An-Najah National University

Faculty of Graduate Studies

Comparative Study of Hyperbaric Bupivacaine Plus Ketamine vs. Bupivacaine Plus Fentanyl for Spinal Anesthesia During Cesarean Section. A prospective, Randomized, Double-Blind, Controlled Study

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الإقرار

أنا الموقع أدناه، مقدم الرسالة التي تحمل العنوان:

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أقر بأن ما اشتملت عليه هذه الرسالة أنما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وان هذه الرسالة ككل، أو أي جزء منها لم يقدم من قبل لنيل أيّ درجة أو لقب علميّ لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher`s own work and has not been submitted from anywhere else, for any other degree or qualification.

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List of Abbreviation

Abbreviations	Meaning
NMDA	N-methyl-D-Aspirate
CNS	Central Nervous System
CVS	Cardio Vascular System
RS	Respiratory Systems
ICP	Intra Cerebral Pressure
C/S	Cesarean Section
UK	United kingdom
SA	Spinal Anesthesia
Ml	Milliliter
Kg	Kilogram
VS	Verses
Mg	Milligram
Mcg	Microgram
K	Ketamine
F	Fentanyl
B	Bupivacaine
IT	Intrathecally
N	Number
PCA	Patient Control Analgesia
CSF	Cerebro Spinal Fluid
SAH	Special Arab Hospital
RCT	Random-Controlled Trial
ASA	American Society of Anesthesiologists
CBC	Complete Blood Count
IRB	Institutional Review Board
MAP	Mean Arterial Pressure
ECG	Electronic Cardio Gram
SPO2	Peripheral Capillary Oxygen Saturation
HR	Heart Rate
BP	Blood Pressure
NS	Normal Slain
Fr G	French Gouge
l/min	Liter/Minuit
T	Temperature
PACU	Post Anesthesia Care Unit
IV	Intravenous
RR	Respiratory Rate
SPSS	Statistical Package For The Social Sciences
SBP	Systolic blood pressure
DBP	Diastolic blood pressure

Conceptual definition of the terms

Hypotension: was defined systolic blood pressure was lower than 90 mm Hg or 20% below the pre induction level. (Khezri, Ghasemi and, Mohammadi in 2013)

Bradycardia: defined as Heart rate below 50 bpm , it is managed by 0.5 mg of atropine (Khezri, Ghasemi and, Mohammadi in 2013) .

Onset of sensory block: was defined as the time from the end of injection of the intrathecal anesthetic to the time at which pain at the T10 dermatome was absent.(Khezri, Ghasemi and, Mohammadi in 2013)

Duration of sensory blockade: is a time from onset of sensory blockade till sensory recovery at thoracic 10 (Sowmya, Ravi, Sujatha, Dinesh, & Kavya, 2016)

Duration of analgesia: is a time from spinal solution injection till first complain of pain > 4 in VAS score and need for analgesic drugs (Venkata et al., 2015) .

Onset of motor blockade: is a time injection of study drug till patient unable to flex lower limbs at hip joint (Sowmya et al., 2016).

Comparative Study of Hyperbaric Bupivacaine Plus Ketamine vs. Bupivacaine Plus Fentanyl for Spinal Anesthesia During Cesarean Section. A prospective, Randomized, Double-Blind, Controlled Study

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Abstract

Background: the effective postoperative pain management is a key priority of women undergoing cesarean delivery. Inadequate pain management in acute postoperative period is associated with persistent pain, greater opioid use, delayed functional recovery and increased postpartum depression.

The current study compared the analgesic effects of bupivacaine plus ketamine, bupivacaine plus fentanyl and bupivacaine alone for spinal anesthesia on postoperative pain and total analgesia consumption in patients undergoing elective cesarean section.

Method: this was a double blinded randomized control trial (RCT), 105 full-term parturient were randomly allocated into three groups: group F received (10mg) of 0.5% Bupivacaine plus 25μg Fentanyl, group B received (10mg) of 0.5% Bupivacaine alone and group K received (10mg) of 0.5% Bupivacaine plus 15mg ketamine. Pain incidence and intensity, Nausea, incidence and intensity, frequency of vomiting, bradycardia, hypotension episodes, headache, pruritus, shivering, sedation, time to the first analgesia requirement, and, patients' satisfaction. Moreover, onset and duration of sensory and motor block, and hemodynamic parameters were

recorded pre-, intra-, and postoperatively, every 3 min in the first time of operation then every 5min intraoperative, every 5 min for 15 min in the post-anesthesia care unit and every hour to 4hr in the floor**.**

Result: Demographic data was comparable between the groups. Patient who received fentanyl had rapid in onset of sensory block with (p value<0.001), and faster in onset of motor block with mean (2.68min)(P value<0.001), and had significant prolong in duration of sensory, motor block, in fentanyl group (P value<0.05), and had significant elongate in duration of analgesia (P value<0.000).Also, had significant decreased in the total analgesia consumption with decreased in pain intensity. There were no significant different between three group regarding: incidence of intraoperative Bradycardia there were 1\35 (2.9%) in fentanyl group vs. 1\35(2.9%) in ketamine group, incidence of intraoperative hypotension there were 25\35 (71.4%) in bupivacaine group vs. 29\35(82.9%) in fentanyl group and 30\35 (85.7%) in ketamine group, occurrence of side effects and complications during the caesarean section was few in the three groups, as the pain, itching, and vomiting did not occur in any participants within the three groups. Postoperatively, incidence of hypotension were 1\35 (2.9%) in three group, incidences and intensity of postoperative shivering where1\35 (2.9%) in bupivacaine group, 3\35 (8.6%) in fentanyl, 2\35 (5.7%) in ketamine, (p value> 0.58). Incidences and intensity of postoperative nausea where1\35(2.9%) in bupivacaine group, (p value> 0.36) and no one in the other groups, theoccurrence of side effects in postoperative period, as the bradycardia, headache, pruritus, shivering,

nausea, vomiting, and respiratory distress did not occur in any participants within the three groups.

Conclusion: In spinal anesthesia for the elective cesarean segment, 25 mic fentanyl to 10mg bupivacaine showed faster onset of sensory and motor block and better hemodynamic stability with minimal side effects, longer sensory and motor block duration, and duration of analgesia, decreased total analgesic consumption and reduce pain intensity in the post-operative period. and higher patient satisfaction. Furthermore, the incidence of sedation is higher with the ketamine group.

Keyword: ketamine, fentanyl**,** Bupivacaine, spinal anesthesia, cesarean section.

Chapter one
Introduction

1.1 Introduction

Can be performed cesarean section under general anesthesia or regional anesthesia. Due to the smaller impact on the airway in the cesarean section, the regional C/S anesthesia is better than the general anesthesia. It reduces the risk of aspiration and greater recognition during the entire operation and reduces. Weak uterine contractions are a dangerous complication (Wong CA, 2010).

Spinal anesthesia is a fantastic anesthesia technique and is largely used due to it has many benefits over general anesthesia, such as a lower response to stress, less blood loss, inexpensive, and a lower rate of morbidity and death in high-risk patients. (Gaiser RR, 1997).It is used in all emergency and non- compulsory surgeries and involves injecting a local anesthetic into the cerebrospinal fluid to block nerve transmission (Charles BB2005), regional anesthesia has been recommended as a favorite to general anesthesia to eliminate or reduce exposure to general anesthetics. (McGowan FX Jr, 2008).In addition, It is considered a safe and efficient modality for a wide range of operative procedures, although it is not free of risks (Ghani et al., 2015).

Administering anesthesia for the cesarean segment is one of the most challenging duties facing anesthesiologists. Bupivacaine is the most common local anesthetic used in cesarean sections. The anesthesia

administered by bupivacaine alone may be too short for the prepared operation, so the accuracy of the blockade is too low. Commonly used additives include fentanyl, buprenorphine, ketamine, and neostigmine.Additives can be combined with local anesthetics to obtain beneficial responses, like decreasing the systemic toxicity of local anesthetics, extending the duration of action of local anesthetics, and enhancing the efficacy of blockers. (L.R &Veena., 2017).

The parturient prefer being awake during childbirth so, the most popular method in cesarean deliveries is regional anesthesia, it's safer than general anesthesia because when you use small amounts of local anesthetics, make fetal uptake and placental transfer of drug negligible if it compared with regional anesthesia (RaoAnnavarapu., Kumar SongaMD, &SravanthiK, 2015).

During cesarean section, you've to remove the visceral pain caused by traction on the peritoneum and intraperitoneal organs and related to bradycardia and nausea and vomiting, hypotension, and shorter duration of action so would require larger doses of local anesthetics and early postoperative analgesics (Chakrabarti, Debroy, & Ray, 2015).

Ketamine is an N-methyl D aspartate (NMDA) receptor blocker. It has an analgesic influence if inserted intrathecally and has a synergistic effect with bupivacaine (Togal T., 2004). Ketamine is a phencyclidine derivative that has a strong analgesic effect. Compared with other local injections, it has several benefits as an anesthetic. For example, it leads to exciting the

cardiovascular system and keeps the respiratory response to carbon dioxide. Ketamine affects the central nervous system (CNS), cardiovascular system (CVS), and respiratory systems (RS).

On CNS, ketamine produces a unique impact as it can do dissociative analgesia additionally ketamine make amnesia, profound analgesia, and emergence phenomena (a feeling of floating, vivid dreams, hallucinations, and delirium), as ketamine increase cerebral blood flow, which leads to increase intra cerebral pressure (ICP), this mechanism can be avoided by administration of benzodiazepine (D. A. Haas, and, D. G. Harper, 1992).

Ketamine outcomes on CVS are specific from another analgesia by increased heart rate, cardiac output, blood pressure as ketamine consider a negative inotropic agent, so ketamine makes bigger oxygen blood demand for that it as a contraindication in ischemic heart disease patient. On coronary heart rhythm, ketamine has no proven outcomes as it can produce dysrhythmia (D. A. Haas, and, D. G. Harper, 1992).

On RS ketamine make a characteristic impact in comparison with a different anesthetic agent by maintains residual capacity, bronchodilators, and might also cause slight respiratory depression (D. A. Haas, and, D. G. Harper, 1992).

Intrathecal injection of ketamine is favorable because it has positive influences on the cardiovascular system, and respiratory function can be mixed with the analgesic influences of spinal anesthesia. The non-

competitive inhibition of NMDA ionophores is the initial mechanism of action of the spinal anesthetic ketamine (Schug SA, 1999).

Bupivacaine act by using stabilize cell membrane to prevent and the initiation and transmission of neural impulse, for that, think about it as a true regional anesthesia drug.

The effects of bupivacaine on CVS two are more serious as can lead to atrioventriculer block, limit heart conduction with peripheral vasodilation which leads to minimizing cardiac output and blood pressure, ventricular arrhythmia, and cardiac arrest.

On CNS the effects vary from stimulation to depression as bupivacaine may lead to tremors, restlessness progressive to convulsion, or bupivacaine can lead to coma and respiratory depression.

Nevertheless, the extensive usage of bupivacaine for pain control is based primarily on the supposition that it is safe. Bupivacaine is a local anesthetic used for nerve blocks, epidural anesthesia, and intrathecal anesthesia. It is usually used to control pain before, during, and after spinal surgery. (Kotilainen E., 1997&Sice PJ., 2006).

Fentanyl is a lipophilic opioid drug that works on many gelatinous in the spinal cord's dorsal horn, blocking nerve fibers. (MokhtarY, &Khaled G., 2019), additionally, fentanyl has a rapid onset with a short duration of action, in addition when used intrathecally concentrate in small quantity in

the fourth ventricle by using this fentanyl reason respiratory depression is unusual (Anupam C., Debashis D., 2015).

This study intended to examine ketamine plus bupivacaine vs. fentanyl plus bupivacaine vs. bupivacaine alone for spinal anesthesia during cesarean section.

1.2 Background

1.2.1 Cesarean section delivery

Cesarean delivery is a surgical procedure that includes an incision opening abdominal layers and the uterus to terminate the pregnancy and remove the fetus from the uterus. Many indications for elective cesarean include genital herpes in the mother and previous cesarean section and fetal mal-presentation, pregnant with twins, and mother with HIV. The most common complications of the cesarean segment include injury to another organ such as the bladder, nausea and vomiting, heavy blood loss, wound infection, and neonatal tachypnea (Sami & Ussbah., 2016).

1.2.2 Regional anesthesia

Regional anesthesia is expanding as an alternative to general anesthesia. Later, local anesthesia can be used for postoperative pain relief. At present, spinal anesthesia and epidural anesthesia have a significant influence on obstetrics, and they are extensively used for analgesia in women who give birth and cesarean segment. Cesarean section can use epidural anesthesia or spinal anesthesia. Both have their advantages. The mother can stay awake

to experience the birth of the child. Regional anesthesia for cesarean section performs reduction in the incidence of failed intubation and pulmonary aspiration so, it is associated with less maternal morbidity and mortality than is general anesthesia Butterworth Iv et al.,(2013).Regional anesthesia involves the right placement of a needle or catheter adjacent to nerve plexus that innervate the area of the physique where surgical treatment is to be performed; it is a safe technique and an positive approach to supply top anesthesia and analgesia in the course of intra and post-operative, which include: (i) Spinal anesthesia; (ii) epidural anesthesia; and (iii) peripheral nerve block (Morgan, 2013).

1.2.3 Spinal anesthesia (SA)

Spinal anesthesia one of the preferred and extensively used techniques for conditions like cesarean segment; it is easy to administer and rapid onset of action, and provides analgesia and muscular relaxation. Compared with epidural anesthesia, it is more reliable sensory and motor blockade, but the lack of long-lasting postoperative analgesia stays the main disadvantage in spinal anesthesia (Sun, Li, & Gan, 2015).

SA is an invasive anesthetic procedure, entails insertion of a spinal needle between lumbar vertebrae (3-4 or 4-5) to inject nearby anesthetic such as Bupivacaine into the intrathecal, subarachnoid space. The local anesthetic is used to block sensory and motor nerves from fourth thoracic to fourth sacral dermatomes, which leads to sympathetic block out flow. Its earliest viable complication is hypotension (Sami & Ussbah, 2016).

1.2.4 Ketamine

Ketamine is an N-methyl D aspartate (NMDA) receptor blocker. It has an analgesic influence if inserted intrathecally and has a synergistic effect with bupivacaine (Togal T., 2004). Ketamine is a phencyclidine derivative that has a potent analgesic effect. Compared with other local injections, it has several benefits as an anesthetic. For example, it leads to exciting the cardiovascular system and keeps the respiratory response to carbon dioxide. Ketamine has an influence on the central nervous system (CNS), cardiovascular system (CVS), and respiration systems (RS) Ketamine is used as an anesthetic in diagnosis and surgery. When used by intravenous or intramuscular injection, ketamine is very suitable for short-term surgeries. Ketamine can be used for more extended operations with additional doses or by intravenous infusion. If you need skeletal muscle relaxation, you should use muscle relaxants and supportive breathing.Its contraindications are patients with allergies, people with high blood pressure that may pose a critical risk, and patients with eclampsia or pre-eclampsia, severe coronary artery disease, stroke, or brain trauma.Unwanted outcomes include anaphylactic reaction, Hallucination, Abnormal dreams, Nightmare, amnesia, Confusion, Agitation, Abnormal behavior, Delirium, Blood pressure increased, Heart rate increased, and Nausea, Vomiting. Pharmacodynamics: Ketamine is a fast-acting general anesthetic used for intravenous or intramuscular use and has excellent pharmacological effects. Ketamine hydrochloride can produce dissociative anesthesia defined by catalepsy, amnesia, and significant analgesia and

may continue during recovery. The throat reflex remains normal, and skeletal muscle tension may typically increase or to differing measuresmild irritation of the heart and airways, sometimes respiratory depression. The related pharmacokinetic property is that ketamine is rapidly distributed to perfusion tissue composed of the brain and placenta. The rate of placental movement of ketamine to the umbilical vein during delivery was 47%. From the injection of ketamine to the vaginal delivery, the average mother's delivery time has 12 minutes.The alteration of the drug occurs in the liver. The end of anesthesia is the redistribution of the brain to different tissues and partially through metabolism.The exclusion of half-life is approximately 2to3 hours, and the kidney usually excretes it as a binding metabolite. (emc, 2020)

1.2.5 Fentanyl

Fentanyl, an opioid can be administered intrathecally to enhance the quality and duration of postoperative analgesia to a significant extent and improves the quality of sensory blockade intraoperative without significant side effects on the neonate nor increasing sympathetic or motor blockade (Prabha et al., 2014)

Fentanyl is a lipophilic opioid with a faster onset than morphine. It enters the spinal cord from the cerebrospinal fluid faster than hydrophilic opioids. Additionally, fentanyl does not cause delayed respiratory depression. (L.R & Veena, 2017).

