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HEMODYNAMIC AND ANALGESIC EFFECT OF INTRATHECAL FENTANYL AS ADJUVANT WITH LOW AND CONVENTIONAL DOSE OF BUPIVACAINE IN PATIENTS UNDERGOING ELECTIVE CESAREAN SECTION UNDER SPINAL ANESTHESIA AT GHANDI MEMORIAL HOSPITAL ADDIS ABABA ETHIOPIA,2018/2019

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TITLE

Hemodynamic and analgesic effect of intrathecal fentanyl as adjuvant with low and conventional dose of bupivacaine in patients undergoing elective cesarean section under spinal anesthesia

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Acronyms

AAU: Addis Ababa University

ASA: American Society of Anesthesiologists

CB: conventional dose of bupivacaine alone

CBF: conventional dose bupivacaine with fentanyl

CD: Cesarean Delivery

CS: Cesarean Section

DBP: Diastolic blood pressure

ECG: Electrocardiograph

EDHS: Ethiopia Demographic and Health Survey

GA: General anesthesia

LBF: low dose of bupivacaine with fentanyl

PIH: Pregnancy Induced Hypertension

SA: Spinal anesthesia.

MAP: Mean arterial blood pressure

PI: Principal Investigator

SBP: Systolic blood pressure

VAS: Visual Analogue Score

SPSS: Statistical Package for social sciences

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Abstract

Background: Spinal anesthesia with local anesthetic agents, especially bupivacaine, has side effects such as hypotension, respiratory depression, vomiting and shivering .Its side effects are dose dependent, therefore different approaches have been attempted in order to avoid spinal-induced complications including the use of small dose of bupivacaine or by lowering the dose of local anesthetic and mixing it with additives like Neuraxial opioids.

Objective: The objective of this study is to compare Hemodynamic and analgesic effect of intrathecal fentanyl as adjuvant with low and conventional dose of bupivacaine in patients undergoing elective cesarean section under spinal anesthesia

Methodology: An institutional based prospective cohort study was conducted on 90 patients who fulfill inclusion criteria for cesarean section under spinal anesthesia from December 1-March 30, 2019.Study participants was selected by systematic random sampling technique. Data collection methods include preoperative chart review, intraoperative observation and postoperatively patient interview after informed consent and aim of study is explained to the patient. Two trained anesthetists with continuing supervision from principal investigator collected data. The data was entered into EPI INFO and transport to SPSS version 23 for analysis of variable using one way ANOVA, kruskal wallis H rank test and chi-square.

Result: The comparison of data showed that there is significant difference in arterial blood pressure between LBF vs CBF group and LBF VS CB group with adjusted p value of < 0.05.duration of analgesia was prolonged in LBF and CBF group which is 248± 35.6 and 260.3±40.3 minute respectively compared with CB group (167.10 ± 31.45) with p-value <0.05.time for analgesic request also prolonged in fentanyl added groups which is 304±47.8 minute, 294.6±99.5 and 177±25.88 for LBF,CBF and CB group respectively.

Conclusion and recommendation: use of intrathecal fentanyl as adjuvant with low dose bupivacaine for cesarean section is effective in maintaining hemodynamic stability with improved intraoperative and early postoperative analgesia without any effect on the mother and fetus. We recommend the use of 25mcg intrathecal fentanyl with 8mg bupivacaine as appropriate to improve the hemodynamic status of patients in addition to improve intraoperative and early postoperative analgesia for elective cesarean section in hospital.

CHAPTER ONE: INTRODUCTION

1.1 Background Information

Cesarean section is one of the most common surgeries in the world, which has been increased in the last 21 years [1].As 2016 EDHS program found that the rate of cesarean delivery in Ethiopia is around 2% even if it varies across the seven administrative regions of Ethiopia, of all Addis Ababa had highest rate of cesarean section which accounts around 21.4% [2].

Cesarean delivery requires traction of peritoneum and handling of intraperitoneal organs, resulting in intraoperative visceral pain which is a poorly localized type of pain from deep structures in the body. With higher doses of hyperbaric bupivacaine the incidence of intraoperative visceral pain is reduced, but increasing the dose of bupivacaine increases the risk of high block [3].

Spinal anesthesia has become the anesthetic technique of choice for CD, and has resulted in a reduction in maternal mortality [4, 5]. Simple technique, fast in its effect, and uniform sensory and motor blocks are the advantages of spinal anesthesia. SA also helps to avoid the risk of tracheal intubation as well as maternal risks of GA, facilitate early bonding between mother and baby, and provide effective Neuraxial postoperative analgesia, enabling quicker maternal recovery [6]. It is, however, associated with hypotension in more than 80 % of parturient if not properly managed [7].

Hormonal and mechanical factors make obstetric patients need strict dose calculations of local anesthetics intrathecally for spinal anesthesia. Any greater dose of local anesthetics can cause hemodynamic instability, maternal morbidity and any lesser dose can produce inadequate block [8].

Bupivacaine is the most commonly used drug worldwide for spinal anaesthesia in CD. Spinal anaesthesia with local anesthetic agents, especially bupivacaine, has side effects such as hypotension, respiratory depression, vomiting and shivering in a dose dependent fashion. Hypotension is one of the commonest side effects and can affect both the mother and the fetus or the neonate [9]. Its side effects are dose dependent, therefore different approaches have been attempted in order to avoid spinal-induced complications including the use of small dose of bupivacaine [10, 11] or by lowering the dose of local anesthetic and mixing it with additives like

Neuraxial opioids [11].studies have also shown that by adding intrathecal opioids to bupivacaine in cesarean section enhance the quality of surgical anesthesia [12].

The incidence hypotension was reported to be 58.4 % in spinal anesthesia practices in caesarean operations, and fluid preloading, positioning the patient to the left and the use of vasoconstrictor agents were recommended to prevent hypotension [13, 14].

Postoperative pain after CD is reported to be higher (an unpleasant outcome for women and may result in delayed ambulation, prolonged time for discharge from hospital, poor bonding with the newborn, low satisfaction scores and delay breastfeeding. In addition to this inadequate analgesia leads to elevated plasma catecholamine concentrations, resulting in adverse effect on all organ systems [15]. In contrast, effective analgesia may permit improved mother - child bonding, early ambulation and discharge, greater patient satisfaction and early breast feeding [16]. Neuraxial administration of opioids along with local anesthetics improves the quality of intraoperative analgesia and provides postoperative pain relief for a longer duration than local anesthetics alone [17, 18].

Among synthetic opioids fentanyl is favorable due to greater potency, faster onset of action and rapid redistribution with an associated decrease in the plasma concentration of the drug [19] and thus enhancing the early postoperative analgesia. Intrathecal fentanyl has faster onset of action, it improves quality of intraoperative analgesia, reduces intrathecal doses of local anesthetic drugs and is associated with less side effects and good postoperative analgesia [20].

1.2 Statement of the Problem

Postoperative pain after CD is an unpleasant outcome for women and may result in delayed ambulation, prolonged time for discharge from hospital, poor bonding with the newborn, low satisfaction scores and delay breastfeeding. In addition to this inadequate analgesia leads to elevated plasma catecholamine concentrations, resulting in adverse effect on all organ systems [15]. In contrast, effective analgesia may permit improved mother -child bonding, early ambulation and discharge, greater patient satisfaction and early breastfeeding [16].

Post spinal hypotension is common in women who receive spinal anesthesia for cesarean delivery, with an incidence of up to 58.4 % [13]. Spinal hypotension is commonly associated with maternal nausea and vomiting, reduces uteroplacental blood flow, which may cause fetal acidosis, particularly in situations in which there is already fetal compromise and it may be an important contributory factor for maternal death related to regional anesthesia [12]. Hemodynamic control during CD under SA is therefore very important for the well-being of both the mother and the fetus.

Studies on hemodynamic alterations in spinal anesthesia show that the hypotension after spinal anesthesia is caused due to the enhanced sympathetic segmental block after higher doses of local anesthetic [21, 22, and 23].

Whereas using low dose of intrathecal bupivacaine alone compromises the adequacy of anesthesia for surgical incision even if maternal side effects related with high dose of bupivacaine decreases [10, 24]. Neuraxial administration of opioids along with local anesthetics are studied to be safe to avoid usage of higher dose of bupivacaine by improving the quality of intraoperative analgesia and provides postoperative pain relief for a longer duration than local anesthetics alone [18,19].

Among the synthetic opioids, fentanyl is favorable due to greater potency, faster onset of action and rapid redistribution with an associated decrease in the plasma concentration of the drug [19] and thus enhancing the early postoperative analgesia, improves quality of intraoperative analgesia, reduces intrathecal doses of local anesthetic drugs and is associated with fewer side effects. Unlike morphine fentanyl has fewer tendencies to migrate rostral to the fourth ventricle in sufficient concentration to cause delayed respiratory depression [20].

Despite year of advances in the availability of drugs the main stay of Drug administered for subarachnoid block in CS in many settings in our country is still bupivacaine alone. Use of bupivacaine alone has significant side effects especially in obstetrics populations. Therefore use of intrathecal fentanyl as adjuvant for spinal anesthesia is safe and effective. This can be the solution for increasing the safety and satisfaction of patients undergoing cesarean section under spinal anesthesia by reducing the incidence of hypotension as well as increasing the quality of postoperative pain management. So that the aim of this study will be to compare analgesic effectiveness and hemodynamic change of intrathecal fentanyl as adjuvant with low dose and

conventional dose of bupivacaine in parturients undergoing elective cesarean section under spinal anesthesia.

1.3 Justification of Study

Many studies have been performed to compare quality of anesthesia and hemodynamic effect of intrathecal fentanyl and bupivacaine in cesarean section. Most of these studies have been conducted in the developed world and in western populations. The presence of racial, cultural, genetic and socio demographic difference in the perception of pain and also on blood pressure has been well documented [22,23], meanwhile intraoperative and early postoperative pain as well as intraoperative hypotension are a major problems which needs an immediate and sustainable solution in our set up.

