A COMPARATIVE STUDY OF INFUSION OF EPHEDRINE AND PHENYLEPHRINE ON HEMODYNAMIC STABILITY AFTER SPINAL ANESTHESIA IN ELDERLY PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERIES

By

DR. SYED SUFIAN IBRAHIM Dissertation submitted to the B.L.D.E.(DEEMED TO BE UNIVERSITY),

VIJAYAPURA, KARNATAKA



In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

Under the guidance of

DR. BASAVARAJ PATIL MD

ASSOCIATE PROFESSOR

DEPARTMENT OF ANAESTHESIOL0GY

B.L.D.E(DEEMED TO BE UNIVERSITY)

SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE,

VIJAYAPURA

B.L.D.E. (DEEMED TO BE UNIVERSITY) SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA.

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DR. SYED SUFIAN IBRAHIM

DATE: PLACE:

B.L.D.E. (DEEMED TO BE UNIVERSITY) SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA.

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Date:	Bai
	DR.BASAVARAJ PATIL
Place:	ASSOCIATE PROFESSOR
	DEPARTMENT OF ANAESTHESIOLOGY
	B.L.D.E (DEEMED TO BE UNIVERSITY)
	SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL
	AND RESEARCH CENTRE, VIJAYAPURA, KARNATAKA

B.L.D.E. (DEEMED TO BE) UNIVERSITY SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE, VIJAYAPURA.

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Fili

DR. RENUKA HOLYACHI HEAD OF DEPARTMENT DEPARTMENT OF ANESTHESIOLOGY B.L.D.E (DEEMED TO BE UNIVERSITY) SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA, KARNATAKA

Date:

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> DR ARAVIND PATIL PRINCIPAL B.L.D.E (DEEMED TO BE UNIVERSITY) SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA, KARNATAKA

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DR. SYED SUFIAN IBRAHIM.

ABBREVIATIONS

- SA- Spinal Anaesthesia
- NIBP- Non invasive blood pressure
- **BP-**Blood pressure
- MAP- Mean arterial pressure
- HR- Heart rate
- PR-Pulse Rate
- SpO2- Percentage of oxygen saturation
- ECG- electrocardiography
- BMI- Body Mass Index
- CO- Cardiac Output
- ASA- American Society of Anaesthesiologists
- 0.9% NaCl- Normal Saline
- I/V- Intravenous
- I/M- Intramuscular
- α Alpha
- β Beta
- COMT Catechol-O-Methyl transferase
- MAO Monoamine oxidase
- CABG Coronary artery bypass graft
- p value probability value
- mcg microgram
- mg milligram
- mins minutes

ABSTRACT

AIM

• To compare infusion of ephedrine and phenylephrine on hemodynamic stability after spinal anesthesia in elderly patients aged 60 years and above undergoing lower limb orthopedic surgeries.

BACKGROUND

- Patients aged 60 years and above undergoing lower limb orthopaedic surgeries commonly experience hypotension post spinal anesthesia
- To overcome this effect and to maintain hemodynamic stability prophylactic infusion of vasopressors like ephedrine and phenylephrine are given

METHODOLOGY

Preliminaries:

- Written informed consent was taken.
- Nil per oral status was confirmed.
- The patients were evaluated with a detailed history, general and systemic examinations in the preoperative room.
- The airway, cardiovascular system and respiratory system were examined. Patients were divided into three groups, GROUP P

(PHENYLEPHRINE), GROUP E (EPHEDRINE), and CONTROL GROUP.

INTRAOPERATIVE

- NIBP, electrocardiography, and pulse oximetry were applied to monitor PR, BP, and SpO2.
- Insertion of 18G IV cannula and infusion of Ringer lactate solution 15ml/kg was administered.
- The patients were positioned to sit. Using a 25 G Quincke spinal needle, a lumbar puncture was done at the L3–4 interface following skin disinfection and 2% lignocaine infiltration.
- Premedication was given with Inj. Midazolam 0.5mg to alleviate anxiety of the patients.
- The groups were administered intrathecally with Inj. BUPIVACAINE Heavy 15mg . Patients were turned to the supine position subsequently and Oxygen 5 L/min was delivered via a face mask.
- The sensory level of blockade after spinal anesthesia was assessed by ice cubes or pinprick 5 mins after intrathecal injection.
- GROUP P received a continuous infusion of 30ml 0.9% NaCl with 250 mcg phenylephrine for 30 mins after spinal anesthesia using a infusion syringe pump.
- GROUP E received a continuous infusion of 30ml 0.9% NaCl with 30 mg of ephedrine for 30 mins after spinal anesthesia using a infusion syringe pump.
- CONTROL GROUP were given an intravenous bolus of inj. mephentermine 6 mg after spinal anesthesia as and when required.

The infusion of treatment medication in Group P and Group E was started immediately after spinal anesthesia.

Non Invasive Blood pressure, heart rate, SpO2, ECG were monitored. Incidence of hypotension, bradycardia and the total dose of vasopressor used intraoperatively were noted.

15 minutes before the subarachnoid block and at intervals of 3, 6, 9, 12, 15, 20, 25, and 30 minutes following the subarachnoid block (spinal anesthesia) were used to record hemodynamic data.

PROTOCOL FOR RESCUE TREATMENT;

If SBP fall was greater than 30% from the baseline, bolus dose of Phenylephrine 50mcg/Ephedrine 5 mg was given according to the group.

If heart rate was less than 50 beats per min Inj. Atropine 0.6 mg I/V was given.

In case of hypertension the ongoing infusion was stopped .

RESULTS

- Age, sex , BMI and ASA Grades are comparable and are statistically insignificant.

- The SBP was significantly higher in Group E when compared to other groups at all time intervals after spinal anaesthesia.

- The DBP was significantly higher in Group E when compared to other groups at 3 mins, 6 mins, 9 mins, 12 mins, 15 mins and 25 mins time intervals after spinal anaesthesia

- The MAP was significantly higher in Group E when compared to other groups at 3 mins, 6 mins, 15 mins and 20 mins time intervals after spinal anaesthesia.

- The HR was significantly higher in Group E when compared to other groups and was significantly better at all time intervals after spinal anaesthesia.

- The rescue doses were observed to be statistically insignificant. The rescue doses required in Ephedrine group was less when compared to phenylephrine and control group.

- The number and percentage of Inj. ATROPINE given among all groups were observed to be statistically insignificant. The Inj. ATROPINE was required less in Ephedrine group compared to phenylephrine and control group.

CONCLUSION

The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were better maintained in the ephedrine group than phenylephrine and control group.

The mean arterial pressure (MAP) was significantly higher in all groups but was more effective in ephedrine group.

Heart rate was well maintained and prevention of bradycardia was effectively seen in ephedrine group compared to phenylephrine group.

KEYWORDS

Phenylephrine, Ephedrine, Mean Arterial Pressure, Systolic Blood Pressure, Heart rate

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INTRODUCTION

The elderly aged group people have reduced cardiovascular compensation mechanism which increases the frequency and severity of episodes of hypotension due to sympathetic blockade after subarachnoid block (spinal anaesthesia) significantly.

About one-fourth of surgery patients are elderly, and despite significant medical advancements, they still have chronic illnesses that call for specialized perioperative care.^[12]

In elderly patients, regional anesthesia—most often subarachnoid block, or SAB is favored over general anesthesia due to the potential for many complications and the potential for postoperative disturbance of mental functioning. Yet, the incidence of the related hypotension in the elderly has been estimated to be between 25 and 80%. ^[12]

Vasopressors are commonly used to correct this hypotension during intraoperative period to maintain organ perfusion.

This study was done with the aim to compare the efficacy of vasopressors phenylephrine and ephedrine in maintaining hemodynamic stability intraoperatively after spinal anesthesia in elderly patients who were undergoing lower limb orthopaedic procedures.

