Addis Ababa University

College of Health Sciences

Department of Anesthesia

HEMODYNAMIC RESPONSE OF LOW DOSE BUPIVACAINE WITH FENTANYL, VERSUS NORMAL DOSE BUPIVACAINE ALONE IN ELDERLY PATIENTS WHO UNDERGO LOWER EXTREMITY ORTHOPEDICS SURGERY UNDER SPINAL ANESTHESIA AT, TIKUR ANBESSA SPECIALIZED, HOSPITAL.

BY: BEHAKU AWEL (MSc Student in Anesthesia)

Advisors: Adugna Aregawi (BSc, MSc in Anesthesia, Assistant Professor)

Sulaiman Jemal (BSc, MSc in Anesthesia, Lecturer)

A MASTERS THESIS IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR MASTER OF ANESTHESIA IN ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCE, SCHOOL OF MEDICINE.

JUNE 2019

ADDIS ABEBA, ETHIOPIA

ADDIS ABABA UNIVERISITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE
DEPARTMENT OF ANESTHESIA

HEMODYNAMIC RESPONSE OF LOW DOSE BUPIVACAINE WITH FENTANYL, VERSUS NORMAL DOSE BUPIVACAINE ALONE IN ELDERLY PATIENTS WHO UNDERGO LOWER EXTREMITY ORTHOPEDICS SURGERY UNDER SPINAL ANESTHESIA

PRINCIPAL INVESTIGATOR: BEHAKU AWEL (BSC, MSc STUDENT)
MAIL: behakuawel3@gmail.com
PHONE: +251-920-095-065

ADVISORS: Adugna Aregawi (BSc, MSc in Anesthesia, Assistant Professor)
Sulaiman Jemal (BSc, MSc in Anesthesia, Lecturer)

JUNE 2019
ADDIS ABEBA, ETHIOPIA

ABSTRACT

Background: Spinal anesthesia is a widely used technique for surgery in the elderly. Due to its efficacy, rapidity, reduction of blood loss, and protection against thromboembolic complications. However, associated with exaggerated responses to conventional doses of local anesthetics in elderly patients; thereby increasing hemodynamic complications and as high as 50% hypotension incidence in this patients. An alternative method has been designed to minimize these unwanted hemodynamic effects by administration of adjuvants with low dose of local anesthetics.

Objective: To compare the effectiveness of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone on hemodynamic response, onset and duration of block and complication in elderly patients who undergo lower extremity Orthopedics surgery under spinal anesthesia at Tikur Ambessa Specialized Hospital from November, 2018 - April, 2019

Methods: prospective cohort study design was employed on a total of 64 elderly lower extremity orthopedics procedures, non-exposed group (Group B) received 15 mg of 0.5% isobaric bupivacaine alone and study group (group BF) taken 10mg of 0.5% isobaric bupivacaine with 25mcg of fentanyl to see the effect on hemodynamic changes after spinal anesthesia. SPSS version 25 used for analysis, normality of distribution for continuous variable was tested by Shapiro-Wilk test then parametric data was analyzed by using independent t-test and nonparametric data by Mann-Whitney U-test and categorical data by using chi-square test and fisher exact test. The level of statistical significance for all tests taken $P < 0.05$.

Results: The incidence of hypotension after spinal anesthesia was higher in group B than group BF) (37.5% vs. 9.4%), respectively: p=0.008) and Group BF showed better hemodynamic stability. Considerable difference was noticed in intravenous fluid consumption between groups, group B (1420±97ml) and group BF (1215±94ml) having *(p<0.01).* Higher rate of vasopressor was used in group B than group BF (18.8%), vs. 3.1%), respectively*; (p=0.045).* In our finding group BF had fast onset of sensory block and prolonged time of first analgesia request

Conclusion: Spinal anesthesia for elderly patients undergoing lower extremity surgeries with 10mg of 0.5% bupivacaine and 25µg fentanyl is a reliable and better option, with regard to maintaining hemodynamic stability and lower occurrence of complications without affecting the desirable surgical conditions as well as fast onset of sensory block and prolonged first analgesia request time

Keywords: Spinal anesthesia, bupivacaine, fentanyl 25mcg, hemodynamic response, elderly

ACKNOWLEDGEMENTS

First of all, I would like to thanks to Addis Ababa University for financial and other support

Secondly I wish to acknowledge my debts to my advisor Mrs. Adugna Aregawi and Sulaiman Jemal for their continuous help and guidance, and I wish to thank them for their suggestions, comments and valuable advice to develop thesis paper.

There are no words to express my feeling towards those who enlightened my way throughout the period of conducting my thesis.

Then, I would like to express my great gratefulness towards those authors and researchers of articles, and on-line information for the valuable works I have read and cited in my paper.

Table of Contents

List of tables

List of figures

LIST OF ACRONYMS AND ABBREVATIONS

AAU	Addis Ababa University
ASA	American Societies of Anesthesiology
BMI	Body Mass Index
BP	Blood Pressure
BSc	Bachelor science
DBP	Diastolic blood pressure
DC	Data Collector
Group B	Bupivacaine alone
Group BF	Bupivacaine with fentanyl
Intra-OP	Intra-operative
IV	Intravenous fluid
LA	Local Anesthetics
MAP	mean arterial pressure
NRS	Numeric rating scale
OR	Operation theater
PR	Pulse rate
RCT	Randomized control trial
RD	Respiratory depuration
RR	Respiratory rate
SA	Spinal Anesthesia
SBP	Systolic blood pressure
SpO_2	Oxygen saturation
SPSS	Statistical Package for the Social Sciences
TAR	Time of first analgesia request
TASH	Tikur Anbessa specialized hospital

CHAPTER ONE: INTRODUCTION

1.1 Background

Spinal anesthesia is a widely used anesthetic technique for surgery in the elderly. It is often preferred for its efficacy, rapidity, minimal effect on mental status, reduction of blood loss, and protection against thromboembolic complications.[1]

It also reduces surgical stress by blocking nociceptive afferent input signals from the traumatized site and prevents sympathetic as well as segmental efferent nerve activity. The application of regional anesthesia in elderly patients has been recommended.[2] Because of its simplicity and high success rate spinal anesthesia (SA) belongs to the most common used regional anesthesia techniques in elderly.[3]

Spinal anesthesia may be indicated as the primary anesthetic for major or minor surgeries. It is most useful as the primary anesthetic technique in surgeries involving the abdomen, perineum, or lower extremities.[4]

Potential outcome benefits of spinal anesthesia techniques include avoidance of intubation and mechanical ventilation, decreased blood loss, better perioperative analgesia, less opioid use, protection against thromboembolic complications, and potentially less postoperative cognitive dysfunction (POCD) in elderly population.[5]

Advanced diagnostic and therapeutic facilities have enhanced the life expectancy of humans, as a result of which elderly population is expected to rise 25% by 2020; 506 million as of 2008 and by 2040 will increase to 1.3 billion across the world.[6]

As humans age, there is a general decline in organ function, although there is wide inter individual variability (e.g., some organs might be affected more than others). Most importantly, the cardiovascular and pulmonary systems have reduced function that might impact patients' physiologic responses during surgery and anesthesia.[7]

Age and concurrent diseases make these patients at high risk for perioperative complications. Despite regional anesthesia has a better postoperative outcome, hypotension and bradicardia is common and increases the risk of myocardial ischemia. The main effect of spinal anesthesia was

the reduction of systemic vasicular resistances (SVR) which were reduced by 18% ± 17.2%. The average cardiac index (CI) was initially reduced by 5.2- 6.6%, and it was persistently reduced during the surgical period.[8, 9]

The elderly population is especially challenging when one has to consider all of the pharmacodynamics changes that occur with normal aging.[10] Blood vessel distensibilty is drastically decreased in elderly patients and, combined with increased intimal thickness and endothelial dysfunction, will increase systolic blood pressure, as well as left ventricular workload. Myocardial hypertrophy, along with increased collagen content, creates a stiff left ventricle that depends on adequate preload to maintain cardiac output. This makes elderly patients much more susceptible to fluid overload.[11]

Fluid overload is associated with edema, ileus, postoperative nausea and vomiting, pulmonary complications, and increased cardiac demands.[4] This is due failure of autonomic reflexes responsible for of cardiovascular homeostasis in aged population.[12]

In addition; blunted baroreflex make geriatric patients less able to respond normally to hypovolemia and much more affected to orthostatic hypotension with drug therapy.[13] Orthopedic injuries, especially to the long bones such as the femoral neck, were the most common injury in elderly patients.[14] Osteoarthritis and rheumatoid arthritis increase with age, so does procedures to treat these conditions. High prevalence of skeletal disease plus increased fall risk leads to high incidence of fractures.[15]

Spinal anesthesia in the elderly is associated with exaggerated responses to conventional doses of local anesthetics, thereby increasing the incidence of hemodynamic complications. Some studies suggested that Spinal anesthesia for elderly patients undergoing lower limb surgeries with 2cc bupivacaine 0.5% and 25 μg fentanyl is a safer and better option, both in terms of maintaining hemodynamic stability and lower incidence of complications without compromising the surgical conditions.[16]

Bupivacaine is a widely used local anesthetic agent, is an amide-type, long-acting local anesthetic.[17]

Intrathecal opioid neither by itself nor in combination with LA causes any further depression of efferent sympathetic activity. Therefore, it can enhance sensory blockade without changing the degree of sympathetic blockade, and hence a decrease incidence of intraoperative hypotension.[18] Fentanyl is synthetic opioid with no histamine release thus less hemodynamic effect. Addition of fentanyl for neuraxial anesthesia produces a better- quality of block and reduces anesthetic requirments.[19]

1.2 Statement of the problem

Hypotension after conventional dose of bupivacaine during spinal anesthesia in elderly patients accounts about 50%.[16]

Elderly patient is not simply an older adult, but, rather, a truly different physiologic entity.[20]
The high incidence of coronary disease in this population increases the risk of ischemia secondary to the hypotension. Aging also associated with decreased baro-reflex activity. There is considerable controversy over the use of vasopressors and intravenous fluids to treat or prevent the hypotension of spinal anesthesia (HSA). Unfortunately, none of these methods are without potential ill effect.