1.2.6 Bupivacaine

Bupivacaine (trade name: Marcaine spinal 0.5% heavy) is a clear, colorless, high-pressure sterile solution without particles. The intrathecal route (into subarachnoid) is given for all ages to produce Spinal anesthesia for urology and lower extremity operation for a two to three hours and gastric procedure for forty-five to sixty minutes. Bupivacaine is a long-acting anesthetic of amides with a quick start and extended period. The duration of analgesia in segment T10 to T12 was two to three hours. Marcaine may produce moderate muscle relaxation of the lower limbs for two to two and half hours. The motor block duration did not exceed the analgesia period. In the elderly and patients in the third trimester, the risk of high or complete spinal block increases, leading to cardiovascular and respiratory depression. Therefore, these patients should reduce the dose. During cesarean section under spinal anesthesia, the dose of bupivacaine hydrochloride ranges from seven and a half mg to ten and half mg. Bupivacaine should be taken care of when patients with other local anesthesia or other medication with the same structure, such as specific antiarrhythmic drugs, like lidocaine and mexiletine, are additive due to their systemic toxicity. Undesirable effects include hypotension, Bradycardia, and post-dural puncture headache, nausea, vomiting urinary retention, or urinary incontinence. The pharmacodynamics properties of bupivacaine are a prolonged acting amide-type local anesthetic. Moderate relaxation of the muscles in the lower limbs can cause a blockage of the motor of the abdominal muscles. Finally, heavy marcaine is high-pressure,

and gravity affects its early distribution in the intrathecal space. In terms of pharmacokinetics, the onset of action is fast and extended in the period of activity; that is, the T10 to T12 segment lasts for two to three hours, the lower extremity muscles relax for two to two and half hours, and the abdominal blockage lasts for a long time. The muscles last forty-five to sixty minutes. (Emc, 2018)

1.2.7 Meperidinedrug

Meperidine hydrochloride (trade name: Meperidine) is a narcotic analgesic used to relieve moderate to severe pain. Meperidine is mainly a μ receptor agonist. Although pethidine and morphine have different structures, they contain multiple characteristics, especially reactivity against naloxone. The original drug and metabolites are eliminated in the urine after significant metabolization throughout the hepatic. Nomepiperidine is a pharmacologically active metabolite. It will produce central hyperactivity and possibly seizures if it accumulates after a long intravenous injection or renal failure. Pharmacodynamics: Meperidine is a pain killer drug comparable to morphine but with shorter power plus a smaller duration of action. Its analgesic action lasts two to four hours on average. The analgesic impact will feel the pain-relieving effect about 10 minutes after the injection. It affects the center neural system as well as the smooth muscles via the peripheral nervous system. Meperidine stimulates histamine release within immune cells, resulting in a sequence of anaphylaxis. Pethidine, like other opioids, connects to opiate receptors and

has major pharmacological effects on the central nervous system. Its analgesic and hypnotic actions have a unique therapeutic effect in the central nervous system. Meperidine has similar effects as atropine on the respiratory depression caused by pethidine, including dry mouth and blurred vision. Naloxone and nalorphine can antagonize respiratory depression. Dosage: twenty-five to hundred milligrams, administered subcutaneously or intramuscularly. Twenty-five to fifty milligrams intravenous injection. Pharmacokinetics: After intramuscular or subcutaneous injection, pethidine is rapidly absorbed, with an average time of about 3 hours. The liver undergoes metabolism through hydrolysis, and pethidine is excreted in urine (70% excretion within 24 hours). Urine excretion depends on pH, the lower the pH, the higher the clearance rate. Meperidine passes through the placenta and is secreted in human milk Pethidine and norpethidine pass through the blood-brain barrier and are found in spinal fluid.(Emc, 2019).

1.2.8 Diclofene drug

Diclofeneac sodium: NSAIDs operate by blocking prostaglandin production by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) proportionally. The solution, which can be injected intramuscularly, is helpful in acute pain situations such as renal colic, osteoarthritis, acute backache, acute injury, and pain in the post-operative period. A lower dose may be sufficient for mild to moderate pain. For severe pain, such as renal colic, a dose of 75 mg may be required. To avoid

local tissue injury, the substance should be administered slowly. Furthermore, There is a serious complication in the presence of an active gastrointestinal ulcer, hemorrhage, or rupture, as well as a history of intestinal bleeding or ulceration caused by recent non-steroidal anti-inflammatory drugs (NSAIDs) treatment, Diclofene, like other non-steroidal anti-inflammatory drugs (NSAIDs), is not recommended for persons who have asthmatic or acute sinusitis that is made worse by acetylsalicylic acid or other NSAIDs. Fluid retention and edema have been observed in conjunction with NSAID treatment; thus, patients with a history of hypertension and mild to moderate congestive heart failure require appropriate monitoring and counseling.

Effects of pharmacodynamics: Solution for Injection is a non-steroidal medication containing important analgesic characteristics. It functions as a prostaglandin synthase blocker (cyclooxygenases). Diclofeneac sodium didn't reduce proteoglycan synthesis in the cartilage at concentrations equivalent to those used in people. When taken in association with narcotics to treat post-operative pain, diclofene sodium frequently lowers the requirement for analgesia. Pharmacokinetic characteristics include: Absorption is fast after giving seventy-five mg/ml Solution for Administration through the IM method, and the plasma concentration is achieved within thirty-four minutes. Distribution: Diclofene penetrates the synovial fluid, where the highest levels are measured two to four hours after peak plasma concentration is reached. The observed half-life for synovial fluid clearance is three to six hours. Concentrations of the active

ingredient in synovial fluid are already higher than in plasma and remain high for up to twelve hours. Eliminationthe terminal half-life in plasma is one to two hours. The plasma half-life of four metabolites, including two active metabolites, is also very short, only one to three-hour. Around sixty percent of the administered dose is excreted in the urine in the form of intact molecules of glucuronic acid conjugates and metabolites, most of which are also converted into glucuronic acid conjugates. Only about one percent of the material is excreted in its original form. The remaining dose is excreted as metabolites in the stool via the bile. (emc, 2020).

1.2.9 Metoclopramide

Metoclopramide: (trade name: pramine) is a sterilized solution that is plain and colorless. It is used to prevent postoperative nausea and vomiting (PONV) and to prevent nausea and vomiting (NIRV) caused by radiation therapy. The solution can be given intravenously or intramuscularly. A gradual bolus injection should be used for intravenous delivery (at least three minutes or more). The highest everyday dose is Thirty mg. Its contraindication is gastrointestinal bleeding; mechanical stimulation of gastrointestinal peristalsis or gastrointestinal perforation represents a danger; -combination use with levodopa or dopamine agonists; -seizures (increased frequency and intensity of seizures). Pharmacological treatment group: drugs that stimulate gastrointestinal motility. The function of metoclopramide is to promote normal peristaltic action and is closely related to the control of the parasympathetic nervous system in the upper

gastrointestinal tract. This provides a basic treatment method for the treatment of diseases where impaired gastrointestinal motility is a common underlying factor. Metoclopramide is a dopaminergic antagonism with strong anti-emetic action on medulla chemoreceptor stimulated areas. Metoclopramide is extensively metabolized from the intestinal tract and undergoes considerable first-pass metabolism inside the hepatic. It is eliminated mainly in the urine as free and bound metoclopramide, as well as metabolites. It is eliminated from breast milk and crossing through the placenta. (emc, 2019)

1.3 Aims of the study

This study aims to examine the influence of intrathecal ketamine combined with bupivacaine, intrathecal fentanyl combined with bupivacaine, and hyperbaric bupivacaine alone in patient undergoing elective cesarean section.

1.4 Objective of the study

- To determine the length of sensory and motor blockade in the postoperative period in three groups of patients undergoing elective cesarean section under spinal anesthesia.
- To compare the duration of analgesia in the postoperative period in three groups of patients following elective cesarean section under spinal anesthesia.

- To examine the hemodynamic parameters in three groups of patients undergoing elective cesarean delivery under spinal anesthesia.
- To compare the total of analgesia consumption in the postoperative period in three groups of patients following elective cesarean section under spinal anesthesia.
- To assess in the pain intensity in the postoperative period in three groups of patients undergoing elective cesarean section under spinal anesthesia

1.5 Problem statement

Cesarean deliveries are becoming more common around the world, and adequate postoperative pain treatment is a significant focus for women who have them. Inadequate surgical pain treatment is linked to chronic pain, increased opioids consumption, delayed functional recovery, and postpartum depression. In addition to relieving pain, effective management of patients following cesarean delivery should include the goals of minimal maternal and neonatal adverse effects, rapid return to baseline functionality, and early discharge home. A multimodal analgesic approach, including neuraxial approaches, is performed around the world. (Sutton, C. D., 2017).

During a cesarean section, you must relieve the visceral pain created by traction on the peritoneum and intraperitoneal organs, which is correlated with Bradycardia, nausea and vomiting, hypotension, and a shorter duration

of action, requiring higher doses of local anesthetics and early postoperative analgesics(Chakrabarti, Debroy, &Ray, 2015).

1.6 Significant of the study

Cesarean delivery rate are increasing worldwide, and spinal anesthesia is the most common method. (Sutton, C. D., 2017)

Regional anesthesia is preferred against general anesthesia for cesarean section due to the fact of decreasing impact on an airway, decrease aspiration risk, and higher consciousness during surgery (Wong CA, 2010). In Palestine, there are different approaches in adding some medications to the hyperbaric bupivacaine in spinal anesthesia, in the absence of evidence and studies to guide the use of these drugs. Both of these drugs have side effects and effects. It affects the mother and child during and after cesarean section. However, in Palestinian hospitals, there is no study on the effect of ketamine added to intrathecal hyperbaric bupivacaine in cesarean sections.

The most commonly used intrathecal drugs for spinal anesthesia are local anesthetic with opioids worldwide. Opioids have side effects of itching, nausea, vomiting, urinary retention, and respiratory depression. (Chakrabarti et al., 2015). In our study, we add ketamine as an alternative additive to local anesthetic and compare it to Fentanyl as an additive and local anesthetic without additives.

1.7 Hypothesis of the study

- H (0): There are no significant differences at 0.05 level related to duration of analgesia, between ketamine, fentanyl and bupivacaine groups intraoperative and post-operative.
- H (0): There are no significant differences at 0.05 levelrelated to duration of motor block between ketamine, fentanyl and bupivacaine groups.
- H (0): There are no significant differences at 0.05 levelrelated to duration of sensory block between ketamine fentanyl and bupivacaine groups.
- H (0): There are no significant differences at 0.05 levelrelated to sedation effect between ketamine, fentanyl and bupivacaine groups.
- H (0): There are no significant differences at 0.05 levels related to intra and post-operative nausea and vomiting between ketamine, fentanyl and bupivacaine groups.
- H (0): There are no significant differences at 0.05 level related to intra and post-operative blood pressure, heart rate and respiratory rate between ketamine, fentanyl and bupivacaine groups.
- H (0): There are no significant differences at 0.05 level related to intra and post-operative side effects (pruritus, headache, shivering, and sedation) between ketamine, fentanyl and bupivacaine groups.
- H (0): There are no significant differences at 0.05 level related to total analgesia consumption between ketamine, fentanyl and bupivacaine groups.

- H (0): There are no significant differences at 0.05 level related to pain intensity between ketamine, fentanyl and bupivacaine groups.

Chapter Two
Literature Review

2.1 Literature Review

The provided section concludes the experience and result of other they found many studies toke about ketamine plus bupivacaine vs. fentanyl plus bupivacaine vs. bupivacaine alone for spinal anesthesia during cesarean section regarding post-operative pain management.

2.2 Intrathecal ketamine

A prospective, double-blind, randomized study that added ketamine & fentanyl to bupivacaine intrathecal to perform a cesarean delivery in affected people, this study aimed to evaluate the effect of analgesia for bupivacaine in participants underwent cesarean section, Ninety patients aged 18 to 40 years in a random manner divided to 3 groups: Group K got bupivacaine 10 milligrams mixed to 0.1 mg/kg ketamine. Group F received 10 milligrams of bupivacaine mixed to 25 mcg fentanyl, and group P received 10 milligrams of bupivacaine mixed to 00.50 milliliter pure water. Period between the first analgesia requirement and the need for analgesics during the first 24 hr. postoperatively, sensory & motor block onset time, incidence of detrimental results was evaluated and documented. The finding of this finding is that the first analgesic time of group K (296.80±32.46) was longer than F group (277.87 ± 94.25) and P group (235.43 ± 22.35). Although a significant difference wasn't exited within-group K & group F (P = 00.504), group K and group P (P 0.001) and group

F and group P (P = 0.042) differ significantly. The authors conclude that in cesarean sections deliveries, adding ketamine or fentanyl to spinal bupivacaine improved analgesic effect postoperatively, and that, based on the particular client's need, Ketamine, at the concentrations mentioned early, should be an excellent choice for achieving postoperative analgesia. (Khezri et al, 2016).

Unlugenc H et al. (2006) conducted a study titled "Compared of S (+) ketamine and fentanyl combination to bupivacaine 0.5 percent intrathecally for cesarean section." 90 ASA 1 or 2 adult participants underwent cesarean sections in a random manner assigned into three groups: 1.00 milliliter of 00.9% normal solution in S group (number=thirty), 0.05-milligram \kilogram -1 of S(+) ketamine (one milliliter) in group K (n =30) or twenty-five micrograms (one milliliter) of fentanyl in F group (number=thirty) with ten milligram of 0.5 percent simple bupivacaine intrathecally,They measured the onset and length of sensory and motor blockade, the time required to reach a maximal sensory block of the dermatome, and the length of spinal analgesia. Result were the sensory & motor blockade onset in groups K and F were significantly shorter than in group S (P< 0.014).Their period differed in a significant difference where longer in group F than in group K and group S (P= 00.009). The time required to reach the greatest dermatome stage of block in sensory was substantially reduced in groups K and F than in group S (P 0.001).In group F, the spinal analgesia period was once considerably greater than in K groups and S group (P value= 00.001). This study concluded that participants do

cesarean delivery under analgesia spinal, the addition of S (+) ketamine (00.05-milligram\ kilograms) intrathecally to ten milligrams of plain spinal bupivacaine (00.50 percent) achieve a faster sensory & motor onset block and improved the segmental dissemination of spinal block, while fentanyl supplied prolonged analgesia.

Shrestha, Bhattarai, and Shah. (2013) Conducted research to evaluate the effects of ketamine intrathecally combined to bupivacaine & fentanyl intrathecally mixed to hyperbaric bupivacaine, in which patients were randomly randomized to two groups: group A given two milliliters (ten milligrams) bupivacaine 0.5 percent with twenty-five milligram of ketamine preservative-free, and group B given 2 milliliters (10 milligrams) Group B took two milliliters (10mg) of 0.5 % bupivacaine hyperbaric plus 25microgram fentanyl. Intraoperative, the sensory blockade onset, the extent of motor blockade, and the analgesia period.The needed time to gain Bromage scale three motor blockade used to be minimal in A group than B group. (p= 0.445).However,in group A, the time required to reach the largest dermatome stage of sensory block was shorter than in group B (p= 0.143). Group B had a longer duration of spinal analgesia than group A (p= 0.730).The occurrence of adverse effects, including sedation rating, was greater in group A than in group B (p= 0.048). The incidence of pruritus was greater in B group than in A group in a significant difference (p = 0.001). The authors conclude that adding preservative-free ketamine caused a faster start of sensory and motor blocks. However, it did not prolong the

spinal analgesia duration compared to adding fentanyl in a parturient patient having cesarean sections under spinal anesthesia.

Khezri, Ghasemi, and Mohammadi. (2013) conducted a RCT to study the analgesic properties of ketamine intrathecallyto bupivacaine after cesarean sections, in which 60 participants planned for cesarean delivery via spinal anesthesia they in a random manner assigned into two groups to be given both ten milligram bupivacaine mixedto ketamine, or ten milligram bupivacaine mixedto 0.5 mL pure water intrathecally. The period between the first analgesia need and the need for analgesics during the initial twenty-four hours following operation, the start time of sensory and motor blockades, the sensory and motor blockades length, as well as the occurrence of adverse reactions like lowering blood pressure, consumption of ephedrine, decrease in heart rate, and hypoxemia, were all documented. The examination's result Participants who received ketamine had substantially longer durations of anesthesia than those in the control group who did not [95 percent confidence intervals ($p = 0.001$)]. In addition, the ketamine group showed a considerably greater mean time to the first analgesic requirement (p-value < 00.001). The ketamine group had a lower 24 hr. overall analgesia intake following surgical treatment was in comparison to the control group with significant difference ($p < 0.001$). The intraoperative and postoperative side effects, the two groups no longer differed significantly. The author concludes that ketamine 0.1 mg/kg when given with bupivacaine intrathecally prolonged the first analgesic needs time and decreased overall analgesia intake within the first 24 hr.

postoperatively as compared to bupivacaine solely in the control group in elective cesarean section deliveries.

To evaluate the efficacy of using ketamine in anesthesia spinal into day-case surgical procedure regarding spinal block onset, length of the block, hemodynamic stability, postoperatively the time to intact motor electricity, time to ambulate, and facet effects. 60 participants planned to undergo day case procedures through spinal anesthesia had been enrolled in the study. Patients had been allotted to acquire either three milliliters hyperbaric bupivacaine (0.50%) (Group 1) or 2 milliliters of hyperbaric bupivacaine (0.50%) mixed with l ketamine (25 mg) + ml everyday saline (group 2). This study revealed that in group 2 the block length and its onset time were lower than in group 1. Postoperatively, the needed time to ambulate, and entire motor electricity recovery, and the spinal analgesia lengthwere lesser in number 2 group. There had been no widespread variations in the hemodynamic measures or in the possible adverse undesired outcomes. The authors concluded that ketamine administered to hyperbaric bupivacaine in spinal anesthetic reduces the needed block onset time, the length of the block, and the needed time to regain the complete motor strength and ambulation ability for participant undergone day case procedures.

Hemanth et al. (2013) showed a randomized, double-blind study titled a comparative study of ketamine intrathecal as an additive to 0.5 percent bupivacaine during anesthesia intrathecally. 60 participants have been scheduled for lower abdominal and lower extremities procedures. The

participants were split to be two groups, 30 for each group. Both groups got 3 milliliters of 0.5 % hyperbaric bupivacaine intrathecal. Additionally, the ketamine (Gr K) group received an intrathecal injection of 0.1 mg/kg of body weight ketamine (overall volume is 0.5 ml),the normal saline (Gr S) group given an identical volume of 0.9% normal saline into spinal subarachnoid space. The length and onset of sensory and motor blockade, and also hemodynamics measures intraoperative were assessed. The author revealed that adding ketamine compared to N/S 0.9% administration yields significantly faster onset, the longer of sensory block duration, and extended in the postoperative analgesia period. According to the author to add intrathecal ketamine to hyperbaric bupivacaine gives improved spinal block, stable hemodynamics intraoperative, and a prolonged duration of post-operative analgesic effect.

