausea, vomiting, desaturation or hypoxemia (SpO2<90%) and blood loss during the surgical procedure. Hypotension was defined as a decrease in systolic blood pressure (SBP) more than 20% from the base line. If hypotension occurred in any 6 of the patients they were treated first with head down position, then rapid infusion of ringer lactate was done. If hypotension continued following these measures, then they were treated with Inj. Ephedrine administered intravenously in 5mg boluses at 2 minute interval until the SBP returned to within 20% of the baseline values. Inj. Atropine 0.6mg was administered intravenously to any patient if the heart rate decreased below 60beats/ minute.

STATISTICAL ANALYSIS

The observations are expressed as Mean ± one standard deviation. The baseline haemodynamic values and the postspinal haemodynamic changes at various time intervals were compared using Unpaired "t" and Chi-square tests. The values of $p<0.05$ were considered statistically significant.

RESULTS

The demographic data showed that two groups were similar with respect to age, height and weight(Table 1).

Table 1: Statistical comparison of age, height and weight of the two groups of patients

Parameter	Group A		Group B		t Value	p Value
	Mean	S.D.	Mean	S.D.		
Age (Years)	33.54	8.14	36.68	8.87	1.844	0.0682
Height(Cm)	159.00	5.44	158.96	5.64	0.0361	0.9713
Weight (Kg)	57.32	7.32	56.52	5.57	0.6150	0.5400

The mean, the standard deviation (S.D) and the unpaired 't' test value of age, height and weight of the two groups of patients are presented. It is seen that the groups are matched in respect of these parameters.

Table 2: Statistical comparison of SBP (mm Hg) in the two groups

Period	Group A		Group B		t Value	p Value	Significant
	Mean	SD	Mean	SD			
Baseline	121.98	7.36	123.85	11,45	*0.9715*	0.3337	No
At SAB	127.14	7.36	123.96	10.47	*1.757*	0.137	No
2 minutes	128.74	8.18	116.2	10.95	*6.487*	0.0001	Yes
4 minutes	126.84	7.90	107.72	9.73	*10.787*	0.0001	Yes
6 minutes	121.94	10.10	102.52	9.56	*9.874*	0.0001	Yes
8 minutes	120.34	11.84	100.1	11.09	*8.822*	0.0001	Yes
10 minutes	118.7	11.44	100.78	8.91	*8.739*	0.0001	Yes
20 minutes	118.6	9.10	101.18	7.87	*10.238*	0.0001	Yes
30 minutes	119.92	8.14	104.18	7.44	*9.695*	0.0001	Yes
40 minutes	118.84	6.60	107.46	7.28	*8.189*	0.0001	Yes
50 minutes	117.74	6.90	109.72	6.76	*5.871*	0.0001	Yes
60 minutes	115.6	7.53	118.33	10.41	*1.503*	0.1379	No

The differences are highly significant except at baseline, at SAB and at 60 minutes.

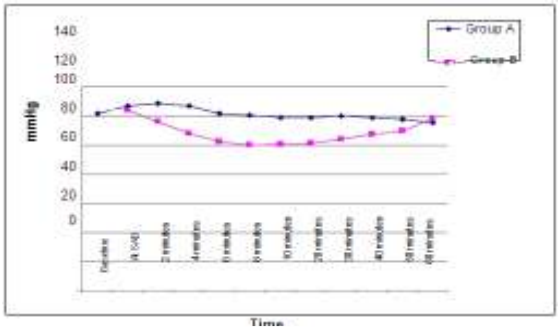

Figure 1: The SBP of the two groups of patients at different time intervals

Table 3: Statistical comparison of DBP (mmHg) in the two groups

Period	Group A		Group B		t Value	p Value	Significant
	Mean	SD	Mean	SD			
Baseline	79,32	4.97	79.0	6.73	*0.271*	0.1455	No
At SAB	81.7	5.95	78.82	6.60	*1.496*	0.1379	No
2 minutes	81.72	7.59	75.66	6.25	*4.358*	0.0001	Yes
4 minutes	80.44	7.69	71.76	5.54	*6.476*	0.0001	Yes
6 minutes	77.78	7.58	68.46	6.4	*6.643*	0.0001	Yes
8 minutes	76.5	7.40	67.38	7.92	*5.590*	0.0001	Yes
10 minutes	75.54	7.49	66.4	6.53	*6.504*	0.0001	Yes
20 minutes	75.44	6.01	67.6	6.01	*6.522*	0.0001	Yes
30 minutes	75.78	5.20	67.62	4.25	*8.592*	0.0001	Yes
40 minutes	75.76	6.10	70.1	5.19	*4.997*	0.0001	Yes
50 minutes	75.48	5.76	70.96	4.88	*4.234*	0.0001	Yes
60 minutes	73.2	3.27	76.66	6.66	*3.298*	0.0014	Yes

The differences are highly significant except at baseline and at SAB. The lowest DBP was 73.2 mmHg at 60 minutes in group A, and 66.4 mmHg at 10 minutes in the other group.