In addition to this the effect of intrathecal fentanyl as adjuvant with conventional dose of bupivacaine on maternal hemodynamic remains as a controversy since different studies shows different result. Some of studies shows as there is no change on maternal hemodynamics but increases the quality of sensory block. in contrast with this some other studies shows as addition of fentanyl on conventional dose of bupivacaine results a better hemodynamic stability and prolonged post op analgesia(1) and they justify as it may be due to reduced activity of sympathetic afferent.

As we observe in our experience different anesthetists administer intrathecal fentanyl in different dose of bupivacaine despite the controversy is made on the conventional dose of bupivacaine. So we want to observe the effect of intrathecal fentanyl on maternal hemodynamic and its analgesic effect when added in low and conventional dose of bupivacaine.

In our country as far as my knowledge and searching ability, there is no similar research done and there has no published evidence on the same topic in the same area. So that, it can be used as a source of information for further researchers and a sole input to the literature. in addition to this the result of this study will be helpful for program planners and policy makers so as to devise different strategies which help to improve and select appropriate combination of bupivacaine and fentanyl to increase maternal satisfaction with spinal anesthesia.

CHAPTER TWO: LITERATURE REVIEW

A randomized control study done by Himbandu G. et al 2016 in USA on 50 parturient to compare maternal hemodynamic and duration of analgesia of intrathecal 7.5 mg of bupivacaine with 25 mcg of fentanyl mixture(group-s) to 10 mg of hyperbaric bupivacaine(group-c) for cesarean section shows The systolic blood pressure significantly decreased with >25% fall from the baseline in group-C (98.76 ± 8.36) than in group-S (117.32 ± 12.21) with $P < 0.001$.The duration of effective analgesia was significantly prolonged in the study group than in the control group ($P < 0.001$) [8].

A randomized control trial study done by Dhumal PR et al on 2013 to compare effectiveness of sensory and motor blockade after spinal anaesthesia with plain bupivacaine (7.5mg of 0.5%) and bupivacaine(5mg of 0.5% Bupivacaine) with fentanyl (25mcg) for elective cesarean section shows the mean time required to reach peak sensory level and duration of motor recovery time was earlier in Group BF than Group B (P= <0.001) but, mean time of two segment regression of sensory analgesia and complete sensory recovery was significantly early in Group B (P<0.05). This shows the duration of effective analgesia was significantly more in Group BF (225.3 ± 29.2) compared with control group (110.33 ± 8.90) [11].

In another randomized control trial study done by Singh H et al in Texas to compare duration of sensory block between 13 mg bupivacaine with 25 mcg of fentanyl (group 1) and bupivacaine 13.5 mg alone (group 2) shows the addition of fentanyl with bupivacaine reduced postoperative analgesia consumption by 28% for 143 minutes. episode of hypotension were more frequent in the fentanyl treated group than in the control group (43% Vs 14 %) which is statistically significant but in terms of other side effects patients in Group BF had fewer side effects (16.66%) compared to control group 36.66%)[25].

A randomized control trial study done in iran on 2017 by Farzi F. et al shows adding 25 mcg of fentanyl to 12.5 mg of intrathecal bupivacaine for elective cesarean section increased the duration of analgesia and provided hemodynamic stablity with no major complication[1].

Another randomized control trial study, conducted in Turkey by Selim TSK et al in 2009 on 40 pregnant women to asses the incidence of hypotension after administration of low dose bupivacaine (4 mg) with fentanyl (25mcg) and l0 mg of bupivacaine alone in elective cesarean section. They found that sensory block was adequate for surgery in all patients. Hypotension occurred in 75 % patients in the fentanyl group and 100% in the control group. They conclude that the incidence of hypotension, number of ephedrine treatments, and need for ephedrine was significantly greater in the non-fentanyl group [26].

In contrast, a randomized control trial study done by Gajanan et al 2014 in india to evaluate the effects of intrathecal administered fentanyl (25mcg) on the characteristics of hyperbaric bupivacaine induced subarachnoid block and adverse effects of fentanyl found no significant difference in intraoperative hypotension (94.20 ± 5.07 vs 96.90 ± 6.30), pulse rate (86.47 ± 3.30 vs 87.13 ± 5.03) and respiratory rate (16.07 vs 16) between treatment and control group. But 5% of the treatment group develops mild Pruritus which did not need treatment [42].

Another single blinded randomized control trial study done in India by jaishri B.et al 2005 on 120 parturients to compare hemodynamic stability , postoperative pain and shivering between 8 mg of bupivacaine ,10mg of bupivacaine,12.5 mg of bupivacaine alone and adding 12.5 mcg of fentanyl in 8mg,10mg and 12.5 mg of bupivacaine in parturient undergoing cesarean section shows bupivacaine fentanyl combination leads to abolishment of visceral pain, reduction in incidence of nausea and vomiting, increased hemodynamic stability and increases the duration of postoperative analgesia; however no effect can be seen on bradycardia, nausea vomiting,shivering,maternal or neonatal respiration. [9].

double blinded randomized control trial done by Misirlioglu K et al 2014 in turkey on 72 patients that underwent elective cesarean section to assess the Effect of Intrathecal Low Dose Levo bupivacaine or Bupivacaine Combined with Fentanyl on the level of motor-sensory block, analgesia duration, patient satisfaction and newborn's well being showed as None of the parturient experienced an inadequate block and finally they conclude that the addition of 20 μg of fentanyl in low doses of intrathecal 7.5 mg of 0.5% isobaric levobupivacaine and 7.5 mg of

0.5% isobaric bupivacaine in elective caesarean section operations provided sufficient analgesia for surgery, and this had no negative effect on the mother or the baby [29].

A randomized control trial study done by Wojciech W on 2010 in Warsaw university of medicine, Poland by department of obstetrics and gynecology to compare analgesic efficacy, hemodynamic change and neonatal outcome of intrathecal bupivacaine supplemented with normal saline (control group) or with fentanyl 25 mcg (fentanyl group) which is adjusted based on their height starting from 7.5 mg to 15 mg in patients undergoing elective cesarean section under spinal anesthesia shows intrathecal fentanyl extended the period of effective analgesia to 4 hours ,reduces total opioids consumption but somewhat increase in incidence of pruritus(10%) of parturient And they concluded that supplementation of spinal anesthesia with intrathecal fentanyl provides effective intraoperative analgesia and decrease opioids consumption during the period of the highest analgesic demand after CS ,without an increase in maternal or neonatal side effects [30].

Other studies in different parts of Europe and Asia have shown that patients who received intrathecal fentanyl (25mcg) with Spinal Bupivacaine had not only improved or prolonged intraoperative analgesic time and reduced analgesic requirements, but also reduced postoperative analgesic requirements for at least 6hrs [16,20]. The incidence of nausea and shivering is significantly reduced as well. Postoperative pain relief and hemodynamic stability are increased by adding fentanyl. Pruritus, maternal respiratory depression and changes in Apgar score do not occur, as not affected by low doses of intrathecal fentanyl [28].

a prospective double blinded control trial done by Mhammed S.et al in Tunisia 2010 on 80 parturients that underwent elective cesarean section to compare hemodynamic change of 10 mg (group A) and 7.5 mg (group B) of isobaric bupivacaine both with 25 µg of fentanyl and 100 µg of morphine in spinal anaesthesia showed the incidence of low blood pressure was markedly higher in the group A than in group B (88% vs 68 %p = 0.03) and the doses of ephedrine used were 30 (larger in group A than in group B. the incidence of intraoperative pain tended to be higher in group B than in group A although the difference did not reach statistical significance (5 versus 2; p = 0.24). intraoperative events such as nausea and vomiting were markedly lower in

group B than in group A, while the incidence of shivering was very low and similar in both groups and when we see the effects of the spinal anaesthesia on the neonates, All the babies were live born. No neonate required tracheal intubation and none died during the study. The baby, whose mother had received intraoperative intravenous fentanyl, had 1' and 5' Apgar scores at 9 and 10 respectively [31].

A Nigerian randomized control trial study done by Olanrewaju NA et al to compare analgesia efficacy of intrathecal fentanyl for patients undergoing elective open reduction and internal fixation of lower limb fractures (ORIF) found that intrathecal fentanyl provided prolonged analgesia for 4 hours post operatively. In addition, spinal anaesthesia complications were reduced [32].

A prospective cohort study done in gondor university hospital ,Ethiopia by kassahun et al in 2016 on 100 parturient to compare analgesic efficacy of 12.5 mg of bupivacaine alone(BS) and 10 mg of bupivacaine with 12.5 mcg of fentanil(BF) reveals total duration of analgesia was longer in BF group (275.10 ± 42.43) than BS group (156.10 ± 34.45) in minutes, P= 0.001, analgesia request time in BF (301.00 ± 46.55) vs. (200.20 ± 44.19) in minute in BS group, P= 0.001 also longer. Not only this but also total amount of tramadol consumption 50(50) mg in BF vs. 100 (50) mg in BS, P= 0.001. VAS score also reduced at 2hrs, 3hrs, 4hr, 5hrs and 6hrs in BF group. In terms of perioperative complications13 (26%) patients in BF group & 19(38%) in BS group were developed hypotension P= 0.198, 3(6%) patients in BF & 18(36%) in BS group developed nausea, P =0.001, Vomiting occurred in one patient in BF group compared with 12 patients in BS group with p-value = 0.002. None of group BS patients developed pruritus but 7(14%) in group BF developed mild pruritus, which did not need treatment. Shivering occurred 15(30%) patients in BF vs29 (58%) in BS group with p-value of 0.005 [33].