Another study conducted by Gunasty. (2007) They evaluated the analgesia block, sensory, and motor block features, In a parturient undergoing cesarean phase, the effects of S (+) ketamine administered into intrathecal space mixed to 0.75 percent undeniable ropivacaine (15 fifteen milligrams) in spinal analgesia were compared to S (+) ketamine +0.5 percent simple bupivacaine (10mg) aggregate administered intrathecally. A hundred &twenty ASA I or II parturient planned for C/S in a random manner divided into four groups. Group 1 (number= thirty) obtained ten milligrams of 0.5% (two milliliters) undeniable bupivacaine plus 0.9 percent of normal saline (one milliliter) in institution B, Group 11 (number= thirty) obtained ten milligrams of 0.5% (two milliliters) simple bupivacaine plus 0.05

milligram\kilogram of ketamine (one milliliter) in BK group, Group III (number= thirty) received 15 milligrams of 0.75% (two milliliters) simple ropivacaine +0.9 percent normal solution(one milliliter) in R group, Group II (number= thirty) took fifteen milligrams of 0.75% (two milliliters) plain ropivacaine +0.05 milligram\kilogram of ketamine (one milliliter)) in the RK group, intrathecally. They measured sensory &motor block onset &duration, the extent of the maximum level of sensory, length of analgesia, sedation, & pain rates at five, ten, fifteen, twenty, twenty-five, also thirty minutes following the injection, and then every fifteen minutes to 2 hr. Finally, this author stated participants undergo C/S under spinal anesthesia, the combination of S (+) ketamine (0.05-milligram \ kilograms) intrathecally to fifteen milligrams of simple ropivacaine (0.75 %) resulted in a quicker start of sensory and motor blockade and a more beneficial segmental distribution of spinal blockade despite increasing the spinal analgesia length while causes sedation within the dosage utilized in this research (0.05 mg kg−1).

A Prospective double blinded comparative research concluded by Patel et al. (2011), fifty parturient (ASAI, II) planned for cesarean deliveries, in a random manner grouped into two groups: 25 parturient for each: Group-A (control) 1.8 milliliter bupivacaine 0.50%+0.50 milliliter normal saline. Total 2.3 milliliter and Group-B (study) 1.8 milliliter bupivacaine 0.50% plus twenty fivemilligram ketamine 0.50 milliliter to give a complete volume of 2.3 milliliter. They concluded that combining 0.50 % bupivacaine intrathecally with preservative-free ketamine intrathecally

results in rapid in sensory block onset, improved stability of hemodynamic and postoperative analgesia without affecting the neonate.

2.3 Intrathecal fentanyl

A potential double-blind, randomized research with the title "analgesia effect for fentanyl intrathecally at the period of maximum analgesic demand following cesarean segment deliveries, which have the goal to compare the effects of postoperative analgesic of fentanyl intrathecally for the duration regarding the length of best postoperative analgesic demand after C/S, this look at consist of 60 parturient planned to undergo elective C/S, parturients were given spinal anesthetic by bupivacaine mixed with normal saline (manipulate group), or by 25 μg fentanyl (fentanyl group), in an attempt to investigate the primary objectives; overall pethidine requirement for the duration of best patient control analgesia and the needed of pethidine was calculated. For the second goals investigation, measurements were taken for patient control analgesia intravenous needs at various interval points; length of strong analgesia, pain evaluations measured using a visual analog scale, opioid side effects, hemodynamic variables, newborns' "Apgar score," & intra-operative pain. The end result for this study was adding fentanyl intrathecally to spinal anesthesia yield a powerful analgesic effect intraoperative and decreased opioid requirement throughout the duration of the best analgesic call postoperatively, with no increase in maternal or newborn side effects. (Weigl, 2016).

Another study conducted by Bogra, (2005), involved 120 participant undergone cesarean section deliveries split to be 6 groups: B8, B10, and B 12.5 8.10 and 12.5 milligram of bupivacaine and FB8, FB10, and FB 12.5 received a combination of 12.5 microgram fentanyl intrathecally respectively. Study variables assessed involved visceral pain-score, hemodynamic measures, intra-operative sedation, intra-operative and post-operative shivering and pain. The sensory block onset to T6 was quicker with higher bupivacaine dosages in bupivacaine-only and bupivacaine plus fentanyl mixture treatment. Lower doses of bupivacaine alone were unable to completely remove the visceral pain. Blood pressure measurements dropped when Bupivacaine and Fentanyl mixed. The use of fentanyl significantly decreased nausea and shivering while increasing post-operative pain relief and hemodynamics. Fentanyl does not cause pruritus, respiratory distress in mothers, or changes in baby Apgar scores.

A prospective double-blinded manipulation study evaluated the efficacy of fentanyl intrathecally at variant dosages, clinical effectiveness, and adverse reactions in parturient present process cesarean-sections deliveries. This examine was accomplished on 243 females undergone cesarean deliveries via spinal anesthesia had been allocated in a random manner to acquire 10, 15, or 25 μg of fentanyl intrathecally with ten milligrams of 0.5% bupivacaine. Participants have been evaluated for clinical efficacy via assessing ache score, rescue analgesic requirement, shifting to general anesthesia and proceedings of inefficient surgical anesthesia via the surgical doctor. The study's findings patients who received 25 mic of

fentanyl showed significant higher incidence of dizziness, nausea, pruritus as well as significant enhanced and increased sensory & motor blockage (P < 00.001).The author concludes that for participants undergo cesarean-section delivers, 10 or 15 mic of fentanyl intrathecally with 10 milligrams of bupivacaine achieved sufficient surgical anesthetic and analgesia while having minimum adverse-effects. Ali et al., (2018).

Himabindu et al in. (2015), a randomized controlled prospective have a look at was purpose to examine the hemodynamic variables and analgesic effect time span by use a small dosage (7.5 milligrams) bupivacaine fentanyl combination into a traditional dose (ten milligrams) of hyperbaric bupivacaine in cesarean deliveries, the observe was behavior on 50 singleton parturient, planned to undergo optional caesareans phase have been allotted in a random manner: Study group (group-S) acquired a admix of twenty fivemicrogram fentanyl and 7.5 milligrams of hyperbaric bupivacaine, while the manage group (group-C) obtained ten milligrams of hyperbaric bupivacaine. The delivery mother's hemodynamic variables, sensory and motor blockade, length of analgesia, and the new child's Apgar score were evaluated among the study participants. The result of the look at turned into the blood-pressure substantially Fell down by >25% reduction of base-line readings in organization-C (98.76 ± 8.36) than in organization-S (117.32 ± 12.21) with P < 0.001. The duration of efficient analgesia was significantly longer in the examine group than in the control group.(P < 0.001).

Another study developed by Kang in. (1998) the title of research “fentanyl intrathecally in combination with diluted small-dose bupivacaine for cesarean section, the process of study 30 parturient with no major diseases underwent cesarean sections taken randomly then split to 2 groups. Each participant given five milligrams of hyperbaric bupivacaine in addition to twenty five microgram of fentanyl (0.5 milliliters) & 0.6 milliliters of cerebrospinal fluid (CSF) (Group M + F) or eight milligrams of hyperbaric bupivacaine with 0.5 milliliters of cerebrospinal fluid (CSF) (Group M + F) (Group M). the consequence on hemodynamics stability, adverse effects, and total analgesic time span were evaluated, the author concluded that combined small-dose bupivacaine with fentanyl can achieve further hemodynamic stability, prolonged analgesic effect postoperatively, and reduce shivering occurrence rate. The prevalence of pruritus in institution M + F was great, however it turned into normally mild.

A Prospective double blinded comparative research operated by Archana et al. (2017) on participants undergoing cesarean section to confirm the capacity and efficacy of intrathecal bupivacaine in combination with intrathecal fentanyl and bupivacaine alone. Sixty participants were prorated for 2 groups, thirty patients in each group. Group I obtained 1.6 mL of 0.5% of bupivacaine added to 20mcg fentanyl; Group II received two milliliters of 0.5percent of bupivacaine alone. Participants’ hemodynamics was appraised and a neonatal outcome was checked out by Apgar score at one minute & five minutes. Complexity likes nausea, bradycardia, vomiting, and pruritus was deliberated. The first rescue

analgesics drugs request time, the time of effective analgesia were measured. There were no observed neonatal side effects in both two study groups. In the bupivacaine and fentanyl, group the means time of analgesia was two hundred and fourteen minutes. However, in the bupivacaine, the only group was one hundred ninety-five minutes ($p<0.5$). The bupivacaine (alone) group had a quicker onset of action. Showed significant value, the decline in MAP in the bupivacaine and fentanyl group, was fifteen percentage while in the bupivacaine (only) group was twenty-three percentage ($p<0.001$). Remarkably in the cesarean section under spinal anesthesia, the inclusion of intrathecal 20 µg of fentanyl to bupivacaine 8 mg, perpetuated the length of postoperative analgesia, enhanced analgesia quality intraoperative, and introduced enhanced hemodynamic constancy without disturbing the newborn clinical condition.

A Prospective double blinded research was conducted by Idowu OA et al. (2011), in participants undergoing cesarean section to evaluate the length of analgesia after the combination of fentanyl into bupivacaine during cesarean delivery; sixty participants were prorated to two groups, thirty patients in every group. BF Group obtained 2.5 mL of 0.5% of bupivacaine added to 25mcg fentanyl; Group B obtained 2.5 mL of 0.5% of bupivacaine alone. Participants' hemodynamics, such as maternal pulse rate, blood pressure, and respiration rate, were assessed. Sensory level, motor block, pain ratings (numeric rating scale), and adverse reactions were evaluated every two minutes for the first fifteen min, then every five minutes throughout the remainder of the operation. Afterward, at thirty-minute

intervals, till the first complaint of pain, time of request of rescue analgesia, and the time of effective analgesia were documented. The analgesic time in the bupivacaine and fentanyl group was two hundred forty minutes than bupivacaine only group nighty nine minutes with a ($p<0.05$). The length of analgesia in the bupivacaine and fentanyl group was longer than in the bupivacaine-only group.($p<0.05$). The author summarized that inclusion of intrathecal 25 µg of fentanyl to bupivacaine, prolonged the length of postoperative analgesia, and enhanced the quality of intraoperative analgesia.

Another study was conducted by Seyedhejazi, M & Madarek, E., (2007), with a title the effect of low-dose bupivacaine plus fentanyl in spinal anesthetic on hemodynamic nausea and vomiting in cesarean delivery, with the goal of comparing In a parturient having cesarean delivery, the hemodynamics, nausea, and vomiting with low dosage bupivacaine-fentanyl in spinal anesthetic were compared to a standard dose of spinal bupivacaine.which they use method prospective double-blind randomized, Forty patients between the ages of 17 and 35 who undergone cesarean section were randomly assigned to one of two groups. Group A was given spinal anesthetic with eight-milligram bupivacaine and ten microgram fentanyl, whereas Group B was given twelve milligrams bupivacaine, the author noted that a lowdosage of bupivacaine plus fentanyl offers effective spinal anesthetic for cesarean delivery with less hypotension, nausea, and vomiting than a large dose of bupivacaine and fentanyl.

Chapter Three
Methodology

3.1 Introduction

This chapter presents an overview of the research methodology that was used for this study. It includes: study design, site and setting, Population, inclusion and exclusion criteria, sample size and sampling process, Pre-enrollment assessment, Randomization, Blindness, Ethical consideration, Data collection procedure, Anesthesia protocol, Study measures (variable), Validity of the questionnaire, Privacy and Confidentiality. A sample of 105 women selected, random sample used, definition as recruited (every elective c/s pregnant woman whose age is (18-45years), who delivered in SAH in Palestine (Nablus).

3.2 Study design

The research was performed as a prospective, controlled, randomly selected, double-blind trial. This design has been chosen because of its power on scientific evidence hierarchy, reducing error chances and more reliable results.

3.3 Study site and setting

This research was done at a specialized Arab hospital, a private hospital in Nablus, Palestine, Caesarian sections operation rooms.

3.4 Study population

The target population is a pregnant women with age (18-45) years old and planed for elective cesarean sections delivery with ASA Classification I &II, at specialized Arab hospital.

3.5 Sample size

G power was used to estimate sample size, using an effect size of 0.8 and an α error probability of 0.05. Each group will include Thirty-five patients. A total of 105 patients will be included in the study. To find the appropriate sample size for research that provides enough power to identify statistical significance, the study's power set at 80% and the level of alpha set at p 0.05.

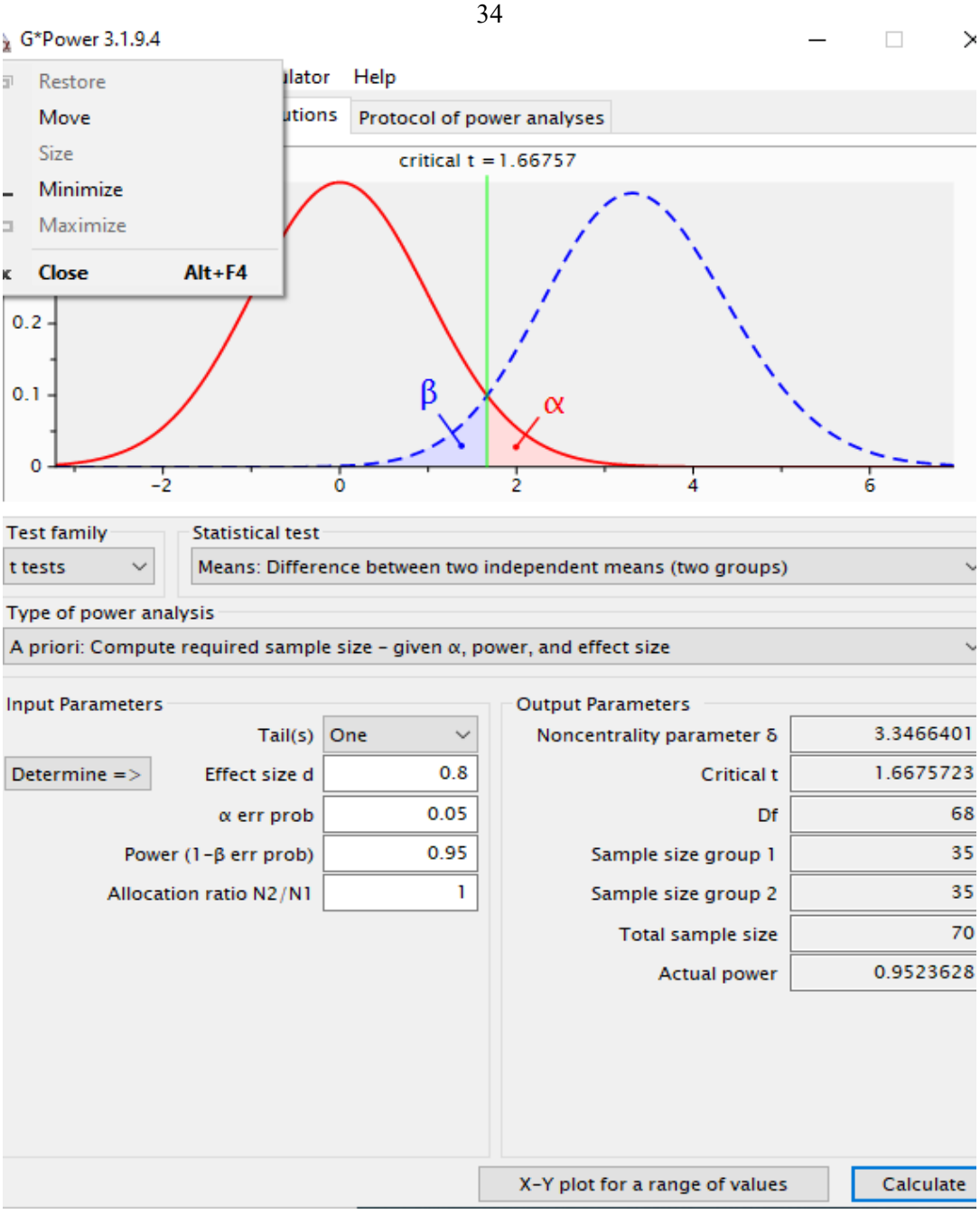

Figure 1: Randomization list.

3.6 Randomization

Randomization is performed by opaque and well-sealed envelopes. The sequence was generated on a computer using random allotment software 1.0. The number is imprinted on envelopes, and the group type, together with the sequential number, is recorded on the card. When the patients

arrived, envelopes were opened to determine which group they would be assigned. In this prospective double-blind comparative study, 105 women were designated into threegroup's35ofeach. Dose respond in each group K group was received intrathecal bupivacaine 10mg plus 15mg ketamine. Group F was received intrathecal bupivacaine 10mg plus fentanyl 25mcg. Group B was receivedbupivacaine 10 mg. (Appendix 4)

3.7 Blindness

Both pregnant women and the data collector (researcher) who participates in the surgeries wereblinded in the group allocation, and anesthesiologistwas not blinded.

3.8 Inclusion criteria

- Patients undergoing cesarean sections delivery under spinal anesthesia
- Patients between the ages of 18 to 45
- Class 1 and 2 of the American Society of Anesthesiologists (ASA)
- The patient agreed to collaborate in the research.

3.9 Exclusion criteria

- Patients who have a history of ketamine drug allergies.
- ASA 3 and above
- Complicated surgeries.

- Contraindications to spinal block
- Any contraindication to regional anesthesia such as local infection or bleeding disorders.
- Long-term opioid use.
- A history of chronic pain

3.10 Pre-enrollment assessment

Every patient that will be recruited in the study must have done a complete blood count (CBC) to check hemoglobin levels and platelet counts to exclude any patient that had a low platelet count (less than 80 x 10*3). Low platelet count patients have increased probability to form epidural hematomas, so spinal anesthesia is contraindicated in those patients.

3.11 Data collection procedure

After getting study approval from An- Najah National University's institutional review board (IRB) and agreement from the hospital research committee, the study objectives and procedure was explained to potential participant before being invited to participate. Once they agree, a written consent form was signed by participants. One hundred and five parturient women with ASA1 or 2who were planned for elective cesarean section with spinal anesthesia were recruited and randomized into three groups. Group K was received ketamine15mg plus bupivacaine10mg intrathecally,

Group F was received 25mic fentanyl, plus 10mg bupivacaine intrathecally and Group B was received 10mg bupivacaine alone intrathecally.

For each woman, a data collection sheet including the following information was filled out: name, age, weight, gestational age, blood pressure, pulse rate, respiration rate, and Electrocardiogram rhythm, skin body temperature was measured, and Spo2 was used as a baseline.