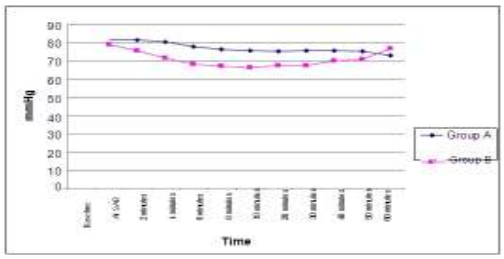

Figure 2: The DBP of the two groups of patients at different time intervals

Table 4: Statistical comparison of MAP (mmHg) in the two groups

Period	Group A		Group B		t Value	p Value	Significant
	Mean	SD	Mean	SD			
Baseline	93.54	5.19	93.95	7.27	*0.325*	0.5454	No
At SAB	96.84	6.01	93.80	7.26	*2.281*	0.0247	Yes
2 minutes	97.39	7.17	89.17	7.13	*5.748*	0.0001	Yes
4 minutes	95.91	7.36	83.75	6.33	*8.857*	0.0001	Yes
6 minutes	92.5	8.05	78.88	8.01	*8.481*	0.0001	Yes
8 minutes	91.11	9^9	94.87	5.51	*2,462*	0.0156	Yes
1 0 minutes	89.92	8.25	94.99	5.31	*3.654*	0.0042	Yes
20 minutes	89.82	6.45	95.90	5.12	*5.221*	0.0001	Yes
30 minutes	90.49	5.23	96.11	5.31	5.3521	0.0001	Yes
40 minutes	89.21	8.66	96.11	5.06	*4.861*	0.0001	Yes
50 minutes	89.57	5.70	96.31	5.07	*6.247*	0.0001	Yes
60 minutes	87.33	4.52	103.44	5.7	*15.659*	0.0001	Yes

The differences are highly significant except at baseline. The MAP of the two groups of patients at different time intervals is presented in Graph 4 and Table 3. In group A, the lowest MAP was 87.33 mmHg at 60 minutes, and the highest was 97.39 mmHg at 2 minutes. In group R, the lowest was 78.88 mmHg at 6 minutes, and the highest was 103.44.

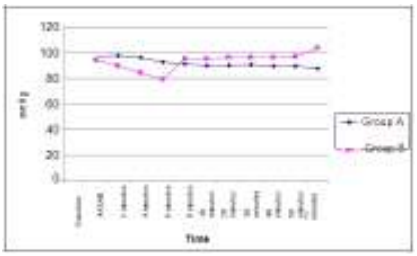

Figure 3: The MAP of the two groups of patients at different time intervals

Table 5: Statistical comparison of HR (beat /minute) in the two groups

Period	Group A		Group B		t Value	p Value	Significant
	Mean	SD	Mean	SD			
Baseline	78.34	7.97	81.14	8.05	1.748	0.0836	No
At SAB	81.98	8.29	83.2	6.77	0.806	0.4222	No
2 minutes	83.08	8.33	85.26	7.35	1.388	0.1684	No
4 minutes	83.2	8.76	88.32	8.3	3.000	0.0034	Yes
6 minutes	83.3	8.27	89.58	8.66	3.708	0.0003	Yes
8 minutes	82.56	8.11	92.26	9.07	5.637	0.0001	Yes
10 minutes	82.62	8.04	92.1	8.41	5.761	0.0001	Yes
20 minutes	81.84	6.48	93.26	7.63	8.067	0.0001	Yes
30 minutes	81.6	6.56	92.08	7.87	7.233	0.0001	Yes
40 minutes	80.56	5.95	90.44	6.96	7.826	0.0001	Yes
50 minutes	81.26	5.53	89.6	6.59	6.855	0.0001	Yes
60 minutes	79.2	4.55	96.0	12.49	8.937	0.0001	Yes

The differences are highly significant from 4th minute onwards. The HR of the groups of patients at different time intervals is presented in Table 5 and graph 4.