Research hypothesis

Hemodynamic changes and duration of analgesia are different in patient who receive low dose bupivacaine with fentanyl and conventional dose of bupivacaine compared to those receive conventional dose of bupivacaine alone

HO1: There is no statistically significant difference in maternal hemodynamic among groups.

HA1: There is statistically significant difference in maternal hemodynamic among groups

HO2: There is no statistically significant difference in time to analgesic request among groups.

HA2: There is statistically significant difference in time to analgesic request among groups.

HO3: There is no statistically significant difference in duration of analgesia among groups.

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

CHAPTER THREE: OBJECTIVES

3.1 General Objective

The aim of this study is to compare the hemodynamic and analgesic effect of low dose bupivacaine with fentanyl and conventional dose of bupivacaine with fentanyl in parturients undergoing elective cesarean section under spinal anesthesia from December 1, 2018 to march 30, 2019.

3.2 Specific Objectives

- ✓ To compare hemodynamic changes among groups
- ✓ To compare first analgesic request among groups
- ✓ To compare duration of analgesia among groups

CHAPTER FOUR: METHODS AND MATERIALS

4.1 Study place and Period

The study was conducted at Gandhi Memorial Hospital which is located in capital city of Ethiopia, Addis Ababa. It was established in 1958 G.C when it was called the only maternity hospital in Ethiopia. The hospital was named as Gandhi Memorial Hospital for the memory of Mahatma Gandhi. It is one of the thirteen governmental hospitals found in Addis Ababa and one of the hospitals which was administered by Addis Ababa Health Bureau. The Hospital primarily gives services for women and children. The Hospital provides Gynecologic, Obstetric and reproductive health services including Mother and Child Health (MCH), infertility and sexual violence services. Currently, it is providing inpatient, outpatient services and emergency cases. The hospital has 110 beds and delivers 25 neonates each day. The hospital has two operation tables and average number of caesarian deliveries done at the hospital is eight to ten per day and from this average of 3 to 4 parturients undergo elective cesarean section. The study was conducted from December 1, 2018 to march 30, 2019.

4.2 Study design

An institutional based prospective cohort study was employed from December 1, 2018 to march 30, 2019.

4.3 populations

4.3.1 Source population

All parturient that underwent cesarean delivery at Gandi Memorial Hospital.

4.3.2 Study population

Elective parturient that underwent cesarean delivery under spinal anesthesia at Gandi Memorial Hospital during study period.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

All pregnant women, who were candidate for elective cesarean section with ASA class I and II

4.4.2 Exclusion criteria

- Patients with preexisting hypertension or PIH requiring treatment [1,9]
- Patients with cardiac/renal or other end organ disease [33].

- Patients with extreme height (<140 cm and >175 cm) [1].
- Patients delivering under spinal anesthesia with added adjuvant like trans abdominal plane block(TAP block) and adjuvants other than intrathecal fentanyl
- Patents delivered with cesarean section under spinal anesthesia with lidocaine
- Those having volume of surgical bleeding more than 1500 cc
- Lack of sufficient sensory level for cesarean section, and the need for general anesthesia

4.5 study Variables

4.5.1 Dependent variables

Hemodynamic changes

First analgesic request

Duration of analgesia

4.5.2 Independent variables

- ✓ Socio demographic variables (age,sex,weight,height and BMI)
- ✓ ASA physical status
- ✓ exposure status(LBF or CBF or CB)
- ✓ Duration of surgery
- ✓ Estimated total intraoperative blood loss
- ✓ Amount of fluid preloaded
- ✓ Intraoperative fluid balance
- ✓ History of previous surgery

4.6 Sample size and sampling technique

4.6.1 Sample size determination

The primary endpoint of our study was to compare hemodynamic status and analgesic effect so that sample size estimation based on largest sample size were used and calculated by using a priori power analysis (G Power version 3.01) based on the results of a pilot study done at Ghandi memorial hospital on 15 patients (5 for each group) and taking mean systolic blood pressure measurement in mmhg at 10 minute which is 99.6,90 and 94 for LBF, CBF and CB group respectively. The common pooled standard deviation was 9.6 for all three groups. Controlling for the probability of a Type I error at alpha = 0.017 (the alpha level was reduced using a Bonferroni

correction, 0.05/3= 0.017, to allow for comparisons of all three groups),and a power of 80% was used .The calculated sample size was 81; by adding 10%, attrition rate and assuming balanced design the total sample size was 90.

4.6.2 Sampling Technique and procedure

As Gandi memorial hospital surgical log book shows 360 patients estimated to undergo cesarean section within the hospital during study period, So 90 participants were recruited by systematic sampling technique with the probability of about 25%. k = N/n =4. The first study participant will be selected by lottery method.

n = total sample size

k = skip interval

N = Total study population

4.7 Data Collection Technique and Patients

After providing training for data collectors, data collected using pretested questionnaires with multiple close and open-ended questions on respondents. All patients who scheduled for elective cesarean section that fulfill inclusion criteria and volunteer to take part in the study were thoroughly assessed before surgery by history taking, and chart review following informed consent. On the morning of the surgery data collector, instructed the patient on how to self-report pain using VAS score. Sociodemographic and intraoperative variables are filled by intraoperative data collector and the remaining postoperative data was collected by the other data collector who is unaware of group allocation.

On arrival of the patients to the operative theater, and after application of the routine hospital monitoring protocol, HR, noninvasive blood pressure, and SPO2 has been recorded before performing spinal anesthesia and it was taken as a base line vital sign. During each procedure the data collectors observes the intraoperative condition of the patient. After SA is performed the data collectors recorded the maximum sensory block assesed with the patient's ability to distinct the sharpness created by the tip of the needle(pin prick method) and motor block level which is routinely examined by examining skeletal muscle strength criteria using modified bromage scale. The neonates Apgar score had also recorded.

Post operatively each patient was interviewed and their chart also reviewed. Group LBF are those laboring mothers taking 25 mcg of intrathecal fentanyl with 0.5% of 8 mg bupivacaine, group CBF are those who take 25 mcg of intrathecal fentanyl with 0.5% of 10 mg bupivacaine

and group CB are those taking 0.5% of 10 mg of bupivacaine only. The fentanyl dose of 25mcg is chosen based on the recommendations in the review of Hamber and Viscomi [35]. One of the data collectors take and observe intraoperative necessary information.

Starting from the immediate postoperative time, presence and scale of pain, time for the first analgesic request as well as analgesics need was assessed by the other trained data collector. This assessment was done at 1hr, 2 hrs, 3hrs, 4hrs, 5hrs and 6hrs for VAS score. All patients were also assesed within 12 hrs after surgery for potential drug complications such as nausea and vomiting, itching etc and the neonatal Apgar score also assessed in the first and fifth minute of delivery.

The categories of patients was identified by the by data collectors. The VAS was determined by the patient marking their pain intensity on a line which 10 cm long. Two BSC anesthetists were selected to collect data and one day training was given on how to collect data. Another Msc anesthetist was assigned to assist and supervise data collectors.

4.9 Data quality assurance

To ensure quality of data, pre-test of the questionnaire was performed on study populations. The completed questionnaire was submitted and reviewed daily to avoid loss of data. Close supervision and daily information exchange was used as a means to correct problems during the course of data collection. Data consistency and completeness was made throughout the data collection, data entry and analysis.

4.10 Data processing and analysis

Data were entered into Epi-info 7 and exported to SPSS V 23 for analysis. The data were tested for normality using histogram and Shapiro–Wilk normality test (p value >0.05 taken as normally distributed) and homogeneity of variance were tested by Levene's test (p value >0.05). Normally distributed and continuous data were analyzed using one way analysis of variance (ANOVA) with post hoc analysis for multiple test and non-normally distributed data were analyzed using kuruska-wallis H rank test. The comparisons of categorical variable were analyzed using Pearson chi-square test. Data were presented as mean ±SD for normally distributed, median ± IQR for non normally distributed and categorical data were presented as numbers and frequencies (percentages). P-values <0.05 was considered statistically significant.

4.11 Ethical Consideration

The study was conducted after obtaining ethical approval from Addis Ababa University institutional review board (IRB). After the permission from IRB, Official letter was submitted to the Addis Ababa health bureau, and then the letter of recommendation was obtained and distributed to Gandi Memorial hospital.

The purpose of the study was explained to the patients under the study and oral informed consent was obtained from them. Patients were informed that the care to be given will not compromised in any way and confidentiality was assured. Name and other identifying information wasn't used in the study.

4.12 Presentation and dissemination plan

The result of the study will be presented using tables and figures. The copies of final results will be disseminated to AAU department of anesthesia, Ethiopian anesthetists association, and Addis Ababa health bureau and at large for Minister of health. It will be presented on workshop and different seminars and finally submitted to a relevant scientific journal for publication.

4.13 Operational Definitions

Hemodynamic: in this research tend to refer arterial blood pressure**.**

Hypotention:defined as a systolic blood pressure of below 90mmhg or lower than 30% of starting systolic blood pressure or MAP less than 70mmhg(12).

Bradycardia: defined as heart rate less than 50 beats/minutes (21).

Time for first analgesic request: is the time from intrathecal injection to first request for analgesia [27].

Duration of sensory block: The duration between the ends of intrathecal injection to decrease pin prick sense below T10.

Duration of motor block: the duration between the ends of intrathecal injection to free feet movement.

Duration of analgesia: is considered as time duration from spinal injection to the time when patient had discomfort or pain.

Bromage scale: is a criteria used for examining skeletal muscle strength which is rated as 0=no paralysis, 1=only able to move the knee, 2=only able to move feet, 3=inability to move the leg or knee [34].

VAS score: is a visual analogue scale is a method of pain assessment determined by the patient making a mark of their pain intensity on a line which is 100 millimeter long [17].

No pain _____ worst imaginable pain

Pruritus: defined as any scratch or itching complained by the patient.