REASON FOR SELECTION OF THIS TOPIC

Hypotension is frequently observed after induction of spinal anesthesia in elderly patients undergoing lower limb orthopedic surgeries^[1]

It is due to reduction of cardiac output and systemic vascular resistance, which raises the possibility of myocardial ischemia. It also lowers middle cerebral artery velocity as a result of compromised cerebral autoregulation during the perioperative phase.^[2,18]

The elderly are more likely to have comorbid diseases, which increases their risk of hypoperfusion, which is brought on by hypotension, the primary risk factor for which is hypovolemia^{. [3, 4]}

As crystalloids are frequently ineffective in sustaining blood pressure, their administration can soon result in volume overload and congestive heart failure.^[2]</sup>

Vasopressors such as phenylephrine and ephedrine can be immediately infused into elderly people to prevent hemodynamic abnormalities following spinal anesthesia.^[5]

The alpha-adrenergic agonist phenylephrine is typically linked to reflex bradycardia^{.[6]} It raises blood pressure due to venoconstriction and arterial vasoconstriction. This increases venous tone and venous return (preload), as well as systemic vascular resistance.

Ephedrine is a mixed action (alpha and beta) adrenergic agonist which increases the cardiac output and prevents a decrease in heart rate as it leads to greater venoconstriction than arteriolar constriction and thus improves venous return (preload) and increases cardiac output, Blood pressure and heart rate.

AIMS AND OBJECTIVES

AIM:

• To compare infusion of ephedrine and phenylephrine on hemodynamic stability after spinal anesthesia in elderly patients aged 60 years and above undergoing lower limb orthopedic surgeries.

OBJECTIVES:

PRIMARY:

• To evaluate the effectiveness of prophylactic intravenous ephedrine or phenylephrine infusion on the prevention of hypotension and effect on heart rate in patients aged 60 years and above undergoing lower limb orthopedic surgeries.

SECONDARY:

• No. of rescue doses of ephedrine and phenylephrine given after spinal anesthesia.

REVIEW OF LITERATURE

- Zunic M et al, $2019^{[7]}$ conducted a prospective, randomized, double blind, placebo-controlled study in 2019 to determine the impact of an infusion of phenylephrine or ephedrine given just after spinal anesthesia (SA) on the hemodynamics of older orthopedic patients. The final analysis included 70 patients. After completion of the measurements, the Control (C) group experienced a substantial decrease in mean arterial pressure (MAP) compared to the baseline value. However, the Phenylephrine (P) and Ephedrine (E) groups experienced no significant changes in MAP. After SA, the cardiac index decreased in the control group, remained constant in the P group, and significantly increased in the E group. At the conclusion of the measures, there were significant differences between the C and E groups (p = 0.049) as well as between the P and E groups (p = 0.01).
- W. Mon et al, 2017 ^[8] conducted a randomized, double-blind study to assess the effects of phenylephrine or ephedrine infusions titrated to maintain baseline systolic blood pressure (bSBP) during spinal anesthesia in 40 patients. The results concluded that while both phenylephrine and ephedrine groups were able to achieve good systolic blood pressure, ephedrine increased cardiac output in comparison to phenylephrine. The study determined that phenylephrine was linked to a decrease in the mother's heart rate and cardiac output; however, umbilical cord gases remained higher in the phenylephrine group than in the ephedrine group. Despite maintaining uteroplacental perfusion and systolic blood pressure and cardiac output, ephedrine was linked to a mixed respiratory and metabolic acidosis in the fetus.

- Asokan A et al, $2021^{[9]}$ in a study of 50 patients who were randomized into two groups and of ephedrine and phenylephrine in a comparative study. Vital signs including blood pressure, heart rate, and oxygen saturation were monitored in all parturients for the initial five minutes of the procedure after spinal anesthesia. These vital parameters were then recorded every minute for the next five minutes of the procedure. Records were kept on the prevalence of bradycardia, hypotension, and the need for vasopressors (phenylephrine and ephedrine). To ascertain the newborn outcome, the Apgar score and a blood sample from the umbilical cord were obtained for blood gas analysis. Upon completion of the study, it was shown that the phenylephrine group consumed more vasopressors (92±112 µg) than the ephedrine group (4.8±5.5 mg), with a statistically significant difference.
- Abbasivash R et al,2016 conducted a randomized double-blind clinical trial on 92 patients aged between 40 and 70 years old, ASA class one and two under hip fracture surgery under spinal anesthesia in two groups of patients receiving ephedrine as the control group and phenylephrine as the experimental group. In MAP, systolic, and diastolic pressures, the frequency of hypotension was considerably reduced in the phenylephrine group 3, 6, and 9 minutes after spinal anesthesia. At different time of study there was no apparent differences in heart rate between the two groups. Lesser vasopressor use was observed in the phenylephrine group. The usage of atropine for nausea and vomiting did not significantly differ between the two groups.
- Sinha G et al, $2020^{[10]}$ conducted a study in which three groups(P, E, M) (n = 20) were randomly assigned to receive intravenous boluses of phenylephrine 100 mcg, ephedrine 6 mg, and mephentermine 6 mg, respectively, following hypotension in a prospective, double-blind, randomized controlled study involving 60 ASA physical status class II patients undergoing elective caesarean section under spinal anesthesia. The phenylephrine group experienced a decrease in mean heart rate subsequent

to vasopressor delivery. All three groups showed a similar overall trend (P = 0.1). The phenylephrine group had a greater prevalence of bradycardia (P = 0.003). It was determined that during the subarachnoid block for a cesarean delivery, the three vasopressors efficiently preserved arterial blood pressure. When compared to ephedrine and mephentermine, phenylephrine significantly lowered heart rate.

- Simin Atashkhoie et al, 2018 ^[11] in a randomized, double-blinded study, conducted on 90 pregnant women who underwent spinal anesthesia for an elective cesarean section. Prior to spinal anesthesia, either serum NaCl 0.9% (placebo group) or mixed ephedrine and phenylephrine (study group) were infused over a 15-minute period. Fetal blood gas and hemodynamic parameters were noted. The study group reported less bradycardia and hypotension after spinal anesthesia, according to the findings. Inotropes and vasopressors were required more frequently in the placebo group for treating hypotension, nausea, and vomiting. Study had shown that prophylactic low-dose infusions of phenylephrine and ephedrine prior to spinal anesthesia for cesarean sections reduce the incidence and severity of hypotension in mothers, reduce nausea and vomiting, reduce the requirement for antiemetic medication, and raise the Apgar score of neonates
- Saru singh et al, $2014^{[12]}$ conducted a randomized comparative study, in which 100 patients were randomly allocated to receive ephedrine 30 mg intramuscularly 10 mins before the administration conducted of spinal anaesthesia in Group I and preloading with 500 ml of polygeline 3.5% intravascularly over 10 mins prior to subarachnoid block in Group II. Patients in both groups were closely monitored for pulse rate, systolic blood pressure, hypotension, requirement of rescue therapy and adverse effects. It was concluded that the incidence of hypotension and requirement for rescue therapy was statistically less in Group I compared with Group II (P < 0.05). Heart rates were better maintained in Group I than Group II, with few hemodynamic adverse effects in both groups. Ephedrine 30 mg given

intramuscularly in elderly patients was more effective for the prevention of post-subarachnoid block hypotension.

- Fabrice Ferre et al, 2016^[13] conducted a prospective, randomized, doubleblind, and placebo-controlled study on 54 patients above 60 years of age who underwent elective lower limb procedures under spinal anesthesia were included in the study. Patients were randomly assigned to either the control group C (0.9% isotonic sodium chloride solution) or group P (100µg/mL phenylephrine solution at 1 mL/min after spinal anesthesia). Group P's MAP was better than Group C's. Group P had a higher percentage of patients without hypotension (cumulative survival) (P=.04). Prophylactic phenylephrine infusion was found to be an effective means to lessen spinalinduced hypotension in elderly patients. It reduces the number of hypotensive episodes in patients and delays the onset of hypotension when compared to control group.
- AB Filani et al, 2023 conducted a randomized, double-blind study on patients aged ≥ 65 years undergoing elective lower limb and urological surgeries under subarachnoid block concluded that 19 patients from each of the three groups (A, B, and C) constituting a total of 57 patients ,who were randomly allocated. Following the induction of spinal anesthesia, groups A, B, and C were administered phenylephrine infusions at rates of 50 µg/min, 75 µg/min, and 100 µg/min, respectively. In group A, phenylephrine reduced hypotension without causing any negative side effects. Lastly, they concluded that an infusion of 50 µg/min of phenylephrine prevented elderly individuals from experiencing spinal-induced hypotension without eliciting any of the known side effects, and that an infusion of 50 µg/min caused reactive hypertension.