The question of an adequate treatment for avoidance of hypotension during SA are still subject to debate.[2] Preloading the patient with intravenous fluid (electrolyte and/or colloid) is widely used; however any increase in cardiac output, stroke index and central venous pressure that may be achieved is of short duration and the vasodilatation, as the primary cause of hypotension, remains uncorrected. [21,22]
Another approach has been to minimize HSA by using small or titrated doses of local anesthetic with adjuvant. A comparison of spinal with titrated dosing *versus* single-dose spinal anesthesia found that the former technique led to less frequent and less pronounced decreases in mean arterial pressure with significantly less use of vasopressors and fluid requirements.[23]

"Mini-dose" bupivacaine in combination with fentanyl provides completely satisfactory spinal anesthesia for surgical repair of hip fracture in the elderly. This combination, in comparison with a conventional dose of bupivacaine alone, caused dramatically less hypotension and nearly eliminated the need for vasopressor and fluid support of blood pressure.[23, 24]

Intrathecal opioids enhance analgesia from sub therapeutic doses of local anesthetic and make it possible to achieve successful spinal anesthesia using otherwise inadequate doses of local anesthetic. Yet because intrathecal fentanyl causes neither by itself nor in combination with bupivacaine any further depression of efferent sympathetic activity, it is possible to enhance the sensory blockade without altering the degree of sympathetic blockade.[25]

Elderly patients having insertion of a Richards pin and plate and compared 7.5 mg hyperbaric bupivacaine with added fentanyl 20 mcg (group BF) to 12.5 mg hyperbaric bupivacaine alone (group B). An overall incidence of hypotension was 59.5%. There was no difference in the incidence or severity of hypotension between the two groups.[26]

CHAPTER TWO: LITERATURE REVIEW

With addition of low-dose sufentanil, dose of a local anesthetic can safely lowered by 40% in the elderly population. This can avoid the hemodynamic instability, providing a stable perioperative and postoperative condition and prolong duration of sensory analgesia.[18]

A comparative study conducted by Bhrigu in India(2017) on efficacy of 12.5mg hyperbaric bupivacaine plus saline (group 1) versus bupivacaine 12.5mg plus 25mcg fentanyl (group 2) in geriatric patients undergoing hip replacement surgery. Hypotension was present in 9 and 11 subjects of group 1 and group 2 respectively. Nausea and vomiting was present in 3 and 1 subject of group 1 and group 2 respectively.[27]

A double blinded, prospective, randomized, comparative study done In India, 2015 by Mehta et al. on elective elderly orthopedic lower limb surgeries under spinal anesthesia. Onset of adequate level of sensory block (T10) was longer for group B (Bupivacaine 10 mg and fentanyl 25mcg) (128 +/- 8.3sec) than group A (Bupivacaine 15mg) (95 +/- 10.32sec) and was statistically significant. Duration of motor blocks in group A (162.5 +/- 7.5min) and in group B (129.4 +/- 9.9min) and the difference was statistically significant. Lower pulse rates and less fall in blood pressure was occurred in group B than group A. Incidence of hypotension and use of vasopressors was much higher in group A and was statistically significant. Bradycardia and pruritus was common in group B. Shivering was higher in group A.[28]

a. <u>To evaluate the effect on hemodynamic changes in the intra operative and post-operative period.</u>

RCT had done by Faisal M, in Pakistan (2012) on hemodynamic response of spinal anesthesia in elderly orthopedic patients. Group-A received hyperbaric bupivacaine 7.5 mg and fentanyl 15 µgm while group-B received hyperbaric bupivacaine 15 mg. thirty patients in each group. Fall in MBP at 15 minutes, 30 minutes and 60 minutes in group B (bupivacaine alone) was statistically significant difference (p= 0.010, 0.011 and 0.026 respectively) between the two groups. Hypotension in the group B was significantly higher 73.3% (22 of 30 patients) and 10% (3 of 30 patients) in the group A and statistically significant. Mean ephedrine usage was highly

significant in group B than group A (40mg to 10mg respectively). In group B 22 patients from 30 (73.3%) needed ephedrine and in group A, 3 patients from 30 (10%) and (p-value < 0.05) between groups.[29]

.

Study done by Yucel A, et al, in Turkey (2012) on hemodynamic effects intratecal fentanyl 25 mcg (Group F) alone and fentanyl 25 mcg plus hyperbaric bupivacaine 2.5 mg (Group BF), or epidural anesthesia adding fentanyl 50 mcg (Group E) by combined spinal epidural anesthesia technique in elderly patients. Intrathecal hyperbaric bupivacaine 2.5 mg plus fentanyl 25mcg administration provides shorter motor block onset time, less local anesthetic usage and adequate hemodynamic stability in elderly patients.[30]

Study done by Khanna et al. in India (2012) forty geriatric patients undergoing hip replacement surgery under spinal anesthesia with 12.5 mg bupivacaine plus saline (SS; n = 20) or 25mcg fentanyl (FN; n = 20). Group FN had more pruritis (p <0.02) and lower SaO2 (p <0.007), but prevalence of side effects was similar. Pain intensity (visual analog scale [VAS]), at the time of analgesia request (FAR) was lower in group FN (p <0.01). 25 *mc*g fentanyl during spinal anaesthesia to elderly patients premedicated with benzodiazepines for sedation, does not alter characteristics of motor block; prolongs the sensory block; improves intraoperative analgesia; produces postoperative pain relief; preserves the cognitive function, but induces pruritus and decreases O2 desaturation.[31]

Study done by Khanna et al in India (2002), Systolic B.P. decreased in bupivacaine alone (group A) and bupivacaine with fentanyl (Group B), maximum fall occurred at 15 to 20 min in both the groups: decreases were more severe in group A than in group B,(P<0.O5).heart rates were better maintained in group B than in group A. Group B had lesser duration of motor blockage without significantly compromising the duration of sensory block or the operative conditions. None of the patients required intraoperative anesthetic supplementation. From 30 of them 8 patients in group B had pruritus while none of the patients developed respiratory depression.[16]

In contrast, study done in Australia by Martyr JW, Clark MX in 2001 studied 42 elderly patients having insertion of a Richards pin and plate and compared 7.5 mg hyperbaric bupivacaine with

added fentanyl 20mcg (group BF) to 12.5 mg hyperbaric bupivacaine alone (group B). An overall incidence of hypotension was 59.5%. There was no difference in the incidence or severity of hypotension between the two groups. Two patients from group B and one from group BF experienced mild discomfort. Pruritus was more common in group BF.[25]

b. <u>To compare onset of block</u>

A double-blind, prospective, comparative study done by Kumar S in India(2016) on combined spinal epidural anesthesia using low dose local anesthetic with addition of sufentanil in lower limb surgery for elderly patients. Group I (control group) had a greater incidence of hypotension and, consequently, higher use of vasopressors ($P<0.05$). Onset of sensory analgesia, time to achieve peak sensory level, and recovery from motor blockade were significantly earlier in group II (bupivacaine with sufentanil) ($P<0.05$). Significantly higher incidence of shivering in group I ($P<0.05$).[18]

RCT conducted by Zakir N et al in Iran (2014), to compare the duration of spinal anesthesia with bupivacaine alone and in combination with fentanyl in opium abusers undergoing lower extremity orthopedic elective surgical operations. Fifty patients participated and the mean duration of sensory block was much shorter in the control group (70.47 ± 5.45 minutes) compared with the study group (87.8 ± 7.22 minutes) ($P < 0.001$). Also mean time of achieving to maximum level of block and Mean time of two-segment regression in studied group were significantly higher than control group ($P < 0.01$).[32]

c. <u>Comparing perioperative complications.</u>

Study done by Chico A. *et al* in France, 2003, on comparison of the hemodynamic response of subarachnoid anesthesia with bupivacaine versus bupivacaine with fentanyl in traumatology surgery in elderly patients. Group F given 5 mg of bupivacaine and 15 mcg of fentanyl and Group B received 7.5 mg bupivacaine. Group F patients were more hemodynamically stable and more hypotensive episodes occurred in group B. Group B consumed significantly more ephedrine ($p < 0.05$), administered to 22 patients in group B and 6 in group F. The total dose of ephedrine administered was greater in group B (190 mg) than in group F (40 mg).[33]

In 2000, comparative study done by Ben-David et al. Twenty patients aged ≥70 yr undergoing surgical repair of hip fracture were randomized into two groups of 10 patients each. Group A received a spinal anesthetic of bupivacaine 4 mg plus fentanyl 20mcg, and group B received 10 mg bupivacaine. One of 10 patients in group A required ephedrine, a single dose of 5mg. Nine of 10 patients in group B required vasopressor support. Group B required an average of 35 mg ephedrine, and two patients required phenylephrine. The lowest recorded systolic, diastolic, and mean blood pressures as fractions of the baseline pressures were, respectively, 81%, 84%, and 85% versus 64%, 69%, and 64% for group A versus group B.[23]

A prospective, single, blind, randomized study conducted Goel S. *et al* in 45 adult males (15 in each 3 group) and bupivacaine 0.17% 5mg-with fentanyl 7.5mcg, 10mcg or 12.5mcg those patients scheduled for minor urological procedures using intrathecal anesthesia on a day care basis. The time to two-segment regression and S2 regression with fenta-12.5 was significantly longer than with fenta-7.5 and fenta-10 ($P < 0.01$). Fenta-7.5 had a significantly higher number of failed blocks (four patients) compared with fenta-12.5 ($P < 0.05$). Hemodynamic stability did not differ for all the drug combinations.[34]

Study done by Gurbet A et al. in out-patient anorectal surgery with addition of 25 mcg fentanyl to an ultra-low (sub-anesthetic) dose of intrathecal 2.5mg of 0.5% bupivacaine plus 25mcg fentanyl (group BF, n=18) or 5mg 0.5% bupivacaine alone (group B, n=17). There were no significant differences in intraoperative outcomes, but mean recovery significantly shorter in group BF. There were no between-group differences in hypotension, bradycardia or respiratory depression and post-operative complications were comparable, apart from pruritus which was significantly more frequent in group BF. Fewer patients requested analgesic medication in the early post-operative period in group BF than in group B.[35]

2.1 Significance of the study

For elderly patients, currently, no target anesthesia method and medicines to be provided. But, when selecting anesthesia method and medicines "easy, safe, good effect" is mainly considered as general principle.[36]

Hypotension after conventional dose of bupivacaine during spinal anesthesia in elderly patients accounts about 50%.[16]

In contraries to the earlier report, there were studies that show no significant difference in incidence or severity of hypotension between the two groups.[26, 37]

Prevention of hypotension in elderly population is much more important than that in normal population for a favorable hemodynamic outcome. One approach has been to lower spinal anesthesia induced hypotension is by using small doses of local anesthetics with adjuvant techniques.[38]

Although the use of a single shot low dose local anesthetic for spinal blockade may limit hypotension, it may not provide acceptable anesthesia.[39] Low dose bupivacaine associated with short durations of motor and sensorial block.[40]

More studies are needed to better identify which anesthetic techniques are most beneficial, and perhaps which subsets of patients will benefit from particular regional as well as adjuvant techniques mostly.

