# Prevention of Hypotension Following Subarachnoid Block; Efficacy of Preloading with Hydroxyethyl Starch Versus Ringer's Lactate Solution

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#### **Abstract**

Background: Arterial hypotension is a potential hazard associated with spinal anesthesia. Routinely, crystalloids and colloids are used for managing hypotension. While crystalloids easily move out of the intravascular space, colloids are confined to the intravascular space, thereby minimizing the risk of hypotension. This study was carried out to compare the efficacy of 10% Hydroxyethyl starch with Ringer's lactate solution. Methods: This double blind randomized controlled trial was carried out on 100 patients who underwent spinal anesthesia during the study period. The study participants were randomized into experimental group (6% Hydroxyethyl starch, 10 ml/Kg) and control group (Ringer's lactate, 20 ml/Kg). Blood pressure and heart rate were recorded periodically up to 60 minutes. Sensory level of blockade was checked after 5 minutes. Results: It was observed that as the surgery prolonged, the incidence of hypotension increased among the controls compared to the experimental group. While the initial incidence was higher among the experimental group (24%), the incidence was greater for the controls beyond 25 minutes (42%). The difference in the incidence was statistically significant (p<0.05). Conclusion: Hydroxyethyl starch is superior to Ringer's lactate solution in prevention of Hypotension following spinal anesthesia. Incidence of hypotension is reduced but not completely eliminated. Hydroxyethyl starch also has several other advantages such as prophylaxis against venous thrombosis and decreased allergic potential.

Keywords: Hydroxy ethyl starch; Hypotension; Ringer lactate; Spinal anesthesia.

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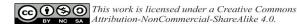
# Introduction

Spinal anesthesia is one of the widely practiced anaesthetic techniques over years for lower abdominal and lower limb surgeries. If spinal anesthesia is applied with proper skills and care, it is a safe procedure which provides satisfactory outcomes. It is a preferred method of choice among the patients and surgeons considering the benefits and comforts achieved on-table. Spinal anesthesia for routine surgical procedures assumes special importance in developing countries because of economic reasons, lack

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of availability of sophisticated anaesthetic apparatus and compressed gases in the remote areas.

The potential hazard associated with spinal anesthesia is arterial hypotension. This can cause significant morbidity and mortality. Methods used to reduce the incidence and severity of spinal hypotension includes head down position, prophylactic vasopressors, leg elevation and strapping, use of inflatable boots and preloading the patients with intravenous fluids. Crystalloids solutions being of lower molecular weight will enter the interstitial space due to lack of intrinsic colloid osmotic pressure resulting in pulmonary edema which interferes with tissue oxygen exchange. Colloids are higher molecular substances than crystalloids and are similar to plasma in oncotic pressure and remain confined to intravascular space with little expansion of interstitial space.

It is indeed a challenge to manage arterial hypotension on table. Although several studies have been carried out to evaluate the effectiveness of spinal anesthesia, very few studies have been carried out to address the adverse effect, mainly hypotension. An analysis into the therapeutics involved in the management of arterial hypotension will go a long way in minimizing the morbidity and mortality associated with spinal anesthesia.

#### **Objectives**

- To compare the preloading efficacy of Ringer's lactate, 20 ml/kg and Hydroxyethyl starch 6%, 10 ml/kg body weight, for prevention of Hypotension following subarachnoid Block.
- 2. To evaluate the adverse outcomes of Hydroxyethyl starch among the study participants.

# Methodology

# Study setting and participants

This double blind randomized controlled trial was carried out in the Department of Anesthesiology of a tertiary teaching institution for a period of 10 months. All the patients who were scheduled for surgeries involving spinal anesthesia during the study period were selected for the study. Based on the selection criteria, a total of 100 participants were included in the study.

#### Inclusion criteria

- Patient belonging to ASA Grade I & II.
- Body Weight 40 to 80 kilograms.
- Age 20 to 60 years of both the sexes.
- Patients undergoing various elective and emergency operations under spinal anesthesia in whom minimal blood loss is anticipated.

## Exclusion criteria

- Any patients in whom spinal anesthesia is contraindicated.
- Patients with cardio vascular, respiratory & central nervous system disorders.