Hemodynamic parameter was measured on time series way: pre, intra, post-operative. Intraoperative data was recorded every 3-min interval from the time of induction of spinal anesthesia then every 5min in intraoperative, until delivery then every 5 minute in the PACU during the first 15 min and every 1hr in the floor. Systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), heart rate, and respiration rate were all involved. Furthermore, the incidence of nausea and vomiting, shivering, and pain assessment were all observed, and all of this data was recorded and documented for each group.

Monitored a mother's body temperature during and after surgery, and shivering was evaluated by a blind examiner and use a 5-item score during and after surgery. The scale approved through (Crossley & Mahajan., 1994) & (Tsai & Chu., 2001) as [0 = no tremor, 1 = erect hair or peripheral vasoconstriction but no visible tremor, 2 = only one muscle group Muscle activity, 3 = muscle activity of more than one muscle group, but no whole-body tremors, 4 = whole-body tremor]. Shivering for at least 3 minutes in levels 3 & 4 was rated positively. Treated positive shivering or lower level

shivering characterized by the patient as distressful with an IV bolus of Meperidine (0.5 mg/kilogram).And the pain was measured intra- and post-operatively using a numerical rating scale (NRS), a subjective metric in which patients score their pain on an eleven-point scale. These scales were used to determine pain intensity on a scale of 0 to 10, with less than or equal five corresponding's to mild pain, 6 to 7 moderate pain, and more than or equal eight referring to severe pain in terms of pain-related check with functioning, and ten corresponding's to the worst pain. (Boonstra et al., 2016) & (Ferreira, Valente, Pais-Ribeiro& Jensen, 2011).

Table 1: Shivering 5-item scale.

Score	Definition
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 shivering
4	Shivering involving the whole body

3.11.1 Anesthesia protocol

Anesthesiologists performed a physical examination on all patients, and non-invasive blood pressure, pulse, and respiration were monitored and recorded. Laboratory tests were assessed (complete blood count, specifically the platelet count). The anesthesia machine was checked and anesthesia equipment also was prepared for an emergency. Equipment for spinal anesthesia and drugs was prepared. Standard monitoring, according to the American Society of Anesthesiologists that includes a continuous

electrocardiogram (ECG), non-invasive blood pressure, and pulse oximetry was followed. Intravenous cannula G18-20 Fr was inserted and given 500 cc normal slain (NS) solution stat was given as routine before spinal injection per the targeted hospital protocol for all patients. Before anesthesia commences, women were briefed on the method of sensory and motor evaluation. An anesthesiologist performed the spinal puncture by pencil-point spinal needle (27 Fr) between the L3 to L4 or L4–L5 vertebrae with the patient in a sitting position on the side of the operation table. For the F group, a solution containing bupivacaine10mg (Marcaine) 0.5% plus 25 mcg fentanyl was administered, for the k group was administered Preservative-free ketamine15mg plus bupivacaine 10mg (Marcaine) 0.5%, and in the B group was administered bupivacaine 10mg (Marcaine) 0.5% alone, Patients were put in a supine posture directly following injection, and a Crawford wedge was inserted under her right hip to achieve left uterine displacement. All patients received oxygen treatment (6 L/min) using a face mask till birth, and routinely assessed sensory and motor blockade, as well as monitored cardiac and breathing parameters. The grade of sedation was evaluated, conforming to the Ramsay sedation scale. Heart parameters such as heart rate and BP are documented directly after subarachnoid block, oxygen saturation and respiratory frequency are also documented at certain intervals. If the SBP becomes less than Ninety mmHg, hypotension was managed by a vasopressor as follows: phenylephrine one microgram\kg as an intravenous bolus (if hearts rate more than or equal 70 bpm) or ephedrine 5–10 mg (if heart rate less than 70

bpm), and intravenous bolus of normal saline 0.9 %(N\S) as hospital protocol Specialized Arab hospital (SAH), 0.5 mg I V Atropine was used to managing maternal bradycardia. The Ramsay sedation score was used to measure sedation. (Appendix5).

Assessing dermatome levels after administering a subarachnoid block every minute after the puncture by using swap soaked in alcohol was under taken. The use of the alcohol sponge to test the level of the block was determined by (Rocco et al., 1985).Surgical incision was acquiesced when sensor level is ≥ T6 dermatome and motor blocking is satisfactory. The total duration of analgesia was the period after medication injection and the first demand for analgesics. The degree of the motor blockade in the lower extremities was separately measured by requesting the patient move the lower limbs according to the Bromage scale during the intraoperative and postoperative period using a four-item rating approved through (Bromage. 1965) also with (Hocking. 2004). (Appendix4). Hypotension, bradycardia, pruritus, nausea and vomiting, shivering, patient satisfaction, and respiratory depression were evaluated as side effects. Intravenous Metoclopramide 10 mg was used to treat nausea when the patient specified a nausea intensity more than or equal two on the Likert scale of zero to six (0=no nausea, 1=very light, 2=mild, 3=moderate, 4=severe, 5=extremely severe, 6=unacceptable).Theincidences of side effects during the first 24 hours were documented. Time for first utilization for analgesic is registered. Post-operative analgesia to control pain intramuscular 75mg

diclofene was used as specialized Arab hospital protocol (SAH) when the patient got pain ≥4 on NRS.

3.12 Data Collection plan

Vital signs observations was taken and recorded in formed data collection sheet including: BP, Pulse, Spo2, Temp, ECG rhythm, and RR was recorded every 3-min interval from the time of induction of spinal anesthesia then every 5min intraoperative until delivery, then every 5 minute in the PACU during the first 15 min and every 1hr in the floor. Other variables were recorded: nausea, vomiting, headache, cardiac arrhythmias, pain on scale 0-10.

3.13 Study measures (variable)

(a)Dependent variable: Time of analgesia, hemodynamic parameters (systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, peripheral capillary oxygen saturation (SpO2), Pain intensity , the duration of sensory ,motor block and duration of analgesia, nausea, vomiting, shivering, purities, sedation, headache, bradycardia and hypotension.

(B) Independent variable: ketamine, fentanyl, bupivacaine, spinal anesthesia.

3.14 The validity of the data sheet

To validate the data sheet and determine whether the data sheet and its sections truly measure what they are designed to measure. Datasheets were presented to two doctoral-level arbitrators, two anesthesiologists, two PACU nurses, and a statistician. The arbitrators approved the objects, and there were agreement on the tool for the study as well as a final report.

Pilot testing: Because the findings of the pilot study can aid in the improvement and modification of the study tools, a pilot study was conducted prior to data collection as a pretest to test the data sheet suitability and validity, to identify areas of vagueness, to assess the real time required to fill the data sheet, to predict response rate, and to highlight any weaknesses in the data sheet contents. It involved a total of 10% of the piloting of the study data sheet on 10 mothers from SAH, who were not included in the study .

3.15 Data analysis plan

The data were analyzed with SPSSversion22 for Windows (IBM Corp., Armonk, NY, USA).Data normality wastested using Kolmogorov-Smirnovtest. The data were normally distributed. Thus, parametric statistics tests were used. Means, standard deviations, percentages and frequencies were used to describe data for each group, Chi Square test was utilized to examine differences between Percentages, Turkey HSD Post-Hoc test examined pairwise differences between mean $p < 0.05$ is considered significant.

3.16 Ethical considerations

The research reported in this thesis was carried out in line with the Declaration of Helsinki and was certified by the institutional review board (IRB) and the Specialized Arab Hospital. Before participation, patients were asked to sign a permission form. Because the patient is not able to choose her therapy, randomization provides an ethical dilemma. Additionally, before considering a part in the research, all patients were given verbal and written information about the study's purpose and goals. It was produced clear that participation was entirely optional, that it could be finished at any time, and maintained confidentiality. As a result, the ethical dilemma is seen as minor. All patients were given life-saving drugs depending on which group the patients are randomized.

3.17 Privacy and confidentiality

The major study tool was a questionnaire filled in by the researcher himself, standardized questionnaire. All data were collected through this tool. The principal investigators took the whole responsibility for the confidentiality and the privacy of the collected data by allowing no access to anyone except the researcher themselves and their supervisor from the faculty of Medicine, health sciences and anesthesiologist.

All data were entered in statistical software by entering the information to each participant without knowing her name, and kept the privacy for information.

Chapter Four
Results

4.1 Introductions

The purpose of this study was to compare Bupivacaine with Fentanyl, Bupivacaine with Ketamine, and Bupivacaine alone in cesarean section women under spinal anesthesia in terms of time to sensory and motor block, postoperative pain, time to the first analgesia requirement, and anticipatory adverse effects (nausea, vomiting, purities, sedation, shivering, bradycardia, and hypotension)

4.2 Demographic characteristics of women underwent cesarean section

When examining the personal characteristics of the study participants, it was found that the average age of women who underwent a cesarean section was 28.5 years with a standard deviation of 4.6, which means that around 70% of the sample ranges between 24 to 32 years old, and additionally, the age did not have any statistically significant difference (ANOVA test were fulfilled Test of Homogeneity of Variances and normality) between the three groups (Bupivacaine, Fentanyl, and Ketamine).(Table 2).

As for the weights of the study participants, it was found that the average weights of women who underwent a caesarean section were 77.3 kilograms, and that most of them ranged between 69 and 86 kilograms, and

the weight did not have any statistically significant difference between the three groups (Bupivacaine, Fentanyl, and Ketamine).(Table 2).

Parity and gravida ranged among women who underwent caesarean section surgery among study participants between zero to 6 births and 1-8 respectively. And they did not have any statistically significant difference between the three groups.(Table 2).

The average of gestational age was 38 weeks and the range was between 35-41weeks with no any statistically significant difference between the three groups.(Table 2).

Table 2: Participants' characteristics among the three groups.

Variable	Group	N	Mean	SD	Min	Max	F	Sig.
Age (years)	Bupivacaine	35	28.2	4.46	20.0	36.0	.305	.738
	Fentanyl	35	28.4	4.51	20.0	40.0		
	Ketamine	35	29.0	5.03	22.0	40.0		
	Total	105	28.5	4.64	20.0	40.0		
Weight (Kg)	Bupivacaine	35	77.1	7.99	58.0	95.0	.010	.990
	Fentanyl	35	77.4	9.01	60.0	98.0		
	Ketamine	35	77.3	10.20	58.0	111.0		
	Total	105	77.3	9.02	58.0	111.0		
Parity	Bupivacaine	35	1.8	1.53	.0	6.0	.307	.736
	Fentanyl	35	1.6	1.21	.0	6.0		
	Ketamine	35	1.6	1.45	.0	6.0		
	Total	105	1.7	1.40	.0	6.0		
Gravida	Bupivacaine	35	3.0	1.82	1.0	8.0	.280	.756
	Fentanyl	35	2.8	1.25	1.0	7.0		
	Ketamine	35	2.8	1.77	1.0	8.0		
	Total	105	2.9	1.62	1.0	8.0		
GA (weeks)	Bupivacaine	35	38.2	1.15	36.0	41.0	.361	.698
	Fentanyl	35	38.0	1.09	36.0	41.0		
	Ketamine	35	37.9	1.12	35.0	40.0		
	Total	105	38.0	1.11	35.0	41.0		

With regard to the particular history of exposure to spinal anesthesia, it was found that there was no statistically significant difference between the three groups (Bupivacaine, Fentanyl, and Ketamine). (Table 3)

Table 3: History of spinal CS among the three groups participants Cross tabulation.

			Group				
		Total	**Bupivacaine**	**Fentanyl**	**Ketamine**	X^2	**Sig.**
History of spinal CS	**No**	50(47.6%)	18(51.4%)	14(40.0%)	18(51.4%)	1.22	0.57
	Yes	55(52.4%)	17(48.6%)	21(60.0%)	17(48.6%)		

Time from spinal block to incision, onset of motor block, & onset of sensory block among the three groups (Bupivacaine, Fentanyl, and Ketamine):

4.3Time from spinal block to incision

The average time was 7 minutes from the spinal block tostart of the incision for the cesarean section, and it ranged between 5 and 9 minutes among the participants of the three groups (Bupivacaine, Fentanyl, and Ketamine). See figure 1.

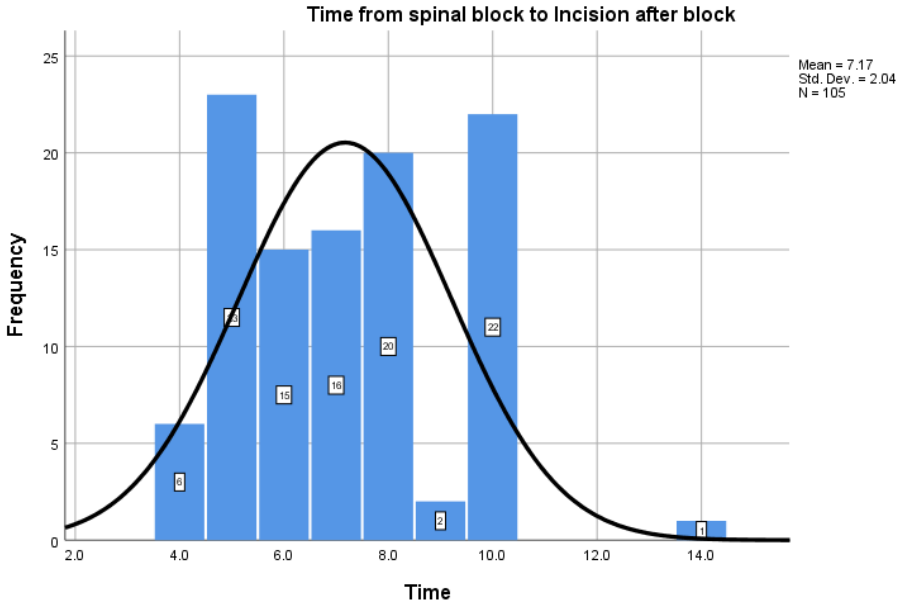

Figure 2:time from spinal block to incision after block.

Figure 2: distribution of time from spinal block to incision among the participants of the three groups (Bupivacaine, Fentanyl, and Ketamine).

4.4 Onset of motor block

The average of motor onset time was 3 minutes after the spinal block, and it ranged between 2.5 and 3.5 minutes among the participants of the three groups (Bupivacaine, Fentanyl, and Ketamine) as seen in figure 2.

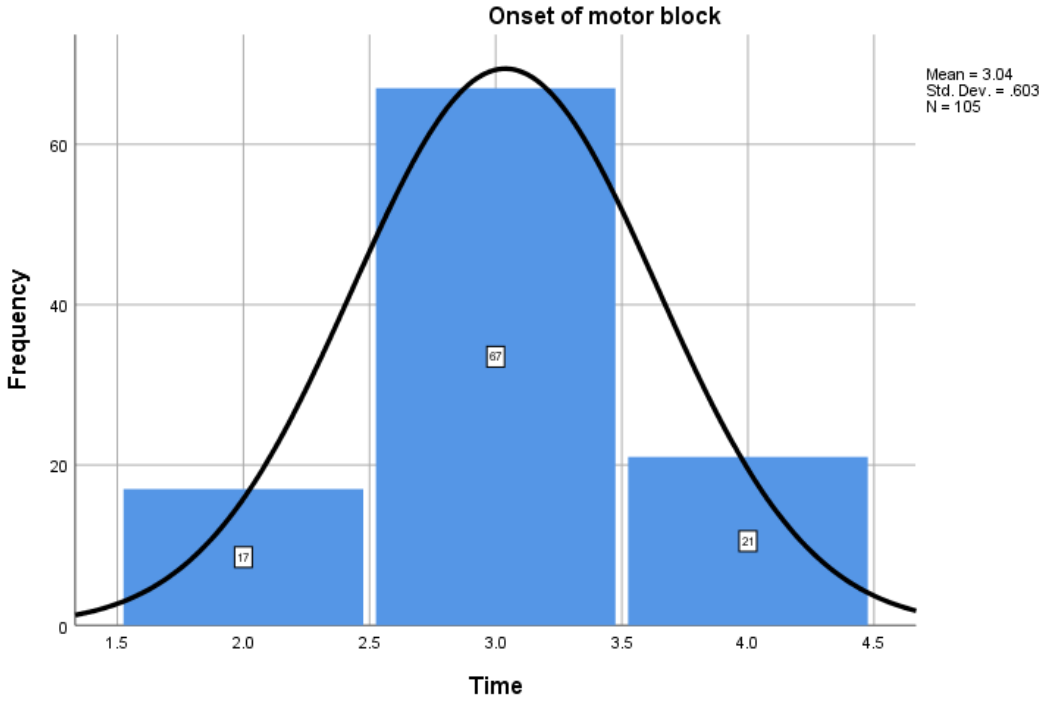

Figure 3: distribution of onset of motor block time among the participants of the three groups (Bupivacaine, Fentanyl, and Ketamine).

4.5 Onset of sensory block

The average of sensory onset time was 1.87 minutes after the spinal block, and nearly 70% ranged between 1.4 and 2.3 minutes among the participants of the three groups (Bupivacaine, Fentanyl, and Ketamine).