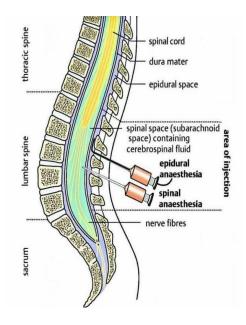
- **Das Neves et al** ¹⁴ in a randomized comparative study in 120 patients found that a prophylactic continuous infusion is better in lowering the risk of hypotension and adverse effects on both the mother and the fetus than a therapeutic phenylephrine bolus dosage.
- Mostafa et al, 2019 ^[15] in a randomized controlled trial of 62 patients , taken into consideration for the final analysis, with a mean age of 71 ± 6 years. Compared to the phenylephrine group, the norepinephrine group showed higher mean heart rate and cardiac output. Reactive Bradycardia was less common in the NE group than in the PE group. At the end, the study concluded that NE provided better hemodynamic stability than PE, stabilizing heart rate, cardiac output, reactive bradycardia, and hypertension.

CLINICAL ANATOMY

SPINAL ANAESTHESIA:

Spinal anaesthesia is a technique wherein a local anesthetic is administered into the subarachnoid space, temporarily inhibiting nerve impulse transmission.

Leonard Corning first used the term "spinal anesthesia" in 1885 to evaluate the influence of cocaine on neurological disorders. He administered a dog with cocaine injection that temporarily paralyzed its hind limbs. He then injected cocaine in a man to carry out a neuraxial block. The patient's legs felt fatigued after taking the second dose, while the first dose had no effect at all. The man had impaired sensibility in his lower extremities after about 20 minutes. Leonard did not describe the free flow of CSF in either scenario, but it is most likely that the man had an epidural and the dog received a spinal anesthesia.



In 1899, a German surgeon named August Bier achieved recognition for being the first to introduce spinal anesthesia. Professor Bier instructed Dr. Hildebrandt, his assistant, to puncture the lumbar region. However, due to dural puncture, Hildebrandt was unable to secure the syringe to the needle, causing a significant amount of spinal fluid to leak out. Hildebrandt volunteered to be the subject for a second try, and they were rewarded with success, even though they were intended to abandon on the study.

August Bier observed that a powerful blow to the tibia with an iron hammer did not cause pain 23 minutes after the spinal injection. After 25 minutes, pulling on a testicle and applying intense pressure were not painfull.

PHYSIOLOGICAL EFFECTS OF SPINAL ANESTHESIA

Autonomic blockade:

The efferent autonomic system with inhibition of neural transmission results in a greater degree of parasympathetic blockade than sympathetic blockade. The parasympathetic outflow is craniosacral, while the sympathetic outflow is thoracolumbar. Neuraxial anesthesia has no effect on the vagus nerve^[19]

Effects on Cardiovascular System:

The most important clinical side effects of sympathetic blockade during subarachnoid block are on the cardiovascular system. All at but the lowest levels of spinal blockade, vasodilation occurs. Vasodilation in the venous side is more marked than the arterial side of circulation which results in the pooling of blood in the venous capacitance vessels. This reduction is well tolerated at low levels of spinal anaesthesia in the circulating blood volume in healthy patients. With increasing level of subarachnoid block, this effect becomes more marked and the venous return becomes gravity dependent. Cardiac output and organ perfusion decline steeply if the venous return decreases too much.

By a modest (100-150 degrees) head down tilt or elevating the legs the venous return can be increased. The cardio-accelerator fibers that leave the spinal cord at T1 to T4 are inhibited at increasing levels of subarachnoid block. In addition to impairing one of the compensatory mechanisms available to maintain the organ perfusion during vasodilation, this is detrimental to patients who depend on higher sympathetic tone to maintain cardiac output (such as during hypovolemia and congestive heart failure).

If the spinal block level is not closely monitored or treated, the rate of cardiovascular compromise will accelerate. Although parasympathetic activity at the sinoatrial node still persists, sudden asystole may occur due to lack of sympathetic innervation.

Effects on respiratory system:

The changes in pulmonary function during neuraxial block are typically not significant in healthy individuals. The tidal volume remains unaltered even at high levels of spinal anesthesia. Since hemodynamic resuscitation commonly treats apnea, phrenic nerve block may not occur with total spinal anesthesia. This shows that brain stem hypoperfusion rather than phrenic nerve block is the cause of the problem.

Effects on Gastrointestinal System:

Predominant parasympathetic activity after neuraxial block causes gastrointestinal hyperperistalsis leading to nausea and vomiting. Hepatic blood flow decreases with reductions in mean arterial pressure from any anaesthetic technique^[19]

Theories of causation of hypotension:

Due to the decreased venous return to the heart and the absence of muscular propulsive forces on the venous system, the cardiac output is reduced.

- Paralysis of vasoconstrictor nerve fibres causes dilation of post arteriolar capillaries and small venules.

- Paralysis of sympathetic cardio-accelerator fibres(T1-T4) leading to subsequent fall in cardiac output and bradycardia.

- Paralysis of the splanchnic nerves, which supply the adrenal glands as sympathetic nerves, leading to a decrease in catecholamines.

- Absorption of the drug into the circulation is more common with extradural than intradural analgesia because of large volume of drugs administered.

- Ischaemia and hypoxia of vital organs.

- Hypovolemia if present may cause fall in blood pressure if central neuraxial blockade is attained.

- Compression of great vessels by tumors within the abdomen.

ADRENERGIC DRUGS

EPHEDRINE

It is an alkaloid which is obtained from Ephedra vulgaris. It is a mixed action ($\alpha+\beta$) sympathomimetic drug. It acts indirectly but also has direct action on alpha and beta receptors. The site of action is by exchange diffusion on the membrane noradrenaline (NA) pool.

PHENYLEHPRINE

It is a selective alpha-1 agonist which has very negligible action on beta receptors. It is a direct acting sympathomimetic agent. It is a non-catechol derivative which is not inactivated by COMT and has a longer duration of action compared to other catecholamines.

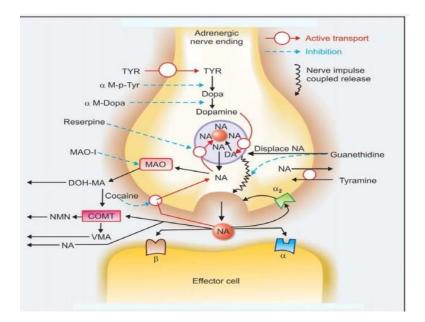


Fig 2.Schematic representation of adrenergic neurotransmission

This figure represents the adrenergic synaptic transmission in the central and peripheral nervous system and at the site of target tissues.

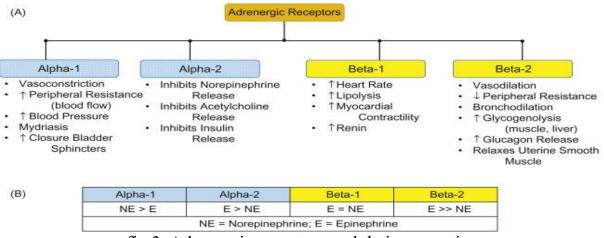
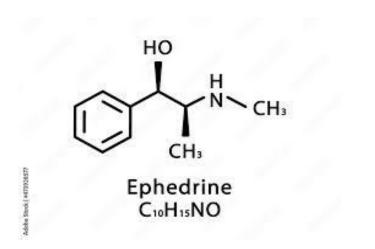
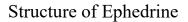


fig 3. Adrenergic receptors and their properties

PHARMACOLOGY OF EPHEDRINE





Pharmacokinetics:

It is absorbed through oral, I/V, I/M and subcutaneous route and its oral bio-availability is 85%. It is metabolised in liver by oxidative deamination. The onset of action through intravenous route(few seconds), intramuscular (10-20 minutes) and orally(15-60 minutes).

The duration of action through I/V and I/M is 60 minutes and orally is 2-4 hours which is longer than the catecholamines. The elimination half-life is 3-6 hours and excretion is through urine with high proportion of drug in unchanged form(22%- 99%).

Pharmacodynamics:

It is a direct and indirect sympathomimetic amine. As a direct effect, ephedrine activates the alpha and beta adrenergic receptors.it stimulates alpha-1 causing vasoconstriction and rise in BP. Beta-1 stimulation increases heart rate and force of myocardial contraction thus increasing cardiac output and stimulation of beta-2 adrenergic receptors causes vasodilation and brochodilation.