All studies have been conducted in this particular group of patients are from the developed world and Asian populations. As we know functional capacity altered by physical and mental activity level, comorbidities, social habits, diet and genetic background.

The aim of the study is to compare hemodynamic response of conventional dose of bupivacaine versus low dose bupivacaine with fentanyl in elderly orthopedic patients so as to provide reliable spinal block for the elderly, with better hemodynamic stability, few side-effects, using a single-shot and low-dose technique, clear management option and add to the existing knowledge as well.

The result of the study is also helpful for program planners and policy makers to devise strategies which in turn help to improve patient's safety. There are limited researches in this topic. So it could be used as a baseline data.

2.2 Statement of Statistical Hypotheses

Ho1: we hypothesize that low dose bupivacaine with fentanyl will not produce statistically significant hemodynamic difference than bupivacaine alone on elderly orthopedics.

HA1: we hypothesize that low dose bupivacaine with fentanyl will produce statistically significant hemodynamic difference than bupivacaine alone on elderly orthopedics.

Ho2: There is no statistically significant difference in onset of block between groups

HA2: There is statistically significant difference in onset of block between groups

Ho3: There is no statistically significant difference in duration of analgesia between groups.

HA3: There is statistically significant difference in duration of analgesia between groups.

Ho4: There is no statistically significant difference in side effects between groups.

HA4: There is statistically significant difference in side effects between groups.

Experimental method we will measures quantities that can vary hemodynamic-variables such as heart rate, blood pressure, oxygen saturation, total IV fluid used, vasopressors used.

Experimental method we will measures quantities that can vary side effects are pruritus, nausea, vomiting, shivering etc.

CHAPTER THREE: OBJECTIVES

3.1 General Objective

To compare the effectiveness of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone on hemodynamic response, onset and duration of block and complication in elderly patients who undergo lower extremity Orthopedics surgery under spinal anesthesia at TASH from November, 2018 - April, 2019

3.2 Specific Objectives

1. To compare hemodynamic changes in the intra operative and post-operative period of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone in elderly patients who undergo lower extremity Orthopedics surgery under spinal anesthesia at TASH from November, 2018 - April, 2019

2. To compare onset of block of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone in elderly patients who undergo lower extremity Orthopedics surgery under spinal anesthesia at TASH from November, 2018 - April, 2019

3. To compare the duration analgesia of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone in elderly patients who undergo lower extremity Orthopedics surgery under spinal anesthesia at TASH from November, 2018 - April, 2019

4. To compare the perioperative complications of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone in elderly patients who undergo lower extremity Orthopedics surgery under spinal anesthesia at TASH from November, 2018 - April, 2019

CHAPTER FOUR: MATERIALS AND METHODS

4.1 Study Area and Period

The study was conducted at Tikur Anbesa specialized hospital which is a very large referral hospital and sees approximately 370,000- 400,000 patients a year but the exact number is not known. The hospital is the largest teaching hospital for Addis Ababa University, School of Medicine in Ethiopia. It is one of the thirteen governmental hospitals found in Addis Ababa. The Hospital gives orthopedics services for all age groups. It has three functional orthopedic operation theatres and one in the way of functionality. The durations of the study extends from November, 2018 - April, 2019

4.2 Study Design

Institutional based prospective cohort study design was employed.

4.3 Population

4.3.1 Source Population

All elderly patients who undergone orthopedics lower extremity surgery under spinal anesthesia at TASH

4.3.2 Study population

All elderly patients who undergone elective orthopedics lower extremity surgery under spinal anesthesia at TASH from November, 2018 - April, 2019

4.4 Eligibility criteria

4.4.1 Inclusion criteria

(1)Age ≥60 years old;

(2) ASA Class I-II

(3) spinal anesthesia with 15mg of 0.5% isobaric bupivacaine alone and 10mg of 0.5% isobaric bupivacaine with 25 mcg fentanyl

4.4.2. Exclusion criteria

1. Failed spinal converted to general anesthesia
2. Analgesic or preoperative medication given patients that might influence analgesia or sedation to the patients
3. Preoperative hyper or hypotensive pts.
4. Emergency procedures are excluded from the study.

4.5 Sample size determination and sampling technique

4.5.1. Sample size determination

Hemodynamics response (hypotension) was one of our primary outcome indicators and from previous observational study which was done in India (Mehta S. et al, 2015).[28] Since there is no documented similar study that is done in the same topic with same study population to my title in our country and there result showed that the incidence that was developed intraoperative hypotension in conventional dose of bupivacaine alone and low dose of bupivacaine with fentanyl group were 40% and 10% respectively. By assuming equal sample size for two groups, the sample size was determined by double population proportion formula as,

$n_1=n_2 = (Z_{\alpha/2}+Z_{\beta})^2 * (p_1 (1-p_1) +p_2 (1-p_2)) / (p_1-p_2)^2 \ =\sim 28.7 = 29$

Where, n1= number of patients that will take low bupivacaine with fentanyl (BF) Group

n2 = number of patients that will take conventional dose of Bupivacaine alone (CB)

Z= 95% confidence interval =1.96

f (α, β) = the power function at 80%= 0.84

P1= proportion of patients that had intraoperative hypotension in BF group

P2 = proportion of patients that had intraoperative hypotension in CB group

Therefore, the total sample size was32 patients in each group adding 10 % contingency

4.5.2 Sampling Technique:

Patients' age ≥60 years who undergoing orthopedics lower extremity surgery were recruited by systematic random sampling into the study. From TASH Orthopedics operation registration book we got 88 elective orthopedics lower extremity procedures were performed in age ≥60 years for four consecutive months before study period. We got skipping interval of 1.5 to recruit 64 study participants. Two patients from every 3 patients were recruited from the schedule during the study period. Adequate history were taken about demographic data interviewed for inclusion and exclusion criteria and cross checked to their charts and consent for voluntary participation in the study was obtained from the participants. Based on the decision of anesthetists selected participants were placed on either group till the required sample size filled.

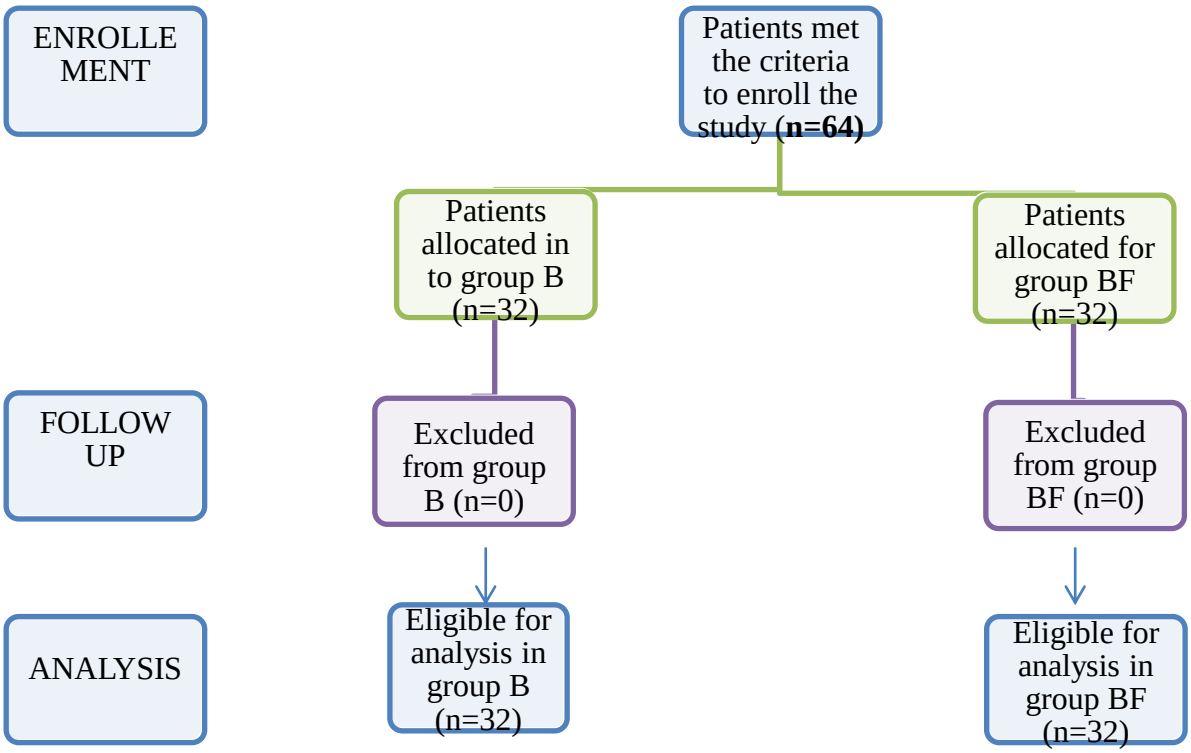


Figure 1*: Flow chart of clients enrolled in the study period at Tikur Anbessa Specialized Hospital from November 15, 2018-April 15, 2019, Addis Ababa, Ethiopia,*

4.6 Study variables

Independent variables:

Age (yr.), body weight (kg), height (cm), body mass index (kg/m2), baseline SBP, baseline MAP, baseline HR, baseline SaO_2, baseline iv fluids, block height (dermatome level), duration of surgery (min), estimated blood loss (ml), , dose of LA drugs (isobaric 0.5% of 15mg bupivacaine alone , isobaric 0.5% bupivacaine of 10mg with 25mcg fentanyl)

Dependent variable: hemodynamic response (hypotension), onset of sensory and motor block, duration of analgesia, and complications.

4.7 Operational Definitions

Anesthetist: is a licensed professional to administer general as well as regional anesthesia to the Patient undergoing surgery.

ASA status: is a surgical risk stratifications validated by American Society of Anesthesiologist; described as follows: [41]

ASA I: A normal healthy patient. Example: Fit, no obese (BMI under 30), a nonsmoking patient with good exercise tolerance.

ASA II: A patient with a mild systemic disease. Example: Patient with no functional limitations and a well-controlled disease (e.g., treated hypertension, obesity with BMI under 35, frequent social drinker or is a cigarette smoker).