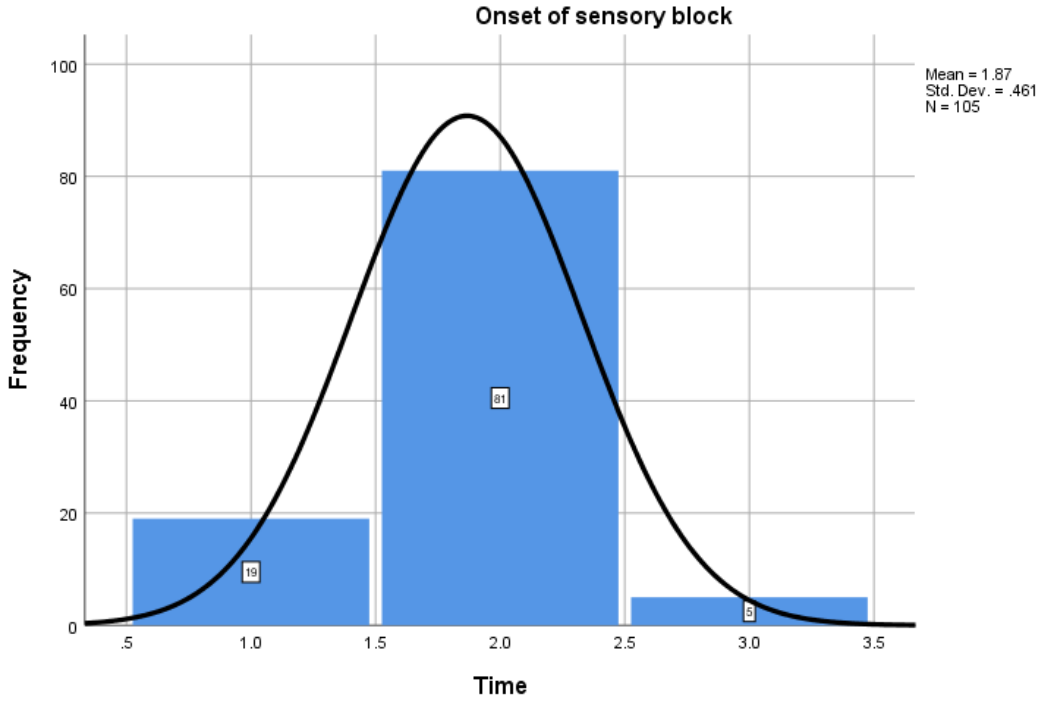

Figure 4: distribution of onset of sensory block time among the participants of the three groups (Bupivacaine, Fentanyl, and Ketamine).

Table (4)indicates that there were statistically significant differences in the level (p <0.05) of time from the spinal block to the start of the operation incision comparison between bupivacaine 7.68(2.06), fentanyl6.11 (1.52), and ketamine7.71 (2.09),(p=0.001).There was also a significant difference in the onset of sensory blockage to T10 betweenbupivacaine2.05(0.33) fentanyl1.57 (0.55) and ketamine1.97 (0.29) (p=0.001).In addition There was a significant difference in the onset of motor blockage betweenbupivacaine3.22 (0.49), fentanyl2.68 (0.63) and ketamine3.20 (0.53) (p=0.001).These results indicate that the timefrom the spinal block to the start of the operation incision, onset of sensory and motor block in the fentanyl group is significantly shorter than the ketamine and bupivacaine group. This means that the fentanyl was the best.

Table 4: Time from spinal block to incision, onset of motor block, & onset of sensory block Among the three groups (bupivacaine, Fentanyl, and Ketamine) Data is presented as Mean ±.

		N	Mean	SD	Min	Max	F	Sig.
Time from spinal block to Incision after block (min)	Bupivacaine	35	7.68	2.06	5.0	14.0		
	Fentanyl	35	6.11	1.52	4.0	10.0	7.99	<.001
	Ketamine	35	7.71	2.09	4.0	10.0		
	Total	105	7.17	2.04	4.0	14.0		
Onset of motor block to T10 by (min)	Bupivacaine	35	3.22	.49	2.0	4.0	10.64	
	Fentanyl	35	2.68	.63	2.0	4.0		<.001
	Ketamine	35	3.20	.53	2.0	4.0		
	Total	105	3.03	.60	2.0	4.0		
Onset of sensory block(min)	Bupivacaine	35	2.05	.33	1.0	3.0	13.76	
	Fentanyl	35	1.57	.55	1.0	3.0		<.001
	Ketamine	35	1.97	.29	1.0	3.0		
	Total	105	1.86	.46	1.0	3.0		

Post hoc multiple comparisons revealed thatthe Fentanyl group did the statistically significant differences and it had the lowest mean in time from spinal block to incision after block ,onset of sensory and motor block in comparing with Bupivacaine and Ketamine groups($p<0.05$) (Table5).

Table 5: Post hoc multiple comparisons for time from spinal block to incision, onset of motor block, & onset of sensory block among the three groups (bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Time from spinal block to Incision after block (min)	Bupivacaine	Fentanyl	1.5714*	.4579	.004	.434	2.709
		Ketamine	-.0286	.4579	.998	-1.166	1.109
	Fentanyl	Bupivacaine	-1.5714*	.4579	.004	-2.709	-.434
		Ketamine	-1.6000*	.4579	.003	-2.737	-.463
	Ketamine	Bupivacaine	.0286	.4579	.998	-1.109	1.166
		Fentanyl	1.6000*	.4579	.003	.463	2.737
Onset of motor block (min)	Bupivacaine	Fentanyl	.5429*	.1325	.000	.214	.872
		Ketamine	.0286	.1325	.977	-.300	.358
	Fentanyl	Bupivacaine	-.5429*	.1325	.000	-.872	-.214
		Ketamine	-.5143*	.1325	.001	-.843	-.185
	Ketamine	Bupivacaine	-.0286	.1325	.977	-.358	.300
		Fentanyl	.5143*	.1325	.001	.185	.843
Onset of sensory block to T10(min)	Bupivacaine	Fentanyl	.4857*	.0988	.000	.240	.731
		Ketamine	.0857	.0988	.687	-.160	.331
	Fentanyl	Bupivacaine	-.4857*	.0988	.000	-.731	-.240
		Ketamine	-.4000*	.0988	.001	-.645	-.155
	Ketamine	Bupivacaine	-.0857	.0988	.687	-.331	.160
		Fentanyl	.4000*	.0988	.001	.155	.645

* The mean difference is significant at the 0.05 level.

4.6 Intra operative Hemodynamic parameters among the three groups

4.6.1 Intra operative systolic blood pressure (SBP)

Showedthat there were statistically significant differencesat the level (p <0.05) at thebaseline of intraoperative SBP M (SD) bupivacaine131.9 (13.0), fentanyl 128.5 (11.5) and ketamine123.1 (13.6) (p=0.018).

On the other hand, the systolic blood pressure at the 9th minutes showedthat there were statistically significant differences at the level (p <0.05)M (SD) bupivacaine 99.4 (11.2), fentanyl 108.6 (16.4) and ketamine99.9 (11.9) (*p* = 0.007). When the fentanyl group's systolic pressure at the 9th minute is compared to the other groups, there is a statistically significant difference (p = 0.007) (Table 6).

Table 6: Intra operative systolic BP among the three groups (bupivacaine, Fentanyl, and Ketamine).

	bupivacaine		**Fentanyl**		**Ketamine**			
Systolic BP at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
Baseline	131.9	13.0	128.5	11.5	123.1	13.6	4.19	**.018**
Induction	117.7	9.3	112.9	11.6	112.4	12.1	2.42	.093
3 min	101.2	12.7	101.0	15.5	96.8	14.7	1.03	.359
6 min	95.4	16.0	98.0	15.9	100.3	11.9	.959	.387
9 min	99.4	11.2	108.6	16.4	99.9	11.9	5.15	**.007**
15 min	105.1	11.8	107.0	10.3	102.7	11.5	1.25	.290
20 min	103.8	12.9	104.6	10.9	101.5	9.6	.730	.484
25 min	104.6	8.50	102.9	11.2	102.6	8.4	.408	.666
30 min	105.8	7.26	103.6	9.1	105.5	5.8	.405	.669
35 min	.	.	107.5	.70	119.5	16.2	1.08	.407

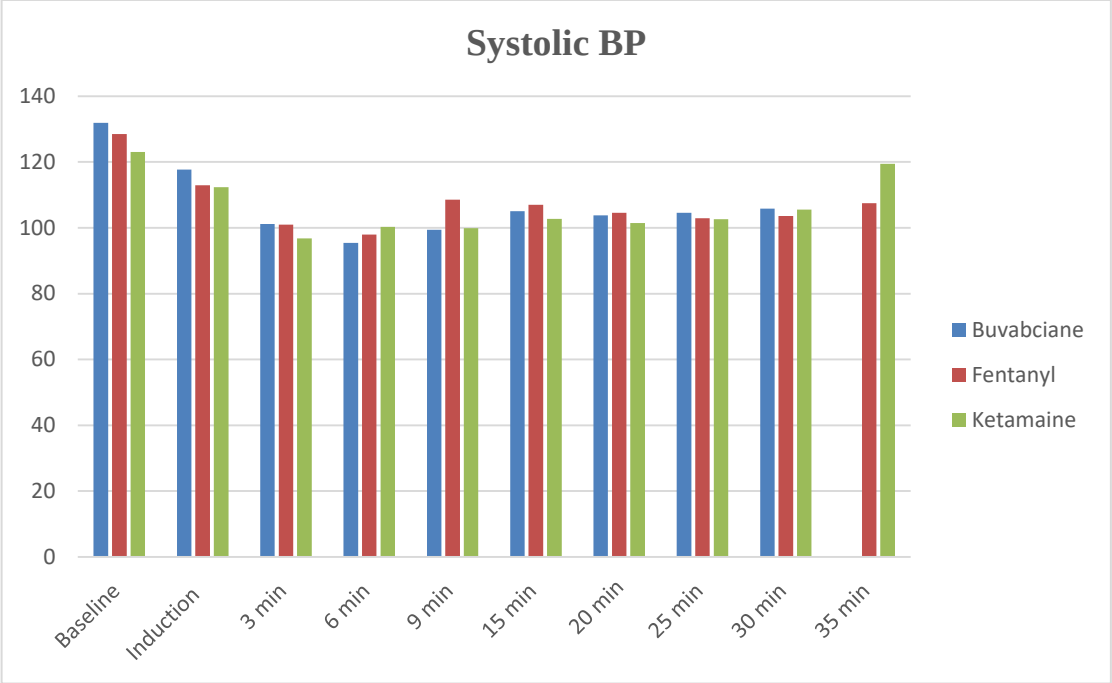

Figure 5*:* Intra operative systolic BP among the three groups.

Post hoc multiple comparisons for intraoperative systolic BP among the three groups (bupivacaine, Fentanyl, and Ketamine) revealed a statistically significant difference in intraoperative baseline systolic blood pressure between bupivacaine group and Ketamine group (p 0.05). Furthermore, systolic blood pressure at the 9th minute in the Fentanyl group was statistically significant when compared to bupivacaine and Ketamine groups (p 0.05) (Table 7).

Table 7: Post hoc multiple comparison forintra operative systolic BP among the three groups (bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
intraoperative Systolic BP mmHg						Lower Bound	Upper Bound
Baseline	Bupivacaine	Fentanyl	3.4000	3.0546	.540	-4.188	10.988
		Ketamine	8.7714*	3.0546	.019	1.183	16.360
	Fentanyl	Bupivacaine	-3.4000	3.0546	.540	-10.988	4.188
		Ketamine	5.3714	3.0546	.218	-2.217	12.960
	Ketamine	Bupivacaine	-8.7714*	3.0546	.019	-16.360	-1.183
		Fentanyl	-5.3714	3.0546	.218	-12.960	2.217
9min	Bupivacaine	Fentanyl	-9.1429*	3.2053	.020	-17.105	-1.180
		Ketamine	-.4857	3.2053	.989	-8.448	7.477
	Fentanyl	Bupivacaine	9.1429*	3.2053	.020	1.180	17.105
		Ketamine	8.6571*	3.2053	.030	.695	16.620
	Ketamine	Bupivacaine	.4857	3.2053	.989	-7.477	8.448
		Fentanyl	-8.6571*	3.2053	.030	-16.620	-.695

* The mean difference is significant at the 0.05 level.

4.6.2 Intra operative Diastolic blood pressure

Table (8) showed that there were statistically significant differences in the level ($p < 0.05$) at the 9minutes M (SD) bupivacaine 55.0(10.1), fentanyl 58.5(10.9) and ketamine52.8 (6.6) ($p=0.043$), the fentanyl group was statistically significant at 9 min($p=0.043$).when compared to diastolic pressure of the other groups .There were also statistically significant differences at 20th minutes bupivacaine 55.8 (6.9), fentanyl 52.2 (7.7) and ketamine50.9 (5.0) ($p=0.008$). In addition there were statistically significant differencesat 25minutes bupivacaine 55.0 (5.2), fentanyl 53.1 (8.3) and ketamine50.7(6.9)($p=0.008$),Bupivacaine group diastolic BP was the one who had a higher and did the significance difference in compare with ketamine at (20&25min)

Table 8: Intra operative Diastolic BP among the three groups (Bupivacaine, Fentanyl, and Ketamine).

	Bupivacaine		Fentanyl		Ketamine			
Diastolic BP at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**Mean**	**F**	**Sig.**
Baseline	77.2	7.2	77.2	8.8	73.5	9.7	2.11	.127
Induction	67.8	9.6	64.8	10.8	62.7	8.3	2.46	.090
3 min	57.8	9.8	54.9	11.7	53.1	12.6	1.49	.229
6 min	53.3	11.6	54.8	10.0	55.6	9.91	.420	.658
9 min	55.0	10.1	58.5	10.9	52.8	6.6	3.24	**.043**
15 min	59.3	10.0	55.9	9.4	54.2	6.9	2.90	.059
20 min	55.8	6.9	52.2	7.7	50.9	5.0	5.04	**.008**
25 min	55.0	5.2	53.1	8.3	50.7	6.9	3.19	**.045**
30 min	56.0	3.8	52.2	7.7	50.4	7.4	2.76	.073
35 min	.	.	58.5	9.1	59.0	11.3	.002	.966

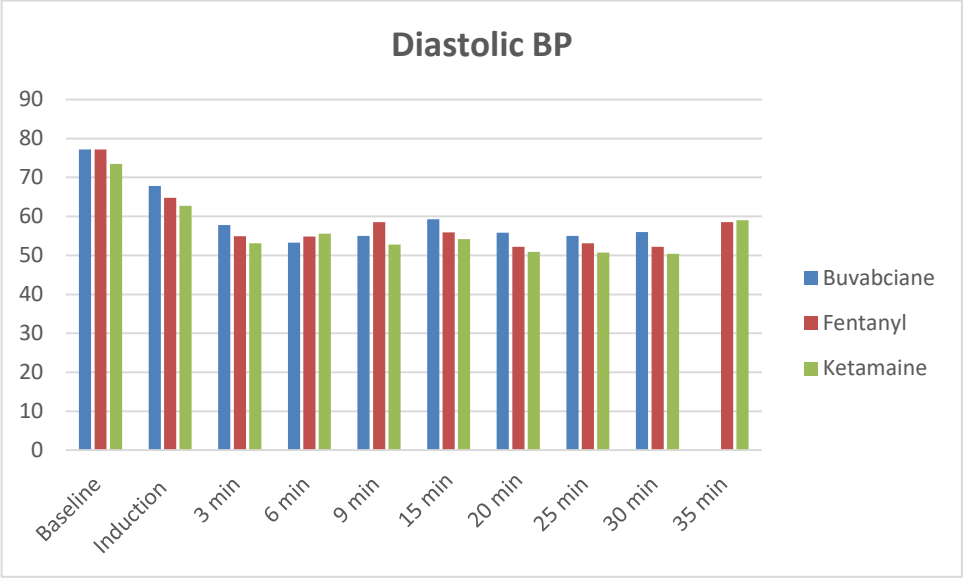

Figure 6: Intra operative diastolic BP among the three groups.

Table (9) showed that intra operative diastolic blood pressure at 9th minutes in the Fentanyl group was statistically significant ($p < 0.05$) compared with the 9th minute's diastolic pressure of the Ketamine group. And Bupivacaine group diastolic BP was the one who had a higher and did the significance difference in compare with ketamine at both times points (20th& 25th minutes) ($p<0.05$)

Table 9: post hocmultiple comparisons for intra operative Diastolic BP among the three groups (Bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
Diastole BP mmHg						Lower Bound	Upper Bound
9 min	Bupivacaine	Fentanyl	-3.5429	2.2550	.295	-9.145	2.059
		Ketamine	2.1429	2.2550	.638	-3.459	7.745
	Fentanyl	Bupivacaine	3.5429	2.2550	.295	-2.059	9.145
		Ketamine	5.6857*	2.2550	.046	.084	11.288
	Ketamine	Bupivacaine	-2.1429	2.2550	.638	-7.745	3.459
		Fentanyl	-5.6857*	2.2550	.046	-11.288	-.084
20 min	Bupivacaine	Fentanyl	3.6000	1.5941	.083	-.360	7.560
		Ketamine	4.8857*	1.5941	.011	.926	8.846
	Fentanyl	Bupivacaine	-3.6000	1.5941	.083	-7.560	.360
		Ketamine	1.2857	1.5941	.723	-2.674	5.246
	Ketamine	Bupivacaine	-4.8857*	1.5941	.011	-8.846	-.926
		Fentanyl	-1.2857	1.5941	.723	-5.246	2.674
25 min	Bupivacaine	Fentanyl	1.9127	1.7006	.533	-2.314	6.139
		Ketamine	4.2589*	1.6886	.046	.062	8.455
	Fentanyl	Bupivacaine	-1.9127	1.7006	.533	-6.139	2.314
		Ketamine	2.3462	1.6758	.379	-1.818	6.511
	Ketamine	Bupivacaine	-4.2589*	1.6886	.046	-8.455	-.062
		Fentanyl	-2.3462	1.6758	.379	-6.511	1.818

* The mean difference is significant at the 0.05 level.

4.6.3 Intra operative Mean arterial pressure

Table (10) showed thatKetamine group MAP at intra operative baseline was statistically significant differenceat the level ($p < 0.05$) and lower than the MAP of both Fentanyl and Bupivacaine groupsM (SD) bupivacaine 96.3 (9.6), fentanyl 94.2 (8.9) and ketamine87.3 (9.7) ($p=0.043$). There were also statistically significant differencesat induction the Bupivacaine group was statistically significant ($p < 0.05$) and higher than the MAP of KetamineM (SD) bupivacaine 83.2 (8.7), fentanyl 81.8 (10.6) and ketamine76.6 (9.2) ($p=.013$).In addition MAP at 9^{th}minutes in the Fentanyl group was statistically significant ($p < 0.05$) and higher than the MAP of both Bupivacaine and ketamine groupsM (SD) bupivacaine 69.5 (10.7),

fentanyl 76.2 (14.2) and ketamine 67.8 (8.2) (p=0.006).While, at 20th minutes Bupivacaine group was statistically significant ($p < 0.05$) and higher than the MAP of Ketamine group,M (SD) bupivacaine 72.1 (7.1), fentanyl 69.8 (9.0) and ketamine 67.0 (6.4) (p=0.019).