Uses:

- To treat significant hypotensive episodes post spinal anaesthesia.
- Bronchial asthma, nasal congestion, reversible airway obstruction.
- Nocturnal enuresis.
- Narcolepsy, CNS stimulation, myasthenia gravis.

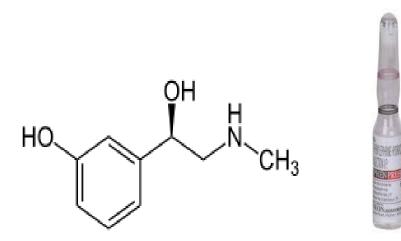
Side effects:

Dizziness, irritability, anxiety, arrhythmias, tachycardia, hypertension, stroke, heart attack, palpitations, restlessness, urinary disturbances.

Contraindications:

Parenteral administration is contraindicated in patients with high BP and ventricular tachycardia. Hyperthyroidism, bradycardia, partial heart block, myocardial disease or severe atherosclerosis, cardiac arrythmias and closed angle glaucoma.

PHARMACOLOGY OF PHENYLEPHRINE



Structure of phenylephrine

Pharmacokinetics:

Its onset is immediate through I/V and I/M (5-10 minutes).

The duration of action is 5-10 minutes(I/V), 1 hour (I/M).

It is metabolized in the gastrointestinal tract and liver by monoaminase oxidase. Bioavailability is 38% through GI tract and protein binding is 95%.

The elimination half life is 2-3.5 hours.

Pharmacodynamics:

On cardiovascular system it causes a rapid increase in systolic blood pressure and diastolic blood pressure due to an increase in systemic vascular resistance. It decreases the heart rate through baroreceptor response. It improves coronary perfusion and increases pulmonary artery pressure. It does not cause CNS stimulation.

It reduces gastrointestinal, renal, uterine, and cutaneous blood flow and can cause alterations in glucose metabolism.

Uses and Dosage:

- Hypotension secondary to neuraxial blockade or general anaesthesia.
- Therapeutic dose I/V bolus 50-200mcg, may be repeated I/M 2-5mg bolus.
- Intravenous continuous infusion as 1-10 mcg/kg/min solution, rate is titrated to effect.
- It is particularly used in patients with coronary heart disease and in patients with aortic stenosis because it increases coronary perfusion pressure with chronotropic side effects unlike other sympathomimetics.
- Mucosal decongestant (1% solution is directly administered intranasally because intense nasal vasoconstriction precludes significant systemic absorption.

Side effects:

Headache, anxiety, dizziness, insomnia, tremor, hallucinations, confusion, weakness, restlessness, drowsiness, bradycardia, hypertension, dysrhythmias, nausea and vomiting.

Contraindications:

Hypersensitivity, hypertension, hyperthyroidism, patients with MAO inhibitors.

When administered phenylephrine, patients on quinidine, tricyclic antidepressants, or cardiac glycosides are at greater risk to dysrhythmias.

MATERIALS AND METHODS

SOURCE OF DATA

This study was conducted in the Department of Anaesthesiology, "B.L.D.E (Deemed to be University) Shri. B.M. Patil Medical College Hospital and Research center, Vijayapura". Study was conducted from January 2023 to June 2024.

METHOD OF COLLECTION OF DATA:

Study Design: A randomized comparative study.

Study Period: 1.5 year study from January 2023 to June 2024

SAMPLE SIZE:

Using the G*Power ver. 3.1.9.4 program to calculate sample size, this study needs a total sample size of 174 (for each group of 58, assuming equal group sizes). The MAP(mmHg) for Control (Mean = 90, SD = 12), Phenylephrine (Mean = 85, SD = 12), and Ephedrine (Mean = 84, SD = 9). Therefore, in order to detect a difference in means (t tests - Means: Difference between two independent means (two groups)) with 80% power.

STATISTICAL ANALYSIS:

The data was entered into a Microsoft Excel document, and SPSS (Version 20) the statistical tool for the social sciences—was implemented to conduct the statistical analysis. The findings were displayed as graphs, counts and percentages, mean, and SD.

The independent sample t-test was used to compare the two groups for continuous variables in normally distributed data.

The Mann-Whitney U test was used for variables that were not normally distributed. To compare categorical variables between the two groups, Fisher's exact test or the Chi-square test were used.

The Kruskal-Wallis test was used for not normally distributed groups, and the ANOVA test was applied if there were more than two groups. It was considered statistically significant if p<0.05. All statistics were calculated two tailed.

STUDY POPULATION

This study was done on inpatients undergoing various elective lower limb orthopedic surgical procedures under spinal anesthesia.

INCLUSION CRITERIA:

- Age 60 years and above patients undergoing lower limb orthopedic surgeries.
- ASA Grade I and II

EXCLUSION CRITERIA:

- Infection at the site of injection.
- Uncontrolled hypovolemia.
- Allergy or hypersensitivity to vasoconstrictors.
- Increased intracranial pressure.
- Coagulopathy, sepsis, fixed Cardiac output states, neurological disease.
- Uncontrolled hypertension, hypothyroidism, uncontrolled diabetes, untreated or uncontrolled heart failure, phaeochromocytoma.
- Patients on MAO inhibitors, tricyclic antidepressants, phenothiazine compounds, recent MI, and recent CABG.

This study was started after CTRI Registration (Reg no: CTRI/2023/04/051451) and was carried out in the operation theatre complex of Shri B M Patil medical college hospital and research centre.

METHODOLOGY

PRELIMINARIES

- Written informed consent was taken.
- Nil per oral status was confirmed.

INVESTIGATIONS:

- Complete blood count, bleeding time, clotting time.
- Blood sugars, blood urea and serum creatinine.
- X-ray chest and 2D Echocardiography.
- Serology(HbsAg, HIV, HCV).

PRE-ANESTHETIC EVALUATION

Before taking the patient for surgery, detailed history of underlying medical illness, previous history of surgery, anesthetic exposure, and hospitalization was elicited. General and systemic examination was carried out. Airway, respiratory and cardiovascular system were assessed.

PHYSICAL EXAMINATION:

- The general condition of the patient
- Vital signs -heart rate, blood pressure, respiratory rate.
- Height and weight.
- Examination of the respiratory system, cardiovascular system, central nervous system, and vertebral system.
- Airway assessment by Mallampati grading.
- Patients were divided into three groups, GROUP P(PHENYLEPHRINE), GROUP E(EPHEDRINE), and CONTROL GROUP.

INTRAOPERATIVE:

• NIBP, electrocardiography, and pulse oximetry were applied to record baseline values of PR, BP, and SpO2.

- Insertion of 18G IV cannula and infusion of Ringer lactate solution 15ml/kg was administered.
- The patients were positioned in a sitting posture. Using a 25 G Quincke spinal needle, a lumbar puncture was done at the L3-4 or L4-L5 Interface following skin disinfection and 2% lignocaine infiltration.
- Premedication was given with Inj. Midazolam 0.5mg to alleviate anxiety of the patients.
- The groups were administered intrathecally with Inj. Bupivacaine Heavy 15mg. Subsequently, patients were turned to the supine position and Oxygen 5 L/min was delivered via a facial mask.
- The sensory blockade level of spinal anesthesia was assessed by ice cubes or pinprick 5 mins after intrathecal injection.
- GROUP P received a continuous infusion of 30ml 0.9% NaCl with 250 mcg phenylephrine for 30 mins immediately after spinal anesthesia using a infusion syringe pump.
- GROUP E received a continuous infusion of 30ml 0.9% NaCl with 30 mg of ephedrine for 30 mins immediately after spinal anesthesia using a infusion syringe pump.
- CONTROL GROUP received an intravenous bolus of Inj. mephentermine 6 mg after spinal anesthesia as and when required.

- The infusion of treatment medication in Group P and Group E was started immediately after spinal anesthesia.
- Non Invasive Blood pressure(NIBP), heart rate, and SpO2 were monitored . Incidence of hypotension, bradycardia and the total dose of vasopressor used intraoperatively were noted.
- Hemodynamic parameters were noted at 15 mins, 10 mins, 5 mins prior to the subarachnoid block and for 0 mins,3 mins, 6 mins, 9 mins,12 mins, 15 mins, 20 ins, 25 mins and 30 mins time intervals after the subarachnoid block (spinal anesthesia).

