

**EFFECTIVENESS OF EPHEDRINE USED IN PERIOPERATIVE MANAGEMENT OF
SPINAL ANAESTHESIA INDUCED HYPOTENSION DURING LOWER LIMB
ORTHOPAEDIC SURGERY**

BY

Dr. Ngugi Peter Kariuki

**A dissertation presented in part fulfillment of the requirements for the award of the degree
of Master of Medicine in Anaesthesia of the University of Nairobi**

2017

PRINCIPAL INVESTIGATOR:

Dr. Ngugi Peter Kariuki

M.B.Ch.B (KIU)

Postgraduate Student, Department of Anaesthesia

University of Nairobi.

SUPERVISORS:

Dr. Patrick O.R. Olang'

M.B.Ch.B, MMed (Anaesthesia) (UoN) Fell Paeds&Obs Anaesth, Cert Res UoN

Senior Lecturer, Department of Anaesthesia

University of Nairobi.

Dr. Thomas M. Chokwe

BSc (Anat), M.B.Ch.B, MMed (Anaesthesia) (UoN)

Senior Lecturer, Department of Anaesthesia

University of Nairobi.

DECLARATION

This dissertation is my original work and to my knowledge has not been submitted for examination or Award of a Degree in any other University.

Dr. Ngugi Peter Kariuki

Signature

Date

This dissertation has been submitted with our approval as University Supervisors.

Dr. Patrick O. R. Olang'

Signature

Date

Dr. Thomas M. Chokwe

Signature

Date

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to

- My supervisors, Dr. Patrick O.R. Olang' and Dr Thomas M. Chokwe for their guidance and supervision when carrying out this study.
- To my lecturers colleagues and friends in the department of Anesthesia for their constant encouragement and input in writing this dissertation
- Mr. Philip Ayieko for his input in data management and analysis
- Mr. Martin Njenga for his assistance in data collection
- To my family for their patience, support and prayers throughout this period
- KNH/UON Ethics and Research Committee for giving me the approval to carry out the study

TABLE OF CONTENTS

PRINCIPAL INVESTIGATOR:	ii
DECLARATION	iii
ACKNOWLEDGEMENTS	iv
ABSTRACT.....	xi
CHAPTER ONE: INTRODUCTION.....	1
CHAPTER TWO: LITERATURE REVIEW	2
Complications of spinal anaesthesia	3
Spinal-induced Hypotension (SIH).....	3
Management of spinal-induced hypotension	4
Ephedrine	5
Contraindications to spinal anaesthesia	10
Study justification and rationale	11
Study question.....	13
Hypothesis.....	13
Study objectives	14
Broad objective	14
Specific objectives	14
CHAPTER THREE: MATERIALS AND METHODS	15
Study Design.....	15
Study Area	15
Study Population.....	15
Eligibility Criteria	15
Sample size determination	16
Sampling Procedure:	16
Data collection	17
Data management.....	18
Data analysis	19
Ethical Considerations	19

CHAPTER FOUR: RESULTS	20
Demographic characteristics	20
Block height	22
Prophylactic ephedrine dose	23
Perioperative haemodynamics	24
Baseline haemodynamics	24
Incidence of hypotension	27
Rescue therapy for post spinal hypotension.....	29
Perioperative fluid therapy and blood loss.....	30
Duration of surgery	31
Adverse effects of ephedrine	32
CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS.....	33
DISCUSSION	33
Ephedrine administration	33
Dermatomal sensory block height	34
Perioperative blood pressure and heart rates trends.....	34
Incidence of hypotension	34
Rescue vasopressors requirements.....	35
Adverse effects of ephedrine	35
Overall outcome.....	36
CONCLUSIONS.....	37
RECOMMENDATIONS	38
Study limitations	39
References	40
APPENDICES	43
Appendix 1: Data collection tool	43
Appendix ii: The informed consent for the patient.....	45
Appendix iii: Consent for the anaesthetist	51
Appendix iv: Antiplagiarism certificate.....	54
Appendix v: Ethical approval letter	55

LIST OF TABLES

Table1: Demographic characteristics stratified by administration of ephedrine prophylaxis	20
Table2: Frequency of Ephedrine doses used for prophylaxis	23
Table 3: Mean baseline haemodynamics in patients undergoing spinal anaesthesia for lower limb surgery.....	24
Table 4: Total number of patients in each group who developed hypotension	27
Table 5: Number of patients with clinically significant hypotension	27
Table 6: Rescue vasopressors requirement	29
Table7: Average amounts of fluids used peri-operatively and the estimated blood loss.....	30
Table 8: Duration of surgery in minutes	31

LIST OF FIGURES

Figure 1: Bar graph showing age distribution.....	21
Figure 2: Sensory level of spinal anaesthesia	22
Figure 3: Average perioperative systolic blood pressures	25
Figure 4: Average mean arterial pressure during the perioperative period	26
Figure 5: Mean heart rate during the perioperative period	26
Figure 6: Perioperative prevalence of hypotension in lower limb surgery patients receiving spinal anaesthesia	28
Figure 7: Correlation between duration of surgery and fluid treatment	32

LIST OF ABBREVIATIONS

ASA- American Society of Anaesthesiologists

BP-Blood Pressure

SBP-Systolic Blood Pressure

DBP- Diastolic Blood Pressure

MAP-Mean Arterial Pressure

IV-Intravenous

IM –Intramuscular

SC- Subcutaneous

SAB- Sub arachnoid blockade

PRN- Pro re nata (as need arises)

KNH- Kenyatta National Hospital

RL- Ringers Lactate

NS- Normal Saline

WHO- World Health Organization

Important definitions

1. American Society of Anesthesiologists Physical Status Classification

ASA 1	Healthy patient without organic, biochemical, or psychiatric disease
ASA 2	Mild to moderate systemic disease that is well controlled and causes no organ dysfunction or functional limitation
ASA 3	Significant or severe systemic disease that limits normal activity
ASA 4	Severe disease that is a constant threat to life or requires intensive therapy
ASA 5	Moribund patient who is equally likely to die in the next 24 hours with or without surgery
ASA 6	Brain-dead organ donor

- 2. Emergency management.** Treatment of any life threatening condition arising during the duration of anaesthesia and requiring immediate treatment. The condition may arise from anaesthesia, surgery or both.

ABSTRACT

Background: Hypotension is the commonest adverse effect that is encountered after spinal anaesthesia. It is usually an exaggeration of the physiological effects of the spinal blockade. The sympathectomy that occurs after the spinal blockade is responsible for the hypotension and bradycardia which, if not adequately managed, leads to organ hypoperfusion; and if severe, to multiple organ failure and death.

Objective: Our objective was to assess the effectiveness of ephedrine used prophylactically or interventionally in the perioperative management of spinal-induced hypotension among ASA I and ASA II patients undergoing elective lower limb orthopaedic surgery at The Kenyatta National Hospital.

Methodology: This was a comparative observational study in which consenting ASA I and ASA II adult patients undergoing orthopaedic surgery under spinal anaesthesia were conveniently sampled. Data was collected by observing the perioperative ephedrine use by the anaesthetists and also the perioperative changes in blood pressure and heart rate and the management of spinal induced hypotension when it occurred.

Results: Overall incidence of hypotension was 50%. The cumulative incidence of post spinal hypotension was lower in the prophylaxis group 46.2% as compared to the no prophylaxis group 53.8%. The requirement for rescue vasopressors was also higher in the no prophylaxis group 32.1% as compared to the prophylaxis group 23.1%. These differences were however not statistically significant. Hypertension and tachycardia occurred in 3% and 9.2% of patients respectively who received prophylactic ephedrine.

Conclusion: There was no statistically significant reduction in the incidence of post spinal hypotension or the requirement for rescue vasopressors following administration of prophylactic intramuscular ephedrine. Ephedrine is a safe drug and anaesthetists should continue to use either of the regimens safely.

CHAPTER ONE: INTRODUCTION

Spinal anaesthesia is a mode of anaesthesia that is achieved by administering an anaesthetic agent into the subarachnoid space. Dural puncture was first described by Essex Wynter in 1891 followed shortly by Heirich Quincke 6 months later. Augustus Karl Gustav Bier, a surgeon, successfully used cocaine intrathecally on six patients for lower extremity surgery in 1898. Arthur Barker, a professor of surgery at the University of London reported on the advancement of spinal techniques in 1907, including the use of a hyperbaric spinal local anaesthetic; with emphasis on sterility and ease of midline over paramedian dural puncture techniques. Advancement of sterility and the investigation of hypotension after injection helped make spinal anaesthesia safer and more popular. ⁽¹⁾

In KNH, spinal anaesthesia is a preferred mode of anaesthesia among majority of the anaesthetists for patients presenting for lower limb orthopaedic surgery due to its numerous advantages as compared with general anaesthesia. These benefits include avoidance of airway manipulation, reduced blood loss and better pain control.

Subarachnoid local anaesthetics effect their sensory block at the spinal cord which is continuous cephalad with the brainstem through foramen magnum and terminates distally in the conus medullaris. ⁽²⁾

Cardiovascular side effects, principally hypotension and bradycardia, are arguably the most important and most common physiologic changes during spinal anesthesia. ⁽³⁾ Spinal induced hypotension is a decrease in systolic blood pressure to less than 80% of the baseline or in absolute terms a decrease in systolic blood pressure to 90-100 mmHg. ⁽¹⁹⁾.

Several strategies are available for the management of spinal induced hypotension. These include fluid loading, positioning and use of vasopressors. Of the vasopressors used for management of post spinal hypotension, ephedrine is the most commonly used because it's cheap and readily available. Ephedrine can be administered either prophylactically or interventionally. In KNH these two regimens are equally used by anaesthesia providers but there is no information on which is more superior to the other.

The purpose of the study was to compare the effectiveness of the two regimens of ephedrine use in the perioperative management of spinal induced hypotension during lower limb orthopaedic surgery.

CHAPTER TWO: LITERATURE REVIEW

Physiological effects of spinal anaesthesia

Following intrathecal administration, the local anaesthetic is found in all sites between the spinal rootlets and the interior of the spinal cord. The spinal rootlets are the principal site of neural blockade ⁽³⁾

a) **Differential nerve block**; nerve fibres subserving different functions display varying sensitivity to local anaesthetic blockade, sympathetic nerve fibres appear to be blocked by the lowest concentration of local anaesthetic followed in order by fibres responsible for pain, touch and motor function. Spinal anaesthesia also produces sedation, potentiates the effect of sedative hypnotics and markedly decreases minimum alveolar concentration of volatile anaesthetics ⁽²⁾

b) **Cardiovascular physiology**; mainly brought about by blockade of sympathetic efferents. Principle effects are bradycardia and hypotension.

c) **Respiratory physiology**; spinal anaesthesia to mid-thoracic levels has little effect on pulmonary function in patients without pre-existing lung disease. The ventilatory response to hypercapnoea is actually increased by spinal anaesthesia. High blocks associated with abdominal and intercostal muscle paralysis can impair ventilatory functions requiring active exhalation.

c) **Gastrointestinal physiology**; GIT effects of spinal anaesthesia are largely the result of sympathetic blockage of T6-L2 fibres. There is as a result, unopposed parasympathetic activity. Consequently secretions increase, sphincters relax and the bowels become constricted. Nausea is common in spinal anaesthesia either from increased parasympathetic activity or spinal –induced hypotension

d) **Endocrine-metabolic physiology**; Spinal anaesthesia inhibits many metabolic changes associated with stress response to surgery. The inhibitory effect is greatest with lower abdominal and lower extremity procedures and least with upper abdominal and thoracic procedures.

Complications of spinal anaesthesia

Backache-aetiology is not clear although needle trauma, local anaesthetic irritation and ligamentous strain secondary to muscle relaxation have been offered as explanations.