# Randomization and grouping

The study participants were grouped into experimental and control groups. The experimental group consisted of 50 participants who received 6% Hydroxyethyl starch, 10 ml/Kg. The control group consisted of 50 participants who received Ringer lactate, 20 ml/Kg. All the participants were randomly allocated into the groups using computer generated random numbers.

# Ethical approval and informed consent

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to the commencement of data collection.

## Procedure

Followingroutineinvestigations and pre-anaesthetic evaluation, all participants were pre-medicated with injection Midazolam 0.02 mg/kg and injection Atropine 0.6 mg, through intra venous route, 30 minutes before surgery.

Basal parameters like heart rate, Oxygen saturation and blood pressure were monitored. A peripheral intravenous line with 18 or 20 gauge canula was secured in one of the upper limbs. Volume infusion was determined in accordance to the body weight. In both the groups, the solutions were infused over a period of 20 minutes. After preloading all patients received ringer lactate infusion for fluid maintenance.

Under aseptic precautions lumbar puncture was performed with 23 gauge spinal needle (Quinke's

Needle) through midline approach with patient in the right lateral or left lateral decubitus position, 10° head down tilt. After free flow of CSF, 2 ml of Lignocaine with 200 mcg of adrenaline was injected. Immediately after the injection the needle was withdrawn the patient turned to supine position.

#### Data collection

Blood pressure and heart rate were recorded at an interval of every minute up to 5 minutes, every 5 minutes up to 30 minutes, every 10 minutes up to 60 minutes. Sensory level of blockade was checked after 5 minutes. Hypotension was defined as decrease in the systolic blood pressure more than 25% from the basal parameter. Hypotension was managed with Trendelenberg's position, increase in fluid infusion rate, and 100% oxygen by mask. If hypotension continued despite the above measures, injection Mephenteramine sulphate was administered intravenously 3 mg bolus at 1 minute interval until the blood pressure increased to acceptable levels. Bradycardia was treated with intravenous injection of Atropine 0.6 ml.

## Data analysis

Data was entered and analyzed using SPSS version 20 software. Difference between the mean for values of systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate was tested for statistical significance using student 't' test for independent group at 5% level of significance.

### Results

Majority of the participants in both the groups belonged to 21-30 years (48% and 52% respectively). Most of the participants weighed between 51-60 kilograms in both the groups (54% and 48% respectively). The level of sensory blockade was at T4 for the controls (52%) and T6 for experimental group (48%) (Table 1).

The incidence of hypotension between the groups is given in table 2. It was observed that as the surgery progressed, the incidence of severe hypotension increased among the controls compared to the experimental group. While the initial incidence was higher among the experimental group (24%), the incidence was greater for the controls beyond 25 minutes (42%). The difference in the incidence was statistically significant (p<0.05).

The difference in the mean systolic blood pressure over the duration of anesthesia is given in table 3. It was observed that although the initial fall in the systolic blood pressure occured in both the groups, there was a significantly higher reduction in the systolic blood pressure in the controls compared to the experimental group, as evidenced by increase in the difference of mean systolic blood pressure. The observed difference was statistically significant. (Table 3) Similar observations were seen with mean diastolic pressure (Table 4).

Our study observed a significant reduction in the mean arterial pressure among the controls within 5 minutes of start of surgery while the mean arterial pressures among the experimental group remained fairly stable throughout the surgery. The observed difference was statistically significant (p<0.05). (Table 5) However, the overall differences in the mean heart rate compared between the two groups at different time intervals did not show significant variation between the groups and also within the groups. (Table 6) Overall, the number of participants requiring Inj. Mepheteramine was higher among the controls (14%) compared to the experimental group (4%) (Table 7).