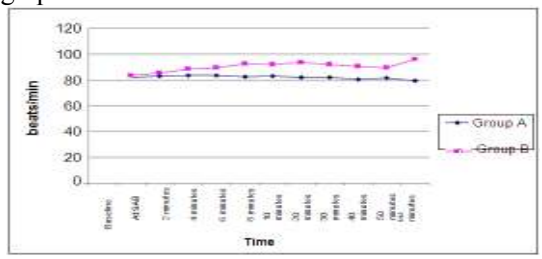

Figure 4: The HR of the two groups of patients at different time intervals

DISCUSSION

The ease and long history of success has made subarachnoid block the anaesthetic procedure of choice for caeserean section. Though spinal anaesthesia has a wide range of advantages like the simplicity of technique, its rapid onset of action, economical and minimal postoperative complications, it is not without the risk of physiological side effects on the various systems[9]. The most common serious side effects from spinal anaesthesia are hypotension and bradycardia [10]. The most common among the Vasopressors a mixed adrenergic agonist such as Ephedrine more ideally corrects the non cardiac circulatory sequel of spinal anaesthesia than does either a pure α-or β-adrenergic agonist[11]. There are mixed results to prophylactic administration of I.M. Ephedrine as to its postoperative incidences of hypertensive episodes and alleged unpredictable absorption from the site of injection[12]. The belief that a relative overdose may result in hypertension, tachycardia or both postoperatively, and may therefore be detrimental[13]. Nevertheless, administration of Ephedrine 37.5mg I.M. was not associated with reactive hypertension or tachycardia in women undergoing caesarean section. In other studies patients aged >60years received I.M. Ephedrine for prevention of hypotension. Although the incidence of hypotensive episodes was effectively reduced, all patients experienced a significant decrease in systolic pressure after spinal anesthesia[14]. Studies related to prophylactic bolus or infusions of I.V. Ephedrine have proved their efficacy in preventing the episodes of hypotension without unwanted side effects[15,16,17]. In our study, incidence of hypotcnsion is 8 % in Group A patients and 40% in patients of Group B. All these patients who developed hypotension showed a fall in systolic arterial pressure of more than 20% of the base line value within the first 20minutes of intrathecal block. The incidence of hypotension is greater in Group B when compared to Group A which is statistically highly significant ($x\sim = 12.336$, $p < 0.0001$) **Kafle *et al* 199418**in there study found the incidence of hypotension to be 55% in Group I (ephedrine group) and 83% in Group II (control group). These high incidences of hypotension may be attributed to the high level of sensory block T3-T4 level, higher doses of bupivacaine heavy 0.5% used and non exclusion of patients who had intraoperative bleeding above 10% in both the groups. **Eroglu *et al* 2003** [19] in this study found the incidence of hypotension to be 23.33% in Group I (ephedrine group) and 50% in Group II (control group). These values differ in comparison to our values as the patients enrolled into there study were aged >60years (range 60-87) and belonged to ASA Grades II and III. Both the studies have shown that the incidence of hypotension is statistically lower in patients who have received prophylactic Oral Ephedrine before Subarachnoid block; our studies is in support with their studies. In our study patients in whom we noticed a fall in blood pressure, we adopted active measures like head down position, increasing the rate of infusion and oxygenation. If the hypotcnsion continued despite the above measures Inj. Ephedrine hydrochloride 5mg bolus were administered I.V. at 2 minute interval until the blood pressure returned to within 80% of baseline values. In our study 18% of patients in Group B required vasopressors therapy and larger volumes of additional intravenous fluid. In Group A none of the patients received vasopressors and the 8% of patients who had hypotensive episodes were rectified by application of active measures. **Kafle *et al* 1994** [36] in their study supplemented Inj. Ephedrine I.V. as soon as there was a fall in blood pressure and did not use any form of measures used in my study. Patients in Group I (ephedrine group) received 4.3±4.8mg I.V. Ephedrine and Group II (control group) received 11.6±9.4mg I.V. Ephedrine which was statistically significant ($p<0.01$). **Eroglu *et al* 2003** [44] in there study supplemented Inj. Ephedrine I.V. as soon as there was a fall in blood pressure and did not use any form of measures used in my study. Patients in Group I (ephedrine group) received 3.42±0.97mg I.V. Ephedrine and Group II (control group) received 8.86±1.24mg I.V. Ephedrine which was statistically highly significant ($p<0.0001$). In both the above mentioned studies there is a statistically significant reduction in the supplemental doses of intraoperative I.V. Ephedrine in patients who received prophylactic oral

Ephedrine which is consistent with them In our study even though both the groups had a statistically non significant variation in the heart rate up to the 2nd minute, there was a steady rise in the heart rate of Group B patients from 4th minute onwards when compared with Group A patients who had none. This can be explained by the intravenous supplements of Ephedrine boluses and increased infusion of Ringer solution in Group B patients who had blood pressure < 80% of baseline values. **Kafle *et al* 1994** [36] found in their study that tachycardia did occur in patients given intravenous Ephedrine to treat the hypotension and none of the patients who received oral Ephedrine prophylactically had tachycardia. This finding is consistent with their study. **Eroglu *et al* 2003** [44] receded six cases of bradycardia in Group II (control group) who responded to Inj. Atropine. Intraoperatively, These cases of bradycardia were attributed to the high level of sensory block (T4 level). None of their patients who received Oral Ephedrine had episodes of tachycardia which is consistent with their study.

CONCLUSION

The prophylactic administration of oral Ephedrine in ASA Grade I and II patients undergoing caeserian section under spinal anaesthesia is an effective measure in preventing hypotension without causing untoward side effects like central nervous system stimulation, tachycardia or arrhythmias.

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