Post dural puncture headache-the headache results from the loss of CSF through the meningeal needle-hole resulting in decreased buoyant support for the brain. In the upright position, the brain sags in the cranial vault, putting traction on pain sensitive structures. Traction on cranial nerves is believed to cause cranial nerve palsies that are seen occasionally.

Total spinal anaesthesia- occurs when the local anaesthetic spreads high enough to block the entire spinal cord and essentially the brainstem during spinal anaesthesia. Profound hypotension and bradycardia are common secondary to complete sympathetic blockade. Respiratory arrest may occur as a result of respiratory muscle paralysis or dysfunction of brainstem respiratory control centres

Neurologic injury- Persistent paraesthesias, and limited motor weakness are the commonest injuries. Paraplegia and diffuse injury to cauda equina roots occur rarely. Injury may result from direct needle trauma to the spinal cord or spinal nerves, spinal cord ischaemia, from accidental injection of neurotoxic drugs or chemicals, from introduction of bacteria or from the local anaesthetics injected

Spinal haematoma- coagulation defects are the principal risk factors for epidural/intrathecal haematoma. Patients most commonly present with persistent numbness or lower extremity weakness.

Spinal-induced Hypotension (SIH)

Hypotension occurring post spinal anaesthesia is an exaggeration of the physiological effect of the spinal blockade. Hypotension occurs in approximately 33% of the non-obstetric patients. ⁽¹⁾ The sympathectomy produced by spinal anaesthesia induces haemodynamic changes. The block height determines the extent of sympathetic blockade which determines the amount of change in cardiovascular parameters

High sensory block height, age older than 40 years, obesity, combined general and spinal anaesthesia, chronic alcohol consumption, history of hypertension; all increase the likelihood of hypotension after spinal anaesthesia. ⁽¹⁾

Arterial and veno-dilation both occur in spinal anaesthesia and combine to produce hypotension. Venodilatation increases the volume in capacitance vessels thus reducing venous return and right sided filling pressures. This fall in preload leads to a fall in cardiac output. Arterial dilatation on the other hand reduces the peripheral resistance. ⁽³⁾ The hypotension is thus as a result of decrease in preload, cardiac output and a reduction in the peripheral vascular resistance.

Management of spinal-induced hypotension

Various strategies have been adopted to help prevent hypotension occurring after spinal blockade. One of the strategies is volume preloading /co-loading. The preloading is usually given approximately 30 minutes before the spinal blockade while co-loading is usually administered concurrently with the spinal blockade. The fluid given is usually 20 mL/kg body weight. Studies have however shown that co-loading is superior to preloading. ⁽¹⁸⁾ The use of fluid load has, however, been disputed by researchers who have demonstrated that patients who received volume preload or co-load required almost similar amounts of rescue vasopressors. ⁽¹⁹⁾

Positioning can also prevent spinal-induced hypotension. The most effective and simplest way to achieve this is by positioning the patient in trendelenburg position. This position should not exceed 20 degrees because extreme trendelenburg can lead to a decrease in cerebral perfusion due to an increase in the jugular venous pressure. If the level of spinal anaesthesia is not yet fixed, the trendelenburg position can alter the level of spinal anaesthesia and cause a high level of spinal anaesthesia in patients receiving hyperbaric local anaesthetic solutions. ⁽¹⁾

Treatment of hypotension arising from spinal anaesthesia is essential so that the myocardium and brain remain adequately perfused. If a patient is asymptomatic, decrease in blood pressure of up to 33% need not to be treated. If pharmacologic treatment of hypotension is indicated, vasopressors remain the mainstay of treatment. Combined alpha and beta adrenergic agonists may be better than the pure alpha agonists for treating blood pressure depression. Ephedrine is currently the drug of choice and it elevates blood pressure by increasing the cardiac output and peripheral vascular resistance. ⁽²⁾

Ephedrine

Ephedrine is one of the most commonly used non-catecholamine sympathomimetic agents. It is used extensively for treating hypotension following spinal or epidural anesthesia. Ephedrine stimulates both α and β receptors by direct and indirect actions. It is predominantly an indirect-acting pressor, producing its effects by causing nor-epinephrine release. Tachyphylaxis develops rapidly and is probably related to the depletion of norepinephrine stores with repeated injection. The cardiovascular effects of ephedrine are nearly identical to those of epinephrine, but it is less potent. Its effects are sustained about 10 times longer than those of epinephrine. Ephedrine produces venoconstriction to a greater degree than arteriolar constriction. This may be its most important and unappreciated effect. It causes a redistribution of blood centrally, improves venous return and increases cardiac output. The mild β action restores heart rate simultaneously with improved venous return. An increased blood pressure is noted as a result rather than a cause of these events. Mild α_1 -arteriolar constriction does occur, but the net effect of improving venous return and heart rate is increased cardiac output. This response, however, depends on the patient's state of hydration ⁽³⁾

Ephedrine can be administered orally or parenterally. The dosage in hypotension ranges from 25-50 mg I/M or S/C every 3-4 hours or 5-25 mg I/V every 5-10 minutes until stable. Maximum dose is 150 mg/24 hours. The onset of action after intramuscular administration is 10-20 minutes. The half life ranges from 2.5-3.6 hours. It's minimally metabolized in the liver and the metabolites excreted in urine. Frequently encountered adverse effects are hypertension, tachycardia, dysrhythmias, anxiety, anorexia, nausea, vomiting, tremors and palpitations. ⁽²⁰⁾

Ephedrine is usually administered intravenously in bolus doses as need arise when the blood pressure drops or prophylactically either intramuscularly or as an intravenous infusion. The use of prophylactic ephedrine versus on demand has been evaluated by several researchers on its efficacy in the management of spinal-induced hypotension. M. Goel et al studied the haemodynamic effects during combined spinal and epidural anaesthesia, comparing the role of fluid preloading and prophylactic vasopressors. Patients were randomly allocated to 2 groups. Group 1, patients received crystalloid preloading (Ringers Lactate) 20 minutes before procedure at a rate of 15ml/kg and group 2 patients received prophylactic ephedrine intravenously , 5mg at 1st and 2nd minute after the block. In both groups, sustained fall in systolic blood pressure was

observed from baseline. In group 1, the fall in BP was more and the difference was also statistically significant. In group 1, 30% of patients developed hypotension while in group 2, only 10% of the patients developed hypotension. Rescue ephedrine was also required in a higher proportion of patients in group 1 than group 2. The study showed that prophylactic ephedrine is a more effective method in reducing the incidence and severity of fall in systolic blood pressure as compared to volume loading. Nausea was complained of by 3 and 1 patients in group 1 and 2 respectively. Other minor untoward reactions like vomiting, rigors, restlessness were experienced by very few patients. ⁽⁴⁾

SK Kafle et al studied ASA I & II patients undergoing lower abdominal surgery under spinal anaesthesia who were randomized into 2 groups. All patients were given routine oral premedication consisting of diazepam 10 mg and ranitidine 150 mg at bed time and at 90 min before surgery. Group I patients received ephedrine 30 mg orally, 30 minutes before subarachnoid block was administered. Group II patients only received routine premedication. Patients with decreases in blood pressure of 20% were given ephedrine i/v in increments, in addition to crystalloids. Despite a similar level of block (T3-T4) and i/v fluids the total dose of ephedrine supplement in group I was 4.3+/-4.8mg compared with 11.6+/-9.4mg in group II. They concluded that oral premedication with ephedrine is a simple and effective way of reducing the incidence of hypotension in patients undergoing lower abdominal surgery under subarachnoid block. ⁽⁵⁾

Singh S. et al carried out a study to compare efficacy, side effects and limitations of prophylactic ephedrine 30mg IM versus polygelline 3.5%, 500ml intravenously for the maintenance of blood pressure after subarachnoid block (SAB). They studied a total of 100 elderly patients (>50 years) who were randomly allocated to receive either ephedrine 30mg IM 10 minutes before the institution of SAB in group I or preloading with 500ml of polygelline 3.5% over 10 minutes prior to (SAB) in group II. In both groups, rescue ephedrine and other vasoconstrictors were given to treat hypotension if it occurred. They discovered that the incidence of hypotension and requirement for rescue therapy was significantly less in group I compared to group II. Heart rates were better maintained in group I than group II, with few haemodynamic adverse effects in both groups. Tachycardia was observed in three patients in Group I. Hypertension was observed in two cases of Group I but was statistically insignificant (P value 0.153). They concluded that

ephedrine 30mg IM given as pre-treatment before SAB in elderly patients was more effective for the prevention of spinal-induced hypotension than pre-loading with polygelline. ⁽⁶⁾

A study to evaluate pre-loading and vasopressors as a combined prophylaxis for hypotension during subarachnoid anaesthesia was carried out by Hemant Bhagat et al. Ninety patients were randomly allocated into 3 different groups. Group I received pre-loading with 15ml/kg of ringers lactate. Group II patients received prophylactic intravenous ephedrine 28 mg administered over 20 minutes. Group III patients received preloading with half the volume as in group II and ephedrine half the dose as in group II. The incidence of hypotension was only 3.33% in group III, 16.66% in group II and 63.33% in group I. The duration of significant fall in systolic arterial pressure, hypotensive episodes and requirement of intravenous fluids and ephedrine for management of hypotension were least in group III and maximum in group I. In group II one patient had hypertension that resolved in 10 minutes without any treatment. Nausea and vomiting was present in all the groups but was statistically non-significant. They concluded that combination therapy with reduced volume of preloading and reduced dose of vasopressor is an effective method of prophylaxis against spinal-induced hypotension and provides better haemodynamic stability when compared to the use of preloading or vasopressors alone. ⁽⁷⁾

In a double blind, placebo controlled, randomized study, J. E. Sternlo et al investigated the efficacy of intramuscular ephedrine in 98 elderly patients undergoing hip arthroplasty under spinal anaesthesia with plain bupivacaine. Fifty patients received ephedrine 0.6 mg/kg body weight deep in the paravertebral muscles immediately after injection of bupivacaine and 48 received an equal volume of saline. Patients in both groups were given the same volumes of fluids before anaesthesia. Systolic arterial pressure during the first 60 minutes after anaesthesia remained more stable in the ephedrine treated group and there was also a significantly smaller number of patients in this group who had decreases in pressure of more than 30% of pre-block levels and fewer required rescue, intravenous ephedrine. Only one patient in the ephedrine group developed hypertension. No other side effects of ephedrine were reported in this study. They concluded that ephedrine 0.6 mg/kg body weight administered in the paravertebral muscles immediately after plain bupivacaine spinal anaesthesia was a simple and effective means of reducing the incidence of hypotension in elderly patients. ⁽⁸⁾

Elogru F. et al investigated the prophylactic effects of oral ephedrine in spinal anesthesia-induced hypotension during transurethral prostatectomy. Sixty American Society of Anesthesiologists Grade II and III patients scheduled for spinal anesthesia were randomized into one of two groups. Patients in Group I (n = 30) received oral ephedrine 50 mg in addition to premedication whilst those in Group II (n = 30) received only premedication 30 minutes before spinal anesthesia. Systolic arterial pressure values were significantly lower in Group II during the spinal anesthesia, post-spinal and intraoperative periods. The incidence of hypotension was halved in Group I compared to Group II (23.33% vs 50 %). They concluded that a prophylactic oral dose of ephedrine 50 mg was effective for minimizing and managing spinal anesthesia-induced hypotension during transurethral resection of the prostate. ⁽¹⁰⁾