ASA III: A patient with a severe systemic disease that is not life-threatening. Example: Patient with some functional limitation as a result of disease (e.g., poorly treated hypertension or diabetes, morbid obesity etc.

ASA IV: A patient with a severe systemic disease that is a constant threat to life. Example: Patient with functional limitation from severe, life-threatening disease (e.g., unstable angina, poorly controlled COPD, symptomatic CHF, recent (less than three months ago) myocardial infarction or stroke.

Bromage scale:

Activity	**Score**
Able to lift legs against gravity	0
Able to flex knee but unable to flex legs	1
Able to move feet but unable to flex knee	2
Unable to move any joints	3

Conventional dose of bupivacaine is considered as a dose of intrathecal 0.5% of 15mg bupivacaine alone

Elderly patients – elderly refers to people that are 60 years of age and above.[27, 42]

Elective: is surgery done before on set (appearance) of any complication that may constitute urgent surgical indication.

Emergency: is surgery done at onset or near appearance of any complication that may constitute urgent indication

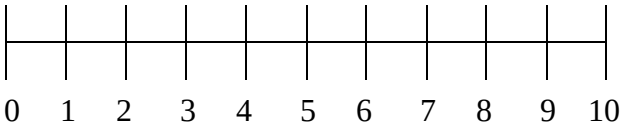
Failed Spinal: The word failed implies that spinal anesthesia was attempted, but without resulting in a sensory block or a block that resulted is inadequate for that surgery

Grading status of shivering= "0"= no shivering, 1=One or more of: pilioerection, 2 = visible muscular activity confined to one muscular group, 3= visible muscular activity more than one

muscular group and 4 =gross muscular activity involving the whole body. Grading of pruritus 1= no itching, 2 =mild itching, 3 = moderate itching 4=severe itching

Low dose of Bupivacaine: is considered as a dose of intrathecal 0.5% 10mg bupivacaine.

Numeric Rating scale (NRS): NRS pain assessment tool was used for grading severity of pain. Patients were informed about this pre-operatively. It has 0-10 (11point scale) numeral and viewing or listening to the numbers the rating by number on how the pain feels whereby 0 is no pain, (1-3) mild pain, (4-6) moderate pain, (7-10) severe pain.[43]



Pruritus: is an unpleasant sensation leading to scratching.

Time for first analgesic request (TAR): is the time from spinal anesthesia injection to first complaint of pain by the patient.[44]

4.8 Data collection tools and procedures

This study was analysed hemodynamic response of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo orthopedics lower extremity surgery. Implementation was done as follows.

Data was collected using pretested structured check list which was prepared in English. Data was collected by 2 BSC anesthetists and supervised by 1 MSc Anesthetists.

Using the method of randomly blocked patients were divided in to two groups. For clarity, we named bupivacaine 15mg alone group as Group B and the 10mg bupivacaine with fentanyl regime as Group BF. Preoperatively method of assessment during and after surgery was explained for the patients, and an informed consent was taken.

Monitoring of hemodynamic response (SBP, DAP, MBP, PR, RR and SpO_2) at baseline then after spinal injection at 05 min, 10min, 15 min, 30 min, 60 min, 90 min and 120 min for both the

groups.[29] Hypotension was defined as systolic blood pressure decrease of more than 25% from baseline.[18],[23] Treatment given for hypotension also was documented.

The mean BP, HR, name of vasopressor, total vasopressor dose for each patient and intraoperative patient complaints were recorded. PR <60/min was graded as bradycardia.[28] Respiratory rate was monitored intra-operatively in all the patients as other vital sign's. Respiratory depression was estimated as a decrease in SaO2 less than 90%.

The cephalic spread of sensory block was assessed by using cold sensation every minute following spinal anesthesia up to onset of sensory block. Motor block was assessed at the same time intervals up to onset of motor block using modified Bromage scale and we decide the motor block, at bromage score of 3.

Duration of analgesia was calculated in both the groups from the time of spinal block to the time of first analgesic requirement. Side effects such as shivering, pruritus, seizures nausea and vomiting and there grade of severity were closely observed and recorded intra and postoperatively.

4.9 Data Quality Control

Pretest was done before actual data collection to ensure quality of data by taking 10% respondents (3 patients in each group). Data collectors and supervisors were trained on each items included in the study tools, objective, relevant of study, right of respondents, confidentiality of information were obtained. During data collection, regular supervision and follow up was made. Investigator was cross checked for completeness and consistency of data on daily basis. Once the data were collected checked for completeness, consistency and accuracy, it was sorted, categorized and summarized. Then, we entered the data into the computer using developed data entry format, coded for each category of variables and again cross checked for error

4.10 Data Processing and Analysis

Data were checked and cleaned manually for completeness and then coded and entered in to SPSS version 25 computer program for analysis. Descriptive statistics were summarized with tables and figures reported as means ± SD for continuous variables, and numbers or percentages for quantitative variables. Normality of distribution for continuous variable was tested by Shapiro-Wilk test and parametric variables were analyzed by independent t-test and Mann-Whitney for nonparametric test as needed, while chi-square test was used for hypotension and fisher exact test for categorical data association (for complications). Association was measured by 95% confidence interval and $p<0.05$ was considered as statistically significant.

4.11 Ethical Consideration

Prior to data collection, proposal was reviewed by Addis Ababa University, department of anesthesia research ethical committee. After obtaining ethical clearance paper and approval from research ethical committee, TASH hospital administration gave me a permission to collect data. During data collection process each parturient was asked for his/her informed oral consent to participate in the study after brief explanation about the objectives of the study by the data collectors. Participants' identification was coded and the check list was kept in proper place by the PI. Data was used only for the study purpose.

4.12. Plan for dissemination

The result of the study will be disseminated by hard copy to Addis Ababa University College of health Science, department of anesthesia and to Tikur Anbessa specialized hospital medical administration office. The result of the study will be presented on different conference including the Ethiopian association of anesthetists to show the effect of low dose bupivacaine with fentanyl on hemodynamic stability after spinal anesthesia and to forward recommendations. The study will be also sent to different journals for publication

CHAPTER FIVE: RESULTS

5.1 Demographic, preoperative and intra-operative characteristics of in elderly orthopedics

A total of 64 patients were included in the study and 32 in each group. Group B given 15mg of 0.5% bupivacaine alone and group BF took 10mg of 0.5% bupivacaine with 25mcg fentanyl. Age, gender, height, weight was compered in our study and they were comparable ($p>0.05$). There were also no statistically significant difference between the groups in ASA physical status, BMI, duration of surgery preload fluid administered and preoperative hemodynamic parameters. Significant difference was obtained while comparing mean of total fluid intake between the two study groups. Which was statistically significant having *($p<0.001$)* (Table 1)

Table 1: Demographic data, preoperative and intra-operative variables among groups from Nov., 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

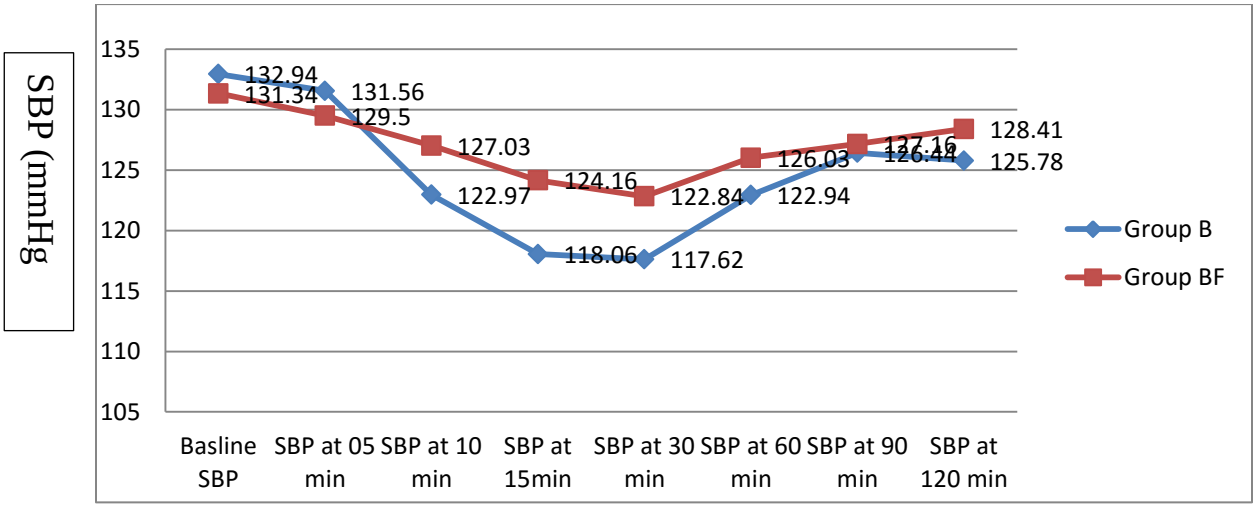
		Group		*p-value*
		Group B	Group BF	
N		32	32	
Gender	Male	19(30%)	15(23%)	.316
	Female	13(20%)	17(27%)	
Age(range and mean ± SD) in Yrs.		60 - 80	60 -79	.429
		68.78 ± 6.1	67.63± 5.5	
Weight (range and mean ± SD) in kg		55 - 80	55 - 81	.478
		67±7.6	65.66±7.45	
Height (cm)		170.2±3.3	170.2±3.1	.969
BMI (Kg/m^2	<18.5	0%	1(1.6%)	.422
	18.5-24.9	24(37.5%)	25(39.1%)	
	25-29.5	8(12.5%)	6((9.5%)	
ASA	ASA I	13(20.3%)	11(17.2%)	.606
	ASA II	19(29.7%)	21(32.8%)	
Fluid preload(ml)		398.44±92.007	387.5±87.067	.625
Total fluid used(ml)		1420±97	1215±94	.000
Amount of blood loss(ml)		273 ±85	282 ±99	.684
Duration of surgery		106.41±31.45	100.88±33.54	.406
Baseline SBP		132.94±10.94	131.34±10.01	.546
Baseline MAP		96.75±9.82	96.76±8.11	.989
Baseline HR		72.91 ±4.55	72.63±5.09	.817
Baseline SaO_2		95.81%±1.87	95.72%±1.46	.779

NB: ASA= American Society Anesthesiologist (surgical risk stratifications) SBP= systolic blood pressure MAP = mean arterial blood pressure HR = heart rate SaO_2 = arterial oxygen saturation

Independent t-test for Mean and standard deviation, Mann- Whitney U- test for median (BMI), Gender and ASA by chi-square test

5.2 Hemodynamic characteristics of elderly orthopedics between groups

In group B maximum fall of 11.5% in mean systolic BP was observed at 30 min following spinal block. In Group BF, maximum fall of 6.5% in mean SBP at 30min. But no statistically significant difference between groups (Figure 2).