Table 10: Intra operative MAP among the three groups (Bupivacaine, Fentanyl, and Ketamine).

	Bupivacaine		**Fentanyl**		**Ketamine**			
MAP at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
Baseline	96.3	9.6	94.2	8.9	87.3	9.7	8.71	**< .001**
Induction	83.2	8.7	81.8	10.6	76.6	9.2	4.56	**.013**
3min	71.6	10.9	70.2	12.3	65.8	13.2	2.19	.117
6min	67.3	14.4	70.0	12.5	70.2	10.1	.590	.556
9min	69.5	10.7	76.2	14.2	67.8	8.2	5.41	**.006**
15min	73.1	9.0	73.3	10.9	69.2	7.0	2.22	.114
20min	72.1	7.1	69.8	9.0	67.0	6.4	4.09	**.019**
25min	70.1	6.1	69.8	10.3	66.7	7.4	1.80	.170
30min	70.5	5.1	68.9	8.4	66.6	6.1	1.26	.292
35min	.	.	74.0	12.7	76.5	6.3	.062	.827

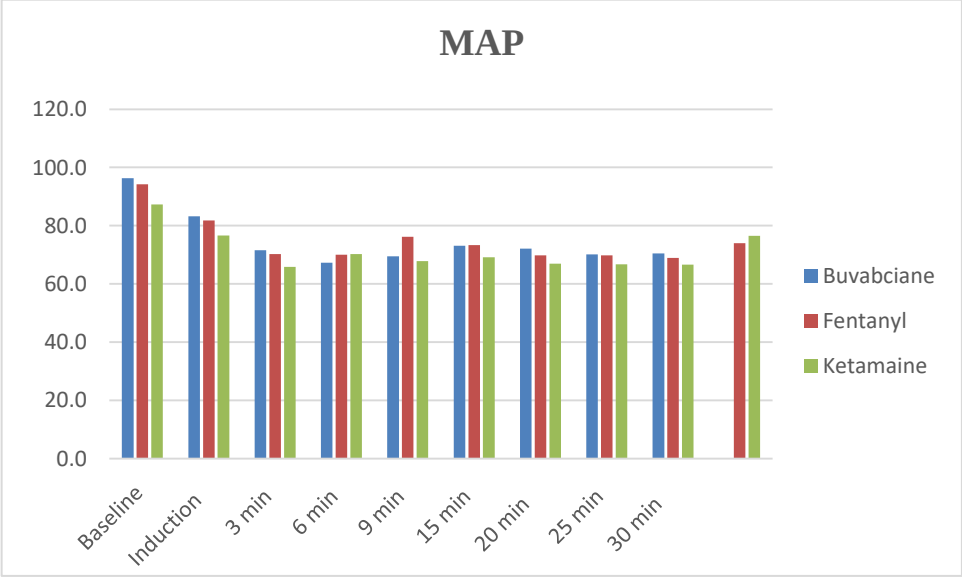

Figure 7: Intra operative MAP among the three groups.

Table (11) post hoc multiple Comparisons for intra operative MAP among the three groups (Bupivacaine, Fentanyl, and Ketamine)revealed that the ketamine group intraoperativeMAP at baseline was statistically significant ($p < 0.05$) and lower than the MAP of both Fentanyl and Bupivacaine groups (87.3 mmHg vs. 94.2 mmHg & 96.3mmHg respectively).

On the other hand, the MAP at Induction in the Bupivacaine group was statistically significant ($p < 0.05$) and higher than the MAP of Ketamine (83.2 mmHg vs. 76.6 mmHg).

Moreover, intraoperative MAP at 9th minutes revealed that Fentanyl group was statistically significant ($p < 0.05$) and higher than the MAP of both Bupivacaine and ketamine groups (76.2 mmHg vs. 69.5 mmHg & 67.8 mmHg respectively). While at 20th minutes Bupivacaine group was statistically significant ($p < 0.05$) and higher than the MAP of Ketamine (72.1 mmHg vs. 67.0 mmHg).

Table 11: post hoc multiple Comparisons for intra operative MAP among the three groups (Bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
MAP mmHg						Lower Bound	Upper Bound
Baseline	Bupivacaine	Fentanyl	2.0286	2.2614	.670	-3.589	7.646
		Ketamine	9.0000*	2.2614	.001	3.382	14.618
	Fentanyl	Bupivacaine	-2.0286	2.2614	.670	-7.646	3.589
		Ketamine	6.9714*	2.2614	.011	1.354	12.589
	Ketamine	Bupivacaine	-9.0000*	2.2614	.001	-14.618	-3.382
		Fentanyl	-6.9714*	2.2614	.011	-12.589	-1.354
induction	Bupivacaine	Fentanyl	1.3429	2.2875	.842	-4.340	7.025
		Ketamine	6.5429*	2.2875	.020	.860	12.225
	Fentanyl	Bupivacaine	-1.3429	2.2875	.842	-7.025	4.340
		Ketamine	5.2000	2.2875	.080	-.482	10.882
	Ketamine	Bupivacaine	-6.5429*	2.2875	.020	-12.225	-.860
		Fentanyl	-5.2000	2.2875	.080	-10.882	.482
9min	Bupivacaine	Fentanyl	-6.7143*	2.7018	.050	-13.426	-.003

		Ketamine	1.6857	2.7018	.823	-5.026	8.397
	Fentanyl	Bupivacaine	6.7143*	2.7018	.050	.003	13.426
		Ketamine	8.4000*	2.7018	.010	1.688	15.112
	Ketamine	Bupivacaine	-1.6857	2.7018	.823	-8.397	5.026
		Fentanyl	-8.4000*	2.7018	.010	-15.112	-1.688
20min	Bupivacaine	Fentanyl	2.3714	1.8084	.426	-2.121	6.864
		Ketamine	5.1714*	1.8084	.020	.679	9.664
	Fentanyl	Bupivacaine	-2.3714	1.8084	.426	-6.864	2.121
		Ketamine	2.8000	1.8084	.306	-1.692	7.292
	Ketamine	Bupivacaine	-5.1714*	1.8084	.020	-9.664	-.679
		Fentanyl	-2.8000	1.8084	.306	-7.292	1.692

* The mean difference is significant at the 0.05 level.

4.6.4 Intra operative Heart rate

Table (12) showed that there were statistical significant differences between M (SD) bupivacaine 98.7 (18.2), fentanyl 93.1 (14.4) and ketamine 86.4 (19.1) (p = 0.015).

Table 12: Intra operative HR among the three groups (Bupivacaine, Fentanyl, and Ketamine).

	Bupivacaine		**Fentanyl**		**Ketamine**			
HR at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
Baseline	95.0	9.5	94.0	11.9	91.7	14.6	.681	.509
Induction	93.9	11.4	94.7	12.8	92.3	14.7	.325	.723
3 min	**98.7**	**18.2**	**93.1**	**14.4**	**86.4**	**19.1**	**4.393**	**.015**
6 min	97.7	17.3	90.4	13.3	89.3	15.3	3.034	.052
9 min	95.4	12.7	89.6	12.1	90.0	13.2	2.313	.104
15 min	91.9	9.9	91.7	11.4	90.9	11.2	.094	.911
20 min	93.6	10.8	90.4	11.5	92.7	11.7	.748	.476
25 min	94.8	9.5	91.6	9.1	93.0	12.8	.774	.464
30 min	98.8	8.9	92.7	9.7	94.9	12.3	1.442	.246
35 min	.	.	108.5	5.0	95.5	7.8	3.976	.184

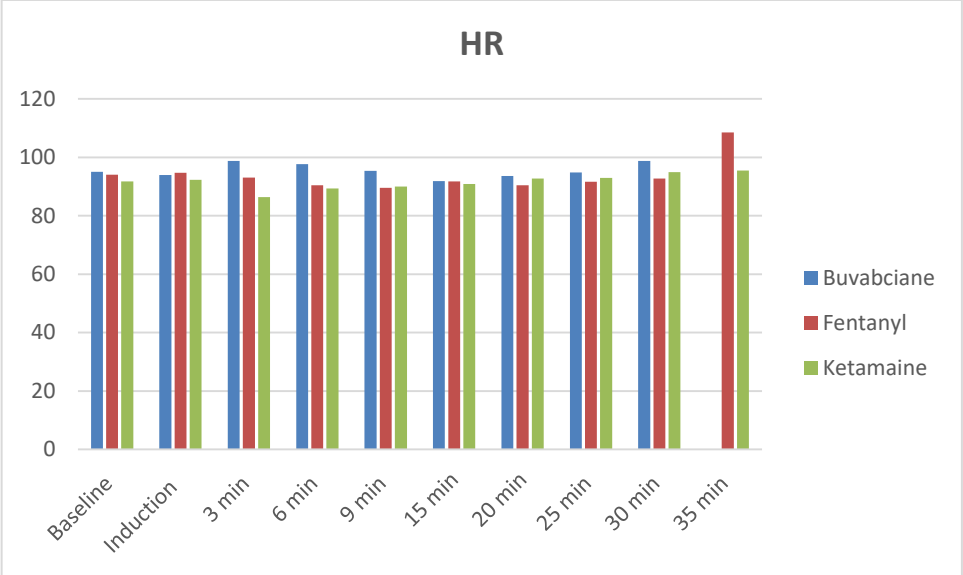

Figure 8: Intra operative HR among the three groups**.**

In Table (13) post hoc multiple comparisons for intra operative HR among the three groups (Bupivacaine, Fentanyl, and Ketamine) showed that the Bupivacaine group HR at 3rd minute was statistically significant ($p < 0.05$) compared toketamine and fentanyl groups

Table 13: post hoc multiple comparisons for intra operative HR among the three groups (Bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
HR (bpm)						Lower Bound	Upper Bound
3min	Bupivacaine	Fentanyl	5.6000	4.1500	.406	-4.709	15.909
		Ketamine	12.2857*	4.1500	.015	1.976	22.595
	Fentanyl	Bupivacaine	-5.6000	4.1500	.406	-15.909	4.709
		Ketamine	6.6857	4.1500	.278	-3.624	16.995
	Ketamine	Bupivacaine	-12.2857*	4.1500	.015	-22.595	-1.976
		Fentanyl	-6.6857	4.1500	.278	-16.995	3.624

* The mean difference is significant at the 0.05 level.

4.6.5 Intra operative Respiratory rate

Table (14) showed thatthere were significant difference regarding intra operative respiratory rate at induction between bupivacaine 16.7 (2.6), fentanyl 15.8 (2.1) and ketamine 17.7 (3.2) (p = 0.013).There were alsostatistically significant differencesat 25th minutes between M (SD) bupivacaine 17.0 (2.6), fentanyl 16.7 (3.1) and ketamine 18.8 (2.6) (p = 0.006).

Table 14: Intra operative RR among the three groups (Bupivacaine, Fentanyl, and Ketamine).

	Bupivacaine		**Fentanyl**		**Ketamine**			
RR at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
Baseline	16.0	1.8	15.6	1.6	15.9	1.8	.525	.593
Induction	16.7	2.6	15.8	2.1	17.7	3.2	4.50	**.013**
3 min	17.1	2.9	16.2	2.6	17.7	3.9	1.93	.149
6 min	16.3	3.4	17.2	3.6	16.6	2.9	.678	.510
9 min	16.8	3.4	17.7	3.7	17.9	3.8	.845	.432
1 5 min	17.4	3.7	16.8	3.9	18.8	3.1	2.69	.072
20 min	17.4	3.8	17.7	3.8	18.9	3.9	1.45	.238
25 min	17.0	2.6	16.7	3.1	18.8	2.6	5.39	**.006**
30 min	16.5	3.0	16.6	2.8	17.8	2.4	1.18	.314
35 min	.	.	16.0	1.4	20.5	0.7	16.2	.057

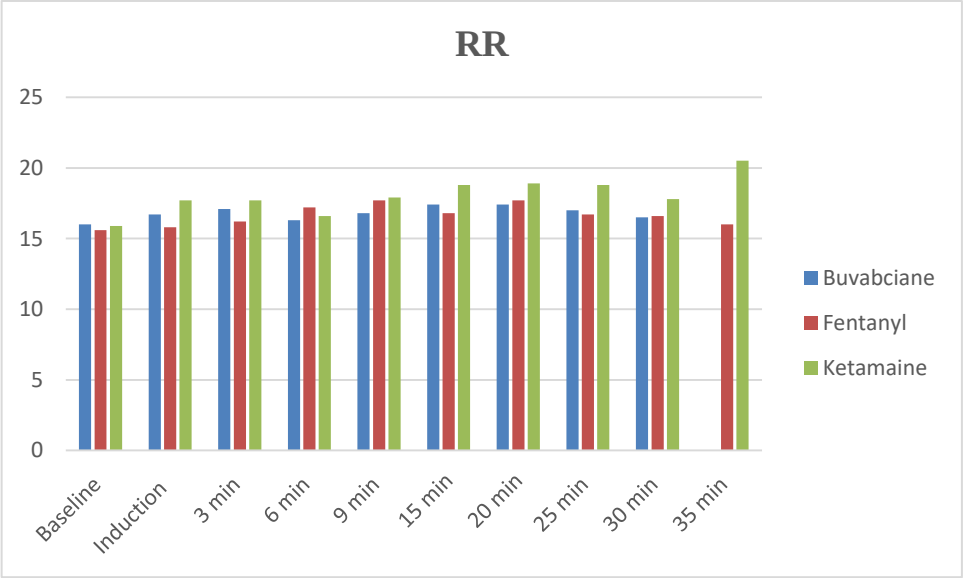

Figure 9: Intra operative RR among the three groups.

In Table (15) post hoc Multiple Comparisons for Intra operative RR among the three groups (Bupivacaine, Fentanyl, and Ketamine)revealed that the significant difference at induction was between ketamine group compared to fentanyl (p=.013).And revealed that the ketamine group RR at 25th minute was statistically significant ($p < 0.05$) and higher than the RR of both Bupivacaine & Fentanyl groups.

Table 15: post hoc Multiple Comparisons for Intra operative RR among the three groups (Bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
Respiratory rate (bpm)						Lower Bound	Upper Bound
induction	Bupivacaine	Fentanyl	.914	.638	.362	-.67	2.50
		Ketamine	-1.000	.638	.297	-2.59	.59
	Fentanyl	Bupivacaine	-.914	.638	.362	-2.50	.67
		Ketamine	-1.914*	.638	.013	-3.50	-.33
	Ketamine	Bupivacaine	1.000	.638	.297	-.59	2.59
		Fentanyl	1.914*	.638	.013	.33	3.50
25min	Bupivacaine	Fentanyl	.324	.687	.895	-1.38	2.03
		Ketamine	-1.741*	.682	.043	-3.44	-.05
	Fentanyl	Bupivacaine	-.324	.687	.895	-2.03	1.38
		Ketamine	-2.066*	.677	.012	-3.75	-.38
	Ketamine	Bupivacaine	1.741*	.682	.043	.05	3.44
		Fentanyl	2.066*	.677	.012	.38	3.75

* The mean difference is significant at the 0.05 level.

4.6.6 Intra operative SPO2

Table (16) showed that there were statistically significant differences regarding Intra operative SPO2 at 15th min and at 20th min between the three groups. At 15minutes M (SD) bupivacaine 98.5(1.2), fentanyl 97.6(1.6) and ketamine 98.3(1.4) ($p = 0.017$).There were alsostatistically significant differencesat 20th between M (SD) bupivacaine 98.5 (1.3), fentanyl 97.3 (1.7) and ketamine 98.1 (1.4) ($p = 0.006$).

Table 16: Intra operative SpO^2 among the three groups (Bupivacaine, Fentanyl, and Ketamine).

	Bupivacaine		Fentanyl		Ketamine			
SpO^2 at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
Baseline	99.0	1.3	99.0	1.0	99.4	0.8	1.69	.190
Induction	99.0	0.9	98.5	1.1	99.1	1.1	3.03	.052
3 min	99.0	1.1	98.5	1.2	98.7	1.3	1.96	.145
6 min	98.9	1.0	98.3	1.4	98.6	1.3	2.01	.139
9 min	98.5	1.0	98.1	1.3	98.5	1.5	1.41	.247
15 min	98.5	1.2	97.6	1.6	98.3	1.4	4.24	**.017**
20 min	98.5	1.3	97.3	1.7	98.1	1.4	5.34	**.006**
25 min	98.3	1.3	97.6	1.7	98.0	1.4	2.15	.121
30 min	98.4	1.5	97.7	1.9	98.2	1.5	.884	.420
35 min	.	.	99.5	0.7	96.0	1.4	9.80	.089

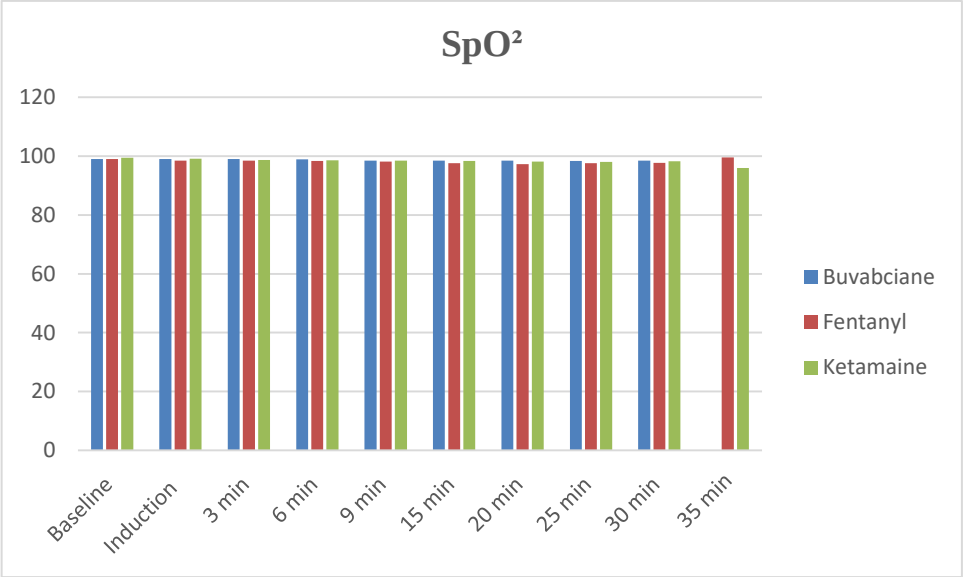

Figure 10: Intra operative SpO^2 among the three groups.