In a double-blind, randomized study, Mohammad Boota et al. sought to evaluate the efficacy of intramuscular ephedrine along with preloading in prevention of spinal-induced hypotension in elderly patients undergoing inguinal hernia surgery. 80 elderly patients undergoing inguinal hernia surgery under spinal anaesthesia were divided into two equal groups. Forty patients received intramuscular injection of ephedrine 45mg deep in the paravertebral muscles immediately after injection of bupivacaine, and 40 received an equal volume of saline. Patients in both groups were given the same volumes of fluid before anaesthesia. The incidence of hypotension was lower in the ephedrine group as compared to the saline group. They concluded that ephedrine 45mg administered in the paravertebral muscles immediately after plain bupivacaine spinal anaesthesia was a simple and effective means of reducing the incidence of hypotensive episodes in the elderly patients. ⁽¹¹⁾

Jabalameli M. et al. conducted a study to evaluate the efficacy of three combinational methods to prevent hypotension following spinal anesthesia. In their prospective double blind trial, 150 candidates for elective cesarean delivery under spinal anesthesia were randomly allocated to three treatment groups; 1---Ringer's Lactate (RL) solution (15 ml/kg) plus Hemacel (7 ml/kg) preload, 2---RL solution (15 ml/kg) preload plus ephedrine (15 mg, IV, bolus), 3---Hemacel (7 ml/kg) preload plus ephedrine (15 mg, IV, bolus). The cumulative incidence of hypotension was 44%, 40%, and 46% in groups 1 to 3, respectively. There were no significant differences in supplementary ephedrine requirement among groups which received or among groups which did not receive prophylactic ephedrine. Groups were not different in the incidence of hypotension

and nausea or vomiting. Incidence of hypertension was highest in group 2 compared with other groups. This incidence was however statistically non-significant and the patients didn't require any treatment. Nausea and vomiting was comparable in all the groups. They concluded that combination of preventive methods decreased the occurrence of hypotension following spinal anaesthesia to an acceptable level. Overall, the most effective method was a combination of crystalloid preload with ephedrine. ⁽¹²⁾

Fawad Ahmed Khan et al conducted a study with an aim of assessing the efficacy of single dose (10mg) of ephedrine given prophylactically to prevent hypotension in patients during spinal anaesthesia. Sixty ASA I and ASAII patients were divided into two groups. Group I (n=30) received Ringers lactate solution 15 ml/kg as preload and group II (n=30) received Ringers lactate solution 15 ml/kg as preload along with single prophylactic dose of ephedrine 10 mg intravenously which was given after administering spinal anaesthesia. The comparison was made between groups I and group II. There was significantly lower incidence of hypotension in group II as compared to group I. They concluded that administration of a single prophylactic dose (10mg) of ephedrine prevents hypotension in patients during spinal anaesthesia ⁽¹⁴⁾. This study was replicated by Madhu Tiwari et al. ⁽¹⁵⁾

R. Vasanthageethan et al carried out a study to determine the efficacy of prophylactic orally administered ephedrine in minimizing the incidence of hypotension following spinal anaesthesia in patients undergoing lower abdominal and scrotal surgeries. 100 ASA grade I patients undergoing lower abdominal and scrotal surgeries were randomly allocated equally into two groups. One group received 30 mg of oral ephedrine and the other group received a placebo 30 minutes before spinal anaesthesia. They found out that the incidence of hypotension and the need to use intravenous ephedrine for treatment of hypotension was lower in the patients who received oral ephedrine prophylaxis. There were no significant side effects noticed due to the administration of oral ephedrine prophylaxis ⁽¹⁶⁾

A study on the haemodynamic effects of prophylactic intravenous ephedrine versus ephedrine use on as need arises basis (PRN) in patients undergoing spinal anaesthesia for Caesarean delivery was conducted by Abdul Rehman et al. Seventy patients undergoing caesarean delivery under spinal anaesthesia were randomly assigned to two groups. Patients in one group received ephedrine only when indicated while patients in the other group received prophylactic ephedrine

15 mg intravenously immediately after the induction of subarachnoid block. In the first group, blood pressure dropped in a higher number of patients 65.7% as compared to the group that received prophylactic ephedrine 17.1%. They concluded that prophylactic ephedrine was better than PRN ephedrine in prevention of hypotension in patients undergoing spinal anaesthesia for caesarean delivery. ⁽¹⁷⁾

In a study in Nigeria, I Desalu and O. T. Kushimo sought to determine whether ephedrine infusion was more effective at preventing hypotension than traditional pre-hydration during spinal anaesthesia for caesarean section in African parturients. Sixty patients for elective caesarean delivery were randomly allocated to group 1: 1 L 0.9% saline before spinal block, and group 2: infusion of ephedrine 30 mg in 1 L of 0.9% saline after spinal block, titrated to maternal systolic pressure. Systolic pressures decreased 5 min after spinal block. Group 2 had higher mean values of systolic pressure throughout most of the study period than group 1. Hypotension occurred in 70% of patients in group 1 and 40% of patients in group 2. Severe hypotension occurred in 40% of group 1 and 13.3% of group 2. They concluded that prophylactic ephedrine given by standard infusion set was more effective than crystalloid pre-hydration in the prevention of hypotension during spinal anaesthesia for elective caesarean delivery ⁽¹⁸⁾

Contraindications to spinal anaesthesia

In certain circumstances, spinal anaesthesia may not be used where it may endanger the health of the patient or be technically difficult to perform. These may be classified as either absolute or relative

- **Absolute contraindications**
 - Patient refusal

- **Relative**
 - Hypovolaemia and shock
 - Increased intracranial pressure
 - Coagulopathy or thrombocytopenia

- Sepsis
- Infection at the puncture site⁽³⁾

Study justification and rationale

Many orthopaedic operations are well suited for regional anaesthetic techniques. Regional anaesthesia may reduce the incidence of major perioperative complications associated with certain surgical procedures, such as deep vein thrombosis, pulmonary embolism, respiratory complications and death. Postoperative pain management is a significant problem after orthopaedic procedures. With regional anaesthetic techniques, there is superior pain relief. Orthopaedic patients often pose difficult airway management problems. Regional anaesthesia avoids manipulation of the airway and conscious patients can aid in the safest and most comfortable positioning for surgery. Regional anaesthesia has also been associated with decreased intraoperative blood loss ⁽²⁾

The most common adverse effect encountered with spinal anaesthesia is hypotension. ^(1, 20) Several interventions can be planned for prevention of spinal-induced hypotension. Preloading/co-loading with a crystalloid fluid is a common strategy used at Kenyatta National Hospital orthopaedic theatres. However, preload has potential disadvantages including risk of haemodilution, fluid overload and anaphylactoid reactions especially when colloids are used. Trendelenberg position may help prevent hypotension but cannot be applied more than 20 degrees without risk of cerebral hypo-perfusion. It may also cause high spinal or total spinal if the spinal blockade has not achieved fixation. Pharmacologic agents, therefore, play a big role in the management of hypotension in some of these patients.

In Kenyatta national hospital, ephedrine, adrenaline and phenylephrine are all used in the management of spinal induced hypotension. Ephedrine is the most commonly used agent because it's cheap, readily available and has a longer duration of action. It's commonly administered intramuscularly prior to the administration of the spinal anaesthesia or as need arises (PRN) after the administration of spinal anaesthesia depending on the preference of the anaesthetist. There is, however, no standard protocol for the administration of ephedrine and the choice is usually at the discretion of the anaesthetist administering the anaesthesia.

Most comparative studies done elsewhere recommend the use of prophylactic ephedrine because it achieves better blood pressure control than ephedrine use on as need arises basis. No local data is available on the effectiveness of prophylactic ephedrine versus PRN ephedrine. This study aimed at bridging this local evidence gap and possibly provide a basis for the introduction of a standard protocol on the administration of ephedrine so as to reduce the incidence of hypotension following spinal anaesthesia and thus lead to an overall improvement in patient care.

Study question

Is prophylactic ephedrine more effective than interventional ephedrine in the perioperative management of spinal anaesthesia induced hypotension during perioperative lower limb orthopaedic surgery?

Hypothesis*Null hypothesis*

The incidence of hypotension and requirement for rescue vasopressors is similar in patients receiving prophylactic ephedrine compared to those receiving ephedrine when need arises.

Alternative hypothesis

The incidence of hypotension and requirement for rescue vasopressors is lower in patients receiving prophylactic ephedrine when compared to those receiving ephedrine when need arises.

Study objectives

Broad objective

To assess the effectiveness of ephedrine used prophylactically or interventionally in the perioperative management of spinal-induced hypotension among ASA I and ASA II orthopaedic patients undergoing elective lower limb surgery at KNH

Specific objectives

- To determine the incidence of spinal-induced hypotension in ASA I and ASA II orthopaedic patients undergoing lower limb surgery when ephedrine is administered prophylactically
- To determine the incidence of spinal-induced hypotension in ASA I and ASA II orthopaedic patients undergoing lower limb surgery when ephedrine is used as need arises.
- To compare the requirement of rescue vasopressors for the treatment of spinal-induced hypotension between ASA I and ASA II patients receiving prophylactic ephedrine versus those receiving ephedrine when need arises.
- To determine the common adverse effects associated with the use of ephedrine

CHAPTER THREE: MATERIALS AND METHODS

Study Design

This was a comparative observational study.

Study Area

The study was carried out at Kenyatta National Hospital's orthopaedics wards, orthopaedics theatre and post anaesthesia care unit (PACU). Kenyatta National Hospital (KNH) was established in 1901 with a capacity of 40 beds. Over the years KNH has grown to its present capacity of 2,000 beds and attends to an annual average of 70,000 inpatients and 500,000 outpatients. Currently it is the largest referral hospital in Kenya and serves as the teaching hospital for the University of Nairobi. KNH has 24 operating theatres of which 3 theatres are allocated to elective orthopaedic procedures.

Study Population

Adult patients (above 18 years of age) who were scheduled to undergo elective lower limb surgery under spinal anaesthesia at KNH orthopaedic operation theatres.

Eligibility Criteria

Inclusion Criteria

- Patients who gave informed consent to participate in the study
- Adult patients (above 18 years of age) assessed to be in ASA class I or II scheduled for elective lower limb surgery under spinal anaesthesia at KNH

Exclusion Criteria

- ASA III and ASA IV patients
- Patients who did not consent to participate in the study.
- Patients who had known contraindications to ephedrine
- Patients who had known contraindications to spinal anaesthesia

- Patients who were converted to general anaesthesia or given sedative drugs
- Pregnant patients

Sample size determination

Sample size calculation was done using the formula for estimating sample size for a single proportion with finite population correction (Daniel 1999):

$$n = \frac{NZ^2P(1 - P)}{d^2(N - 1) + Z^2P(1 - P)}$$

n = sample size with finite population correction

N = Population size = 200 patients assuming 6 spinal anaesthetic procedures per day for a two-month study period

Z = statistic for 95% confidence = 1.96

P = expected incidence of spinal-induced hypotension in ASA I and ASA II orthopaedic patients in KNH (prevalence = 40%, P = 0.4)

d = precision (desired precision = 5%, d = 0.05)

n = 130

Sampling Procedure:

The principal investigator reviewed the patients in the ward on the evening before the day of surgery. He identified participants based on the inclusion and exclusion criteria outlined above and explained the nature of the study and obtained informed written consent.

Patients listed for surgery were assessed for eligibility and enrolled. Those not meeting the inclusion criteria and those who declined to participate were excluded. Convenience sampling was used to identify patients who were included in the study. Every alternate consented patient in

each of the orthopaedics surgery theatre list scheduled to undergo spinal anaesthesia was included. The investigator then recruited patients into the study as they underwent anaesthesia and surgery until the required sample size required was achieved in each group.

Since there were only two regimens of ephedrine for use during spinal anaesthesia; prophylactic and PRN, two groups of patients were obtained without influencing or intervening in their anaesthetic management; a prophylaxis group and a no prophylaxis group. Comparisons were made from these two groups.

Data collection

The principal investigator did not make any decision nor participate in the anaesthetic management of the patient. All the decisions on management were made by the anaesthetist managing the patient following the established KNH spinal anaesthesia protocol.