Table 1: Background characteristics of the study participants

S. No	Characteristics	Control	Experimental (Group B)	
5. NO	Characteristics	(Group A) N=50 (%)	(Gloup B) N=50 (%)	
1	Age (in years)	( )		
	21-30	24 (48.0)	26 (52.0)	
	31-40	13 (26.0)	12 (24.0)	
	41-50	7 (14.0)	11 (22.0)	
	51-60	6 (12.0)	1 (2.0)	
2	Sex			
	Male	34 (68.0)	29 (58.0)	
	Female	16 (32.0)	21 (42.0)	
3	Weight distribution (in kilog	rams)		
	41-50	3 (6.0)	5 (10.0)	
	51-60	27 (54.0)	24 (48.0)	
	61-70	15 (30.0)	17 (34.0)	
	71-80	5 (10.0)	4 (8.0)	
4	Type of surgery			
	Herniorraphy	15 (30.0)	13 (26.0)	
	Appendicetomy	13 (26.0)	13 (26.0)	
	Total abdominal	7 (14.0)	12 (24.0)	
	Hystrectomy			
	Skin grafting	5 (10.0)	3 (6.0)	
	Eversion of Sac of	5 (10.0)	3 (6.0)	
	Hydrocele		- 41	
	Subfasical ligation of varicose vein	2 (4.0)	3 (6.0)	
	Varicocele ligation	1 (2.0)	1 (2.0)	
	Ovarian cyst removal	1 (2.0)	1 (2.0)	
	Orchidopexy	1 (2.0)	1 (2.0)	
5	Level of sensory blockade	. ,	` '	
	T4	26 (52.0)	23 (46.0)	
	T6	22 (44.0)	24 (48.0)	
	T8	2 (4.0)	2 (4.0)	
	T10	0(0.0)	1 (2.0)	

**Table 2:** Showing incidence of severe hypotension in Group A and B following spinal anesthesia

S. No	Time	Control (Group A) N = 50 (%)	Experimental (Group B) N = 50 (%)	p- Value
1	0-5	0	16 (24)	p<0.05
2	6-10	0	12 (24)	<i>p</i> <0.05
3	11-15	5 (10)	7 (14)	p<0.05
4	16-20	6 (12)	3 (6)	<i>p</i> <0.05
5	21-25	10 (20)	3 (6)	p<0.05
6	26-30	21 (42)	7 (14)	<i>p</i> <0.05
7	31-35	7 (14)	2 (4)	p<0.05
8	36-40	1 (2)	0	p<0.05
9	>40	2 (4)	0	p<0.05

**Table 3:** Mean systolic blood pressure at different intervals of time after spinal anesthesia

Time (in minutes)	Group A	Group B	p - Value
0	120 mm Hg	120 mm Hg	<i>p</i> >0.05
1	119 mm Hg	121 mm Hg	<i>p</i> >0.05
2	113 mm Hg	118 mm Hg	<i>p</i> <0.05*
3	107 mm Hg	118 mm Hg	<i>p</i> <0.05*
4	103 mm Hg	116 mm Hg	<i>p</i> <0.05*
5	100 mm Hg	115 mm Hg	<i>p</i> <0.05*
10	98 mm Hg	115 mm Hg	<i>p</i> <0.05*
15	96 mm Hg	115 mm Hg	<i>p</i> <0.05*
20	98 mm Hg	114 mm Hg	<i>p</i> <0.05*
25	99 mm Hg	117 mm Hg	<i>p</i> <0.05*
30	101 mm Hg	117 mm Hg	<i>p</i> <0.05*
40	100 mm Hg	118 mm Hg	p<0.05*
50	104 mm Hg	119 mm Hg	<i>p</i> <0.05*
60	104 mm Hg	118 mm Hg	<i>p</i> <0.05*
75	98 mm Hg	120 mm Hg	p<0.05*

<sup>\*</sup>p value significant at 95% level

**Table 4:** Mean diastolic pressure at different time intervals after spinal anesthesia

Time (in minutes)	Group A	Group B	p - Value
0	75 mm Hg	78 mm Hg	<i>p</i> >0.05
	O	O	p>0.03
1	76 mm Hg	78 mm Hg	<i>p</i> >0.05
2	73 mm Hg	77 mm Hg	<i>p</i> >0.05
3	70 mm Hg	75 mm Hg	<i>p</i> >0.05
4	68 mm Hg	74 mm Hg	<i>p</i> <0.05*
5	69 mm Hg	74 mm Hg	<i>p</i> <0.05*
10	65 mm Hg	72 mm Hg	<i>p</i> <0.05*
15	63 mm Hg	73 mm Hg	<i>p</i> <0.05*
20	64 mm Hg	76 mm Hg	<i>p</i> <0.05*
25	65 mm Hg	75 mm Hg	<i>p</i> <0.05*
30	66 mm Hg	74 mm Hg	<i>p</i> <0.05*
40	66 mm Hg	76 mm Hg	<i>p</i> <0.05*