In Table (17) post hoc multiple comparisons for intra operative SpO^2 among the three groups (Bupivacaine, Fentanyl, and Ketamine)indicated that the Bupivacaine group $SpO^2$was statistically significant ($p < 0.05$) compared to Fentanyl at 15^{th}min (p=022) and at 20^{th}min (p=.007).

Table 17: post hoc multiple comparisons for intra operative SpO^2 among the three groups (Bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
spo2						Lower Bound	Upper Bound
15min	Bupivacaine	Fentanyl	.943*	.335	.022	.11	1.77
		Ketamine	.257	.335	.745	-.57	1.09
	Fentanyl	Bupivacaine	-.943*	.335	.022	-1.77	-.11
		Ketamine	-.686	.335	.128	-1.52	.15
	Ketamine	Bupivacaine	-.257	.335	.745	-1.09	.57
		Fentanyl	.686	.335	.128	-.15	1.52
20min	Bupivacaine	Fentanyl	1.143*	.353	.007	.27	2.02
		Ketamine	.429	.353	.481	-.45	1.31
	Fentanyl	Bupivacaine	-1.143*	.353	.007	-2.02	-.27
		Ketamine	-.714	.353	.134	-1.59	.16
	Ketamine	Bupivacaine	-.429	.353	.481	-1.31	.45
		Fentanyl	.714	.353	.134	-.16	1.59

* The mean difference is significant at the 0.05 level.

4.6.7 Intra operative temperature

Table (18) indicates there was statistically significant difference regarding **Intra operative temperature** at baseline time between M (SD) bupivacaine 36.2 (0.2), fentanyl 36.3 (0.1) and ketamine 36.1(0.2) (p = 0.011).

Table 18: Intra operative Temperature among the three groups (Bupivacaine, Fentanyl, and Ketamine).

	Bupivacaine		**Fentanyl**		**Ketamine**			
Temperature at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
Baseline	36.2	0.2	36.3	0.1	36.1	0.2	4.75	**.011**
Induction	36.3	0.1	36.4	0.1	36.3	0.2	1.3	.272
3min	36.4	0.2	36.5	0.1	36.4	0.1	1.03	.358
6min	36.5	0.1	36.5	0.1	36.5	0.1	.474	.624
9min	36.6	0.1	36.6	0.2	36.6	0.1	.424	.656
15min	36.7	0.1	36.6	0.1	36.7	0.1	1.76	.177
20min	36.7	0.1	36.7	0.2	36.7	0.1	.981	.378
25min	36.8	0.2	36.8	0.2	36.8	0.2	.817	.445
30min	36.9	0.2	36.8	0.2	36.9	0.2	.238	.789
35min	.	.	36.8	0.4	36.9	0.1	.154	.733

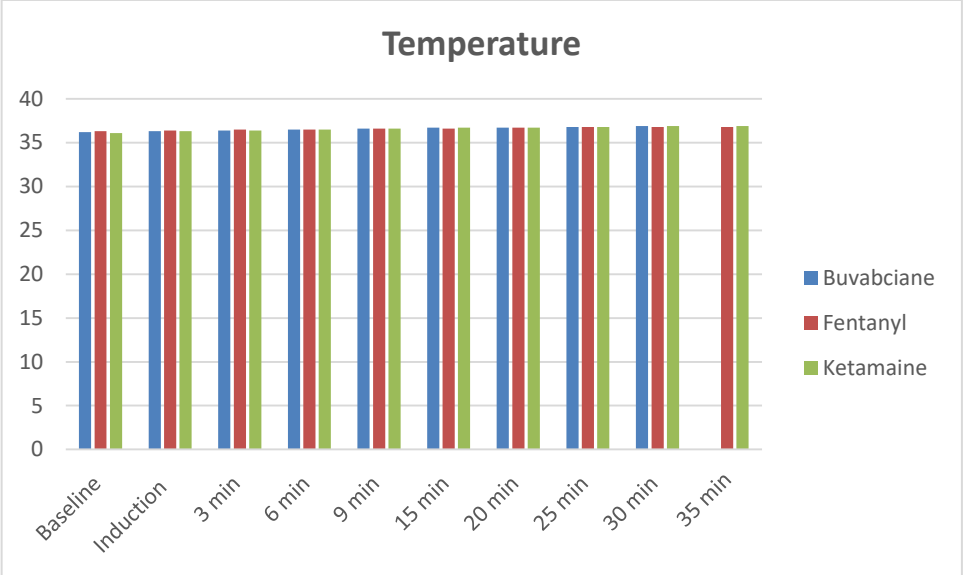

Figure 11: Intra operative Temperature among the three groups.

In Table (19) post hoc multiple comparisons for intra operative temperature among the three groups (Bupivacaine, Fentanyl, and Ketamine) revealed that the temperature of Fentanyl group was statistically significant compared to Ketamine group (36.3 vs. 36.1 c°) (p=.0130).

Table 19: post hocmultiple comparisons for intra operative Temperature among the three groups (Bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
Intraoperative temperature						Lower Bound	Upper Bound
Baseline	Bupivacaine	Fentanyl	-.0886	.0427	.121	-.195	.017
		Ketamine	.0400	.0427	.646	-.066	.146
	Fentanyl	Bupivacaine	.0886	.0427	.121	-.017	.195
		Ketamine	.1286*	.0427	.013	.023	.235
	Ketamine	Bupivacaine	-.0400	.0427	.646	-.146	.066
		Fentanyl	-.1286*	.0427	.013	-.235	-.023

* The mean difference is significant at the 0.05 level

4.6.8 Intra operative complications among the three groups (Bupivacaine, Fentanyl, & Ketamine)

4.6.8.1 Intraoperative bradycardia

In the fentanyl group 1/35 (2.9%) and in the ketamine group, 1/35 (2.9%) bradycardia occurred during surgery, while there was no (0/40) bradycardia in the bupivacaine group. However, there were no significant differences between the groups (P = 0.60) (Table 20).

4.6.8.2 Intraoperative hypotension

There were 25/35 (71.4%) patients in the bupivacaine group, 29/35 (82.9%) patients in the fentanyl group, and 30/35 (85.7%) patients in the ketamine group who had hypotension intraoperative. There was no statistically significant difference between groups (P=0.28) (table 20).

4.6.8.3 Intraoperative pruritus

During the intraoperative, no any cases complain of pruritus. There was no significant difference between the groups (P >0.05 table 20).

4.6.8.4 Intraoperative shivering

Shivering complicated 3 cases out of 35 in the bupivacaine group (8.6%) and 2 cases out of 35 in the fentanyl group (5.7%) during the intraoperative period. However, no cases of shivering were reported in the ketamine group. There was no statistically significant difference between groups (P =0.23) (Table 20).

4.6.8.5 Intraoperative nausea

During the intraoperative period, 8 out of 35 cases (22.9%) in the bupivacaine group, 5 out of 35 cases (14.3%) in the fentanyl group, and 2 cases out of 35 (5.7%) in the ketamine group experienced mild nausea. While 1 case in the bupivacaine group and 1 case in the ketamine group experienced moderate nausea, There was no statistically significant difference between groups (P =0.26) (Table 20)

4.6.8.6 Ramsy sedation scale

Regarding incidence of sedation during intraoperative period, 26 out of 35 cases (71.4%) in ketamine group, 3 out of 35 cases in fentanyl group and no any cases in bupivacaine group.There was significant difference regarding the ramsy sedation scale between the groups (P<0.001); table 20). Thus, ketamine have highly incidence of sedation during intraoperative period.

4.6.8.7 Intraoperative respiratory depression

During the intraoperative period, 3 cases out of 35in thebupivacainegroup (8.6%) and 1 case out of 35in the fentanyl and 1/35 case in ketamine group(2.9%) were complicated by respiratory depression. There was no significant difference between the groups (P =0.23) (Table 20).

Table 20: Intra operative complications among the three groups (Bupivacaine, Fentanyl, & Ketamine)

			Group				
		Total	**Bupivacaine**	**Fentanyl**	**Ketamine**	X^2	**Sig.**
Bradycardia	No	103(98.1%)	35 (100.0%)	34(97.1%)	34 (97.1%)	1.01	.60
	Yes	2(1.9%)	0 (0.0%)	1(2.9%)	1(2.9%)		
Hypotension	No	21(20.0%)	10 (28.6%)	6(17.1%)	5(14.3%)	2.50	.28
	Yes	84(80.0%)	25 (71.4%)	29(82.9%)	30(85.7%)		
Shivering	No	100 (95.2%)	32 (91.4%)	33(94.3%)	35(100.0%)	2.94	.23
	2*	5 (4.8%)	3 (8.6%)	2(5.7%)	0(0.0%)		
Nausea	No	88(83.8%)	26 (74.3%)	30(85.7%)	32(91.4%)	5.23	.26
	Mild	15(14.3%)	8 (22.9%)	5(14.3%)	2(5.7%)		
	Moderate	2(1.9%)	1 (2.9%)	0(0.0%)	1(2.9%)		
Respiratory depression	No	100(95.2%)	32 (91.4%)	34(97.1%)	34(97.1%)	1.68	.43
	Yes	5(4.8%)	3 (8.6%)	1(2.9%)	1(2.9%)		
Pain scale	No	105(100.0%)	35 (100.0%)	35(100.0%)	35(100.0%)	-	-
Pruritus	No	105(100.0%)	35 (100.0%)	35(100.0%)	35(100.0%)	-	-
Vomiting	No	105(100.0%)	35 (100.0%)	35(100.0%)	35(100.0%)	-	-
RSS	2*	76(72.4%)	35 (100.0%)	32(91.4%)	9(25.7%)	57.9	**<.001**
	3*	28(26.7%)	0 (0.0%)	3(8.6%)	25(71.4%)		
	4*	1(1.0%)	0 (0.0%)	0(0.0%)	1(2.9%)		

Shivering 2*: Muscular activity in more than one muscle group but not generalized shivering

Ramsay Sedation Scale (RSS): 2*cooperative, tranquil, oriented, 3*drowsy but responsive to verbal commands, 4*a sleep, brisk response to stimulus

Table (21) showed that the differences between the incidence of ramsy sedation scale in ketamine, bupivacaine and fentanyl group (p=0. 000). The results indicate that patients who received ketamine had significantly more sedation compared to other group.

Table 21: post hocmultiple comparisons intra operative for ramsy sedation scale among the three groups (Bupivacaine, Fentanyl, and Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
Intraoperative Ramsy sedation scale						Lower Bound	Upper Bound
	Bupivacaine	Fentanyl	-.086	.078	.550	-.28	.11
		Ketamine	-.771*	.078	.000	-.97	-.58
	Fentanyl	Bupivacaine	.086	.078	.550	-.11	.28
		Ketamine	-.686*	.078	.000	-.88	-.49
	Ketamine	Bupivacaine	.771*	.078	.000	.58	.97
		Fentanyl	.686*	.078	.000	.49	.88

4.7 PACU: Hemodynamic parameters among the three groups (Bupivacaine, Fentanyl, & Ketamine)

4.7.1 PACU Systolic blood pressure

The systolic pressure of the three groups (Bupivacaine, Fentanyl, and Ketamine) during the PACU period was very close and did not give any statistically significant differences during the whole period (p value > 0.05).

Table 22: PACUSystolic blood pressure among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		Fentanyl		Ketamine			
PACU systolic BP mmHg	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
1 min	105.7	8.6	107.1	10.5	104.9	7.6	.544	.582
5 min	106.2	6.4	109.6	10.2	107.1	6.0	1.84	.163
10 min	108.4	7.7	111.5	7.6	107.6	6.1	2.84	.063
15 min	111.1	7.9	112.6	7.5	108.9	4.8	2.48	.089

4.7.2 PACU diastolic Blood Pressure

The table (23) was shown that the diastolic blood pressure at 5minutes in the bupivacaine group was 58.6 (8.3) mmHg, fentanyl 58.4(9.0)mmHg and ketamine group 53.3(7.3)mmHg, which was statistically significant (p = 0.011).The table also showed that there was a significant different in the level ($p<0.05$) between the three group at 15minutes interval , the bupivacaine group was 62.8 (±7.7) mmHg fentanyl 61.2 (±8.5)mmHg and ketamine group 58.0(±7.8)mmHg(p = 0.040).

Table 23: PACUdiastolic BP among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		Fentanyl		Ketamine			
PACU diastolic BP mmHg	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
1 min	58.1	7.5	57.9	8.7	54.7	8.9	1.77	.174
5 min	58.6	8.3	58.4	9.0	53.3	7.3	4.75	**0.011**
10 min	59.3	8.0	59.1	8.2	56.1	7.2	1.91	.153
15 min	62.8	7.7	61.2	8.5	58.0	7.8	3.31	**0.040**

Table (24) revealed that the diastolic pressure of the Bupivacaine group was statistically significant and higher in comparing with the Ketamine group at 5th PACU time (p=0.028) and at 15th PACU time (p=0.045).

Table 24: post hock multiple compression for PACUdiastolic BP among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
PACU diastolic BP mmHg						Lower Bound	Upper Bound
5 min	Bupivacaine	Fentanyl	.200	1.964	.995	-4.68	5.08
		Ketamine	5.343*	1.964	.028	.46	10.22
	Fentanyl	Bupivacaine	-.200	1.964	.995	-5.08	4.68
		Ketamine	5.143*	1.964	.036	.26	10.02
	Ketamine	Bupivacaine	-5.343*	1.964	.028	-10.22	-.46
		Fentanyl	-5.143*	1.964	.036	-10.02	-.26
15 min	Bupivacaine	Fentanyl	1.657	1.917	.689	-3.11	6.42
		Ketamine	4.857*	1.917	.045	.09	9.62
	Fentanyl	Bupivacaine	-1.657	1.917	.689	-6.42	3.11
		Ketamine	3.200	1.917	.253	-1.56	7.96
	Ketamine	Bupivacaine	-4.857*	1.917	.045	-9.62	-.09
		Fentanyl	-3.200	1.917	.253	-7.96	1.56

4.7.3 PACU MAP

Table (25) showed thatbupivacaine group MAP at 1minutes was statistically significant differencein the level (p <0.05) and higher than the MAP of ketamine groups, bupivacaine 71.9 (8.3), fentanyl 70.0 (7.8) and ketamine 65.9 (13.4) (p=0.048). There were also statistically significant differencesat 15minutes interval the Ketamine group was statistically significant ($p < 0.05$) and lower than the MAP of both group fentanyl and bupivacaine. Bupivacaine 77.8 (8.2), fentanyl 76.1 (7.8) and ketamine71.9 (7.0) (p=0.006).

Table 25: PACU MAP among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		**Fentanyl**		**Ketamine**			
PACU MAP	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
1 min	71.9	8.3	70.0	7.8	65.9	13.4	3.129	**.048**
5 min	72.9	8.4	72.3	7.6	69.6	6.6	1.815	.168
10 min	74.3	8.1	73.4	7.7	70.9	6.2	1.985	.143
15 min	77.8	8.2	76.1	7.8	71.9	7.0	5.403	**.006**

Table (26) post hoc multiple comparisons showed that at 1minute the mean blood pressure of the Bupivacaine group was statistically significant (p value < 0.05) and higher than the mean blood pressure of the Ketamine group. And, at 15th PACU minute, the mean blood pressure of the Ketamine group was statistically significant (p value < 0.05) and lower than the mean blood pressure of the Bupivacaine group, and lower than the mean blood pressure of the Fentanyl group.

Table 26: post hock multiple compression for PACU MAP among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
PACU MAP mmHg						Lower Bound	Upper Bound
1 min	Bupivacaine	Fentanyl	1.829	2.421	.752	-4.19	7.84
		Ketamine	5.914	2.421	.055	-.10	11.93
	Fentanyl	Bupivacaine	-1.829	2.421	.752	-7.84	4.19
		Ketamine	4.086	2.421	.245	-1.93	10.10
	Ketamine	Bupivacaine	-5.914	2.421	.055	-11.93	.10
		Fentanyl	-4.086	2.421	.245	-10.10	1.93
15 min	Bupivacaine	Fentanyl	1.657	1.827	.664	-2.88	6.20
		Ketamine	5.829*	1.827	.008	1.29	10.37
	Fentanyl	Bupivacaine	-1.657	1.827	.664	-6.20	2.88
		Ketamine	4.171	1.827	.079	-.37	8.71
	Ketamine	Bupivacaine	-5.829*	1.827	.008	-10.37	-1.29
		Fentanyl	-4.171	1.827	.079	-8.71	.37

4.7.4 PACU HR

Table (27) showed that there was no significant different between the three group (Bupivacaine, Fentanyl, and Ketamine) in the measure of heart rate at the 0.05 level (p>0.05).

Table 27: PACU HR among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		Fentanyl		Ketamine			
PACU HR	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
1 min	88.8	6.5	89.1	9.8	88.5	10.3	.039	.962
5 min	86.2	7.5	87.2	8.0	88.7	8.5	.872	.421
10 min	86.0	8.2	85.5	7.3	87.0	9.1	.297	.744
15 min	87.9	8.1	86.5	7.5	86.5	9.6	.296	.745

4.7.5 PACU RR

Table (28) showed that there was statistically significant different between the group in the measure of respiratory rate at the0.05 level. The ketamine group at 5minutes was statistically significant differences in compared with the respiratory rate of bupivacaine, bupivacaine 15.0 (±3.4), fentanyl 15.9 (±2.0) and ketamine 16.5 (±1.5) (p = 0.027). There were alsostatistically significant differencesat 15^{th} minute regarding the respiratory rate in ketamine group which was statistically significant, in compared with the RR of Bupivacaine groups, bupivacaine 15.2 (±1.4), fentanyl 15.9 (±1.5) and ketamine 16.5 (±1.7) (p = 0.004).