Upon arrival into the operating room, patients were connected to the monitors, including non-invasive blood pressure (NIBP) monitor, pulse oximetry (SPO₂), and ECG monitors. Baseline vital signs were taken and recorded i.e. pulse rate, non-invasive BP, O₂ saturation (SPO₂) and Respiratory rate. These are standard monitoring for all patients undergoing anaesthesia.

The anaesthetist managing the patient would then decide on the ephedrine regimen to use, whether prophylactic or PRN. The anaesthetist used the regime that He/she was comfortable with. Patients receiving prophylactic ephedrine received an intramuscular injection 10 minutes prior to the administration of anaesthesia. For all patients in both study groups, the anaesthetist prepared a 3mg /mL solution of ephedrine to be administered in the event hypotension occurred. He/ She then proceeded to administer spinal anaesthesia. All the patients recruited in this study received intrathecal bupivacaine 12.5 mg plus fentanyl 25 micrograms. The anaesthetist also chose which strategy to use to treat post-spinal hypotension when it occurred either by using intravenous fluids or boluses of ephedrine or epinephrine. The criteria for treating hypotension were a decrease in the systolic blood pressure to less than 80% of baseline or an absolute value of 90 mmHg and/or signs and symptoms due to hypotension.

Information was collected by means of a specially designed data collection tool. The researcher retrieved the data from the anaesthetic records either in the electronic monitors or patient files.

Data for blood pressure and heart rate of the patients were recorded every 5 minutes for the first thirty minutes and thereafter every fifteen minutes up to a maximum duration of three hours.

The total amount of fluids infused including blood and the total dose of ephedrine boluses or any other vasopressors used were also recorded.

Although literature has shown that ephedrine has been in use for a very long time and is rarely associated with serious adverse effects, any adverse effects suspected by the anaesthetist to be due to ephedrine were also to be recorded. The anaesthetist managing the patient made the decision on the best way to manage any of the adverse effects in the event that they arose. If any severe complications were to occur, the principal investigator, supervisors and the resuscitation team were immediately available to assist.

Data management

Quality assurance and control was ensured through training of research assistants on data collection from the anaesthetist's notes. Standard operating procedures (SOP) outlining the data to be collected for each variable included in the study tool were written and used during data collection. The SOP also contained the expected ranges for physiological measures and data collectors were required to double check to confirm any measurements outside the physiological range. Upon completion of data collection for each patient the principal investigator inspected each data collection tool to ensure that all data had been collected. Incomplete data collection tools were completed. Data entry was done using a database designed in SPSS (IBM) version 20. The database contained range and consistency checks to reduce data entry errors. Any values outside the database ranges were confirmed before entry. The data collection tools were archived in lockable cabinets with restricted access. The database was archived in password-protected computer drive with an external drive backup stored with the questionnaire. The data was archived as required during dissemination of findings in a scientific peer review journal.

Data analysis

Data analysis was conducted using SPSS (IBM) software version 20. Descriptive analysis of simple characteristics included calculating mean (\pm SD) for age and the frequency accompanied with percentages for sex and ASA classification. Patients' vital signs were summarized and presented using mean (\pm SD) for blood pressure and heart rate. In addition percentages of patients with vital signs measurements outside the physiological ranges were calculated. The main outcome of the analysis was based on the frequency of hypotension and the use of ephedrine among adult patients undergoing elective lower limb orthopaedics surgery under spinal anaesthesia presented by calculating a proportion and its 95% confidence interval (CI). The cumulative incidence was calculated as the frequency of spinal-induced hypotension in each group of patients recruited over the period of the study. Apart from the overall incidence of spinal-induced hypotension, cumulative incidence was also calculated for patients receiving ephedrine prophylaxis and those receiving ephedrine as need arises. The two incidences were compared using a Pearson's chi square test to determine whether incidence of hypotension and requirement for rescue vasopressors was similar in patients receiving prophylactic ephedrine compared to those receiving ephedrine when need arises. The decision to fail to reject the null hypothesis was based on the findings of this chi square test of independence. The results were presented using descriptive statistics (mean \pm SD), tables, figures and text.

Ethical Considerations

Approval to carry out the study was obtained from the KNH/UoN Ethics and Research Committee.

Written informed consent was obtained from each participant and filed

There was no additional cost or incentive for participating in the study

Confidentiality was ensured by using patients' initials instead of names

The study did not in any way endanger the participants or expose them to harmful or unapproved procedures.

CHAPTER FOUR: RESULTS

A total of 130 patients scheduled to undergo lower limb surgery under spinal anaesthetic blockade were recruited and included in the study. Data of their demographic characteristics, perioperative haemodynamics, vasopressors and fluid therapy requirements, duration of surgery, estimated blood loss and adverse effects of vasopressors were recorded and analysed.

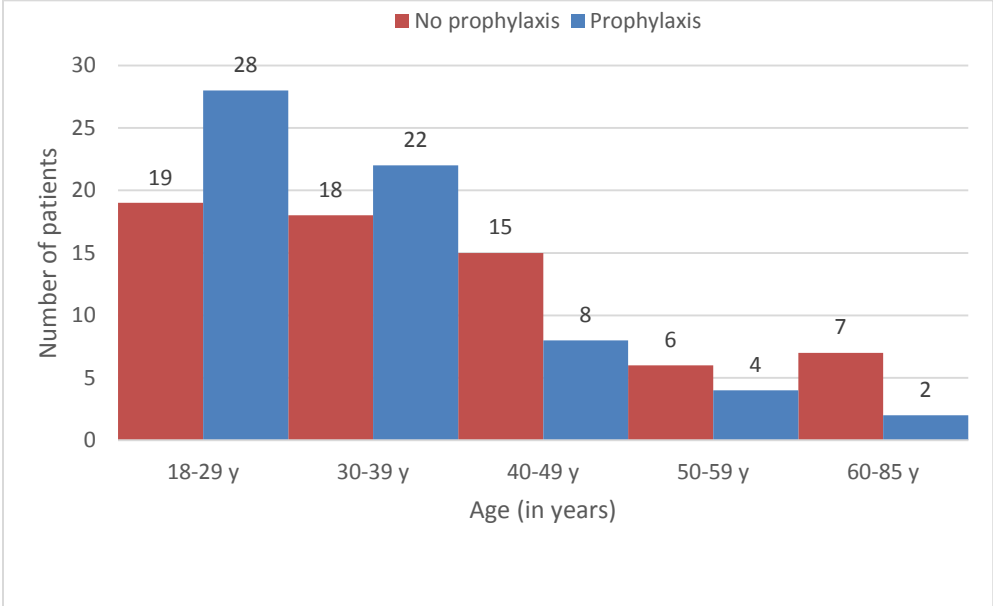
Demographic characteristics

Table1: Demographic characteristics stratified by administration of ephedrine prophylaxis

	Prophylaxis group	No prophylaxis group		
	N (%)	N (%)	OR (95% CI)	P
Gender				
Male	51(78.5)	44(67.7)		
Female	14(21.5)	21(32.3)	0.58(0.26-1.26)	0.169
ASA classification				
ASA I	61(93.8)	57(87.7)		
ASA II	4(6.2)	8(12.3)	0.47(0.13-1.64)	0.234
Age	33.9(±11.9)	37.9(±13.3)	4.0(-0.3-8.3)	0.073

The majority of patients were male in both study groups. Most of the patients were ASA class I and only a small proportion were in ASA class II in both the prophylaxis and the no prophylaxis groups. Their ages ranged from 18-84 years. The mean age for the prophylaxis group was 33.9years (±11.90) while in the no prophylaxis group the mean age was 37.9 years ±13.3). There were no statistically significant differences in the demographic characteristics of the patients.

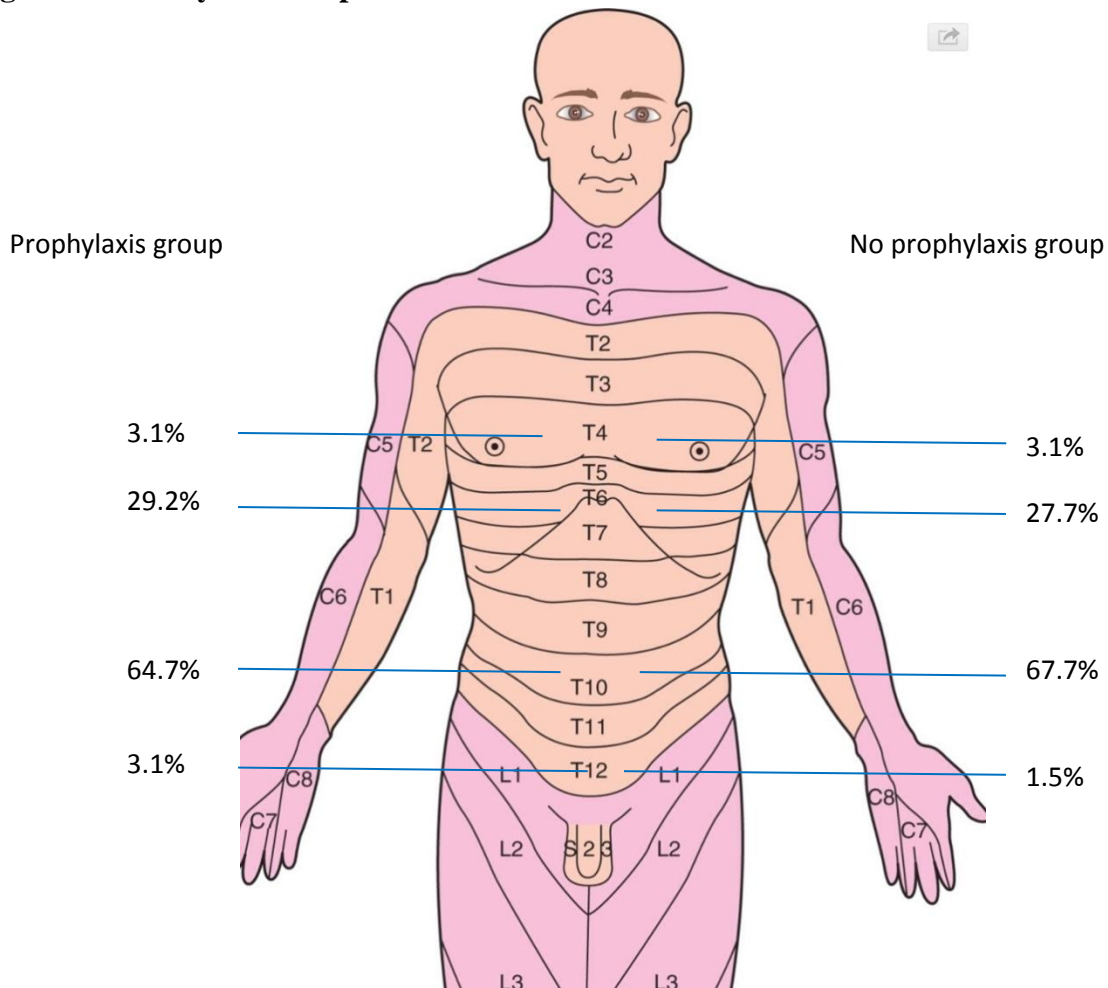
Figure 1: Bar graph showing age distribution



Most of our patients were aged between 18 to 49 years with a majority falling in the age range between 18 to 29 years. Only a few patients were aged 60 years and above.

Block height

Figure 2: Sensory level of spinal anaesthesia



The highest proportion of patients, 64.7% in the prophylaxis and 67.7 % in the no prophylaxis group attained a block height of the T10 dermatome. The lowest dermatome was T12 while the highest dermatome was T4. The block heights were comparable in both groups.