NB: SBP = systolic blood pressure min = minutes

Figure 2: Comparison of mean systolic blood pressure at different time interval of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo lower extremity surgery at Tikur Anbessa Specialized Hospital from November, 2018- April, 2019, Addis Ababa Ethiopia.

Relatively higher incidences hypotension were observed in group B (12(37.5%) than group BF 3(9.4%). Which is statistically significant difference with $X^2 = 7.05$, and (p=0.008) (Figure 3).

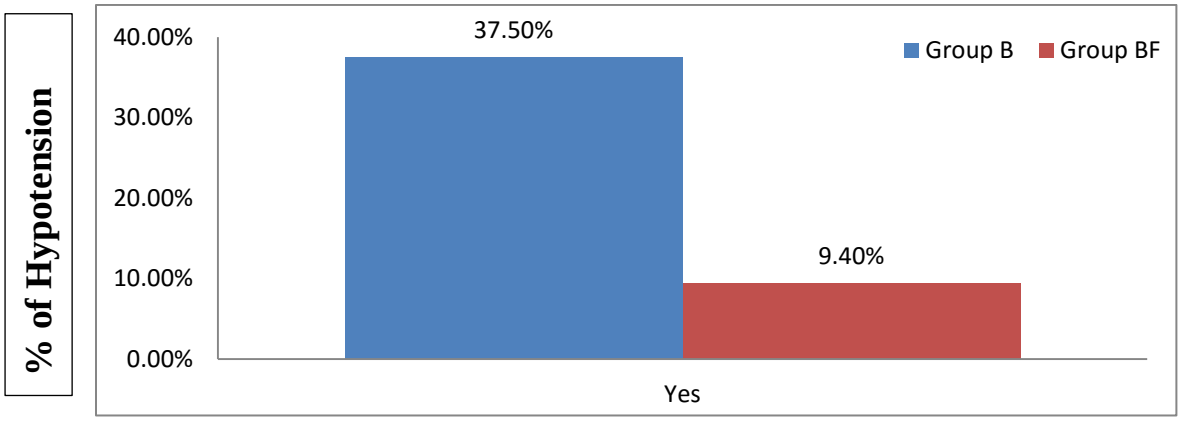
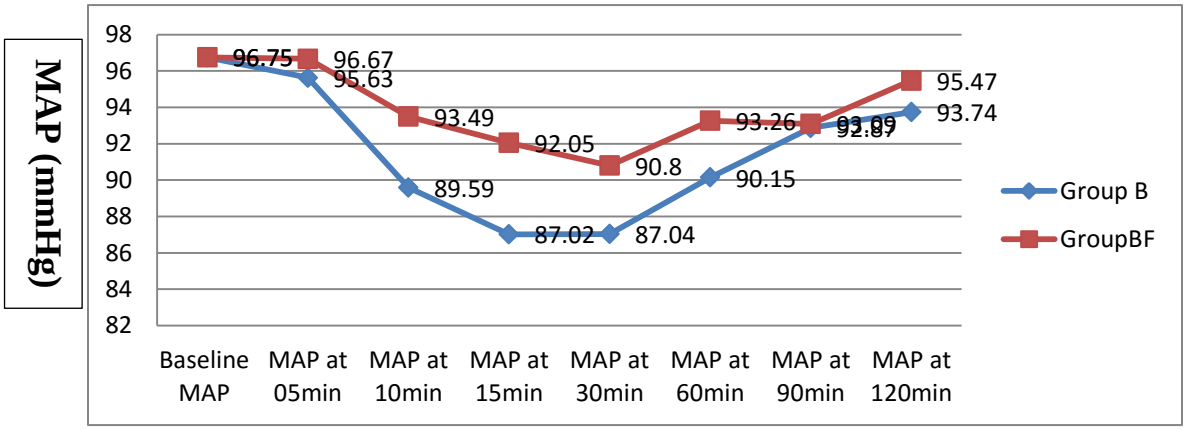


Figure 3: Hemodynamic response (Hypotension) of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo lower extremity surgery from Nov., 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

A maximum fall of 10.1% of MAP in group B was observed at 15 and 30min after subarachnoid block maximum fall of 6% from baseline at 30 min in group BF (Figure 4).



NB: MAP = mean arterial pressure min = minutes

Figure 4: Comparison of mean arterial pressure of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo lower extremity surgery from Nov., 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

HR was compared between groups; a decreased mean heart rate was noticed in Group B at 15 minutes after spinal block but no statistically significant value at all-time intervals and in both groups none of patients treated for bradycardia. (Table 2)

Table 2: Comparison of heart rate change in at different time interval after spinal anesthesia among groups from Nov., 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

	Groups		*P-value*
	B	BF	
N	32	32	
Time in minuets			
05	73.25 ±5.13	73.88±5.08	.500
10	73.19±5	73.66±5.5	.722
15	70.84±5.05	72.53±4.41	.159
30	74.53±5.92	73.22±5.22	.419
60	73.28±4.71	72.91±4.92	.757
90	73.22±4.8	73.25±5.15	.989
120	73.63±4.77	74.47±5.41	.511

Independent t-test for Mean and standard deviation at 10, 15, 60 and 120minutes, Mann- Whitney U- test for median at 05, 30 and 90minutes.

When we compared SaO_2 between groups: there was no statistically significance different at all-time interval but at 30min after spinal anesthesia block lower mean SaO_2 observed in group BF in respect to Group B (Table 3)

Table 3: Comparison of SaO_2 change in different time interval after spinal anesthesia among groups from November, 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

	Groups		*P-value*
	B	BF	
N	32	32	
Time in minuets			
Baseline	95.81±81	95.72±1.46	.779
05	96.3±1.76	95.75±1.59	.412
10	96.34±2.16	96.13±1.64	.347
15	96.5±2.06	95.69±1.69	.361
30	97.09±2	95.94±1.78	.185
60	96.19±1.75	96.14±1.74	.285
90	96.13±1.96	95.81±1.23	.888
120	96.41±1.58	96.15±1.49	.408

SaO_2 =arterial oxygen saturation

When we compared vasopressor consumption between groups, higher rate of adrenaline was used in group B 6(18.8%), and in group BF was 1(3.1%). Which is statistically significant difference with (p=0.045). The maximum and minimum dose of adrenaline used in group B was 50 and 30mcg and in group BF 30mcg was used.

5.3 Spinal anesthesia block characteristics in elderly orthopedic patients between groups

The onset of sensory block and regression of motor block to zero was faster in group BF (*p <0.05*). TAR was also prolonged in BF group *P<0.05*. The mean level of sensory block at surgery, onset of motor block and motor bromage score at start of surgery were compared and found that values were not significant in both the groups (Table 4)

Table 4: Characteristics of the spinal block after spinal anesthesia among groups from November, 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

	Group		*p-value*
	B	BF	
Sensory			
Onset	5.09 ± 1.57	4.31±1.26	0.032*
Level (at surgery)	T8	T9	0.690
TAR (in minutes)	213.19±51.46	233.41±46.46	0.033*
Motor			
Onset	6.72±1.782	6.91±1.573	0.821
Bromage (at surgery)	3	3	.786
Bromage zero (after surgery)	158.88 ±14.661	145.69±15.53	0.01*

TAR= time of analgesia request

Independent t-test for Mean and SD, Mann- Whitney U- test for median (for sensory level and motor bromage)

According to numeric rating scale (NRS) pain severity score in our study statistically significant difference value observed was at 4hrs after spinal block (p=0.014). Otherwise in all-time interval comparable result was seen (Table 5)

Table 5: Comparison of numeric rating score for pain severity at different time intervals from 2.5hrs, 3, 4, 6, 8 and 12hrs among groups from November, 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

	No pain		Mild pain		Moderate pain		Severe pain		*P-value*
	B	BF	B	BF	B	BF	B	BF	
N	32	32	32	32	32	32	32	32	
Time in hours									
2.5	32	32	-	-	-	-	-		1
3	24	26	6	5	2	1	-	-	.777
4	7	18	11	8	14	6	-	-	0.014*
6	3	5	11	11	18	16	-	-	.734
8	4	1	21	25	7	6	-	-	.329
12	2	4	17	18	11	9	2	1	.749

Chi-square test

5.4 Complication of spinal anesthesia between groups

With respect to pruritus there was statistically insignificant difference between groups. In control group (group B) no occurrence of pruritus, but in group BF was 4(12.5%) with mild degree of severity. Incidence of nausea and vomiting in group B was 4(12.5%) with mild degree of severity, but in study group (Group BF) none of them experienced but statistically insignificant *p>0.05*. Rate of shivering in group B was 15.5% with shivering of one muscle group involvement or grade 2, and in group BF was 9.4% of grade 2 (Table 6).

Table 6. Complication of spinal anesthesia among groups from November, 2018-April, 2019 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

	Group		*p-value*
	B	BF	
N	32	32	
Hypotension	12(37.5%)	3(9.4%)	0.008*
pruritus	-	4(12.5%)	0.113
Severity of pruritus	-	2	0.113
Nausea and vomiting	4(12.5%)	-	0.113
Grade of vomiting	2	-	0.113
Shivering	5(15.6)%	3(9.4%)	0.708
Grading of shivering	2	2	0.708
RD	-	-	
Failed Spinal	-	-	

CHAPTER SIX

6.1: DISCUSSION

In our study the demographic characteristics age, height, weight, baseline vital sign, preloaded fluid, duration of surgery, total blood loss and ASA status were comparable between groups $p>0.05$.