50	67 mm Hg	75 mm Hg	<i>p</i> <0.05*
60	64 mm Hg	75 mm Hg	p<0.05*
75	68 mm Hg	76 mm Hg	p<0.05*

<sup>\*</sup>p value significant at 95% level

**Table 5:** Average mean arterial pressure at different time intervals after spinal anesthesia

Time (in minutes)	Group A	Group B	p - Value
0	90 mm Hg	92 mm Hg	<i>p</i> >0.05
1	90 mm Hg	92 mm Hg	<i>p</i> >0.05
2	84 mm Hg	90 mm Hg	<i>p</i> >0.05
3	81 mm Hg	89 mm Hg	<i>p</i> <0.05*
4	78 mm Hg	87 mm Hg	<i>p</i> <0.05*
5	77 mm Hg	87 mm Hg	<i>p</i> <0.05*
10	76 mm Hg	87 mm Hg	<i>p</i> <0.05*
15	74 mm Hg	87 mm Hg	<i>p</i> <0.05*
20	76 mm Hg	89 mm Hg	<i>p</i> <0.05*
25	77 mm Hg	87 mm Hg	<i>p</i> <0.05*
30	77 mm Hg	88 mm Hg	<i>p</i> <0.05*
40	77 mm Hg	89 mm Hg	<i>p</i> <0.05*
50	80 mm Hg	89 mm Hg	<i>p</i> <0.05*
60	81 mm Hg	88 mm Hg	<i>p</i> <0.05*
75	78 mm Hg	93 mm Hg	<i>p</i> <0.05*

<sup>\*</sup>p value significant at 95% level

 ${\bf Table~6:}~{\bf Mean~Heart~Rate~at~different~time~intervals~after~spinal~anesthesia}$ 

Group A	Group B
89 per minute	85 per minute
88 per minute	85 per minute
88 per minute	85 per minute
87 per minute	85 per minute
84 per minute	84 per minute
86 per minute	83 per minute
86 per minute	83 per minute
89 per minute	83 per minute
87 per minute	82 per minute
89 per minute	83 per minute
88 per minute	83 per minute
86 per minute	82 per minute
85 per minute	83 per minute
84 per minute	84 per minute
81 per minute	84 per minute
	88 per minute 88 per minute 87 per minute 84 per minute 86 per minute 86 per minute 89 per minute 87 per minute 89 per minute 89 per minute 89 per minute 89 per minute 88 per minute 86 per minute 86 per minute 86 per minute

**Table 7:** Mephenteramine requirements among the study participants

	Group A	Group B
No. of patients requiring Inj Mephenteramine	7 (14%)	2 (4%)

#### Discussion

Arterial Hypotension is a major and most common complication following spinal anesthesia. The resultant decrease in the cardiac output may cause inadequate cerebral and/or coronary blood flow, culminating in death. Hypotension has been defined differently in many studies. Some define hypotension as fall in blood pressure by 20% and others by 30% from the basal blood pressure, while some studies have defined hypotension as blood pressure less than 80 mmHg. In our study we have considered fall by more than 25% as hypotension. Incidence of Hypotension varies depending upon number of factors such as level of sympathetic blockage, site of operation, nature of operation, patient's age, health condition and blood volume. Since blood pressure can be described as the product of cardiac output and total peripheral vascular resistance, the usual management has been directed towards one of these two factors, namely, use of peripheral vasoconstrictors to increase the total peripheral resistance or the use of drugs with chronotropic or inotropic cardiac action to augment the output of the heart. Another method of increasing cardiac output is to augment the venous return by the expansion of blood volume.

Prophylactic administration of crystalloid before spinal anesthesia has been considered a safe and effective method of reducing the incidence of Hypotension. About 75% of any crystalloid diffuses into interstitial space; its efficacy in expanding plasma volume is only transient. Although crystalloid administration is safe in most patients it may be disadvantageous in certain groups, such as those with renal impairment or congestive cardiac failure if infused in large volumes. Excessive crystalloid administration may rarely produce pulmonary edema and peripheral edema and have little effect on plasma volume, especially in geriatric patients especially after the sympathetic block wears off. Recently attention has been focused on the Prophylactic administration of colloid solutions for the prevention of hypotension during spinal anesthesia. The more logical choice in preventing hypotension during spinal anesthesia is administration of colloids, since it remains in the intravascular compartment for longer period depending on its physical properties.