Prophylactic ephedrine dose

Table2: Frequency of Ephedrine doses used for prophylaxis

Ephedrine dose (mg)	Freq.	Percent
6	3	4.6
9	4	6.2
12	2	3.1
15	52	80.0
18	1	1.5
30	3	4.6
Total	65	100

Half of the patients recruited in the study were given intramuscular ephedrine for prophylaxis against post spinal hypotension. The minimum dose was 6 mg while the maximum dose was 30 mg, the highest proportion of patients received 15 mg (80%). The mean dose of ephedrine used was 14.86 mg. Though all these doses are within the range of doses recommended for prophylaxis, one patient developed hypertension while another developed severe hypotension after receiving 30 mg. This led to most of the anaesthetists preferring to administer half of the total content of a 30 mg ephedrine ampoule prophylactically and then reconstituting the remaining 15 mg to a 3mg/ml solution that would then be administered in boluses in the event that hypotension occurred.

Perioperative haemodynamics

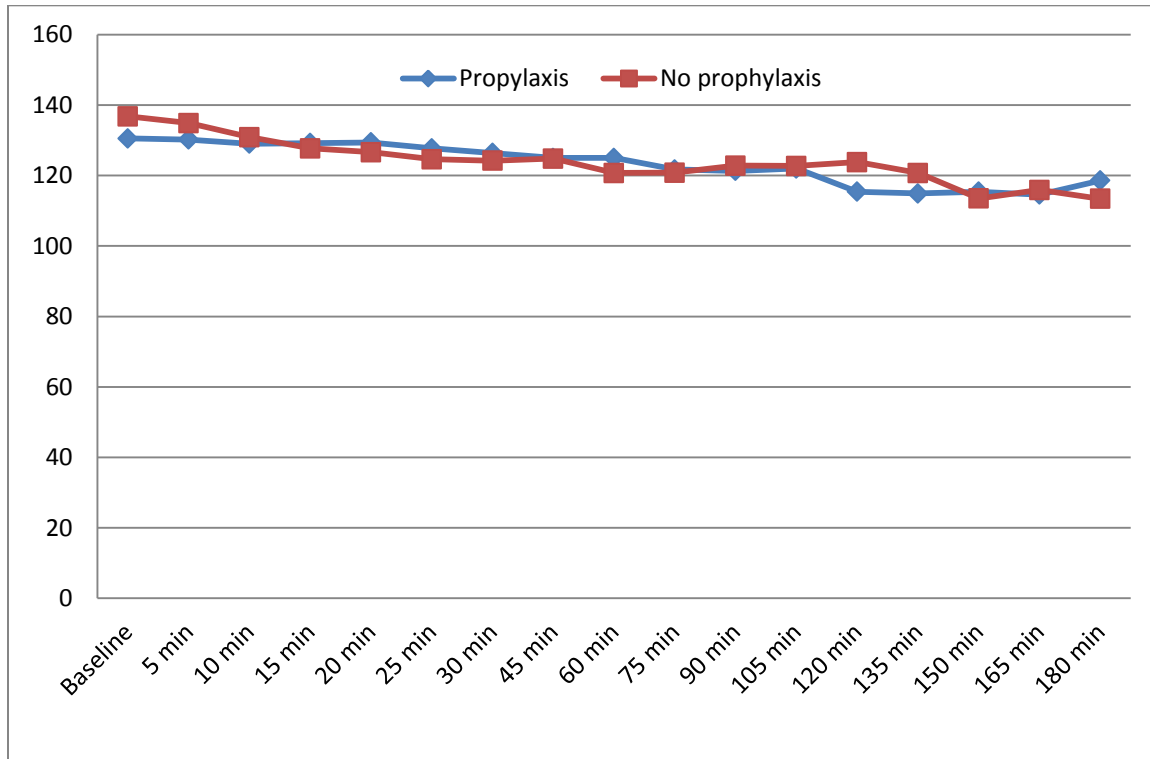
Baseline haemodynamics

Table 3: Mean baseline haemodynamics in patients undergoing spinal anaesthesia for lower limb surgery

	Heart rate	Systolic BP	Diastolic BP	MAP
No Prophylaxis group	92.8	136.8	76.6	92.7
prophylaxis group	94.2	130.5	74.6	89.7
P value	0.695	0.053	0.441	0.254

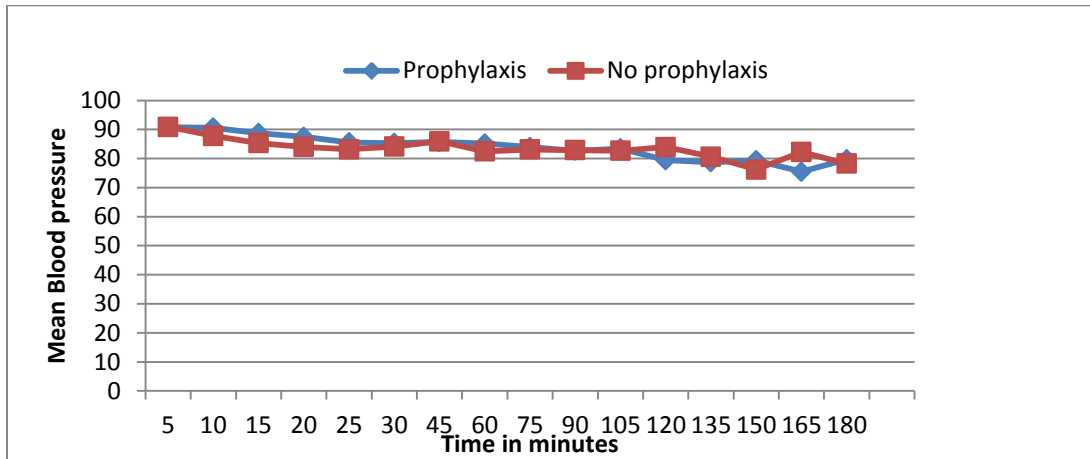
Baseline vitals were taken before administration of prophylactic ephedrine and institution of the spinal blockade. The mean baseline values for systolic, diastolic and mean arterial blood pressures were slightly higher in the no prophylaxis group than the prophylaxis group. Baseline heart rate was higher in the prophylaxis group. There were, however, no significant differences in baseline haemodynamics between the prophylaxis and no prophylaxis groups.

Figure 3: Average perioperative systolic blood pressures



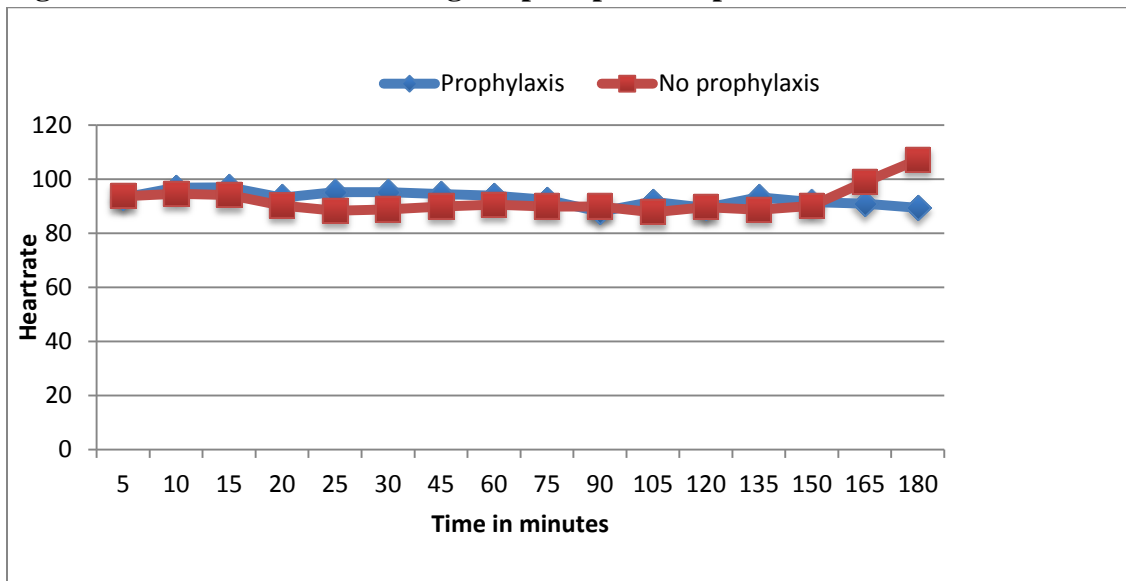
In both groups, there was a gradual decline in the average systolic blood pressure. Maximum initial decline occurred at thirty minutes in the no prophylaxis group and at forty five minutes in the prophylaxis group. Although not statistically significant, the rate of this decline was higher in the no prophylaxis group as compared to the prophylaxis group. ($P>0.77$)

Figure 4: Average mean arterial pressure during the perioperative period



After spinal anaesthesia, there was a gradual reduction in the average mean arterial pressure in both groups. The fall in mean arterial pressure was higher in the no prophylaxis group than in the prophylaxis group. However this difference was not statistically significant. ($P>0.147$)

Figure 5: Mean heart rate during the perioperative period



The mean heart rates were maintained within normal limits for most of the perioperative period in both groups. However, the trends for the heart rates were slightly higher in the prophylaxis group as compared with the no prophylaxis group although this difference was not statistically significant. ($P>0.135$)

Incidence of hypotension

Table 4: Total number of patients in each group who developed hypotension

	Hypotension	No hypotension	OR (95% CI)	P
No prophylaxis group	35(53.8)	30(46.2)	0.73(0.37-1.46)	0.381
Prophylaxis group	30(46.2)	35(53.8)		

Overall incidence of hypotension was 50%. 53.8% of patients in the no prophylaxis group suffered hypotension whereas in the prophylaxis group 46.2% developed hypotension. There was no statistically significant difference in the incidence of hypotension in the two groups (P=0.381).

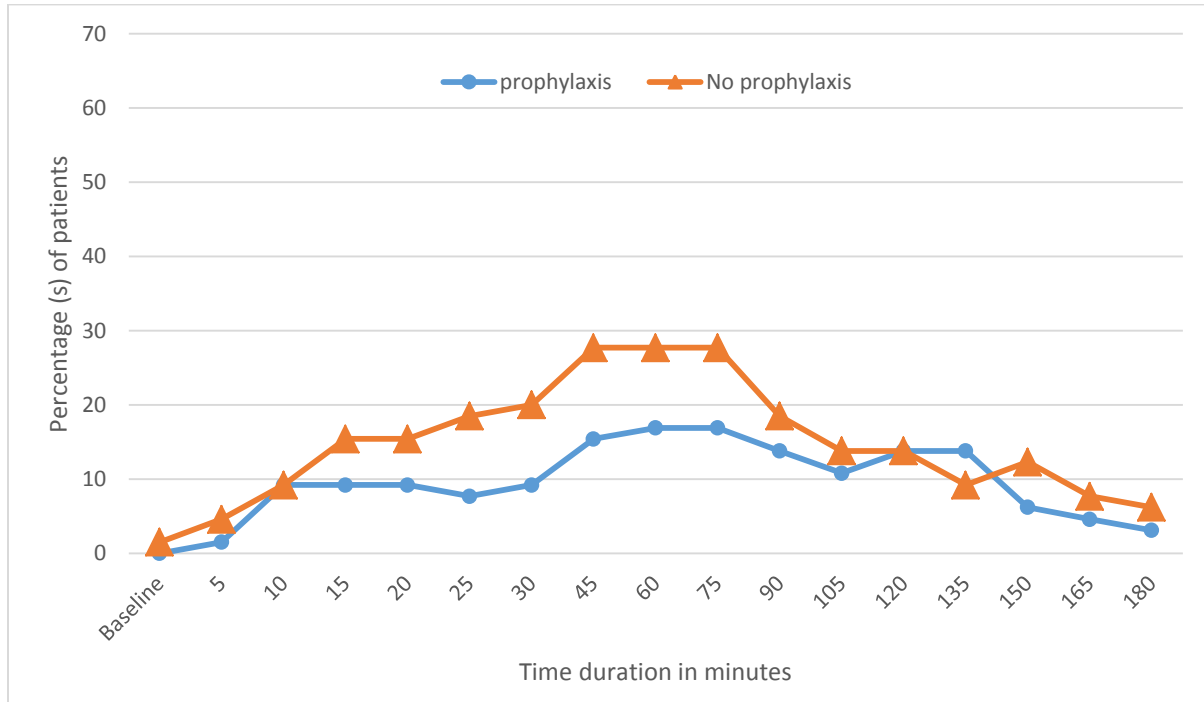
Table 5: Number of patients with clinically significant hypotension

	Prophylaxis group	No prophylaxis group	OR (95% CI)	P value
Hypotension	15(23.1)	21(32.3)	1.59(0.73-3.46)	0.241
No hypotension	50(76.9)	44(67.7)		

The incidence of clinically significant hypotension was deduced from the number of patients requiring rescue ephedrine therapy to treat their hypotension. This is because ephedrine bolus was the initial treatment given to all the patients who developed hypotension requiring intervention. In the prophylaxis group, 23.1% of the patients developed hypotension requiring therapy while in the no prophylaxis group, 32.3% of patients required rescue therapy. This difference was not statistically significant. This incidence was lower than the overall incidence of

hypotension because many patients with hypotension defined as greater than 20% decline from baseline either didn't have clinical signs of hypotension or their absolute systolic blood pressure was higher than 90 mmHg. Most of the anaesthetists were noted to intervene only when the systolic blood pressure fell to less than 90 mmHg in the absence of clinical signs of hypotension.