PROTOCOL FOR RESCUE TREATMENT:

- If SBP fall was greater than 30% from the baseline, intravenous bolus dose of Inj. Phenylephrine 50mcg/Inj. Ephedrine 5 mg was given.
- Inj. Atropine 0.6 mg I/V was administered as a supplement if the heart rate was less than 50 beats per minute.
- In case of hypertension the ongoing infusion was stopped .

OBSERVATION AND RESULTS

- The data collected from my study was listed in the Master Chart.
- The total sample size is 174 (58 in each group).

• Group 1 is Phenylephrine (P)group and group 2 is Ephedrine(E) group and Group 3 is Control Group(C).

• P value less than 0.05 is considered as statistically significant.

	GROUP P		GROUP E		CONTROL		KW TEST	P VALUE
AGE	MEAN	SD	MEAN	SD	MEAN	SD		
	64.13	3.68	64.2	4.23	63.81	4.9	1.4002	0.496

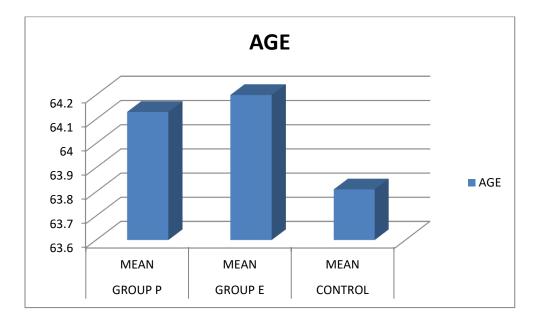


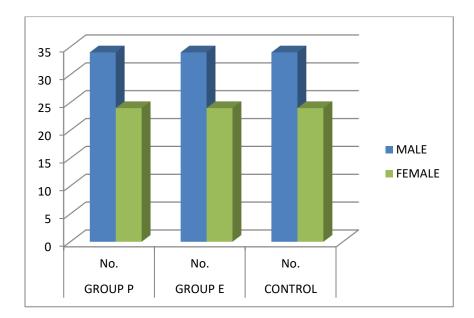
TABLE 1- DISTRIBUTION OF AGE

GRAPH 1- COMPARISION OF AGE DISTRIBUTION

Age (years) of patients in Group P, Group E and Control group were assessed using Kruskal-Wallis test. The groups were comparable with p value of 0.496 and it is statistically not significant.

	GRO	UP P	GROUP E		CONTROL		Chi2 test	p value
SEX	No.	%	No.	%	No.	%		
MALE	34	58.6	34	58.6	34	58.6		
FEMALE	24	41.4	24	41.4	24	41.4	0	1

 TABLE 2 – DISTRIBUTION OF SEX

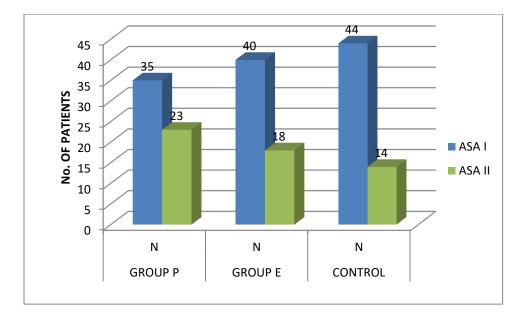


GRAPH 2- DISTRIBUTION OF SEX

Number of Male and Female patients have been compared among groups and evaluated using Chi Square test. The groups were comparable with a p value of 1 which is statistically not significant.

	GROUP P		GROUP E		CON	TROL	Chi2 test	p value
ASA	Ν	%	Ν	%	Ν	%		
ASA I	35	60.3	40	69	44	75.9	3.243	0.197
ASA II	23	39.7	18	31	14	24.1		

TABLE 3 – DISTRIBUTION OF ASA GRADES

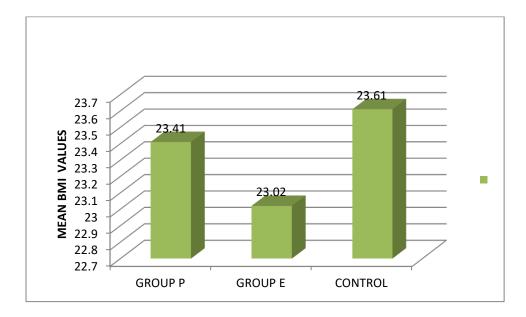


GRAPH 3 – COMPARISON OF ASA GRADES

Number of patients belonging to ASA grades I and II have been compared among all groups and evaluated using Chi Square test. The groups were comparable with a p value of 0.197 and it is statistically not significant.

	GRO	UP P	GRO	UP E CONT		TROL	KW Test	p value
	Mean	SD	Mean	SD	Mean	SD	2 6045	0 271
BMI	23.41	2.76	23.02	1.69	23.61	1.79	2.6045	0.271





GRAPH 4 – COMPARISON OF BODY MASS INDEX (BMI)

Body Mass Index(BMI) (kg/m^2) among three groups have been evaluated using Kruskal- Wallis test. The groups were comparable with a p value of 0.271 which is statistically not significant.

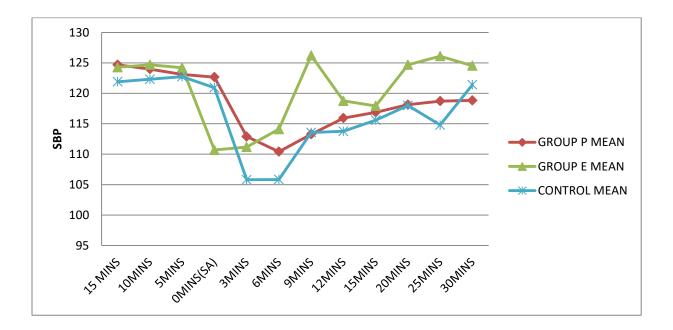
TABLE 5 -DISTRIBUTION OF SYSTOLIC BLOOD PRESSURE (SBP)BEFORE AND AFTER SPINAL ANAESTHESIA

CDD	GRO	UP P	GRO	UP E	CON	TROL		
SBP	MEAN	SD	MEAN	SD	MEAN	SD	KRUSKAL WALLIS TEST	P VALUE
15 MINS	124.69	6.484	124.28	9.218	121.9	8.522	2.909	0.233
10MINS	123.97	5.601	124.69	8.101	122.31	8.112	2.199	0.333
5MINS	123.1	5.659	124.21	9.266	122.72	8.015	0.906	0.636
OMINS(SA)	122.66	5.25	110.69	10.46	120.93	5.419	52.1	0.001*
3MINS	112.9	9.913	111.17	6.292	105.79	11.262	15.417	0.001*
6MINS	110.41	9.717	114.1	7.093	105.83	8.304	24.764	0.001*
9MINS	113.28	9.564	126.21	9.288	113.55	7.109	55.677	0.001*
12MINS	115.93	8.857	118.76	6.689	113.76	8.69	9.269	0.01*
15MINS	116.88	7.446	117.93	5.791	115.59	6.803	2.711	0.258
20MINS	118.14	6.763	124.69	8.23	118	7.293	25.588	0.001*
25MINS	118.72	5.944	126.1	9.002	114.79	8.41	41.998	0.001*
30MINS	118.83	6.269	124.52	9.302	121.41	7.521	12.025	0.002*

*Statistically significant at 5% level of significance (p<0.05)

The mean SBP among Group P, E and C were assessed using Krushkal – Wallis test. A significant p value was obtained[statistically significant data at 5% level of significance(p <0.05)] for mean SBP at 0 mins , 3 mins , 6 mins ,9 mins, 12 mins , 20 mins and 25 mins after spinal anaesthesia.

GRAPH 5- COMPARISON OF SYSTOLIC BLOOD PRESSURE (SBP) BEFORE AND AFTER SPINAL ANAESTHESIA



The mean SBP at different time intervals were plotted for each group . the mean SBP at induction(0 mins) of spinal anaesthesia was higher in Group P compared to Group E and Control group .The mean SBP was higher in Group E when compared to other groups at 6mins , 9 mins, 12 mins, 15 mins, 20 mins, 25 mins and 30 mins time intervals after spinal anaesthesia which was statistically significant.