The result of this study showed that the overall incidence of hypotension was 37.5% in non-exposed group (0.5% of 15mg isobaric bupivacaine) and 9.4% in study groups (0.5% of 10mg isobaric bupivacaine with 25mcg fentanyl), higher incidence of hypotension in non-exposed than study groups $p<0.05$.In this study statistically significant differences were observed between groups. (Kumar S, 2011) explained that intrathecal opioid neither by itself nor in combination with LA causes any further depression of efferent sympathetic activity. Therefore, it can enhance sensory blockade without changing the degree of sympathetic blockade, and hence a decrease incidence of intraoperative hypotension.[17]

(Alwin C, 2014) displayed that fentanyl is synthetic opioid with no histamine release thus less hemodynamic effect. Addition of fentanyl for neuraxial anesthesia produces a better- quality of block and reduces anesthetic requirments.[18] With addition of low-dose sufentanil, dose of a local anesthetic can safely lowered by 40% in the elderly population. This can avoid the hemodynamic instability, providing a stable perioperative and postoperative condition and prolong duration of sensory analgesia.[17]

This result is in line with study done Chico A. et al in France (2003) in their study group F given 5 mg of bupivacaine and 15 mcg of fentanyl and Group B received 7.5 mg bupivacaine alone and Group F patients were more hemodynamically stable and more hypotensive episodes occurred in group B.[33]

This finding shows comparable result with RCT, done in Pakistan (2012), on hemodynamic response of spinal anesthesia in elderly orthopedic patients. Group-A received hyperbaric bupivacaine 7.5 mg and fentanyl 15 µg while group-B received hyperbaric bupivacaine 15 mg.

thirty patients in each group. Hypotension in the group B was significantly higher 73.3% (22 of 30 patients) and 10% (3 of 30 patients) in the group A and statistically significant differences.[29]

Our result is also comparable with findings of another RCTs conducted in India by Mehta S. et al (2015) They studied on 60 elective elderly orthopedic lower limb surgeries under spinal anesthesia. Fewer falls in blood pressure was noted in group B (0.5% of 10mg bupivacaine with 25mcg fentanyl) than group A (0.5% of 15mg bupivacaine alone), 3(10%), 12(40%), respectively and (Kumer S. and Jit S, 2011) studied on 50 elderly patients undergoing lower limb surgery under combined spinal epidural anesthesia. Group I received 2.5 ml of intrathecal hyperbaric bupivacaine (LA), while group II received 1.5 ml of intrathecal LA+0.1 ml sufentanil (5 μg). Incidence hypotension was 44% in group I and 8% in group II. With significant different between groups $p<0.05$. [18, 28]

In contrast, study done by Martyr JW and Clark MX in Australia (2001) studied 42 elderly patients having insertion of a Richards pin and plate and compared 7.5 mg hyperbaric bupivacaine with added fentanyl 20 mcg (group BF) to 12.5 mg hyperbaric bupivacaine alone (group B). An overall incidence of hypotension was 59.5%. There was no difference in the incidence or severity of hypotension between the two groups.[26] This contraries may be due to type of procedure, comorbidities, social habits, diet or genetic background the patients.

In our study mean of total fluid intake in group B was 1420±97 and in group BF was 1215±94 which was statistically significant having (*p<0.001*). When we compared vasopressor consumption between groups, higher rate of adrenaline was used in group B 6(18.8%), and in group BF was 1(3.1%). Which is statistically significant difference with (*p=0.045*). It can be due to higher infusion and vasopressor needed to restore normal blood pressure in B group as hypotension was higher in these groups.

This result in line with RCT study done by Faisal M, in Pakistan (2012) Group-A received hyperbaric bupivacaine 7.5 mg and fentanyl 15 μg while group-B received hyperbaric bupivacaine 15 mg. Mean ephedrine usage was highly significant in group B than group A

(40mg to 10mg respectively). In group B 22 patients from 30 (73.3%) needed ephedrine and in group A, 3 patients from 30 (10%) and (p-value < 0.05) between groups.[29]

Mehta et al. also shows similar finding to our study as 15mg (group A) and 10mg (group B) of isobaric bupivacaine both with 25 µg of fentanyl use of vasopressors was much higher in group A and was statistically significant.[27]This finding also shows comparable result with study done by Chico A. et al in France, 2003, on comparison of the hemodynamic response of subarachnoid anesthesia with bupivacaine versus bupivacaine with fentanyl in traumatology surgery in elderly patients. Group F given 5 mg of bupivacaine and 15 mcg of fentanyl and Group B received 7.5 mg bupivacaine. Group B consumed significantly more ephedrine ($p < 0.05$), administered to 22 patients in group B and 6 in group F. The total dose of ephedrine administered was greater in group B (190 mg) than in group F (40 mg).[33]

Higher incidence of vasopressor use was reported by Ben-David et al. Group A received a spinal anesthetic of bupivacaine 4 mg plus fentanyl 20 mcg, and group B received 10 mg bupivacaine. One of 10 patients in group A required ephedrine, a single dose of 5 mg. Nine of 10 patients in group B required vasopressor support.[23]

In our study time of first analgesia request (TAR) was compared in both the groups and were found that first analgesia request time was longer in group BF than group B which was statistically significant with (P=0.033).

When performing spinal anesthesia, adding adjuvants to the local anesthetic can reduce the amount of local anesthetic, prolong its analgesic effect, and prolong anesthesia time.[44] The administration of a combination of drugs intrathecally targets different spinal receptors resulting in prolonged and superior quality of analgesia.[46]

Effective pain control is crucial for optimum care of all patients in postoperative period. Addition of an opioid like fentanyl to bupivacaine can provide effective intraoperative as well as postoperative analgesia with minimal side effects. Potential synergism between fentanyl and bupivacaine has been reported by BenDavid B et al.[23]

This study in line with study done by (R. Diwakaran, 2017) on lower abdominal and pelvic surgeries, were randomly divided into three groups. Group BC (bupivacaine + clonidine) received 50 µg clonidine while BF (bupivacaine + fentanyl) received 50 µg of fentanyl; the third group received equal volumes of normal saline (Group NS, bupivacaine + normal saline) for subarachnoid block. Duration of analgesia was higher in BC than BF which in turn was higher than the Group NS [281.26 ± 97.57, 237.80 ± 58.49 min and 190.48 ± 61.94 min respectively].[47] Our finding also shows comparable result to study done by Akanmu et al. in Nigeria(2013) bupivacaine saline (SB n=30) 10 mg (2 ml) 0.5% hyperbaric bupivacaine or 10mg bupivacaine-25mcg fentanyl combination (FB n= 30) on patients undergo elective open reduction and internal fixation of lower limb fractures (ORIF) TAR in Group FB was significantly longer than the group SB with a mean ± standard deviation of 239.97 ± 28.58 minutes compared to 129.17 ± 11.61 and p-value of <0.001.[48]

In our study time of onset of sensory blockade was compared between groups and were found that faster in group BF than group B alone (4.3 Vs. 5.1 minutes, *P = 0.032*). In line with study done by Kumar S in India (2016). On combined spinal epidural anesthesia using low dose local anesthetic with addition of sufentanil in lower limb surgery for elderly patients and onset of sensory analgesia were significantly earlier in group II (bupivacaine with sufentanil) than group I(control group) (*P*<0.05). [18]

Similarly another comparative study was done by *Indurkar PS et al.* reported mean time for onset of sensory block was 4.60 ± 0.53 min for control group while for study group; it was 3.07 ± 0.47 min. [49]

I contrast with the finding of a study done by Bhrigu N. in India (2017) on assessment of efficacy of bupivacaine plain versus bupivacaine with fentanyl in spinal anesthesia in geriatric patients undergoing hip replacement surgery. Group B received o.5% of bupivacaine and o.5% of bupivacaine + fentanyl and group B was faster onset of sensory block (6.17±1.44) than group B (6.73±1.52).[27] The likely explanation for this contradiction is the technical difference the used to perform block, difference in study design or the type of the procedure.

Regarding numeric rating scale (NRS) pain severity was statistically significant difference value observed was at 4hrs after spinal block less in group BF than group B (p=0.014). Otherwise in all-time interval comparable result was seen. The reason may be due to the synergistic effect of opioids with local anesthetics on pain receptors blockage.

The administration of a combination of drugs intrathecally targets different spinal receptors resulting in prolonged and superior quality of analgesia.[46]

In our study motor bromage regression to zero after surgery were compared and prolonged in Group B 158.88 ±14.7 that of group BF was 145.69±15.53. Which was statistically significant (*p = 0.01)* minutes. The possible reason for the lower duration of motor blocks in study group was due to decrease dose of bupivacaine. Our finding in line with Bhrigu Nath Singh report in 2017.[27]

There was no statistically significant difference among the groups regarding complication rates of pruritus group BF than group B alone (12.5% vs. 0%) (*P = 0.113*). Nausea and vomiting (0% vs. 12.5%) (*p=0.113*) and shivering (9.4%, 15.5%) (p=0.708). Regarding severity of pruritus, nausea and vomiting and shivering also no statistical difference between groups. (*p>0.05*).

6.2 Limitation of study

The following limitations were seen in this study

Unavailability of invasive arterial blood pressure to measure beat to beat systolic blood pressure.

Time span of hypotension were not measured with every hypotensive episodes

6.3 Strength of study

There were no lost follow up respondents which results in missing data

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATIONS

7.1 CONCLUSION

Spinal anesthesia for elderly patients undergoing lower extremity orthopedics surgeries with 0.5% of 10mg bupivacaine with 25µg fentanyl is a safer and better option, with regard to maintaining hemodynamic stability without affecting the desirable surgical conditions as well as fast onset of sensory block with prolonged first analgesia request time.

7.2 RECOMMENDATION

Based on the current thesis findings the following recommendations were drawn:

- Anesthetists are advocated to use 0.5% of 10mg bupivacaine with 25mcg fentanyl for elderly populations.
- Hospitals are recommended to make bupivacaine and fentanyl sustainably available for spinal anesthesia to manage elderly patients who undergoing orthopedics lower extremity surgeries.
- Future RCT studies are recommended that close the gaps and more strong in study design on the effect of lowering dose of bupivacaine with adjuvant techniques on hemodynamic changes in country wide.