Figure 6: Perioperative prevalence of hypotension in lower limb surgery patients receiving spinal anaesthesia



There was a gradual increase in the prevalence of hypotension beginning in the first five minutes reaching a peak at the 45th minute in the no prophylaxis group and at one hour in the prophylaxis group. The peak prevalence of hypotension was 27.7 % in the no prophylaxis group and 16.9% in the prophylaxis group. The prevalence of hypotension from the 15th to the 105th minute was higher in the no prophylaxis group than in the prophylaxis group. The highest prevalence was noted between the 45th to the 75th minute in both groups and it was higher in the no prophylaxis group as compared to the prophylaxis group. Blood loss could have contributed to this hypotension although this couldn't be ascertained since estimation of total blood loss was only done at the end of the operation.

Logistic regression showed a reduction in the risk of developing hypotension in the prophylaxis group from 15th minute to the 105th minute. The greatest risk reduction occurred from the 25th to the 45th minute. The risk reduction was, however, not statistically significant. (P>0.077)

Rescue therapy for post spinal hypotension

Table 6: Rescue vasopressors requirement

	Prophylaxis group	No prophylaxis group	OR (95% CI)	P value
	N (%)	N (%)		
Ephedrine				
Given	15(23.1)	21(32.3)		
Not given	50(76.9)	44(67.7)	1.59(0.73-3.46)	0.241
Ephedrine boluses				
Single bolus	6(9.2)	11(16.9)		
2 boluses	3(4.6)	9(13.8)	0.61(0.12-3.16)	0.557
3 boluses	6(9.2)	0(0.0)	NA	NA
7 boluses	0(0.0)	1(4.8)	NA	NA
Ephedrine dose				
Mean dose	9.1(±8.4)	9.4(±5.2)	-0.3(-4.7-4.2)	0.910

Several patients in both groups required rescue vasopressors for the treatment of hypotension. In the prophylaxis group, 23.1% of the patients developed hypotension requiring therapy while in

the no prophylaxis group 32.3% of patients required rescue therapy. A total of 30 boluses of ephedrine were administered to all patients in each study group. The dose of each bolus was either 3mg or 6 mg. The mean dose of ephedrine used in the no prophylaxis group was 9.4 mg (± 5.2). This was slightly higher than the prophylaxis group who received a mean dose of 9.1mg (± 8.4). Adrenaline was administered in 4 patients after ephedrine failed to treat their hypotension. In the prophylaxis group, only one patient was treated with adrenaline and received one bolus of 5 micrograms. In the no prophylaxis group, three patients were treated with adrenaline. One patient received one bolus of 5 micrograms. The second patient received 3 boluses totalling to a dose of 15 micrograms while the third patient received a total of 75 micrograms administered in two boluses.

Perioperative fluid therapy and blood loss

Table7: Average amounts of fluids used peri-operatively and the estimated blood loss.

	Prophylaxis group	No prophylaxis group	Difference (95% CI)	P
Crystalloids	1861.5(± 609.2)	1930.8(± 624.2)	69.2(-142.8-281.3)	0.523
Colloids	500.0(± 0.0)	714.3(± 393.4)	214.3(-77.1-505.7)	0.200
Blood	454.2(± 14.4)	450.0(± 0.0)	-4.2(-12.3-4.0)	0.339
Total	1960.8(± 643.8)	2076.9(± 912.2)	116.2(-155.3-387.6)	0.403
Estimated blood loss	325.8(± 293.6)	313.2(± 388.4)	-12.6(-131.9-106.7)	0.837

All patients received intravenous crystalloids during the perioperative period. The average crystalloid amount administered in the prophylaxis group was 1861.5 mL (± 609.2). This was slightly lower than the average amount of 1930 mL (± 624.2) administered to patients in the no prophylaxis group. 11 patients (16.92%) in the prophylaxis group were transfused with whole blood while in the no prophylaxis group, 8 patients (12.30%) were transfused. A few patients,

2(3.07%) in the prophylaxis group and 7 (10.76%) in the no prophylaxis group received colloids other than blood. Total fluid requirement was slightly higher in the no prophylaxis group as compared to the prophylaxis group. The fluid requirements in the two groups did not have statistically significant difference. The estimated blood loss was slightly higher in the prophylaxis group than the no prophylaxis group. This difference was, however, statistically insignificant. Though these differences were statistically insignificant, the maintenance of a slightly higher blood pressure in the prophylaxis group could have contributed to the slight increase in blood loss in this group and a reduction in the need for fluid boluses to treat hypotension and thus lower fluid requirement. However, it was not within the study protocol to standardise procedure and fluid loss which were independent variables as well as the surgeon undertaking the operation.

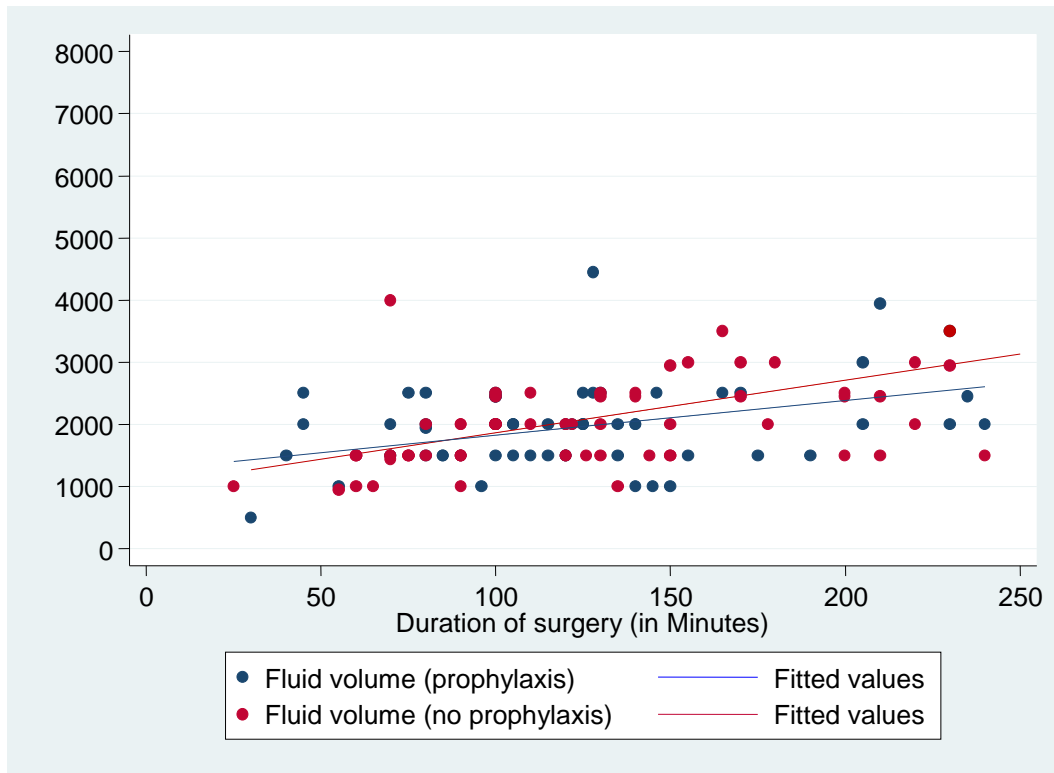
Duration of surgery

Table 8: Duration of surgery in minutes

	Prophylaxis group	No prophylaxis group	Mean difference (95% CI)	P
Duration of surgery	123.8(±53.2)	126.8(±56.7)	3.0(-16.0-22.0)	0.756

The average duration of surgery was slightly longer in the no prophylaxis group, 126.8 minutes (±56.7) versus 123.8 minutes (±53.2) in the prophylaxis group. This difference was, however, not significant.

Figure 7: Correlation between duration of surgery and fluid treatment



The fluid requirement increased with increasing duration of surgery. This could have been attributed to the continued infusion of fluids to meet the body maintenance requirements as well as to replace ongoing losses due to evaporation and bleeding. This requirement was slightly higher in the no prophylaxis group possibly due to use of fluid boluses to treat hypotension whose incidence was slightly higher in this group. This difference was however not statistically significant. (P=0.383)

Adverse effects of ephedrine

Very few patients suffered adverse reactions suspected to be arising from the use of ephedrine. Hypertension occurred in 2 patients in the prophylaxis group. 6 patients, also in the prophylactic group had tachycardia. Tremors occurred in two patients, one in each group.

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

DISCUSSION

Spinal anaesthesia has become the preferred mode of anaesthesia in patients undergoing lower limb orthopaedic surgery. This is because it's associated with better operating conditions with reduced blood loss, lower incidences of deep vein thrombosis and better post-operative analgesia. Spinal anaesthesia also avoids manipulation of the airway and is the ideal mode of anaesthesia for patients with difficult airway manageable with spinal blockade. ^(2, 6)

Despite the clinical benefits of spinal anaesthesia, there exists a major threat of hypotension following its administration which if not adequately managed can lead to severe morbidity or even mortality. This hypotension results from the sympathetic blockade that follows spinal anaesthesia leading to vasodilation and venodilation and pooling of blood in the capacitance vessels. As a result, there's a reduction in venous return which eventually leads to reduction in cardiac output and subsequently blood pressure. Post spinal hypotension is managed by intravenous fluid boluses and vasopressors. Fluid therapy may have limitations in patients at risk of fluid overload. Ephedrine is the most commonly used vasopressor in our set up because it's safe and cost effective. Numerous studies have evaluated the role of ephedrine in prevention of post spinal hypotension in orthopaedic surgery ^(5, 6, 8)

We chose to do a study and evaluate the effectiveness of ephedrine when it's used either prophylactically or interventionally in the management of post spinal hypotension during lower limb orthopaedic surgery. We had a total of one hundred and thirty ASA 1 & 2 patients allocated into two groups depending on whether they received ephedrine prophylaxis or not.