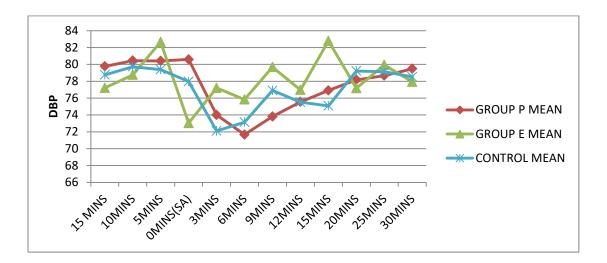
TABLE 6 – DISTRIBUTION OF DIASTOLIC BLOOD PRSSURE
(DBP) BEFORE AND AFTER SPINAL ANAESTHESIA

000	GRO	UP P	GRO	UP E	CON	TROL		DVALUE
DBP	MEAN	SD	MEAN	SD	MEAN	SD	KRUSKAL WALLIS TEST	P VALUE
15 MINS	79.76	4.036	77.21	5.681	78.76	6.244	7.054	0.029
10MINS	80.45	4.337	78.76	4.795	79.72	5.65	3.852	0.146
5MINS	80.41	4.538	82.66	6.932	79.38	6.147	5.72	0.057
OMINS(SA)	80.59	4.694	73.03	6.951	77.97	6.012	41.437	0.001*
3MINS	74	7.912	77.21	5.755	72.1	8.853	12.403	0.002*
6MINS	71.66	7.06	75.83	5.141	73.14	6.99	12.293	0.002*
9MINS	73.81	7.473	79.69	5.642	76.9	5.782	20.863	0.001*
12MINS	75.55	7.361	76.97	5.855	75.52	4.817	2.605	0.272
15MINS	76.9	7.314	82.79	7.659	75.07	5.831	33.183	0.001*
20MINS	78.17	5.497	77.17	5.67	79.21	5.415	5.482	0.065
25MINS	78.66	5.46	79.93	5.493	79.14	5.984	3.505	0.173
30MINS	79.48	5.513	77.93	4.709	78.52	6.07	1.159	0.56

*Statistically significant at 5% level of significance (p<0.05)

The mean DBP among Group P, Group E and Control group were assessed using Kruskal – Wallis test. A significant p value was obtained[statistically significant data at 5% level of significance(p <0.05)] for mean SBP at 5 mins before spinal anaesthesia and 0 mins , 3 mins , 6 mins , 9 mins and 15 mins after spinal anaesthesia.

GRAPH 6 – COMPARISON OF DIASTOLIC BLOOD PRESSURE (DBP) BEFORE AND AFTER SPINAL ANAESTHESIA



The mean DBP at different time intervals were plotted for each group . the mean DBP at induction(0 mins) of spinal anaesthesia was higher in Group P compared to Group E and Control group .The mean DBP was higher in Group E when compared to other groups at 3 mins, 6 mins, 9 mins, 12 mins, 15 mins and 25 mins time intervals after spinal anaesthesia which was statistically significant.

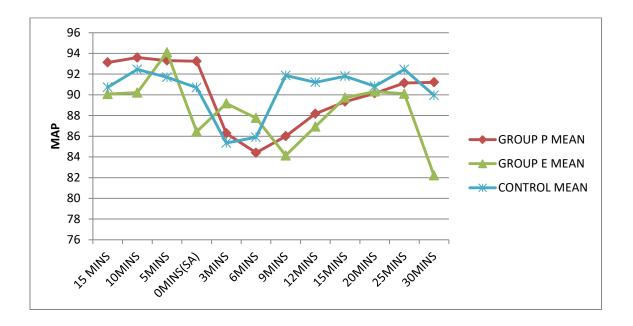
TABLE 7 – DISTRIBUTION OF MEAN ARTERIAL PRESSURE (MAP)BEFORE AND AFTER SPINAL ANAESTHESIA

	GRO	UP P	GRO	UP E	CON	TROL		
MAP	MEAN	SD	MEAN	SD	MEAN	SD	KRUSKAL WALLIS TEST	P VALUE
15 MINS	93.12	5.743	90.07	6.005	90.72	6.42	3.408	0.182
10MINS	93.59	5.641	90.21	5.991	92.45	5.299	9.851	0.007*
5MINS	93.31	5.462	94.1	7.421	91.69	6.222	1.815	0.404
OMINS(SA)	93.24	5.679	86.45	7.465	90.69	5.384	26.693	0.001*
3MINS	86.28	7.181	89.17	7.177	85.34	9.134	7.873	0.02*
6MINS	84.4	7.903	87.76	5.124	85.9	6.8	8.188	0.017*
9MINS	86	7.823	84.14	2.899	91.86	4.926	54.177	0.001*
12MINS	88.17	7.985	86.93	3.732	91.21	4.912	16.763	0.001*
15MINS	89.34	8.305	89.72	6.127	91.79	5.628	9.832	0.007*
20MINS	90.14	6.301	90.31	5.789	90.83	6.325	0.919	0.632
25MINS	91.14	5.206	90.1	6.011	92.45	5.299	5.533	0.063
30MINS	91.21	5.204	82.21	1.926	89.95	1.572	103.305	0.001*

*Statistically significant at 5% level of significance (p<0.05)

The mean MAP among Group P, Group E and Control group were assessed using Kruskal – Wallis test . A significant p value was obtained[statistically significant data at 5% level of significance(p <0.05)] for mean MAP at 10 mins before spinal anaesthesia and 0 mins , 3 mins , 6 mins , 9 mins , 12 mins, 15 mins and 30 mins after spinal anaesthesia.

GRAPH 7 – COMPARISON OF MEAN ARTERIAL PRESSURE (MAP) BEFORE AND AFTER SPINAL ANAESTHESIA



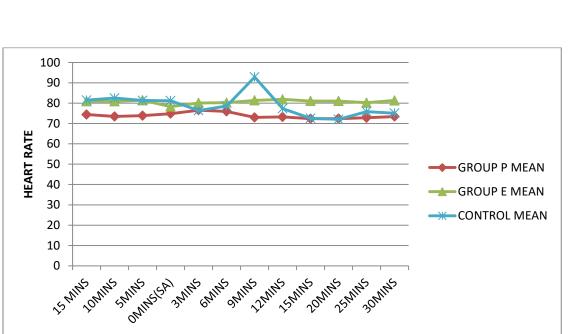
The mean of MAP at different time intervals were plotted for each group .The mean MAP was significant in all groups , but the mean MAP was higher in control group compared to other groups . The mean MAP was higher in ephedrine group compared to phenylephrine group at 3 mins, 6 mins, 15 mins and 20 mins time intervals after spinal anaesthesia which was statistically significant.

UD	GRO	UP P	GRO	UP E	CONTROL			P VALUE
HR	MEAN	SD	MEAN	SD	MEAN	SD	KRUSKAL WALLIS TEST	P VALUE
15 MINS	74.38	8.22	80.86	8.662	81.47	2.879	24.478	0.001*
10MINS	73.45	7.972	80.91	8.585	82.48	2.767	38.165	0.001*
5MINS	73.83	7.798	81.38	8.452	81.29	3.089	34.734	0.001*
OMINS(SA)	74.81	8.159	78.29	8.335	81.19	2.941	28.046	0.001*
3MINS	76.53	10.715	80.1	9.576	76.36	11.105	8.722	0.013*
6MINS	75.93	12.304	80.22	9.793	78.6	9.568	8.511	0.014*
9MINS	72.97	10.364	81.33	8.696	92.84	10.917	68.697	0.001*
12MINS	73.22	9.557	81.86	7.316	77.29	9.722	27.209	0.001*
15MINS	72.33	8.062	81.03	8.572	72.52	8.392	33.083	0.001*
20MINS	72.36	7.873	81.02	8.853	72.02	6.995	35.586	0.001*
25MINS	72.79	6.826	80.22	8.107	75.83	6.261	23.058	0.001*
30MINS	73.38	6.693	81.31	8.876	75.03	7.958	24.668	0.001*

TABLE 8 – DISTRIBUTION OF HEART RATE (HR) BEFORE ANDAFTER SPINAL ANAESTHESIA

*Statistically significant at 5% level of significance (p<0.05)

The mean heart rate (HR) among Group P, Group E and Control group were assessed using Kruskal – Wallis test. A significant p value of <0.014 was obtained [statistically significant data at 5% level of significance (p <0.05)] for mean HR at all time intervals before and after spinal anaesthesia.