Low dose of Bupivacaine: is considered as a dose of intrathecal bupivacaine of <8 mg for cesarean section [24].

Conventional dose of bupivacaine:

Is considered when its intrathecal dose is >8 mg for cesarean section [24].

CHAPTER FIVE: RESUIT

5.1 Socio-demographic characteristics of the participants

All 90 laboring mothers who underwent caesarean delivery under spinal anaesthesia during the study period were included with a response rate of 100%.Of these patients, 30 mothers were given intrathecal fentanyl (25mcg) with (8 mg) 0.5% bupivacaine (LBF group), 30 patients fentanyl 25 mcg with (10mg) (0.5%) bupivacaine (CBF group) and 30 patients 10 mg 0.5% bupivacaine alone (CB group).There was no statistically significant difference among the groups with respect to age, sex, weight, height, duration of surgery and ASA status as shown in **[Table1].**

Table 1: Socio-Demographic Characteristics Of Patients Undergoing Elective Cesarean Section Under Spinal Anesthesia At Ghandi Memorial Hospital Addis Ababa, Ethiopia 2019.

		LBF-group(n=30)	CBF-group(n=30)	CB-group(n=30)	P-value
Age in years		27(6)	26(4)	27(7)	0.530
Height in meter		1.59 ±0.27	1.60±0.28	1.60±1.03	0.394
Weight in kg		60.8±3.4	62.9±7.3	61.3±4.4	0.292
BMI		23.7±0.97	24.3±2.8	23.8±1.8	0.408
ASA	**I**	23(76.7%)	24(80%)	19(63.3%)	0.303
	II	7(23.3%)	6(20%)	11(36.7%)	
Parity	**I**	10(33.3%)	8(26.7%)	6(20%)	0.099
	>I	20(66.6%)	22(73.3%)	24(80%)	
Gestational age in weeks		39.0±1.24	39.3±1,26	39.8±1.76	0.12

Hint:*=Mean (standard deviation); **= Median (inter quartile range) Value are presented as: Mean+SD: One way ANOVA test, Median (IQR):Kuruska-wallis H rank test, Number(%):chi-square test and $p<0.05$ is statistically significant.

There is no significance difference in total amount of preloaded fluid, total amount of estimated blood loss ,total amount of fluid administered intraoperatively and duration of surgery among groups with p value of >0.05 as shown in table 2 below.

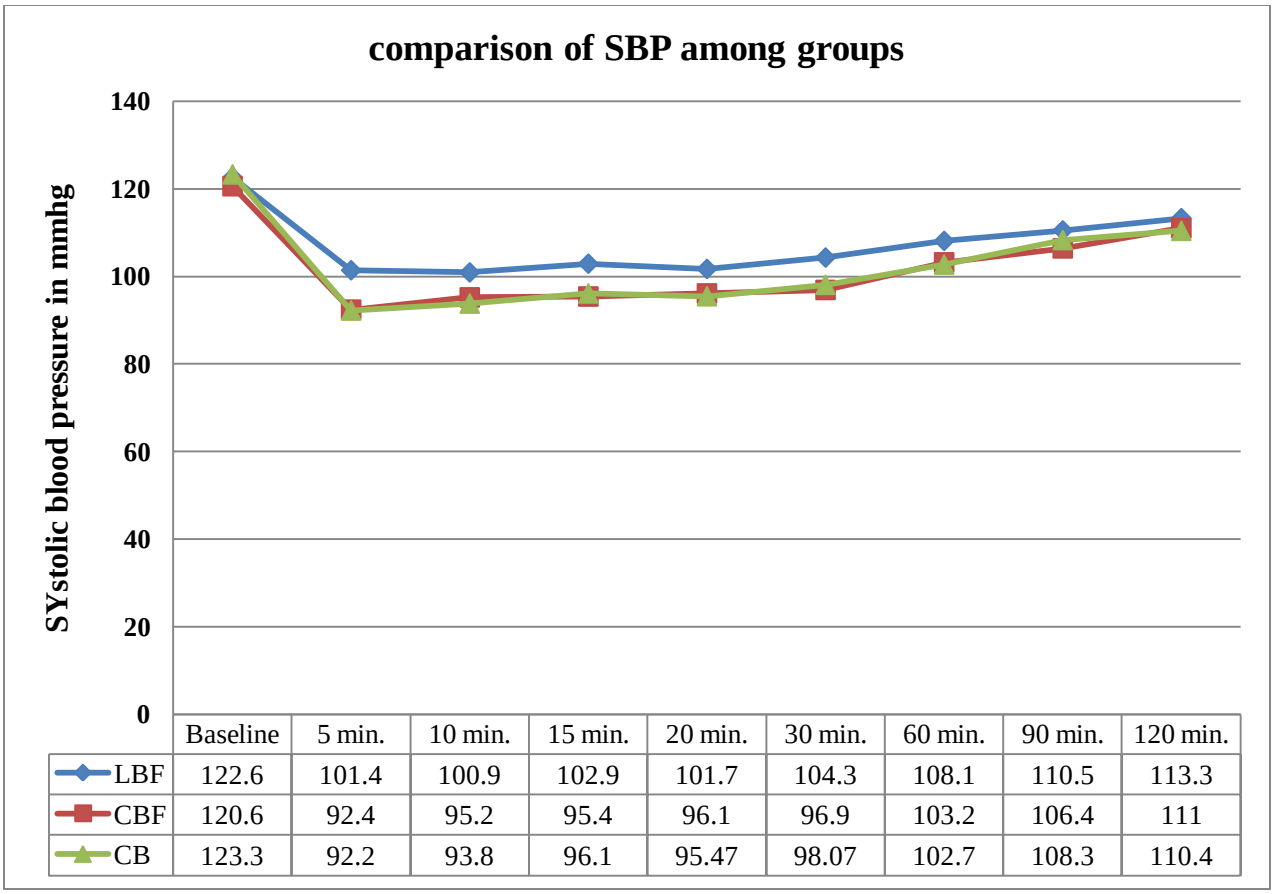
Table 2: Intraoperative Conditions Of Mothers Undergoing Cesarean Section Under Spinal Anesthesia At Ghandi Memorial Hospital Addis Ababa Ethiopia, 2019.

	LBF-group	**CBF-group**	**CB-group**	**P-value**
Amount of fluid preloaded	540±223.7*	550±241.7	603±188*	0.552
Total amount of fluid given intra op in ml	1570±475*	1413±506	1430±521*	0.417
Total surgical blood loss	500(200)**	400(150)	500(250)**	0.114
Duration of surgery in minutes	42(5)**	45(5)	45(6)**	0.942
Apgar score at 1 and 5 minute	7-10	7-10	7-10	NS

Hint:*=Mean (standard deviation); **= Median (interquartile range) Value are presented as: Mean+SD: One way ANOVA test, Median (IQR):Kuruska-wallis H rank test, Number(%):chi-square test and p<0.05 is statistically significant. NS-not significant

5.2 Comparisons of hemodynamic parameters among groups

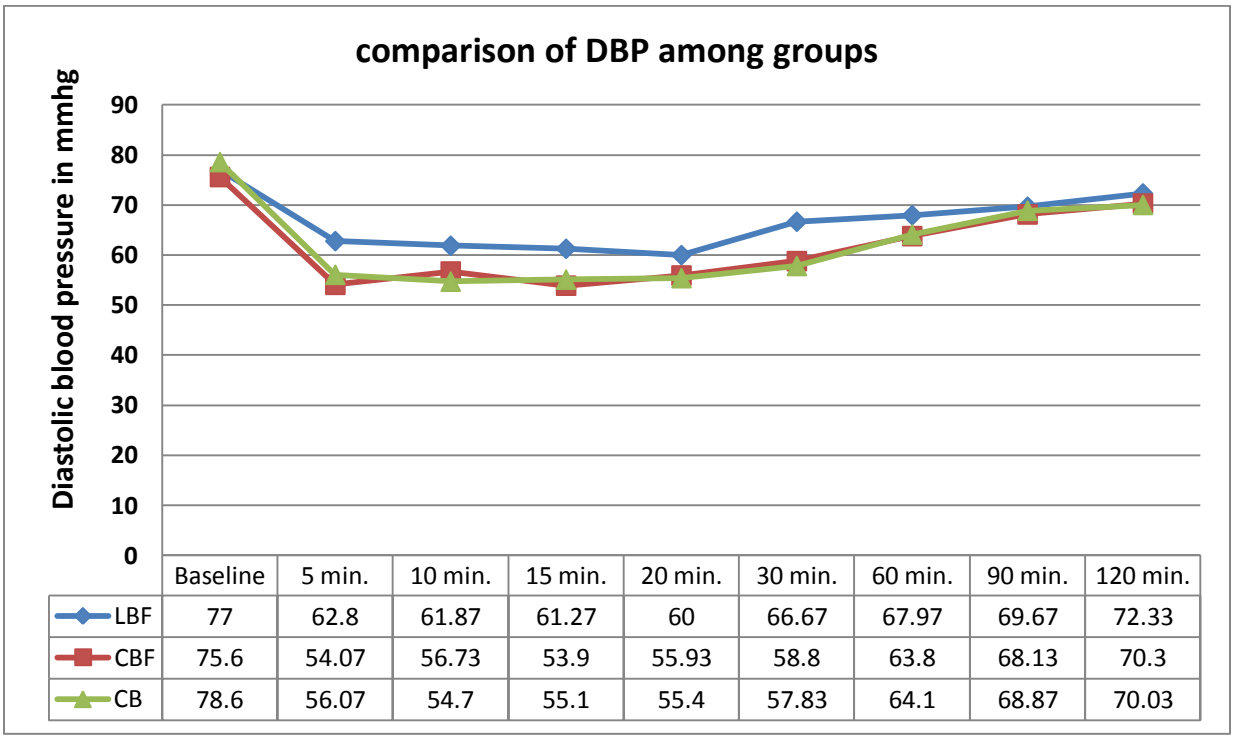
There was no significant difference in baseline hemodynamic parameters among groups with p-value >0.05; however arterial blood pressure over the first 30 minutes was significantly different among groups. In a post hoc analysis, we compare SBP, DBP and MAP between LBF vs CBF, LBF vs CB and CBF vs CB group and there is significant difference in arterial blood pressure between LBF vs CBF group and LBF VS CB group with adjusted p value of < 0.05. The peak decrease in systolic and diastolic blood pressure was recorded in the first 10 to 15 minutes in all three groups. There is no statistically significant difference in arterial blood pressure between CBF and CB group at all time interval [figure 1, 2 and table 3]



	Baseline	5 min.	10 min.	15 min.	20 min.	30 min.	60 min.	90 min.	120 min.
LBF	122.6	101.4	100.9	102.9	101.7	104.3	108.1	110.5	113.3
CBF	120.6	92.4	95.2	95.4	96.1	96.9	103.2	106.4	111
CB	123.3	92.2	93.8	96.1	95.47	98.07	102.7	108.3	110.4

Figure 1: a line graph shows Systolic blood pressure (mmHg) measurement at different time intervals Of Patients Underwent Elective Cesarean Section under Spinal Anesthesia at Ghandi Memorial Hospital Addis Ababa, Ethiopia 2019.