Ephedrine administration

In our study the preferred route of prophylactic ephedrine administration was intramuscular. 80% of the patients received 15mg, 14% received 6-12mg while 4.5% received 30mg. The different prophylactic doses were used because at Kenyatta National Hospital, there is no protocol on the standard dose that should be used for prophylaxis. This was administered 10 minutes prior to administration of the spinal blockade. This timing was ideal because the onset of action of intramuscular ephedrine is 10-20 minutes. All patients in both groups received interventional rescue ephedrine if they developed post spinal hypotension requiring vasopressor therapy.

The timing for our administration of prophylactic ephedrine was similar to a study done by Singh S. et al but our doses were lower. In their randomized controlled trial, Singh S et al administered ephedrine 30mg intramuscularly 10minutes before institution of spinal blockade ⁽⁶⁾.

Dermatomal sensory block height

A block height of T10 dermatome was attained by 66.2% of the patients in this study. T6 dermatome was attained by 28.5 % of patients. Only 3.1% attained T4 sensory block and 2.3% attained T12. This sensory block height was slightly lower than what was achieved in the study by Singh S et al where 56% attained a block height of T6 and 41% attained a T8 level. This could be attributed by the fact that in our study, all patients received the same dose of intrathecal bupivacaine and fentanyl whereas in Singh S, et al study, the dose of intrathecal bupivacaine was calculated basing on the patient's weight. This level is adequate for lower limb surgery. ⁽³⁾

Perioperative blood pressure and heart rates trends

Our study showed a decline in average systolic blood pressure and the mean arterial pressure from the baseline in both group. The onset of systolic blood pressure decline was apparent in the first five minutes in both groups and reached an initial maximum fall at thirty minutes in the no prophylaxis group and at forty five minutes in the prophylaxis group. This decline was higher in patients who did not receive ephedrine prophylaxis. These mean heart rates were also better preserved in prophylaxis group as compared to the no prophylaxis group in the first 75 minutes. In the study by Singh S et al, onset of hypotension was immediate and reached a maximum fall at 10 minutes in the ephedrine group and 20 minutes in the polygelline group. This difference in onset of blood pressure decline could be attributed to higher block height in the study by Singh S et al since block height determines the extent of sympathetic blockade and thus the spinal hypotension ⁽¹⁾

Incidence of hypotension

The overall incidence of post spinal hypotension in our study was 50%. The cumulative incidence in the no prophylaxis group was 53.8%. This was slightly higher than the prophylaxis group whose cumulative incidence was 46.2%. This difference in the incidence of hypotension between the two groups did not attain statistical significance. The incidence of hypotension in

our study was higher than in the study by Singh S et al where they found an overall incidence of 36%. In this study 28% of the patients who received ephedrine prophylaxis and 44% of the patients who received 3.5% polygelline preload developed hypotension. However, the incidence of hypotension in the polygelline preload group was comparable to the incidences of hypotension in the no prophylaxis group in our study. This is in keeping with the study by R Jackson et al which showed that volume preload was not essential in the prevention of spinal-induced hypotension.⁽¹⁹⁾ The reduction in the incidences of hypotension in the ephedrine treated group in the study by Singh S et al could be due to the fact that they used a constant prophylactic dose of 30mg of ephedrine in all their patients while in our study majority of the patients received a prophylactic dose of 15mg.

Rescue vasopressors requirements

Not all the patients who developed hypotension required rescue vasopressors therapy. Only patients with clinical features of hypotension or those whose systolic blood pressures fell below 90mmHg were treated with rescue vasopressors. In the no prophylaxis group, 32.3% of patients required rescue vasopressors therapy while in the prophylaxis group, 23.1% required rescue therapy. All the patients who received rescue vasopressors therapy were treated with ephedrine boluses of either 3mg or 6mg. In both groups, only four patients required the use of adrenaline after ephedrine failed to treat their hypotension. Three of these patients had initially received three boluses of ephedrine each of which was 3 mg. The fourth patient had received prophylactic ephedrine 15 mg plus two boluses of rescue ephedrine each 6 mg. This could have been attributed to tachyphylaxis which occurs when ephedrine is repeatedly administered intravenously. The requirement for rescue therapy in our study was higher than in the study by Singh S. et al. In this study, only 10% of patients in the ephedrine group required rescue therapy while in the polygelline group, 30% of patients required rescue therapy with ephedrine. The requirement for ephedrine in the polygelline group was comparable to the requirement in the no prophylaxis group in our study.

Adverse effects of ephedrine

The adverse effects of ephedrine are not common and include hypotension, tachycardia, dysrhythmias, anxiety, nausea and vomiting, tremors and palpitations. In our study, 3% patients

in the prophylaxis group developed hypertension which was transient and short lived and didn't require any treatment. 9.2% of the patients in the prophylaxis group also developed tachycardia that resolved without any treatment. Our results were comparable to studies done elsewhere. J.E Sternlo et al carried out a study comparing the efficacy of prophylactic intramuscular ephedrine 0.6mg /kg vs a placebo in the control of spinal hypotension. Out of 49 patients given ephedrine, only two patients developed adverse effects to ephedrine. One patient developed hypertension while another one developed tachycardia. This was despite the dose of prophylactic ephedrine in their study being almost 3 times higher than the dosage given to most of our patients. In the study by Mohammed Boota, 40 patients received intramuscular ephedrine 45mg immediately after injection of intrathecal bupivacaine. Only one patient suffering from heart failure and atrial fibrillation had a 31% increase in systolic blood pressure. In the study by Singh S et al, 4% of patients who received prophylactic ephedrine developed hypertension, 2% developed bradycardia and 6% had tachycardia. In all these studies, no treatment for the adverse effects was reported and so they could have resolved on their own. Our study therefore demonstrated that ephedrine is a relatively safe drug. ^(6, 8, 10)

Overall outcome

Although it was not statistically significant, prophylactic treatment with ephedrine was associated with a reduction in both the incidence and prevalence of hypotension in the perioperative period. This effect was similarly noted in comparative studies done elsewhere. ^(5, 6, 8, 10, 11, 12) However, most of these other studies were randomized controlled studies and the dosage of ephedrine used was higher than what was used in this study.

Since the results of this study didn't have statistical significance despite the clinical significance, we were not able to reject the null hypothesis that the incidence of hypotension and requirement for rescue vasopressors was similar in patients receiving prophylactic ephedrine compared to those receiving ephedrine on "as-need-arises" basis.

CONCLUSIONS

- Ephedrine was the vasopressor commonly used in the management of post spinal hypotension among patients undergoing lower limb orthopaedic surgery at The Kenyatta National Hospital
- The incidence of spinal induced hypotension in ASA I and ASA II patients undergoing lower limb orthopaedic surgery was 46.2% when prophylactic ephedrine was used and 53.8% when it was used as per need.
- There was no statistically significant difference both in the incidence of hypotension and requirement of rescue vasopressors for the treatment of post spinal hypotension in ASA I and ASA II patients undergoing lower limb orthopaedic surgery whether ephedrine prophylaxis was used or not.
- Side effects are rare with the use of ephedrine and when they occur; tachycardia is the most common followed by hypertension and tremors in our set up.

RECOMMENDATIONS

- Ephedrine is a safe vasopressor and should be used in the management of spinal anaesthesia induced hypotension
- Both prophylactic and PRN ephedrine are equally effective in management of post spinal hypotension and anaesthetists should work with either protocol safely
- Further studies are required to establish other factors that contribute to the high incidence of post-spinal hypotension during elective lower limb orthopaedic surgery at Kenyatta National Hospital.

Study limitations

There were several limitations in this study.

- Missing and erroneous data from record charts.
- Not able to correlate the weight of the patients and the incidence of hypotension
- Time of rescue therapy not recorded therefore unable to determine whether the hypotension was due to the spinal anaesthesia or other factors related to surgery
- Duration of starvation was not recorded thus unable to correlate fluid deficit versus hypotension and vasopressor requirement
- Types of surgery not classified hence correlation between surgery type, blood loss and hypotension not possible

References

1. New York School Of Regional anaesthesia homepage [http://www.nysora.com/techniques/neuraxial and perineuraxial techniques/landmarks based /3423 spinal anaesthesia.html](http://www.nysora.com/techniques/neuraxial_and_perineuraxial_techniques/landmarks_based_/3423_spinal_anaesthesia.html)
2. Ronald D. Miller, Lars I. Eriksson, Lee A. Fleisher, Jeanine P. Wiener, Kronish William L. Young, *Millers anaesthesia seventh edition*, Churchill Livingstone Elsevier, United Kingdom, 2009.
3. Paul G. Barash, Cullen Bruce F.; Stoelting Robert K., Cahalan Michael K., Stock M. Christine, *Clinical Anaesthesia, sixth edition 2009*, Wolter Kluwer/ Lippincott Williams & Wilkins
4. M Goel, M Sharma, A. Kulshreshtra, S. Mashraqui, *Hemodynamic Effects during Combined Spinal and Epidural Anesthesia: Role of Fluid Preloading and Prophylactic Vasoconstrictors*. The Internet Journal of Anesthesiology. 2008 Volume 22 Number 1.
5. S K Kafle, S. M. malla, B.D.Lekhak, *Prophylactic oral ephedrine reduces the incidence of hypotension aftersubarachnoid block*, Canadian journal of anaesthesia 1994 Nov; 41(11):1091-3
6. Singh S, Shah T D, Gupta R, Kaur P, Walia C S, Sehrawat S. *Post spinal hypotension in elderly patientsundergoingorthopaedic surgery. Prophylactic ephedrine versus polygeline 3.5%*. Anesth Essays Res 2014;8:334-8
7. DrHemantBhagat, DrKiran Malhotra, DrSudhir, K. Ghidyal, Dr Prakash, C. Srivastava, *evaluation of preloading and vasoconstrictors as a combined prophylaxis for hypotension during subarachnoid anaesthesia*, Indian journal of anaesthesia, 2004; 48(4): 299-303
8. J. E. Sternlo, A. Rettrup, R. Sandin, *prophylactic i.m ephedrine in bupivacaine anaesthesia*, British Journal of Anaesthesia (Impact Factor: 4.35). 05/1995; 74(5):517-20. DOI: 10.1093/bja/74.5.517
9. Eroglu F, Yavuz L, Ceylan BG, Sevin G, Soyupek S. *Prophylactic effects of systemic oral ephedrine in spinal anesthesia-induced hypotension during transurethral prostatectomy*. Scand J UrolNephrol. 2003;37(2):145-50.