GRAPH 8 – COMPARISON OF HEART RATE (HR) BEFORE AND AFTER SPINAL ANAESTHESIA

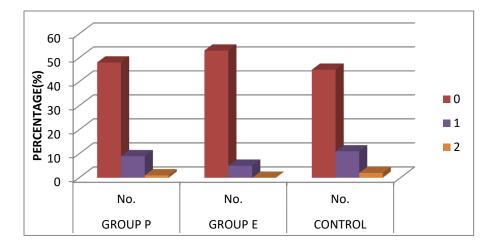
The mean HR at different time intervals were plotted for each group .The mean HR was higher in Group E when compared to other groups and was statistically significant at 3 mins, 6 mins, 12 mins, 15 mins, 20 mins, 25 mins and 30 mins of time intervals after spinal anaesthesia.

TABLE 9 – NO. AND PERCENTAGE OF RESCUE DOSES GIVEN IN ALLGROUPS

		UP P	GROUP E		CONTROL			P VALUE
ESCUE DOSE	No.	%	No.	%	No.	%	CHI SQUARE TEST	P VALUE
0	48	82.80%	53	91.40%	45	77.60%		
1	9	15.50%	5	8.60%	11	19.00%	4.911	0.297
2	1	1.70%	0	0.00%	2	3.40%		

The number and percentage of rescue doses of vasopressors given among all groups were assessed using Chi square test. A p value of 0.297 was calculated and observed to be statistically insignificant.

GRAPH 9- COMPARISON OF NUMBER AND PERCENTAGE OF RESCUE DOSES GIVEN IN ALL GROUPS



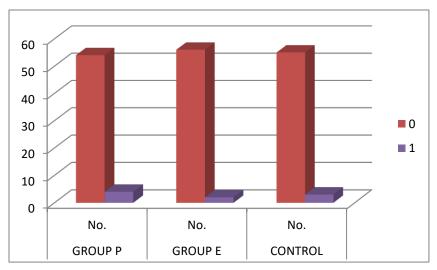
The number and percentage of rescue doses of vasopressors given among all groups were represented graphically and it was observed to be statistically insignificant. The rescue doses required in Ephedrine group was less when compared to phenylephrine and control group.

TABLE 10 – NO. AND PERCENTAGE OF ATROPINE DOSES GIVENALL GROUPS

	GRO	UP P	GRO	UP E	CON	TROL			
ATROPINE	No.	%	No.	%	No.	%	CHI SQUARE TEST	P VALUE	
0	54	93.10%	56	96.60%	55	94.80%	0 702	0.704	
1	4	6.90%	2	3.40%	3	5.20%	0.703		

The number and percentage of Inj. ATROPINE given among all groups were assessed using Chi square test. A p value of 0.704 was calculated and observed to be statistically insignificant.





The number and percentage of Inj. ATROPINE given among all groups were represented graphically and it was observed to be statistically insignificant. The Inj. ATROPINE required to treat bradycardia was less in Ephedrine group compared to phenylephrine and control group.

DISCUSSION

Hypotension is frequently observed after spinal block in elderly patients¹as they have reduced cardiovascular compensation mechanism which increases the frequency and severity of episodes of hypotension due to sympathetic blockade. It increases the risk of myocardial ischemia during the perioperative period and is triggered by a reduction in cardiac output and systemic vascular resistance^{.[2]}

Elderly patients who have a high incidence of coexisting illnesses are at high risk of hypoperfusion, which is due to hypotension, whose primary risk factor is hypovolemia ^{.[3,4]} Hypotension has an incidence of 25-80% in the old age patients. Even with brief episodes of uncorrected hypotension, elderly patients are more vulnerable to long-term consequences due to decreased physiologic reserve and a higher incidence of systemic disease, particularly cardiovascular disease ^[16,17]

Elderly patients with untreated subarachnoid block have lower systolic blood pressure, systemic vascular resistance, and central venous pressure ⁽¹⁶⁾. Restoring preload to the heart during spinal block should be accomplished by administering sufficient intravenous fluids (8–10 ml/kg). Adequate preloading prevents decrease in cardiac output and unexpected cardiac arrests but excessive fluid administration can lead to fluid overload and urinary retention. A vasopressor should be administered if the systolic blood pressure declines by more than 25%–30% of baseline or to less than 90 mmHg.

Since vasopressors are known to cause vasoconstriction by increasing systemic vascular resistance eventually to prevent spinal induced hypotension (SIH), they are a better choice to maintain haemodynamics in the elderly patients.

As per the observed results from our study, Phenylephrine 250 mcg/30ml and Ephedrine 30mg/30ml, both were effective in maintaining hemodynamic stability after subarachnoid block. The systolic blood pressure was maintained in GROUP E> GROUP P>CONTROL groups following induction of spinal block. The attenuation of SBP due to sympathetic blockade was more pronounced within the initial 15 mins after spinal anesthesia, which was well optimized by the ephedrine group compared to phenylephrine and control groups.

The diastolic blood pressure(DBP) was observed to be maintained in GROUP E>GROUP P>CONTROL groups. The mean arterial pressure (MAP) was observed to be almost equally maintained in all groups (GROUP P=GROUP E=CONTROL), however the initial drop in MAP after spinal block was better optimized in Ephedrine group.

The heart rate was observed to be effectively maintained in GROUP E> CONTROL GROUP> GROUP P. 4 patients in 58 samples of phenylephrine group were treated with Inj. Atropine 0.6mg intravenously in response to bradycardia , whereas in Ephedrine group only 2 patients had bradycardia. The rescue doses (phenylephrine 50mcg/ephedrine 5mg) to maintain SBP after fall of more than 30% below baseline, was more required in phenylephrine group compared to ephedrine group.

Zunic M et al⁷ conducted a study on the influence of ephedrine or phenylephrine infusion administered immediately after spinal anesthesia (SA) on hemodynamics in elderly orthopedic patients. It was observed that cardiac index, mean arterial pressure and heart rate was better in ephedrine group than phenylephrine and control groups. In present study it was observed that systolic blood pressure, mean arterial pressure and heart rate was more effectively maintained in ephedrine group compared to other groups.

W. Mon et al ⁸ conducted a study to evaluate cardiac output (CO) changes with phenylephrine or ephedrine infusions titrated to maintain baseline systolic blood pressure (bSBP) during spinal anesthesia in 40 parturients and found that ephedrine increased cardiac output compared to phenylephrine and found that phenylephrine was associated with a higher decrease in the maternal heart rate and cardiac output, although the umbilical cord gases were still better than those of the ephedrine group. Despite maintaining vital parameters, ephedrine was associated with a mixed respiratory and metabolic acidosis in the fetus. In present study , phenylephrine was associated with higher incidence of bradycardia and decrease in systolic blood pressure.

Asokan A et al⁹ conducted study in 50 parturients and concluded that the vasopressor consumption was more in phenylephrine group compared to ephedrine group and ephedrine 6 mg and phenylephrine 100 μ g did not differ in their efficacy to manage hypotension during spinal anaesthesia for caesarean delivery and maternal bradycardia was more in the phenylephrine group with equal incidence of fetal acidosis in the study groups

Sinha G et al. in a study observed that the mean heart rate was lower in phenylephrine group. There was higher incidence of bradycardia in the phenylephrine group. It was found that during the subarachnoid block for a cesarean section, the three vasopressors efficiently controlled arterial blood pressure. The heart rate was substantially reduced by phenylephrine as compared to ephedrine and mephentermine.

CONCLUSION

In present study, prophylactic infusion of ephedrine was found to be better vasopressor agent compared to phenylephrine in maintaining hemodynamic stability.

The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were better maintained in the ephedrine group than phenylephrine and control groups.

The mean arterial pressure (MAP) was maintained in all groups but was well maintained in ephedrine group.

Maintenance of heart rate and prevention of bradycardia was effectively seen in ephedrine group compared to phenylephrine group.

Hence, it is concluded that perioperative use of ephedrine as a low dose prophylactic infusion can be used to maintain vital parameters effectively in elderly patients posted for lower limb orthopaedic surgeries under subarachnoid block(SA).

SUMMARY

"A COMPARATIVE STUDY OF INFUSION OF EPHEDRINE AND PHENYLEPHRINE ON HEMODYNAMIC STABILITY AFTER SPINAL ANESTHESIA IN ELDERLY PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERIES".