Diastolic blood pressure was lower in low dose bupivacaine groups than conventional dose of bupivacaine in the first 60 minutes which is stastically significant (p-value<0.05) after wards no stastically significant difference in DBP was seen up to 2hrs of postoperative period among groups as shown in **figure 2** below. in post hoc analysis there was significant difference between LBF vs CB and LBF vs CBF ; however no significant difference in DBP seen between CBF vs CB groups at different time intervals.



	Baseline	5 min.	10 min.	15 min.	20 min.	30 min.	60 min.	90 min.	120 min.
LBF	77	62.8	61.87	61.27	60	66.67	67.97	69.67	72.33
CBF	75.6	54.07	56.73	53.9	55.93	58.8	63.8	68.13	70.3
CB	78.6	56.07	54.7	55.1	55.4	57.83	64.1	68.87	70.03

Figure 2: A Line Graph Shows Diastolic Blood Pressure (Mmhg) At Different Time Interval Of Patients Undergoing Elective Cesarean Section Under Spinal Anesthesia At Ghandi Memorial Hospital Addis Ababa, Ethiopia 2019.

A one way ANOVA test showed as there was significant difference in mean arterial pressure among groups at all time intervals. in post hoc analysis there was significant difference in mean arterial blood pressure between LBF vs CBF and LBF vs CB with p-value >0.05; however no significant difference in MAP between CB vs CBF group.

Table 3: intraoperative mean arterial blood pressure measurement of Patients Undergoing Elective Cesarean Section Under Spinal Anesthesia At Ghandi Memorial Hospital Addis Ababa, Ethiopia 2019.

Group		**Baseline**	**5 min**	**10 min**	**15 min**	**20 min**	**25 min**	**30 min**	**60 min**	**90 min**	**120 min**
LBF	MEAN ±SD	92.24 ±3.3	75.6 ±9.9	74.9 ±8.9	75.1 ±8.3	73.9 ±5.9	76.1 ±8.0	79.2 ±8.1	81.3 ±4.6	83.7 ±5.3	86.5 ±5.3
CBF	Mean ±SD	90.6 ±11.2	66.8 ±11.8	70.3 ±8.3	67.8 ±9.5	69.5 ±8.2	71.9 ±9.6	71.8 ±8.2	76.5 ±6.3	79.5 ±6.2	83.8 ±5.4
CB	Mean ±SD	93.5 ±4.9	68.1 ±10.7	68.6 ±9.9	68.9 ±7.8	69.0 ±6.8	71.1 ±9.5	71.9 ±7.8	76.2 ±5.9	79.4 ±5.2	82.3 ±4.3
P-value	0.308	0.004	0.004	0.027	0.003	0.015	0.084	0.001	0.001	0.004	0.007

Hint: P-value <0.05 is taken as significant

There was no statistical significant difference in mean heart rate at various time intervals among groups as shown in [Tables 4].

Table 4: Heart Rate Measurement Of Patients Undergoing Elective Cesarean Section Under Spinal Anesthesia At Ghandi Memorial Hospital Addis Ababa, Ethiopia 2019.

		Base line	5 min	10 min	20 min	30 min	60 min	90 min	120 min
LBF-group	Mean ±SD	90.0 ±3.8*	82.23 ±6.87	82.8 ±7	87.8 ±8.3	85.2 ±8.6	85.6 ±10.7	86.8 ±6.4	87.07 ±6.7
CBF-group	Mean ±SD	92.9 ±4.3	78± 8.5	84.5 ±9.4	86.3 ±10.2	84.3 ±7.7	87.6 ±9.0	88.2 ±9.4	88.1 ±6.9
CB-group	Mean ±SD	91.6 ±5.3*	82.1 ±9.4	81.4 ±7.8	85.7 ±10.8	83.8 ±8.8	87.9 ±8.6	87.2 ±7.6	87.9 ±7.0
P-value		0.57	0.086	0.343	0.693	0.494	0.589	0.776	0.814

Hint: P-value <0.05 is taken as significant

5.3 Comparisons of Characteristics of spinal anesthesia among groups

The time required for the onset of the target sensory block of T6 dermatome was significantly faster in group LBF (3.13 min ± 0.6 min) and in group CBF(3.07 min ±0.7 min) than in group CB (4.03 min ± 0.9 min) with ($P < 0.001$). However, there was no significant difference between both the groups in the quality of surgical anesthesia (level of sensory block was above T10 in all three groups).

The duration of postoperative analgesia was significantly prolonged in the LBF group (248± 35.6min) and in CBF group (260.3±40.3 min) than in the CBF group (167.10 ± 31.45min) with $P < 0.001$. in post hoc analysis there was no significant difference in post operative analgesic duration between LBF and CBF group with adjusted P-value = 0.846.

Quality of sensory blockade was good referring to no requirement of any analgesic support intraoperatively in all three groups. Quality of motor blockade assessed by bromage scale showed adequate muscle relaxation in all groups with 90% of patients had level **IV** motor block and the other 10% had level **III** motor block with no significant difference among groups(P-value >0.05).

Table 4: Characteristic of spinal anaesthesia and duration of analgesia of mother's undergone elective cesarean section at Ghandi memorial hospital, Ethiopia, 2019.

	LBF(n=30)	CBF(n=30)	CB(n=30)	P-value
Highest sensory level (dermatome)	T4	T4	T4	-
Time of Onset of sensory level T6 (minute)	3.13±0.57	3.07±0.69	4.03±0.99	0.000
Duration of grade 0 motor block	120(30)	150(50)	150(20	0.002
Duration of analgesia (minute)	248± 35.6	260.3±40.3	167.10 ± 31.45	0.001
Time for first analgesic request	304±47.8	294.6±99.5	177±25.88	0.001

Values are presented as: Mean±SD: One way ANOVA test, Median (IQR): Kuruska-wallis H rank, *P* - value > 0.05 taken as significant

5.4 Comparison of Post operative pain VAS score among groups

As Kruskal Wallis H rank test results in the first 3 hrs of post operative period all three groups of patients had no experience pain with VAS score of zero. In the next 4 and 5 hours of postoperative period fentanyl added groups had lower VAS score than bupivacaine alone group which is stastically significant (p-value <0.05) as shown in table 5 below.

Table 5: Postoperative Visual Analogue scale pain scores median (IQR) in centimeters in each group over the first 12 postoperative hours of patients who undergone elective cesarean section at Ghandi memorial hospital, Ethiopia, 2019.

Group	LBF	CBF	CB	P-value
VAS score at 2 hrs.	0(0)	0(0)	0(0)	1.000
VAS score at 3 hrs.	0(0)	0(1)	0(2)	0.13
VAS score at 4 hrs.	2(3)	1(1)	4(3)	0.000
VAS score at 5 hrs.	2(3)	3(2)	5(3)	0.001
VAS score at 6 hrs.	3(4)	3(3)	6(5)	0.413
VAS score at 12 hrs.	2(1)	3(2)	2(2)	0.368

Median (IQR):kruskal walih H rank test,p-value<0.05 taken as significant

5.5 Comparing Post operative time to first analgesic request among groups

Postoperatively, a one way ANOVA test showed that the time from intrathecal injection to the first analgesic request was significantly different among the three groups (*P* >0.05). Mothers in the LBF group and CBF group had a significant longer time for the first analgesic request compared to the CB group, (304±47.8),(294.6±99.5)and (177±25.88) minutes respectively as shown in **[Fig.3]**.in post hoc multiple test analysis there was no significant difference in time for first analgesic request between LBF and CBF groups with p value of 0.889.