References

1. Maurer SG, Chen AL, Hiebert R, Pereira GC, Di Cesare PE. Comparison of outcomes of using spinal versus general anesthesia in total hip arthroplasty. Am J Orthop (Belle Mead NJ) 2007; 36:E101–E106.
2. Borgeat A. Anesthesia for Orthopedic Surgery in the Elderly: Facts to Think About. J Med Sci 2007; 27(3):101-108 http://jms.ndmctsgh.edu.tw/2703101.pd
3. Gligorijevic S. Spinal anaesthesia – An update. Switzerland, Period biol, 2011: 113(2), 167–170.
4. Farag E., Argalious M., John E., Sharma D. Basic Sciences in Anesthesia. Switzerland: Springer International: 2018. https://t.me/Anesthesia_Books
5. Mears SC, Kates SL. A guide to improving the care of patients with fragility fractures, edition 2. Geriatr Orthop Surg Rehabil 2015;6(2):58–120.
6. Naughton C, Feneck RO. The impact of age on six-month survival in patients with cardiovascular risk factors undergoing elective noncardiac surgery. Int J Clin Pract. 2007;61:768–76. [PubMed]
7. Rivera R., Joseph F. Perioperative Drug Therapy in Elderly Patients. The journal of the American society of anesthesiologists, Inc. 2009:Vol.110, 1176-1181. doi:10.1097/ALN.0b013e3181a10207
8. Messina, A et al. Haemodynamic effects of spinal anesthesia in elderly patients undergoing hip fracture surgery. European Journal of Anesthesiology: 2010:27(47) :241–242
9. Kannan S. Ten milligrams intrathecal bupivacaine is too high for spinal anesthesia for hip surgery in the geriatric population. Anesthesiology 2000;93:1365.
10. Chau DL, Walker V, Pai L, et al. Opiates and elderly: use and side effects. Clin Interv Aging 2008;3:273–8. [PMC free article] [PubMed]
11. Lakatta EG: Age-associated cardiovascular changes in health: Impact on cardiovascular disease in older persons. Heart Fail Rev 2002; 7:29–49
12. Singh S. et al. Postspinal hypotension in elderly patients undergoing orthopedic surgery, prophylactic ephedrine versus polygeline 3.5%. Anesth Essays Res. 2014: 8(3): 334–338.

13. Turnheim K: When drug therapy gets old: Pharmacokinetics and pharmacodynamics in the elderly. Exp Gerontol 2003; 38:843–53
14. Maxwell CA, et al. The aging of America: a comprehensive look at over 25,000 geriatric trauma admissions to United States hospitals. Am Surg. 2015; 81(6):630–6.
15. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. Anesthesiology 2004:101: 950–9
16. Shah S., Shah B., Deb Ch. comparative evaluation of bupivacaine plain versus bupivacaine with fentanyl in spinal anaesthesia in geriatric patients. International Journal of Medical and Health Research. 2016, 2(6): 23-26.
17. Balakrishnan K, Ebenezer V, Dakir A, Kumar S, Prakash D. Bupivacaine versus lignocaine as the choice of local anesthetic agent for impacted third molar surgery a review. Journal of Pharmacy & Bioallied Sciences. 2015;7(Suppl 1):S230-S233. doi:10.4103/0975-7406.155921.
18. Kumar S, Bajwa SJS. Neuraxial opioids in geriatrics: A dose reduction study of local anesthetic with addition of sufentanil in lower limb surgery for elderly patients. Saudi Journal of Anaesthesia. 2011;5(2):142-149. doi:10.4103/1658-354X.82781.
19. Alwin C. & David S. Reginal anesthesia a pocket guide. Oxford: University press. 2014, 1st ED.
20. Reves, J.G., Barnett, S.R., McSwain, J., Rooke, G.A. (Eds.). Geriatric Anesthesiology. Switzerland: Springer international. 2018, 3rd Ed.
21. Riesmeier A et al. Crystalloid/colloid vs crystalloid intraVAScular volume administration before spinal anaesthesia in elderly patients: the influence on cardiac output and stroke volume. Anesth Analg. 2009; 108: 650–54
22. Asehnoune K et al. Small-dose bupivacaine-sufentanil prevents cardiac output modifications after spinal anaesthesia. Anesth Analg. 2005; 101: 1512–15
23. Ben-David B et al. Minidose Bupivacaine–Fentanyl Spinal Anesthesia for Surgical Repair of Hip Fracture in the Aged. Anesthesiology2000;92(1):6
24. Sivevski A. Spinal anaesthesia for cesarean section with reduced dose of intrathecal bupivacaine plus fentanyl. Prilozi. 2006 Dec; 27(2):225-36.
25. Shrestha B, Acharya SP, Roshana A. Comparison of intrathecal bupivacaine with or without fentanyl for urosurgeries. JSAN 2014; 1:18-21.

26. Martyr JW1, Clark MX. Hypotension in elderly patients undergoing spinal anaesthesia for repair of fractured neck of femur. naesth Intensive Care. 2001:29(5):501-5.
27. Bhrigu Nath Singh. Assessment of effcacy of bupivacaine plain versus bupivacaine with fentanyl in spinal anaesthesia in geriatric patients undergoing hip replacement surgery: a comparative study. International Journal of Contemporary Medical Research 2017;4(7):1614-1616
28. Mehta S., Dalwadi H., Shah T. Comparative study of low dose bupivacaine-fentanyl vs. conventional dose of bupivacaine in spinal anaesthesia for orthopedic procedures in elderly patients. Gujarat medical journal. 2015; 70 (1):
29. Faisal M., Ahmed W., Khan S. Hemodynamic response of low dose bupivacaine with fentanyl spinal anesthesia in elderly patients. Journal of Army medical & Dental Corps. 2012; 62(3)
30. Yucel A, et al. Single intrathecal fentanyl for combined spinal epidural anesthesia confers no advantage over hemodynamic effects in elderly patients. Eur Rev Med Pharmacol Sci. 2012; 16(2):207-12.
31. Khanna M S, Singh IK. Comparative evaluation of bupivacaine plain versus bupivacaine with fentanyl in spinal anaesthesia in geriatric patients. Indian J. Anaesth. 2002;46(3),199-203.
32. Zakir N., Soltani Gh., Javdani N., et al. Effect of fentanyl in Spinal anesthesia with bupivacaine in opium abusers. Razavi international Jornal of Medicine. 2014; 2(1): e14271 DOI: 10.5812/rijm 14271
33. Chico A., Pardos C., Grau A., et al. Comparison of the hemodynamic response in subarachnoid anesthesia with bupivacaine versus bupivacaine with fentanyl in traumatology surgery in elderly patients. Rev Esp Anestesiol Reanim. 2003 Jan; 50(1):17-22
34. Goel S., Bhardwaj N, Grover, VK: Intrathecal fentanyl added to intrathecal bupivacaine for day case surgery: A randomized study. Eur J Anaesthesiol 2003; 20: 294-297. Google Scholar, Crossref, Medline, ISI
35. Gurbet A, Turker G, Girgin NK, et al. Combination of ultra-low dose bupivacaine and fentanyl for spinal anaesthesia in out-patient anorectal surgery. Journal of international medical research. 2008; 36 (5): 964-970.

36. Haoyu G, Weidong L, Fan Y. Effectiveness and safety of propofol intravenous total anesthesia on treatment of elders' painless endoscopy. Med Rev 2016; 22(16): 3305-3307.
37. Hofhuizen et al. Spinal anesthesia-induced hypotension is caused by a decrease in stroke volume in elderly patients: 2019:12, 19-26. The Netherlands: Jornal of local and regional anesthesia https://doi.org/10.2147/LRA.S193925
38. Pallavi, et al. Comparison between Fentanyl as an adjuvant. Central Journal of ISA: 2017: 1(2): 64-71
39. Rasooli S. Minidose bupivacaine - fentanyl spinal anesthesia for cesarean section in preeclamptic parturients. Medical Journal of the Islamic Republic of Iran , Vol. 20, No. 2, July, 2006, pp. 94-97
40. Zeynep N. et al. Spinal anesthesia with low-dose bupivacaine-fentanyl combination: Rev. Bras.Anestesiol. vol.62 no.6 Campinas Nov./Dec. 2012:http://dx.doi.org/10.1590/S00347094201200060000
41. Doyle DJ, Garmon EH. American Society of Anesthesiologists Classification (ASA Class) [Updated 2019 Jan 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 https://www.ncbi.nlm.nih.gov/books/NBK441940
42. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA 2010; **303:2043**–2050pmid:20501926
43. Abdel El-Hamid AM, Afifi EE.Transversus abdominal block versus local anesthesia wound infiltration in patient undergoing open inguinal hernia repair surgery .Ain –Sham J Anesthesiol.2016;9:280-3.
44. Akanmu et al. Analgesic Effects of Intrathecally Administered Fentanyl in Spinal *Anaesthesia*. Maced J Med Sci. 2013 Sep 15; 6(3):255-260.
45. So Hui Yun, et al : Spinal anesthesia in cesarean section: Anesth Pain Med 2017; 12: 233-239 https://doi.org/10.17085/apm.2017.12.3.233
46. Cox RF, Collins MA. The effects of benzodiazepines on human opioid receptor binding and function. Anesth Analg. 2001;93:354–8. [PubMed] [Google Scholar]
47. S. Parthasarathy, N. Krishnaveni. Comparative evaluation of addition of either fentanyl or clonidine to bupivacaine in spinal anesthesia – a randomized controlled clinical trial. Anaesth Pain & Intensive Care 2017;21(3):323-327

48. Akanmu et al. Analgesic Effects of Intrathecally Administered Fentanyl in Spinal *Anaesthesia.* Maced J Med Sci. 2013 Sep 15; 6(3):255-260.
49. *Indurkar PS et al.* A comparative study of hyperbaric bupivacaine versus hyperbaric bupivacaine and fentanyl (12.5 mcg) in subarachnoid anesthesia for lower abdominal and lower extremity surgeries *Int J Res Med Sci. 2015 Nov;3(11):3147-3155*
50. *Khanna, Singh:* bupivacaine with fentanyl for sa in geriatric patients*: Indian J. Anaesth. 2002:46(3):199-203*

.

Annex I: Information Sheet

Title of the Research

Hemodynamic response of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo orthopedic lower extremity surgeries at TASH, Addis Ababa, Ethiopia

Name of Principal Investigator – Behaku Awel (MSc student in Anesthesia)

Name of advisors: Adugna and Suleyman.

Name of the Organization: Addis Ababa University, College of Medicine and Health Sciences, department of Anesthesia

Name of the Sponsor: Addis Ababa University

Introduction:

This information sheet is prepared with the aim of assessing hemodynamic response of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergone orthopedic lower extremity surgeries at TASH. The research group includes the principal investigator, two data collectors, and one advisor.

Purpose of the Research

The aim of this study was to compare conventional dose of bupivacaine alone versus low dose bupivacaine with fentanyl in response to hemodynamic change after spinal anesthesia.

The results of this study were used to design appropriate patient management in TASH, as well as in other health institutions in Ethiopia.