In our study the incidence of hypotension has been found to be 62% in control group and 18% in experimental group. After subarachnoid block there was a progressive fall of blood pressure up to 20 minutes and maximum hypotension occurred

within 10–15 minutes. There was a statistically significant difference in the incidence of hypotension in control group compared to experimental group (p<0.05). We found that Hydroxyethyl starch is superior to Ringer lactate in preventing hypotension following spinal anesthesia.

Our observation was close to the study conducted by¹ who observed higher incidence of hypotension (52%) in lactated Ringers solution group compared to (15%) the hetastarch group.² in his study found no hypotension in the albumin group compared with an incidence of 29% in the crystalloid group.³ Also found lower incidence of hypotension (45%) in the Hetastarch group compared to (85%) in Ringer lactate group. Siddik SM *et al.* also had similar findings showing increased incidence of hypotension (80%) in Ringer lactate group when compared to (40%) in 10% hydroxy ethyl starch group.⁴ Similar results were observed in studies done by Hiroshi Ueyama *et al.*⁵

Hydroxy ethyl starch is a colloid which replaces lost albumin, which is mainly responsible for the oncotic pressure in the blood. It is essential that substances like hydroxyethyl starch should have sufficient molecular weight so as to prevent its excretion rapidly out of the body. Hydroxy ethyl starch exerts a colloid oncotic pressure of  $58.5~\rm cm~H_2O$  and one litre of hydroxyethyl starch increases the plasma oncotic pressure of patients in hypovolemic shock by 36%.

In order to achieve a long intravascular stay necessary for an effective plasma volume improvement, Hydroxyethyl starch molecules should be above the renal threshold. Hydroxy ethyl starch is primarily eliminated via the kidneys. Hydroxyethyl starch fraction that is subjected to slower renal elimination is cleaved first by intracellular gamma amylases and their intravascular alpha glomerular filtration. The rate of degradation to renally excretable fraction of Hydroxyethyl starch depends on the degree of molar substitutions and the substitution pattern. Hydroxyethyl starch following acute or chronic administration is subject to transient storage in liver, spleen and other organ until broken down and eliminated by tissue glucosidases. Patients with normal renal function rapidly eliminate hydroxyethyl starch. The residual Hydroxyethyl starch dose is metabolized in tissues by tissue glucosidases and excreted in the kidneys. Patients with total chronic renal failure tend to be subject to extensive tissue storage of Hydroxyethyl starch as a consequence of the non dialyzability. Hydroxyethyl starch is therefore contraindicated in these patients. About 46% of the participants who

were administered Hydroxyethyl starch excreted it in the urine within two days and 64% within eight days.

The more stable hemodynamic status observed after colloid administration probably relates to its remaining in the intravascular compartment longer than crystalloids. Extra vascular redistribution of crystalloids may be so rapid that it may be impossible to infuse them fast enough to maintain intravascular volume. Freported that colloid osmotic pressure decrease by only 1.7 mm Hg after preloading with 3% dextran 70 before epidural anesthesia for caesarean section, compared with a 5.6 mm Hg decrease after preloading with Ringer lactate.

In our study we did not come across any allergic reactions to the Hydroxyethyl starch. In our study we found that hydroxyethyl starch is superior to Ringer's lactate in prevention of Hypotension following spinal anesthesia. Incidence of hypotension is reduced but not completely eliminated. Hydroxyethyl starch also has several other advantages such as prophylaxis against venous thrombosis and decreased allergic potential in comparison to gelatin.

### Conclusion

In our study we have found that Hydroxyethyl starch is more effective, than lactated Ringer's solution in preventing hypotension in patients undergoing surgeries under spinal anesthesia. However, the incidence of hypotension was only reduced but not completely eliminated in this study. The dose response relationship in

eliminating the incidence of hypotension needs to be further explored.

Conflict of interest: Nil

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Ethical approval: Obtained

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