10. Dr Mohammad Boota Dr Sajid Munir, Dr Bilal Baig, Dr Syed Tariq Mohsin, DrSaleem Iqbal, *prevention of post spinal hypotension; a comparison between preloading with and without intramuscular ephedrine in elderly patients undergoing inguinal hernia surgery*. Professional Med J May-June 2012;19(3): 000-000
11. Jabalameli M, Soltani HA, Hashemi J, Behdad S, Soleimani B. *Prevention of post-spinal hypotension using crystalloid, colloid and ephedrine with three different combinations: A double blind randomized study*. Adv Biomed Res 2012;1:36
12. Fawad Ahmed Khan, RuminaTabassum, SaleemSabbar, *Assessment of the efficacy of single dose of ephedrine given prophylactically to prevent hypotension in patients during spinal anaesthesia*, Pak J Surg 2010; 26(1):61-64
13. Madhu Tiwari, Pawan Tiwari, KrishanLalGarg, BalbirChhabra. “*Efficacy of a Single Prophylactic Dose of Ephedrine to Prevent Hypotension in Patients during Spinal Anesthesia*”. Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 48, September 29; Page: 11556-11561, DOI: 10.14260/jemds/2014/3512
14. R. Vasanthageethan, S. Ramesh Kumar, IlangoGanesan. *Prophylactic Oral Ephedrine in Prevention of Hypotension Following Spinal Anaesthesia*. Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 13, February 12; Page: 2138-2143, DOI: 10.14260/jemds/2015/310
15. Abdul Rehman, Harris Baig, M. Zameer Rajput, HumaZeb, *Comparison of prophylactic ephedrine against prn ephedrine during spinal anaesthesia for caesarean section, anaesthesia pain and intensive care* 2011; 15(1);21-24
16. I Desalu, O. T. Kushimo, *Is ephedrine infusion more effective at preventing hypotension than traditional prehydration during spinal anaesthesia for caesarean section in African parturients?*, international journal of obstetric anaesthesia, 2005 Oct;14(4):294-9
17. Mitra J K, Roy J, Bhattacharyya P, Yunus M, Lyngdoh N M. *Changing trends in the management of hypotension following spinal anesthesia in cesarean section*. J Postgrad Med 2013;59:121-6

18. LT Walter Williamson, LT David Burks, LT Jessica Pipkin, Joseph F. Burkard, CDR Lisa Osborne, Joseph E. Pellegrini, *effect of timing of fluid bolus on reduction of spinal induced hypotension in patients undergoing elective Caesarean section*. AANA Journal, April 2009, Vol. 77 No. 2
19. R. Jackson, J. A. Reid, J. Thorburn, *Volume preloading is not essential to prevent spinal induced hypotension at Caesarean section*, British Journal of Anaesthesia 1995;75:262-265
20. reference.[medscape.com/drug/akovaz-ephedrine-342436](http://www.medscape.com/drug/akovaz-ephedrine-342436)

APPENDICES

Appendix 1: Data collection tool

Initials

Age

Sex Male Female

ASA classification ASA 1 ASA II

Block height. (Dermatome level)

Prophylactic ephedrine; Given Not given Dosage if given

Observations

Time (minutes)	Heart rate	SBP	DBP	MAP
Baseline				
5				
10				
15				
20				
25				
30				
45				
60				
75				
90				
105				
120				
135				
150				
165				
180				

Duration of surgery in minutes

Total amount of fluids given

Type of fluid	Amount
Crystalloids	
Colloids other than blood	
Blood	
Total	

Estimated blood loss in mL

Vasopressors used

Agent	Number of boluses	Total dose given
Ephedrine		
Adrenaline		
Others(specify)		

Adverse effects of ephedrine; tick if present

Hypertension	
Tachycardia	
Dysrhythmias	
Anxiety	
Nausea	
Vomiting	
Tremors	
Palpitations	

Appendix ii: The informed consent for the patient

Proposal:

Effectiveness of ephedrine used prophylactically or interventionally in perioperative management of spinal anaesthesia induced hypotension during lower limb orthopaedic surgery

Consent Explanation

My name is DrKariukiNgugi., currently pursuing a postgraduate degree in Anesthesia

I am conducting a study to find out the effectiveness of ephedrine used prophylactically or interventionally in perioperative management of spinal anaesthesia induced hypotension during lower limb orthopaedic surgery

Study purpose

Post spinal hypotension is a common problem arising after the administration of spinal anaesthesia. The current management of this hypotension is use of ephedrine administered either before or after the onset of the hypotension. The purpose of my study is to find out how effective this treatment is in the management of post spinal hypotension.

Study procedure

This study will involve collecting information from the records in your hospital file after spinal anaesthesia has been administered. All the decisions regarding the management of anaesthesia will be determined by the anaesthetist in charge in the theatre where you will be undergoing operation.

Voluntary participation

Your participation in this study is entirely voluntary. Whether you participate or not, all the services you receive in this hospital will continue and nothing will change. You will not be given any money or gifts to participate in this research.

Risks

There are no risks involved for participating in this study since the investigator will only retrieve data from your records and will not intervene in your anaesthetic management.

Benefits of the study

There will be no direct benefits to you for participating in the study but the results from this study will help us in developing strategies for improving patient care in the future.

Study approval

This study is being conducted with the approval of the KNH/UON's Ethics and Research Committee.

Confidentiality

Information about you collected during the study will not be identified by your name but by a number, known only to the researcher, it will not be shared with or given to anyone.

Contact

If there is anything you are concerned about or that is bothering you about the study please feel free to ask me at any time. You may contact me on 0722537927. You may also reach one of my supervisors as follows:

Dr Patrick Olang' 0722532116,

Dr Thomas Chokwe 0722528237,

In addition, for any queries on ethical issues, contact:

KNH/UON Nairobi Ethical and Research Committee - 020 726300-9

Thank you

Consent form for the Patient

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research and understand that I have the right to withdraw from the research at any time without in any way affecting my medical care.

Name of Participant

Signature of Participant

Date

Maelezoyakibaliyamgonjwa

Jina langu ni DrKariuki Ngugi. Mimi ni mwanafunzi katika chuo kikuu cha Nairobi. Ninasomea masomo ya udaktari. Nina fanya utafiti ya kujua umaarufu wa dawa aina ya ephedrine inapotumika kutibu upungufu wa pressure baadaya anaesthesia ya uti wa mgongo. Utafiti huu una lenga baadhi ya wagonjwa wanaofanyiwa oparesheni kwenye sehemu za miguu na mapaja kwa kutumia anaesthesia ya uti wa mgongo katika hospitali ya kitaifaya Kenyatta. Na kukaribisha kushiriki kwa utafitihuu.

Nia yautafiti

Kupungua kwa pressure ni moja yamadhara yanayotokea wakati wagonjwa wanapewa anaesthesia ya uti wa mgongo. Huu upungufu wa pressure unaweza kuleta madhara zaidi iwapo hautagunduliwa mapema na tiba kupeanwa haraka iwezekanavyo. Kwa kawaida wagonjwa wapatao hii shinda ya upungufu wa pressure huwa wanatibiwa na dawa ainaya ephedrine ambayo hundungwa kabla ya anaesthesia au wakati pressure imeenda chini baada ya kupewa anaesthesia. Utafiti wangu una lengo ya kubaini umaarufu wa kwa matumizi haya.

Jinsi utafiti utakaofanyika

Utafiti huu utahusisha kupata rekodi ya utabibu wako kwenye file yako baada ya kutibi wa kwa aina ya anaesthesia ya uti wa mgongo. Uamuzi wowote kuhusu utabibu wowote utafanywa na daktari atakaye kupea hiyo anaesthesia.

Kujumuishwakwako

Kujumuishwa kwako katika utafiti huu ni kwa hiari yako na unaweza kujitoa wakati wowote bila kuingilia matibabu yako kwa vyovyote vile. Utafiti huu hautakugharimu pesa zozote, haitaongeza ada yako ya hospitali. Si lazima unufaike kwa kushiriki katika utafiti huu lakini utafiti huu utatusaidia katika matibabu ya wagonjwa watakaohitaji matibabu yetu hapo baadaye.

Madharayautafiti

Hakuna madhara yoyote yanayo tarajiwa kutokana na kushiriki katika utafiti huu kwa sababu mtafiti hatahusika kwa vyovyote kwenye utabibu. Mtafiti atatumia tu rekodi zako za matibabu

Manufaa ya utafiti

Si lazima unufaike kutoka kwa utafiti huu lakini matokeo ya utafiti huu utatusaidia kuimarisha matibabu ya wagonjwa katika enzi zijazo.

Idhini ya utafiti

Utafiti huu umeidhinishwa na KNH/UON Ethics and Research Committee

Siri

Majina yako, ugonjwa unaogua na mambo yote tutakayo jua kukuhusu yatabaki siri.

Kuwa siliana nami

Kwa maelezo zaidi au malalamishi yoyote, wasiliana name kwa nambari ya simu 0722537927. Aidha, unaweza ukawasiliana na mmoja wa wasimamizi wangu kama walivyoandikwa hapa chini

Dkt Patrick Olang' 0722532116,

Dkt Thomas Chokwe 0722528237,

Pia, kwa maswali ya nayohusu maadili, unaweza kuwasiliana na KNH/UON Ethical and Research Committee -020 726300-9.

Asante.

Kibali cha mgonjwa

Nimesoma/nimesomewa maelezo ya utafiti. Nimepewa fursa ya kuuliza maswali na nimejibiwa kikamilifu. Nimekubali kwa hiari yangu kushiriki katika utafiti huu. Ninaelewa kwamba niko na haki ya kujitoa kwa utafiti huu wakati wowote bila kupoteza haki yangu ya matibabu.

Jina la mshiriki

Sahihi ya mshiriki

Tarehe.....

Appendix iii: Consent for the anaesthetist

My name is Dr. Kariuki Ngugi. I am currently pursuing a postgraduate degree in Anesthesia

The study;

Effectiveness of ephedrine used prophylactically or interventionally in perioperative management of spinal anaesthesia induced hypotension during lower limb orthopaedic surgery. This will be an observational study and will involve extracting information from the anaesthetic record during the course of anaesthesia and surgery.

Participation in the study

Your participation in this study will be voluntary and you may decide to withdraw from it at any stage without any penalty.

Study approval

This study will be conducted with the approval of The Kenyatta National Hospital/University of Nairobi Ethics and Research Committee.

Confidentiality

Your identity will be protected with utmost confidentiality during the study and your personal details will not be recorded in the data collection tool.

Contacts

For any clarifications or queries you may contact me on the telephone number 0722537927. You may also reach one of my supervisors as follows:

Dr Patrick Olang' 0722532116,

Dr Thomas Chokwe 0722528237,

In addition, for any queries on ethical issues, contact:

KNH/UON Nairobi Ethical and Research Committee - 020 726300-9

Consent Form for the Anaesthetist

I..... (Initials only) have read and understood the explanation of this study.

I have freely chosen to participate in the study and understand that whether or not I participate, the care I give patients will not be compromised in any way whatsoever.

I understand that I may choose to withdraw from the study at any stage without any penalty.

Signed..... (Anaesthetist)

Date

Appendix iv: Antiplagiarism certificate

Turnitin Originality Report

EFFECTIVENESS OF EPHEDRINE USED IN PERIOPERATIVE MANAGEMENT OF SPINAL ANAESTHESIA INDUCED HYPOTENSION DURING LOWER LIMB ORTHOPAEDIC SURGERY by Peter Ngugi Kariuki

From Anaesthesia (Masters of Medicine)

- Processed on 29-Sep-2017 11:44 EAT
- ID: 854442800
- Word Count: 10251

Similarity Index

11%

Similarity by Source

Internet Sources:

5%

Publications:

5%

Student Papers:

5%

Appendix v: Ethical approval letter



UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel: (254-020) 2723100 Ext: 44355



KNH-UoN ERC
Email: uonknh_erc@uonbi.ac.ke
Website: <http://www.erc.uonbi.ac.ke>
Facebook: https://www.facebook.com/uonknh_erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC



KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726800-9
Fax: 726272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/18

23rd January 2017

Dr. Ngugi Peter Kariuki
Dept. of Anaesthesia
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Kariuki

Revised Research Proposal: "Effectiveness of Ephedrine used prophylactically or interventionally in perioperative management of Spinal Anaesthesia induced Hypotension during lower limb orthopaedic surgery (P762/011/2015)"

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above revised proposal. The approval period is from 23rd January 2017 – 22nd January 2018.

This approval is subject to compliance with the following requirements:

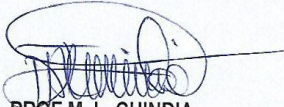
- Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
- All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
- Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
- Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
- Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. *(Attach a comprehensive progress report to support the renewal)*
- Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
- Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Kindly arrange to submit a copy of registration by Pharmacy and Poisons Board and approval when ready..

Protect to discover

For more details consult the KNH- UoN ERC website <http://www.erc.uonbi.ac.ke>

Yours sincerely,



PROF M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
 The Deputy Director, CS, KNH
 The Assistant Director, Health Information, KNH
 The Chair, KNH- UoN ERC
 The Dean, School of Medicine, UoN
 The Chair, Dept. of Anaesthesia, UoN
 Supervisors: Dr. Patrick Olang', Dr. Thomas Chokwe