Person to contact

For any questions or concerns can contact the principal investigator using the following addresses:

Name: Behaku Awel

Telephone: +251 920 095065

E-mail: **behakuawel3@gmail.com.**

Annex II: Consent form (English version)

This questionnaire was used as a guide to collect information for the data collectors! Questionnaires to assess hemodynamic response of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo infra-umbilical orthopedic surgery at TASH, Addis Ababa, Ethiopia

Hello! My name is ----------I am one of the members of the research team. The purpose of this questionnaire is to gather information on hemodynamic response of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo orthopedic lower extremity surgeries at, TASH, Addis Ababa, Ethiopia

I have identified you as a study participant hoping that you would be willing to help me by providing some information. I have some questions, which I would like to ask you, if you have the time and are willing. Your participation is definitely important to assess hemodynamic response of low dose bupivacaine with fentanyl versus normal dose bupivacaine alone for spinal anesthesia in elderly patients who undergo orthopedic lower extremity surgeries at TASH, Addis Ababa, Ethiopia. All information you provide waskept confidential. I will not include any identifiers, such as your name or exact address.

Only honest answers would contribute to improvement of health planning. Your role in the success of the research is important and I appreciate your contribution to the research. Would this be okay with you?

I understood about the advantage of the research and the roles I will have in the research. I have agreed to participate in the research.

A. Agree B. disagree

If Respondent agrees to be interviewed, the interview wasstarted

Questionnaire Code _____

Starting time _____ finishing time _____

Date of data collection_____

Name of data collector _____signature_____

Annex III: Consent form (Amharic version) የአማርኛ መጠይቅ

ይህ መጠይቅ ለመረጃ ሰብሳበው እንደ ጠቃሚ ሆኖ ያገለግላል

መረጃው ሚደረገው በሽማግሌዎች ከወገብ በታች ስብራት ላይ በቀዶ ህክምና ጊዜ ከወገብ በታች የሚሰጡ የአኔስቴዝያ መድሃኒቶች (ቡፒቫኬን ብቻው እና ቡፒቫኬን ከፌንታኒል ጋር) በህመምተኛው ላይ የሚኖረዉን ለውጥ ላይ የሚደረገው ምርምር /ጥናት መረጃ ለመሰብሰብ ነው፡፡ ጥናቱን የሚያካሂዱት በአዲስ አበባ ዩኒቨርስቲ በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል ፣ አዲስ አበባ ፣ አትዮጵያ ነው፡፡የጥናቱ አድራጊ የአኔስቴዝያ ት/ክፍል የሁለተኛ ድግሪ ተማሪ የሆኑት አቶ በህቁ አወል ናቸው፡፡

ሄሎ ስሜ _____ እኔ አንዱ የጥናቱ አባል ነኝ፡፡ የጥናቱ አላማ በሽማግሌዎች ከወገብ በታች ስብራት ላይ በቀዶ ህክምና ጊዜ ከወገብ በታች የሚሰጡ የአኔስቴዝያ መድሃኒቶች (ቡፒቫኬን ብቻው እና ቡፒቫኬን ከፌንታኒል ጋር) በህመምተኛው ላይ የሚኖረዉን ለውጥ ላይ ምርምር /ጥናት ለማድረግ ነው፡፡

እርሶን የጥናቱን ተሳታፊ ሳደርጎት ፈቀደኛ ሆነው የተወሰኑ መረጃዎችን ይሰጡኛል ብዬ በማሰብ ነው፡፡ የርሶ ተሳትፎ በርግጠኝነት በሽማግሌዎች ከወገብ በታች ስብራት ላይ በቀዶ ህክምና ጊዜ ከወገብ በታች የሚሰጡ የአኔስቴዝያ መድሃኒቶች (ቡፒቫኬን ብቻው እና ቡፒቫኬን ከፌንታኒል ጋር) በህመምተኛው ላይ የሚኖረዉን ለውጥ ላይ የሚደረገው ምርምር /ጥናት ላይ በጣም ጠቀሚ ነው፡፡

እርሶ የሚሰጡኝ መረጃ ምስጥርነቱ በጥብቅ እስከ መጨረሻ የተጠበቀ ነው፡፡ የርሶን ማንነት የሚገልፅ ለምሳሌ ስምም ሆነ አድራሻ አይገለፅም እንዲሁም በማንኛውም ሰዓት የጥያቄና መልሱን ሂደት ማቻረጥ ይቻለል፡፡

የርሶ እዉነተኛ ምላሽ ብቻ ጤናን በማሻሻል ላይ አስተዋፅኦ ይኖረዋል፡፡ የርሶ ሚና የጥናቱ መሳካት ላይ ወሳኝ ነው ፤ እናም በጥናቱ በመሳተፍዎ ደስ ሊሎት ይገባል፡፡ ይስማማሉ?

የጥናቱ ጥቅም እና የእኔ ሚና ተረድቻለሁ፡፡ ስለሆነም፣ በጥናቱ ለመሳተፍ

ሀ. ተስማምቻለሁ (ቃለ መጠይቁን መቀጠል ይችላሉ).....

ለ. አልተስማማሁም(ቃለ መጠይቁን ያቁሙ).....

ተሳታፊው ለመጠየቁ ፈቃደኛ ከሆኑ መጠይቁ ይቀጠላል

የመጠይቁ መለያ ኮድ.....

የተጀመረበት ሰዓት..... ያለቀበት ሰዓት.....

መረጃው የተሰበሰበበት ቀን.....

የመረጃዉን ሰብሳቢ ስም..... ፊርማ.....

Annex IV: Check list

Observation sheet Code _____

Date of data collection----------/----------/2018/19GC

Starting time_____ Name of data collector---------- signature_____

Name of supervisor---------- signature----------

Instruction: For each of the following questions, please circle the number of alternative(s) that fit the response or fill the blank space!

SECTION I: Demographic characteristics

S. No	**parameters**	Response	Code
101	Dates Of Surgery	____ /_____ /____	
102	Sex	Male 2. Female	
103	Age in years		
104	Weight in kg		
105	Height in cm		
106	BMI (kg/m^2)	A. 18.5–24.9 B. 25–29.9 C. 30–34.9 D. >35	
107	ASA physical status	ASA I 2. ASA II	
108	Indication of surgery		

SECTION II: baseline preoperative characteristics of patients and interventions

S. No	Parameters	Response	Code
201	Does any preoperative medication given?	A. yes B. no	
202	If above question answer is yes, specify?		
203	Amount of fluid preloaded within 30 minutes before spinal block in ml if any?		
204	Base line BP before SA in mmHg	SBP_____ mmHg DBP_____ MAP_____	
205	Base line PR before SA in bpm	_____bpm	
206	Base line SPO_2	_____%	

Section IV: Hemodynamic measurements during surgery

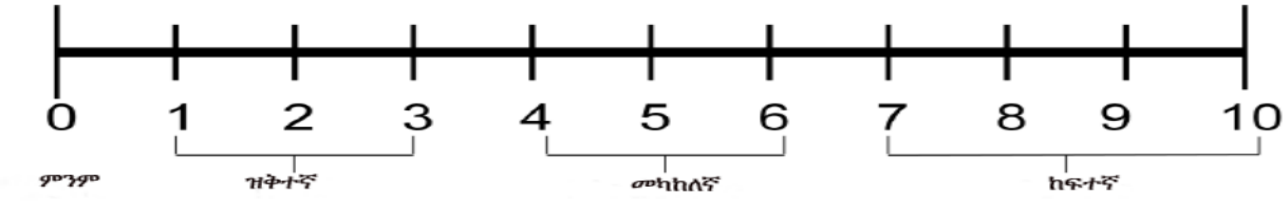
S. No.	Parameters	Time intervals after SA (in minutes)						
		05	10	15	30	60	90	120
301	SBP (mmHg)							
302	DBP							
303	MBP							
304	PR							
305	RR							
306	SaO2							

Section III: intraoperative parameters, adverse events and intervention

S. No.	parameters	Response	Code
401	What was local anesthetic used	bupivacaine 0.5% of 15mg alone bupivacaine 0.5% 0f 10mg and fentanyl 25mcg	
402	Volume of local anesthetic in ml		
403	Onset of Sensory block (in Minutes)		
404	Sensory block level before surgery in terms of dermatome level	T8 2. T9 3. T10 Other specify	
405	Onset of Motor block (in minutes)		
406	Motor block of bromage scale at start of surgery	0 2. 1 3. 2 4. 3	
	Does patient experience after spinal anesthesia?		
407	hypotension	Yes 2. no	
408	Bradycardia	Yes 2. no	
409	Desaturation	Yes 2. no	
410	Nausea	Yes 2. no	
411	If yes what grade?	1. None 2. mild 3. Moderate 4. severe	
412	Vomiting	Yes 2. no	
413	If yes grade of severity?	1. Mild 2. Moderate 3. severe	
414	Seizure	Yes 2. no	
415	Pruritus	Yes 2. no	
416	If pruritus happened what severity?	1. No itching 3. moderate 2. Mild 4. severe itching	

417	shivering	Yes 2. no	
418	If yes what grade?	1. zero 2. One 3. two 4. Three 5. four	
419	Blood loss (ml)		
420	Other_____	yes 2. no	
421	If, any of above are yes is there any intervention done?	Yes 2. no	
422	If yes, what was done?	Vasopressor given Name _____Dose_____ Atropine___mg Pethidine ____mg given Other Specify_____	
423	Time of intervention drugs used	Before spinal During spinal 3. After spinal	
424	Time of motor regressions to Bromage scale 0	_____ (in minutes).	
425	Total intraoperative fluid given during the operation in ml		
426	Duration of surgery in minutes		
427	Duration of anesthesia in minute	_____	

501. Numeric rating scores for pain.



1. No pain (ምንም የህመም ስሜት የለም (0) 2. Mild pain (ጥቂት የህመም ስሜት አለ (1-3)

3. Moderate pain (መካከለኛ የህመም ስሜት አለ (4-6) 4. Severe pain (ከፍተኛ የህመም ስሜት አለ (7-10)

Hrs	At2.5hr	At 3 hrs.	4hrs	6hrs	8hhrs	12hrs
NRS Score						

601. First analgesia request time from start of anesthesia (in minutes) _____

Declaration

I, the undersigned, declare that this thesis is my original work in partial fulfillment of the requirements for the degree of MSc in Advanced Clinical Anesthesia.

I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced

Name: _____

Signature: _____

Submission to MSc Tutor, Dept. of Anesthesia, Addis Ababa University.

Date of Submission: _____

this thesis work has been submitted for examination with my/our approval as Advisors and Tutors on the MSc in Advanced Clinical Anesthesia course

Name Signature

1. _____ _____

2. _____ _____

3._____ _____