This study was carried out on 174 patients undergoing Surgery under Spinal Anaesthesia in B.L.D.E(Deemed to be University), Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura.

Group P received continuous intravenous infusion of phenylephrine 250mcg in 30 ml normal saline, Group E received continuous intravenous infusion of Ephedrine 30mg in 30 ml normal saline and Control Group received intravenous bolus of inj mephentermine as and when required.

The SBP, DBP, MAP and HR were more effectively maintained in ephedrine group compared to phenylephrine and control groups.

The requirement of rescues doses and Inj. Atropine to treat bradycardia were insignificant and less in ephedrine group compared to other groups.

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SAMPLE INFORMED CONSENT FORM

B.L.D.E(DEEMED TO BE UNIVERSITY) SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA – 586103, KARNATAKA

<u>TITLE OF THE PROJECT</u> : A COMPARATIVE STUDY OF INFUSION OF EPHEDRINE AND PHENYLEPHRINE ON HEMODYNAMIC STABILITY AFTER SPINAL ANESTHESIA IN ELDERLY PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERIES

PRINCIPAL INVESTIGATOR :

Dr. SYED SUFIAN IBRAHIM

Department of Anaesthesiology

B.L.D.E (DEEMED TO BE UNIVERSITY)

Shri. B.M. Patil Medical College and Research Centre, Solapur Road, VIJAYAPURA-03

PG GUIDE :

Dr. BASAVARAJ PATIL

ASSOCIATE PROFESSOR

Department of Anaesthesiology

B.L.D.E (DEEMED TO BE UNIVERSITY)

Shri B.M. MPatil Medical College and Research Centre, Sholapur Road, VIJAYAPURA-03

PURPOSE OF RESEARCH

I have been informed that, this study is "A COMPARATIVE STUDY OF INFUSION OF EPHEDRINE AND PHENYLEPHRINE ON HEMODYNAMIC STABILITY AFTER SPINAL ANESTHESIA IN ELDERLY PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERIES". I have been explained about the reason for conducting this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

PROCEDURE

I understand that I will be participating in the study "A COMPARATIVE STUDY OF INFUSION OF EPHEDRINE AND PHENYLEPHRINE ON HEMODYNAMIC STABILITY AFTER SPINAL ANESTHESIA IN ELDERLY PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERIES"

RISKS AND DISCOMFORTS

I understand that I/my ward may experience complications during the study and I understand that necessary measures will be taken to reduce complications as and when they arise.

BENEFITS

I understand that I/my wards participation in this study will help in finding out, "A COMPARATIVE STUDY OF INFUSION OF EPHEDRINE AND PHENYLEPHRINE ON HEMODYNAMIC STABILITY AFTER SPINAL ANESTHESIA IN ELDERLY PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERIES".

CONFIDENTIALITY

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital.

Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number.

The code key connecting name to numbers will be kept in a separate secure location. If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission.

I understand that I may see the photograph and video tapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION

I understand that I may ask more questions about the study at any time.

Dr. SYED SUFIAN IBRAHIM is available to answer my questions or concerns.

I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

And that a copy of this consent form will be given to me for keep for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. SYED SUFIAN IBRAHIM will terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to ______,

the purpose of this research, the procedures required and the possible

risks and benefits, to the best of my ability in patient's own language.

Date:

DR. BASAVARAJ PATIL

DR. SYED SUFIAN IBRAHIM

(Guide)

(Investigator)

STUDY SUBJECT CONSENT STATEMENT

I confirm that DR. SYED SUFIAN IBRAHIM has explained to me

the purpose of this research, the study procedure that I will undergo and

possible discomforts and benefits that I may experience, in my own

language.

I have been explained all the above in detail in my own language and I

understand the same. Therefore I agree to give my consent to participate

as a subject in this research project.

Date_____

(Participant)

Date_____

(Witness to above signature)

PROFORMA

PATIENT DETAILS:

Name: Age: Sex: Address: Height: Weight: BMI: Ward: Diagnosis: Surgical procedure: Past history: Date: IP No.:

General physical examination:

Pallor	

Icterus

Cyanosis

Clubbing

Lymphadenopathy

Edema

Mallampati Grade

Vital parameters:

Pulse

Blood pressure

Respiratory rate

Temperature

Systemic Examination:

CVS

RS

CNS

PA

Investigations:

Haemoglobin:

TLC:

Platelet count:

Urine routine:

HIV:

HbsAg:

ASA grade:

Group allotted by randomization:

Parameters:

Demographic DATA and hemodynamic measurements	Phenylephrine(P)	Ephedrine(E)	Control (C)
No. of Patients			
Gender(M/F)			
Age			
Systolic Blood Pressure(SBP)			
Diastolic Blood Pressure (DBP)			
Mean Arterial Pressure(MAP)			
Heart rate (HR)			

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	20 min					
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	30 min					
Ephedrine(E)	15					
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GROUPS	RESCUE DOSES FOR (Phenylepherine 50mcg/ Ephedrine 5mg/ mephentermine 6mg bolus)	TOTAL
PHENYLEPHRINE		
EPHEDRINE		
CONTROL		

BIO-DATA OF THE GUIDE

Guide Name :	Dr. Basavaraj Patil
Date of Birth:	22/07/1982
Education:	MBBS, MD (MP SHAH Medical College, Jamnagar,
	Gujarat)
Designation:	Associate Professor
	Department of Anaesthesiology
Teaching:	UG Teaching- 13Years
	PGTeaching-10 Years
Address:	Associate Professor
	Department of Anaesthesiology
	B.L.D.E (Deemed to be University)
	Shri B.M. Patil Medical College Hospital and
	Research Center, Vijayapura-586103, Karnataka
	(08352)262770
	Ext 2052, 08352-263266(R)
	Ph-7829655342.
	Email id- drbnp2000@gmail.com.

BIO DATA OF INVESTIGATOR

Name:	Dr. SYED SUFIAN IBRAHIM
Date of Birth:	17-09-1995
Qualification:	M.B.B.S (2013-2019)
	Khaja Banda Nawaz
	Institute of Medical Scienes
	Kalaburagi.
KMC Reg.No:	131955
Address:	Department of Anaesthesiology
	B.L.D.E (Deemed to be University)
	Shri B.M. Patil Medical College
	Hospital and Research Center,
	Vijayapura-586 103 , Karnataka.
	Ph: 8722564874
	Email:syedsufiyaan.95@gmail.com





BLDE (DEEMED TO BE UNIVERSITY) Declared as Deemed to be University u/s 3 of UGC Act, 1956 Accredited with 'A' Grade by NAAC (Cycle-2) The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA BLDE (DU)/IEC/ 787/2022-23 30/8/2022

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on Friday, 26th August, 2022 at 3.30 p.m. in the Department of Pharmacology scrutinizes the Synopsis of Post Graduate Student of BLDE (DU)'s Shri B.M.Patil Medical College Hospital & Research Centre from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "A comparative study of infusion of Ephedrine and phenylephrine on Hemodynamic stability after spinal Anesthesia in elderly patients undergoing Lower limb orthopaedic surgeries".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: Dr.Syed Sufian Ibrahim

NAME OF THE GUIDE: Dr.Basavaraj Patil, Dept. of Anaesthesiology

Dr.Akram A Naikwadi Member Scoretary

Dr. Santoshkumar Jeevangi Chairperson IEC, BLDE (DU), VILAYAPHEA,

titutional Ethical Committee,

BLDE (DU). MEMBER SECRETARY titutional Ethical Committee Institutional Ethics Committee DE (Deemed to be University) DE Follovijagaperaments were placed before Ethical Committee for ScrutiRichtEn (Deemed to be University)

Vijayapura-586103. Karnataka

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India. aramma Sajjan Campus, D. H. Holau (Sholapur Road), Vijayapura - 586103, Karnataka BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principa!@bldedu.ac.in

MASTER CHART – GROUP P(PHENYLEPHRINE)

INO PATIENT NAME	<i>N</i> Œ	SEX	HEIGHT	WEIGHT	BMI ASA GRADE	X			SYSTOI	UC BP(mr	mhg)											DIASTI	DUC BP(1	nmhg)										N	VEAN AR	TERIAL P	RESSURE	E											HEART	RATE									ECG	Sp02	RES	ICUE DOSES	ATRI
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MASTER CHART GROUP E(EPHEDRINE)

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