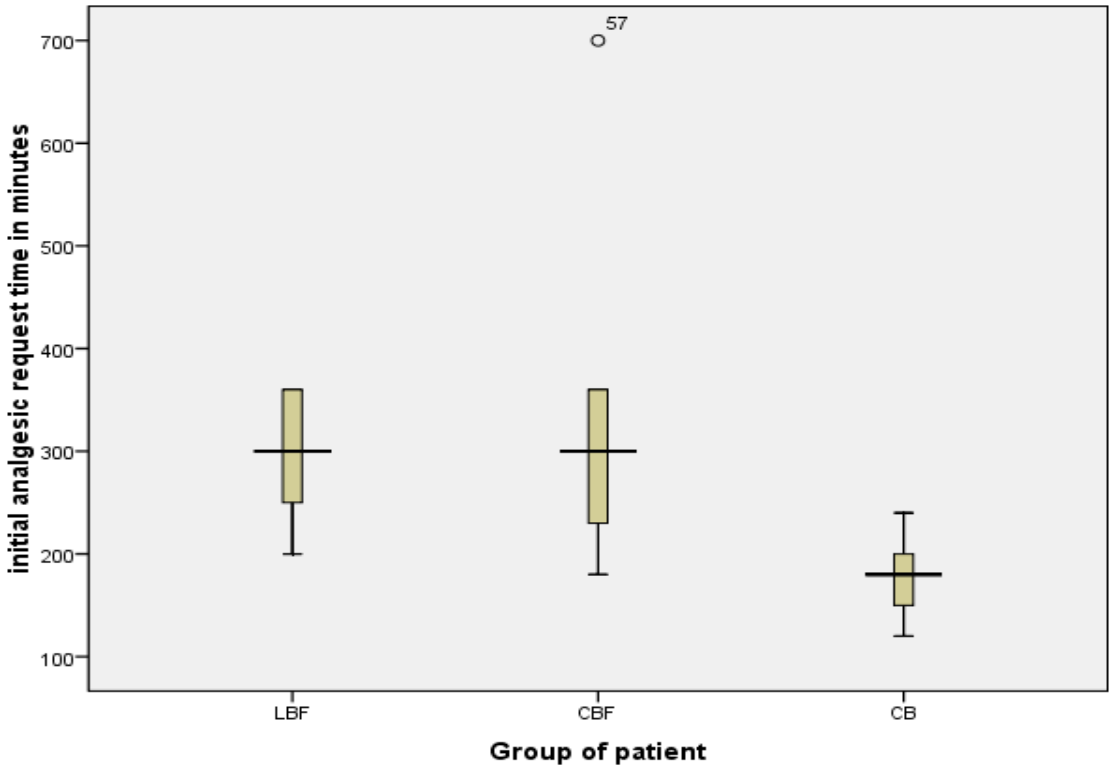


Figure 3: comparison of mean time for postoperative first analgesic request among groups Of Patients Undergoing Elective Cesarean Section Under Spinal Anesthesia At Ghandi Memorial Hospital Addis Ababa, Ethiopia 2019.

5.6 Comparison of Incidence of perioperative complications among groups

In terms of intraoperative complications, 4 (13.3%) patients in LBF group ,13 (42.4%) patients in CBF group and 14(46.7%) patients in CB groups were developed hypotension (P-value>0.05)and treated with IV fluid. None of them needed vaso- active drugs.

2 (6.7%) patients in CBF group and 3(10%) in CB group developed nausea, but none of patients develop nausea in LBF group.Vomiting occurred in two patients of CB group but none of patients develop vomiting in the other two groups with p-value of 0.117.

None of patient developed pruritus in CBF and CB group but one patients in group LBF developed mild pruritus, which did not need treatments

2 (6.7%) of patients developed shivering in LBF, 1(3.3%) in CBF group and 5(16.6%) in CB group with p- value of 0.005. none of patients develop respiratory depression and one and five minute neonatal apgar score was between 7 and 10 in all groups.

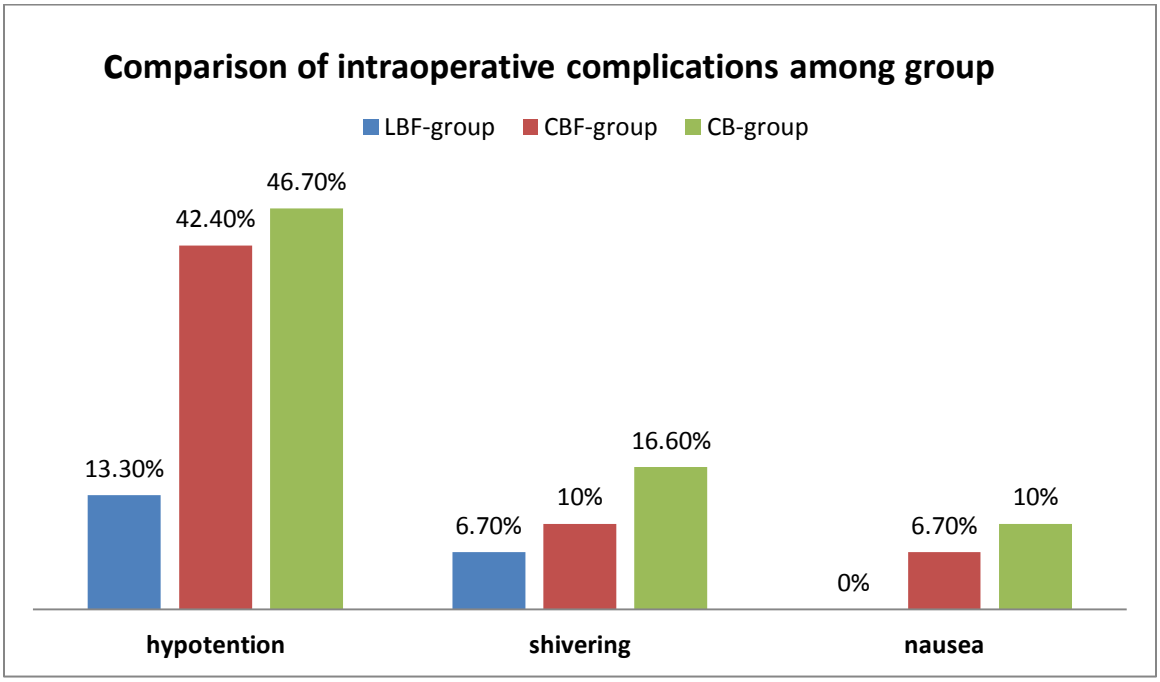


Figure 4: a bar graph representing the commonest intraoperative complications encountered among groups Of Patients Undergoing Elective Cesarean Section Under Spinal Anesthesia At Ghandi Memorial Hospital Addis Ababa, Ethiopia 2019.

Chapter six: Discussion

In our study we observed that the systolic and diastolic blood pressures were decreased significantly($P < 0.05$) in the first 30 minutes of spinal anesthesia in the CBF and CB group when compared to the LBF group, mostly due to more sympathetic blockade by higher doses of bupivacaine both of groups. Similar findings were observed by Himbandu G. et al, that compares hemodynamic stability and analgesic effect of 7.5 mg bupivacaine and 10 mg bupivacaine alone .Bogra et al [40], Seyedhejazi and Madarek [41] also shows similar finding to our study where in they studied by using 8 mg of bupivacaine and 10 µg of fentanyl for spinal anesthesia in caesarean section. Our result had similar finding with the above studies since our dose of local anesthetic we use was relatively equal with them.

In post hoc analysis we observe that there is no significant difference ($p>0.05$) in systolic and diastolic blood pressure between CBF group and CB group in all time intervals .our study is supported by a study done in Ethiopia by kassahun et al. found that no significant change in arterial blood pressure between study group (10 mg bupivacaine and 25 mcg fentanyl) and control group (12.5 mg bupivacaine alone).[33]

Our study showed that the incidence of hypotension was higher in CBF(42.2%) and CB(46.7%) group than LBF group (13.3%) which is stastically significant among groups (p value =0.005).Mhammed S. et al.[31] also shows similar finding to our study as 10 mg (group A) and 7.5 mg (group B) of isobaric bupivacaine both with 25 µg of fentanyl and 100 µg of morphine in spinal anaesthesia for cesarean section shows The incidence of low blood pressure was markedly higher in the group A than in group B (88% vs 68 %p = 0.03).the rate of hypotension is somewhat higher as compared with our study this may be due to the addition of morphine that will have synergetic effect with local anesthetic on sympathetic block.

In regard to our study none of patients need vasopressor treatment for hypotension. in the previous study mentioned above that was done by Mhammed et al [31]shows a larger dose of ephedrine was needed in bupivacaine alone group than fentanyl treated groups (32±23 vs 19±16 mg; p=0.004) respectively. the reason why our patients not taking vasopressor might be due to

the protocol difference in managing spinal hypotension and also the safest medications for managing maternal hypotension like ephedrine are not available in our hospital .

In our study, we observed that the time required for the onset of sensory blockade up to T6 was faster in LBF (3.13±0.57) and CBF group(3.07±0.69) than in the CB(4.03±0.99) and is statistically significant with $P < 0.05$, which corroborate with the study of Himbandu G. et al [8] that compares hemodynamic stablity and analgesic effect of 7.5 mg bupivacaine with 25 mcg fentanyl(group S) and 10 mg bupivacaine alone(group C) shows faster onset of T6 level of sensory block was achieved with group S (3.32±0.8) than group C(4.42±0.41) with p value of 0.001. our study also supported by a study of Gajanan et al [42] and Singh et al [25]who shows fentanyl treated groups had faster onset of sensory block. However, it differs from the observations of Randall's et al.,[27] and Gauchan et al [3] which states that the onset of sensory block to T6 gets faster with increasing bupivacaine dose.

According to our study, mothers in the LBF group and in CBF group had a significant longer time for the first analgesic request compared to mothers in CB group, (304± 47.8), (294.6 ± 99.5) and (177±25.88) in minutes respectively. in contour to our study Biswas BN et al showed that analgesia request time were shorter in bupivacaine alone group (150±10.48 minute) compared to fentanyl treated group (248 ± 11.7 minute) respectively (20).

Our study showed that addition of 25 mcg fentanyl increased total duration of complete analgesia (time from intrathecal injection to when the patients complained of any pain, VAS > 0) which was 248± 35.6 in minutes in LBF group,260.3±40.3 minutes in CBF group compared to bupivacaine alone group which is 167.10 ± 31.45 in minutes with p value = 0.001. our study is in line with a study done by Shashikala TK et al [28] grouped 99 parturients into, FB group who had been given 2ml of 0.5% bupivacaine with 12.5mcg fentanyl and BC group receiving 2ml 0.5% bupivacaine only. They found that the total duration of mean time analgesia between Group BC and Group FB was 165 ± 29.8 minutes in Group BC and 259.4 ± 35.3 minutes in Group FB respectively.

Another study in Nigeria gave 25mcg intrathecal fentanyl to those patient that undergoing lower limb surgery showed that the time of complete analgesia in Group FB was significantly longer than the SB group with a mean ± standard deviation of 239.97 ± 28.58 minutes compared to 129.17 ± 11.61in minutes and p-value of <0.001 respectively(23). Our results are

consistent with the above study even though patient characteristics, type of procedure and duration of surgery were differ from our study. These might be due to similar dose of intrathecal fentanyl (25 mcg) we used [32].

According to our study there was a prolonged motor block in CBF group with a median of 150(50) minute and in CB group with a median of 150(20) minute compared to LBF group with a median of 120(30) minute which is statistically significant with *P*- value = 0.002. Our study is supported by a study done by Dhumal PR, et al shows motor recovery in group BF was 77.2 ±14.7 minutes and in Group B was 98.80 ± 8.91 minutes respectively which was significant but not similar to our study. This might be due to the small dose of bupivacaine used, (Group B patients with 7.5mg of 0.5% heavy Bupivacaine) and in (Group BF patients with 5mg of 0.5% heavy Bupivacaine + 25µg fentanyl) respectively compared to our study (7).

The median or inter quartile range VAS scores at 4hrs ,5hrs and 6hrs was significantly reduced in fentanyl added group than Bupivacaine alone group with p- value < 0.05. Our finding was comparable with a study in Ethiopia by kassahun et al[33] shows significant difference in VAS score at 5 and 6hrs of postoperative period between fentanyl treated and bupivacaine alone group. This significant difference at these hours might be related with the wear off analgesic effects of spinal anesthesia in bupivacaine group and the synergistic effect of intrathecal fentanyl with bupivacaine in BF group continued since the duration of intrathecal fentanyl is expected to stay 6 hours. After 6 hour there was no significant difference in median VAS scores since both groups were treated with diclofenac and tramadol as well as wear of action of intrathecal fentanyl.

In our study there was no statistical significant difference in mean heart rate at various time intervals in all groups, which was similar finding with the previous study by Dhumal PR, et al [11], Shashikala TK et al and jaishri et al [9]. However, a study in Nepal showed that the incidence of bradycardia was 5.7% in control Group and 2.8% in Group BF with no significant variation in the group [3]. A similar study in Texas showed that bradycardia occurred 3 patients in treatment group and 4 patients in control group which was not significant [25]. In comparison to the above two studies there were no cases of bradycardia in our patients. This might be due to relatively lower dose of bupivacaine we used compared with the above studies, as proven scientifically the larger the bupivacaine dose the higher the height of block will result, so that it will block cardio-accelator fibers above T4 and causes bradycardia.

In regard to our study, 2 (6.7%) patients in CBF group and 3(10%) patients in CB group

developed nausea but none of patient in LBF group developed nausea. none of patients developed vomiting in LBF and CBF group but 2(6.7%) of patients experienced vomiting from CB group which is not stastically significant. A study from Iran found that adding 25mcg fentanyl reduced the incidence of nausea (7 patients) and vomiting (4 patients) in Bupivacaine fentanyl group compared with 15 patient developed nausea and 12 patients developed vomiting in their Bupivacaine alone group [1]. Our study is comparable with these results and our possible explanation for the reduction of nausea/vomiting in fentanyl added groups might be due to increased dose of fentanyl (25mcg), better quality of analgesia and good hemodynamic stability in LBF group(43).as different studies shows Intraoperative nausea and vomiting occurs in more than 66% of Caesarean deliveries. This is mainly related to peritoneal traction and exteriorization of the uterus performed with regional anaesthesia [27, 31]. In addition, sympathetic cardio accelerator fibers block with high dose of plain bupivacaine, can result in hypotension. This is strongly related to nausea and vomiting (18).these evidences support our result as fentanyl added groups had lower rate of nausea and vomiting.

In the group-LBF, one patient complained of mild pruritus and none of patients developed pruritus in CBF and CB groups, these might be because of side effect of fentanyl, even the etiology of it was not ascertained, The possible explanation is likely due to the cephalic migration of the opioids in CSF and its subsequent interaction with opioid receptors in the trigeminal nucleus. Similar findings were observed in the previous studies mentioned above by Himbandu G. et al [8] and Cowan et al.[17] and also the study by Jaishri et al.[9] observed no incidence of pruritus in fentanyl treated groups. Another study in India using 12.5 mcg fentanyl with 10mg bupivacaine compared with 10 mg bupivacaine, they found that no patients had pruritus in either of the group (18).

In our study 2 (6.7%) of patients developed shivering in LBF, 1(3.3%) in CBF group and 5(16.6%) in CB group with p- value of 0.005,the incidence of shivering is lower in fentanyl added groups than bupivacaine alone group. the same finding was seen by study of Biswas et al that was done to compare analgesic efficacy and maternal safety between 10 mg bupivacaine alone and 10 mg bupivacaine with 12.5 mcg fentanyl shows 4(20%) of bupivacaine alone group and 1(5%) of fentanyl group develops shivering. jaishri et al,[9] study also shows lower rate of shivering in fentanyl treated groups. a study done by kassahun et al.[33] in Ethiopia shows

shivering occurred in 15 (30%) patients in BF vs. 29 (58%) in BS group with *P*- value of 0.005.according to this study the rate of shivering significantly decreased in fentanyl treated groups but the number is too higher as compared to our study , this might be due to his study populations were emergency cesarean section patients and also environmental factors and operation room conditions may be another reasons.

None of patients in our study developed respiratory depression (spo_2< 90%) which was supported by many studies [3, 20, 28]. This might be due to high affinity of fentanyl with nonspecific binding sites on the lipid surface only a small proportion of the administered dose migrates to the cervical region [33]

In regard to our study one and five minute neonatal Apgar score was between 7 and 10 in all groups. Our result is supported by RCT done on Tunisia in 2010 to compare hemodynamic change of 10 mg (group A) and 7.5 mg (group B) of isobaric bupivacaine both with 25 µg of fentanyl and 100 µg of morphine in spinal anaesthesia for cesarean section shows 1 and 5 minute APGAR score was between 9 and 10 in both groups and also none of mothers develop respiratory depression. A similar study by Gajanan et al [42] using 25mg intrathecal fentanyl in elective cesarean section also showed no APGAR score differences. Also there was no neonatal bradycardia or respiratory depression noticed in our study. These showed that use of 25 mcg intrathecal fentanyl seems safe in cesarean section

Limitation of study

Anesthesia management differs from anesthetist to anesthetist depending on seniority. It was difficult to have a truly blinded data collector. Because during data reviewing, they can easily identify in which group the study subjects belong, so this can be means for bias. Routinely administered analgesics without assessing analgesic need of patient might be a source of bias in pain assessment.

Strength of study

We have tried to make comparable study groups in terms of socio demographic distribution, perioperative factors that affect study outcome so that the difference observed may be due to exposure factors.

Conclusion

Our comparative study shows that the use of intrathecal fentanyl as adjuvant with low dose bupivacaine for cesarean section is effective in maintaining hemodynamics stability with improved intraoperative and early postoperative analgesia, prolonged first analgesia request time and decreased the severity of postoperative pain without any effect on the mother and fetus.

Recommendation

We recommend the use of 25mcg intrathecal fentanyl with 8mg bupivacaine as appropriate to improve the hemodynamic status of patients in addition to improve intraoperative and early postoperative analgesia for elective cesarean section in hospital.

- **Anesthetist**

We also recommend anesthetist to use low dose of bupivacaine with fentanyl as a better choice for spinal anesthesia for elective cesarean section.

- **Researcher**

We also recommended further randomized control trial with adequate sample size and follow up period in order to avoid bias and to assess the exact severity of pain.

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Annex I: Information sheet to get permission for the research

Introduction

This information sheet is prepared to explain the research project that you are asked to join by a group research investigators. The research team includes Msc students, two senior advisors from AAU and two data collector from Ghandi Memorial Hospital.

Name of Principal investigator: -Ayub Mohammed

Advisor's name: -Ms.:-Misrak W/yohanes

Mr.:-Zewetir Ashebir

Name of sponsor: -AAU

Name of organization: -AAU, Health science college, anesthesia department

This information sheet is prepared by the above-mentioned investigator.

Risk

There is no any risk or harm that you will face by participating in this research. Any personal information recorded will not be copied and transferred to other bodies. No need of writing participants' name but by a code. Every piece of information will be kept confidentially.

Benefits

There is no incentive or payment to be gained by taking part in this project. The information collected from this research project will be kept confidential and only accessed by the researcher and research assistant only. This research project will be reviewed and approved by ethical committee of the department. If you want to know more information, you can contact the committee through the address below.

Tel: -+251924415702

Email: yassinmoh1363@gmail.com

Annex II: - Consent form

Dear participants

The aim of this study is to compare hemodynamic stability, analgesic effect and other related complications of intrathecal fentanyl adjuvant with low and conventional dose of bupivacaine among mothers who will give birth under CD in Gandi Memorial Hospital, Addis Ababa Ethiopia, 2019. You are selected to participate in this study by chance. The study will involve various intimate and private life questions. In order to achieve the objective of the research, we are requesting your participation. There are questions for you to answer politely and there is no need to put your name on the questionnaire; no individual response will be reported. Your response will be completely confidential. It is your full right to accept or refuse to give answer for questions. However; your honest answer to those questions will help us to assess and understand the effect. So; we are requesting you to give honest response and keep participation.

Would you willing to participate in the study please? If you are volunteer to participate in the study, you welcome.

For any farther question, please contact the investigator

Address = +251-912-651363

E-mail: yassinmoh1363@gmail.com

የመጠይቅ ፈቃድ

የተከበራችሁ የጥናቱ ተሳታፊዎች

የዚህ ጥናት ዋና አላማ በ2011 ዓ.ም በጋንዲ መታሰቢያ ሆስፒታል ማዋለጃ ክፍል ተኝተዉ ከወገብ በታቸ በሚሰጥ ማደንዘዣ በኦፐራሲዮን የሚገላገሉ ዕናቶቸ በቀዶ ህክምና ወቅት እና ከቀዶ ህክምናዉ በኃላ የሚደርስባቸዉን ህመም እና ተያያዥ ጉዳዮች ለመገንዘብ የሚደረግ ጥናት ነዉ፡፡ በኢጋጣሚ እርስዎም በዚህ ጥናት እንዲሳተፉ ተመርጠዋል፡፡ የዚህ ጥናት ጥቅም እርስዎ በሚሰጡት ምላሽ መሰረት መረጃዎችን በማማላት በሚገኘዉ ን ዉጤት መሰረት መረጃዎችን በማጠናቀር ውጤቱን እየተሰራበት ካለው ጋር ለማገናዘብ እንዲቻል ነዉ፡፡ ጥናቱ በትክክል አላማውን እንዲመታ የእርሶዎን ድጋፉ እንጠይቃለን፡፡ የማንኛውም ግለሰብ ስም አይመዘገብም እንዲሁም ሀሳቡ ብቻውን ይፋ እንዲዎጣ አይደረግም:: ሙሉ በሙሉ በሚስጥር የተጠበቀ ነው፡፡ በጥናቱ መሳተፍ አለመሳተፍ የራስዎ መብት ብቻ ነዉ፡፡ ግልፅ የሆነ ምላሽንና ከልብ የመነጨ ተሳትፎዎን እንዲሰጡን በአክብሮት እንጠይቃለን፡፡

ለመሳተፍ ፈቃደኛ ነዎት ሀ/ አዎ ፊርማ --------- ለ/ አይደለሁም

ለመሳተፍ ፈቃደኛ ስለሆኑ እናመሰግናለን፡፡

Annex III: patient data

Questionnaire

Questionnaire Code _____

Starting time_____

Date of data collection----------

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: Socio Demographic Data (chart review)

Card number:		**Bed no:**	**Code**
S.no	Question	Response	
101	Age		
102	ASA (I/II)	A. ASA I B. ASA II	
103	Weight		
104	Height		
105	Gestational age		
106	Parity		
107	BMI	18.5–24.9 25–29.9 30–34.9 >35	

Section II: Section 2: Preoperative assessment for SA including (Document review) & Intraoperative procedures observation.

Ser. Number	Question	Response	

201	Dates Of Surgery		
202	Plan Of Spinal Anesthesia	8 mg of bupivacaine with 25 mcg of fentanyl 10 mg of bupivacaine with 25 mcg of fentanyl 10 mg of bupivacaine alone	
203	Base line Heart rate	____bpm	
204	Base line Blood pressure(MAP)	____/____(____)mmhg	
205	Base line RR & spo2	_____bpm &_____%	
206	Diagnosis		
207	spinal needle size and type(gauge)		

Section III: Question related to spinal anesthesia and surgery.

S.no	Question	Response	Code	
301	Spinal injection to incision starting time (minutes)			
302	Level of motor blocks (In Bromage scale)& onset of			
303	Level of highest sensory block			
304	Incision starting time to delivery of the child(minute)			
305	Any additional analgesic drug give intraoperativley	If Yes Specify-------- If No Skip		
306	Duration of surgery			

Section IV: Value of hemodynamic parameter after spinal anesthesia intra operatively.

S. No.	**Parameters**	**Time intervals after SA (in minutes)**						
		At 5 min.	At 10 min.	At 15 min.	At 30 min.	At 60 min.	At 90 min.	At 120 min.
401	SBP (mmHg)							
402	DBP							

403	MBP							
404	PR							
405	RR							
406	SpO2							

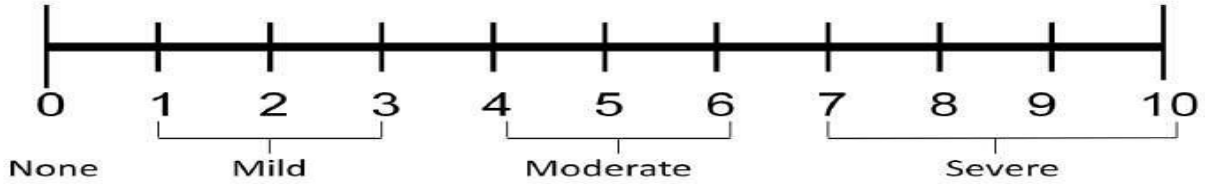
Section V: question related to intraoperative complications

	QUESTIONS	Answer	Management
501	Does hypotention occur intraoperativley (<25% from base line)	Yes No	----------
502	Does Respiratory depression (spo2 <90% or RR <9 bpm) occur for mother	Yes No	
503	Dose Fetal Respiratory depression(spo2 <90%) occur	Yes NO	
504	Does nausea occur intraoperativley?	1. Yes 2. No	
505	If yes what grade?	1. none 2. mild 3. moderate 4. severe	
506	Does pruritus occur intraoperativley?	1. yes 2. no	
507	If yes what severity?	1. no itching 2. mild 3. moderate 4. severe itching	
508	**Does vomiting was occur**	1. yes 2. no	
509	If yes grade of severity?	1. mild 2. moderate 3. severe	

510	APGAR score	At 1 minute ---- At 5 minute ------	
511	Does shivering occur intraoperativley?	1. yes 2. no	
512	If yes what grade?	1. zero 2. one 3. two 4. three 5. four	
513	Total amount blood loss during surgery in ml		
514	Total intraoperative fluid given during the operation in ml		
515	Duration of surgery in minutes		
516	Duration of anesthesia in minute		

Section VI: Question related to pain and postoperative condition of the patient?S

601. Severity of pain scoring using Visual analogue scale.



At 2 hrs. _____ (in centimeters)

At 3hrs. _____ (in centimeters)

At 4hrs. _____ (in centimeters)

At 5hrs. _____ (in centimeters)

At 6hrs. _____ (in centimeters)

At 12hrs. _____ (in centimeters)

602. Total and type of analgesia consumption within 12 hours after patient arrive in the recovery is (_____)

603. Initial Analgesia request time _____ (in minutes) till after the patient arrived in the recovery.

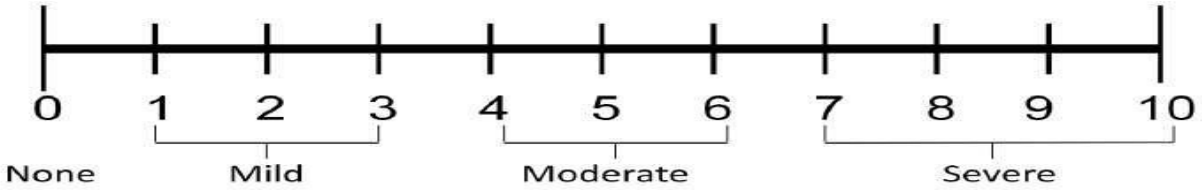
604. Time of motor regressions to Bromage scale 0_____ (in minutes).

Annex IV

Shivering is defined as an involuntary, repetitive activity of skeletal muscles. The presence of shivering was assessed after the completion of subarachnoid drug injection.

0 = no shivering,
1 = piloerection or peripheral vasoconstriction but no visible shivering,
2 = muscular activity in only one muscle group,
3 = muscular activity in more than one muscle group but not generalized, and
4 = shivering involving the whole body.

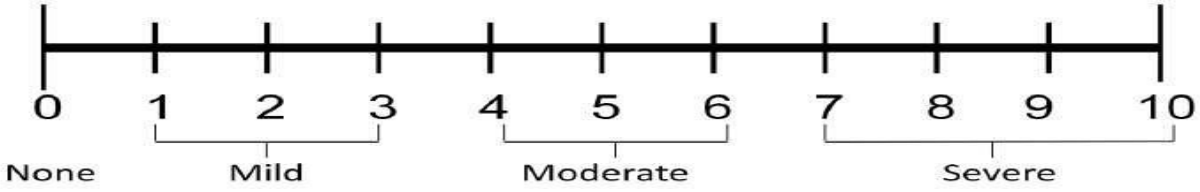
Vomiting was defined as either vomiting (expulsion of stomach contents) or retching (an involuntary attempt to vomit but not productive as regards stomach contents).
Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit.
Severity of nausea and vomiting assessed by verbal pain score (0–10, 0 = no pain, 10 = worst pain imaginable.)



1. none
2. mild
3. moderate
4. severe

Pruritus

The most commonly used tool for self-report of pruritus intensity is the visual analogue scale.



Annex V: American Society of Anesthesiologists (ASA) physical status classification of patients.

Class	Definition
1	Normal healthy patient
2	Patient with mild systemic disease (no functional limitations)
3	Patient with severe systemic disease (some functional limitations)
4	Patient with severe systemic disease that is a constant threat to life (functionality incapacitated)
5	Moribund patient who is not expected to survive without the operation
6	Brain-dead patient whose organs are being removed for donor purposes
E	If the procedure is an emergency, the physical status is followed by "E"

Adopted from Morgan and Mikhail 5thedition

Annex VI: Declaration

I, the undersigned, declare that this thesis is my original work in partial fulfillment of the requirements for the Master of Science degree in Anaesthesia. I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced

Name: _____Signature: _____

Submission to Msc Tutor, Department 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 Master of Science degree in Anaesthesia

Name and Signature

1. _____
2. _____
3. _____