Table 28: PACU RR among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		**Fentanyl**		**Ketamine**			
PACU RR	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
1 min	16.3	1.5	15.7	1.8	16.3	1.5	1.438	.242
5 min	15.0	3.4	15.9	2.0	16.5	1.5	3.736	**.027**
10 min	15.3	1.9	15.5	1.4	15.8	1.6	.831	.438
15 min	15.2	1.4	15.9	1.5	16.5	1.7	5.954	**.004**

Table (29) post hoc multiple comparisons showed that, respiratory rate of the Ketamine group was statistically significant ($p< 0.05$) and higher than the RR of the Bupivacaine group at 5thminute ($p=0.028$) and at 15thminute ($p=0.008$).

Table 29: post hock multiple compression for PACU respiratory rate among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
PACU respiratory rate(bpm)						Lower Bound	Upper Bound
5 min	Bupivacaine	Fentanyl	-.914	.577	.290	-2.35	.52
		Ketamine	-1.571*	.577	.028	-3.01	-.14
	Fentanyl	Bupivacaine	.914	.577	.290	-.52	2.35
		Ketamine	-.657	.577	.525	-2.09	.78
	Ketamine	Bupivacaine	1.571*	.577	.028	.14	3.01
		Fentanyl	.657	.577	.525	-.78	2.09
15 min	Bupivacaine	Fentanyl	1.657	1.827	.664	-2.88	6.20
		Ketamine	5.829*	1.827	.008	1.29	10.37
	Fentanyl	Bupivacaine	-1.657	1.827	.664	-6.20	2.88
		Ketamine	4.171	1.827	.079	-.37	8.71
	Ketamine	Bupivacaine	-5.829*	1.827	.008	-10.37	-1.29
		Fentanyl	-4.171	1.827	.079	-8.71	.37

4.7.6 PACU SPO2

Table (30) showed that the**SPO2**of Bupivacaine group was statistically significant ($p < 0.05$) in compared with the **SPO2**of both group Fentanyl &ketamine at 1minutes interval. Bupivacaine 99.7 (±0.6), fentanyl 98.9 (±1.1) and ketamine 98.8 (±1.2) ($p = 0.001$). There were also Bupivacaine

group statistically significant differences in compared with ketamine at 5 minutes bupivacaine 99.4 (±0.8), fentanyl 98.9 (±1.1) and ketamine 98.8(±1.0) (p = 0.018).

Table 30: PACU SPO^2 among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		**Fentanyl**		**Ketamine**			
PACU SPO^2	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
1 min	99.7	0.6	98.9	1.1	98.8	1.2	7.65	**.001**
5 min	99.4	0.8	98.9	1.1	98.8	1.0	4.20	**.018**
10 min	99.0	1.1	98.9	0.9	98.7	1.1	.496	.610
15 min	99.1	0.9	98.8	1.0	98.6	1.1	2.44	.092

Table (31) the post hoc multiple comparisons reveled that, SPO^2 of the Bupivacaine group was statistically significant (p value < 0.05) and higher than the SPO^2 of the two other groups (Fentanyl & Ketamine) at 1stminute. And, at 15th minute the Bupivacaine group was statistically significant (p value < 0.05) and higher than the SPO^2 of the Ketamine.

Table 31: post hock multiple compression for PACUSPO^2 among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
PACU SPO^2 %						Lower Bound	Upper Bound
1 min	Bupivacaine	Fentanyl	.800*	.240	.005	.20	1.40
		Ketamine	.829*	.240	.004	.23	1.43
	Fentanyl	Bupivacaine	-.800*	.240	.005	-1.40	-.20
		Ketamine	.029	.240	.993	-.57	.63
	Ketamine	Bupivacaine	-.829*	.240	.004	-1.43	-.23
		Fentanyl	-.029	.240	.993	-.63	.57
5 min	Bupivacaine	Fentanyl	.543	.228	.064	-.02	1.11
		Ketamine	.600*	.228	.035	.03	1.17
	Fentanyl	Bupivacaine	-.543	.228	.064	-1.11	.02
		Ketamine	.057	.228	.969	-.51	.62
	Ketamine	Bupivacaine	-.600*	.228	.035	-1.17	-.03
		Fentanyl	-.057	.228	.969	-.62	.51

4.7.7 PACU TEMP

Table (32) indicates that there was statistically significant difference at the level ($p < 0.05$) at 10 minutes interval. Bupivacaine 36.6 (±0.2), fentanyl 36.5 (±0.1) and ketamine 36.6 (±0.3) ($p = 0.011$).The Fentanyl group was the one which made the statistically significant difference at the PACU tenth minute compared with the ketamine group. As well as at the fifteenth minute with both the other two (Bupivacaine and Ketamine) groups 36.5 (±0.1), fentanyl 36.6 (±0.1) and ketamine 36.6 (±0.1) ($p = 0.008$).

Table 32: PACU TEMP among the three groups (Bupivacaine, Fentanyl, &Ketamine).

			Group					
	Bupivacaine		Fentanyl		Ketamine			
PACU TEMP	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
1 min	36.6	0.2	36.6	0.1	36.7	0.2	1.934	.150
5 min	36.6	0.1	36.5	0.1	36.6	0.1	1.095	.338
10 min	36.6	0.2	36.5	0.1	36.6	0.3	3.945	**.022**
15 min	36.6	0.1	36.5	0.1	36.6	0.1	5.103	**.008**

Table (33) the post hoc multiple comparisons showed that, temperature of the Fentanyl group was the one which made the statistically significant difference (p value < 0.05) at the PACU tenth minute compared with the ketamine group ,as well as at the fifteenth minute with both the other two (Bupivacaine and Ketamine groups)(p value < 0.05).

Table 33: post hock multiple compression for PACU temperature among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
PACU temperature						Lower Bound	Upper Bound
10 min	Bupivacaine	Fentanyl	.0829	.0455	.196	-.030	.196
		Ketamine	-.0429	.0455	.643	-.156	.070
	Fentanyl	Bupivacaine	-.0829	.0455	.196	-.196	.030
		Ketamine	-.1257*	.0455	.025	-.239	-.013
	Ketamine	Bupivacaine	.0429	.0455	.643	-.070	.156
		Fentanyl	.1257*	.0455	.025	.013	.239
15 min	Bupivacaine	Fentanyl	.0943*	.0331	.020	.012	.176
		Ketamine	.0057	.0331	.985	-.076	.088
	Fentanyl	Bupivacaine	-.0943*	.0331	.020	-.176	-.012
		Ketamine	-.0886*	.0331	.031	-.171	-.006
	Ketamine	Bupivacaine	-.0057	.0331	.985	-.088	.076
		Fentanyl	.0886*	.0331	.031	.006	.171

4.7.8 PACU complications among the three groups (Bupivacaine, Fentanyl, and Ketamine)

4.7.8.1 PACU bradycardia

There were no cases complicated with bradycardia during the postoperative period, and thus there was no difference between the groups *(P*>0.05; Table34).

4.7.8.2 PACU hypotension

During the postoperative period, 1/35 cases in bupivacaine group (2.9%) and 1 / 35 cases in fentanyl group (2.9%), and1/35 cases in ketamine group were complicated with hypotension. There was no significant differences between the groups (P = 1; Table 34).

4.7.8.3 PACU headache

There were no cases complicated with headache during the postoperative period, and thus there was no difference between the groups *(P*>0.05; Table34).

4.7.8.4 PACU pain (Incidence and Intensity)

During the postoperative period, 1 out of 35 cases in bupivacaine (2.9%)and2 out of 35 cases in ketamine group(5.7%) and no cases in fentanyl were complicated by pain; there was no difference between the groups. Pain intensity was not different between the groups (*P* ≥0.05; Table34).

4.7.8.5 PACU pruritus

There were no cases complicated with pruritus during the postoperative period, and thus there was no difference between the groups *(P*>0.05; Table34).

4.7.8.6 PACU shivering

During the postoperative period, 1 out of 35 cases (2.9%)in bupivacaine group ,3 out of 35fentanyl (8.6%) and 2 out of 35 cases (5.7%) in ketamine group were complicated by shivering (P = 0.58). The fentanyl group had more intense postoperative shivering compared to other group (P = 0.58; Table 34).

4.7.8.7 PACU nausea

During the postoperative period, 1 out of 35 cases (2.9%) in bupivacaine group, and no cases in the other two group were complicated by nausea and thus there was no difference between the groups (P = 0.36;Table 34).

4.7.8.8 PACU vomiting

There were no cases complicated with vomiting during the postoperative period, and thus there was no difference between the groups *(P*>0.05; Table34).

4.7.8.9 PACU respiratory depression

There were no cases complicated with respiratory depression during the postoperative period, and thus there was no difference between the groups *(P*>0.05Table 34).

Table 34: PACU complications among the three groups (Bupivacaine, Fentanyl, &Ketamine)

			Group				
		Total	**Bupivacaine**	**Fentanyl**	**Ketamine**	X^2	**Sig.**
Bradycardia	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	-
Hypotension	No	102 (97.1%)	34(97.1%)	34(97.1%)	34(97.1%)	0.00	1.0
	Yes	3 (2.9%)	1(2.9%)	1(2.9%)	1(2.9%)		
Headache	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	-
Pain	0	102(97.1%)	34(97.1%)	35(100.0%)	33(94.3%)	6.05	.19
	6	1(1%)	1(2.9%)	0(0.0%)	0(0.0%)		
	7	2(1.9%)	0(0.0%)	0(0.0%)	2(5.7%)		
Pruritus	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	NA
Shivering	No	99 (94.3%)	34(97.1%)	32(91.4%)	33(94.3%)	1.06	.58
	2*	6(5.7%)	1(2.9%)	3(8.6%)	2(5.7%)		
Use Meperidine	No	99 (94.3%)	34(97.1%)	32(91.4%)	33(94.3%)	1.06	.58
	Yes	6(5.7%)	1(2.9%)	3(8.6%)	2(5.7%)		
Nausea	No	104(99.0%)	34(97.1%)	35(100.0%)	35(100.0%)	2.01	0.36
	Yes	1(1.0%)	1(2.9%)	0(0.0%)	0(0.0%)		
Vomiting	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	NA
Respiratory Distress	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	NA

Shivering 2*: Muscular activity in more than one muscle group but not generalized shivering

NA: not applicable

Table (35) after surgery, the patients were asked to rate their satisfactionon a 4-point Likert scale. The results showed that there is a statistically significant (p value= 0.011) difference between the three groups (Bupivacaine, Fentanyl, and Ketamine).This result indicates higher satisfaction and better comfort felt by participants in fentanyl group throughout the cesarean section surgery.

Table 35: Patient satisfaction of anesthesia among the three groups (Bupivacaine, Fentanyl, &Ketamine).

			Group				
		Total	**Bupivacaine**	**Fentanyl**	**Ketamine**	X^2	**Sig.**
Patient satisfaction of anesthesia	Mild	2(1.9%)	2(5.7%)	0(0.0%)	0(0.0%)	12.9	0.011
	Moderate	60(57.1%)	18 (51.4%)	15(42.9%)	27(77.1%)		
	Very	43(41.0%)	15(42.9%)	20(57.1%)	8(22.9%)		

Table (36) the post hoc multiple comparisons, revealed that the Fentanyl group was higher and statistically significant compared with the ketamine group ($p<0.05$).

Table 36: post hock multiple compression for patient satisfaction of anesthesia among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
patient satisfaction of anesthesia						Lower Bound	Upper Bound
	Bupivacaine	Fentanyl	-.200	.123	.270	-.51	.11
		Ketamine	.143	.123	.511	-.16	.45
	Fentanyl	Bupivacaine	.200	.123	.270	-.11	.51
		Ketamine	.343*	.123	.023	.04	.65
	Ketamine	Bupivacaine	-.143	.123	.511	-.45	.16
		Fentanyl	-.343*	.123	.023	-.65	-.04

4.8 Floor Hemodynamic parameters among the three groups

4.8.1 Floor Systolic blood pressure

In table (37) was shown that the average systolic blood pressure at 3hr in the bupivacaine group was 116.6 (±5.9), fentanyl 113.5 (±5.9) mmHg, and ketamine group113.0 (±6.7) which was statistically significant (p = 0..037) and higher than the systolic pressure of the other groups.

Table 37: Floor Systolic blood pressure among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		Fentanyl		Ketamine			
Floor Systolic BP	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
30 min	111.2	5.5	111.5	7.5	110.6	5.9	.207	.813
1 hr.	113.1	9.2	112.6	7.8	109.3	6.3	2.415	.094
2 hr.	113.3	6.7	111.8	6.9	111.0	7.2	1.035	.359
3 hr.	116.6	5.9	113.5	5.9	113.0	6.7	3.402	**.037**
4 hr.	118.1	6.8	117.0	6.7	114.7	7.1	2.241	.112

Table (38) Post hoc comparisons showed that 3rd hour floor systolic blood pressure in the Bupivacaine group was statistically significant ($p<0.05$) compared with the systolic pressure of the Ketamine group.

Table 38: post hoc multiple compression forfloor Systolic blood pressure among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
floor Systolic blood pressure (mmHg)						Lower Bound	Upper Bound
3 hour	Bupivacaine	Fentanyl	3.057	1.480	.124	-.62	6.73
		Ketamine	3.571	1.480	.059	-.11	7.25
	Fentanyl	Bupivacaine	-3.057	1.480	.124	-6.73	.62
		Ketamine	.514	1.480	.941	-3.16	4.19
	Ketamine	Bupivacaine	-3.571	1.480	.059	-7.25	.11
		Fentanyl	-.514	1.480	.941	-4.19	3.16

4.8.2 Floor diastolic blood pressure

In table (39) was shown that the average diastolic blood pressure at 4hr in the bupivacaine group, bupivacaine 70.8 (±6), fentanyl 69.8 (±7.3) mmHg, and ketamine group 64.9 (±12.3) which was statistically significant (p = 0..016) in compared with the diastolic pressure of the other groups.

Table 39: Floordiastolic blood pressure among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		**Fentanyl**		**Ketamine**			
Floor Diastolic BP	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
30 min	66.2	5.4	64.3	7.6	63.6	5.8	1.56	.214
1 hr.	66.1	6.6	64.9	9.6	62.3	7.1	2.12	.125
2 hr.	66.8	7.2	65.7	8.1	64.1	7.0	1.11	.333
3 hr.	68.3	5.5	67.4	6.3	64.8	7.5	2.72	.070
4 hr.	70.8	6.0	69.8	7.3	64.9	12.3	4.27	**.016**

In table (40) Post hoc comparisons showed that 4th hour floor diastolic blood pressure in the Bupivacaine group was statistically significant ($p<0.05$) compared with the diastolic blood pressure of the Ketamine group.

Table 40: post hoc multiple compression for thefloor diastolic blood pressure among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
floor diastolic blood pressure (mmHg)						Lower Bound	Upper Bound
4 hour	Bupivacaine	Fentanyl	.971	2.147	.903	-4.36	6.30
		Ketamine	5.857*	2.147	.028	.52	11.19
	Fentanyl	Bupivacaine	-.971	2.147	.903	-6.30	4.36
		Ketamine	4.886	2.147	.080	-.45	10.22
	Ketamine	Bupivacaine	-5.857*	2.147	.028	-11.19	-.52
		Fentanyl	-4.886	2.147	.080	-10.22	.45

4.8.3 Floor HR

Table (41) showed that there was no significant different between the three group (Bupivacaine, Fentanyl, and Ketamine) in the measure of heart rate at the 0.05 level (p>0.05).

Table 41: Floor HR among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		Fentanyl		Ketamine			
Floor HR at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
30 min	84.77	5.472	83.83	7.961	86.14	11.835	.609	.546
1 hr.	85.43	5.632	84.31	6.812	84.66	10.070	.190	.827
2 hr.	83.00	4.917	81.57	5.627	84.94	8.146	2.46	.090
3 hr.	82.57	4.889	81.43	4.761	84.66	8.471	2.37	.098
4 hr.	81.40	5.766	81.34	5.826	82.97	6.771	.793	.455

4.8.4 Floor RR

Table (42) showed that there was statistically significant different between the group in the measure of respiratory rate at the 0.05 level. The ketamine group at 30minutes was statistically significant differences in compared with the respiratory rate of both group (bupivacaine & fentanyl), bupivacaine 15.86 (±1.7), fentanyl 15.86(±1.478) and ketamine 16.77 (1.003) (p = 0. 010). There were alsostatistically significant differencesat 2hour the respiratory rate in ketamine group when compared with the RR of fentanyl groups,bupivacaine 16.06 (±1.187), fentanyl 15.23 (±1.646) and ketamine 16.31 (1.827) (p = 0..013).

Table 42: Floor RR among the three groups (Bupivacaine, Fentanyl, &Ketamine).

	Group							
	Bupivacaine		**Fentanyl**		**ketamine**			
Floors at:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
30 min	15.86	1.700	15.86	1.478	16.77	1.003	4.81	**.010**
1 hr.	15.43	1.754	15.49	1.337	16.23	1.767	2.61	.078
2 hr.	16.06	1.187	15.23	1.646	16.31	1.827	4.53	**.013**
3hr	16.09	1.634	15.40	1.576	16.09	1.502	2.22	.114
4 hr.	15.17	1.706	15.83	1.599	15.80	1.568	1.82	.166

Table (43) the post hoc multiple comparisons showed that, respiratory rate of the Ketamine group was statistically significant (p value < 0.05) and higher than the RR of the Bupivacaine and Fentanyl groups at 30th minute, and Ketamine group was statistically significant (p value < 0.05) and higher than the RR of the Fentanyl group at 2nd hour.

Table 43: post hock multiple compression for the Floor respiratory rate among the three groups (Bupivacaine, Fentanyl, &Ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
Floor respiratory rate						Lower Bound	Upper Bound
30 min	Bupivacaine	Fentanyl	.000	.340	1.000	-.85	.85
		Ketamine	-.914*	.340	.031	-1.76	-.07
	Fentanyl	Bupivacaine	.000	.340	1.000	-.85	.85
		Ketamine	-.914*	.340	.031	-1.76	-.07
	Ketamine	Bupivacaine	.914*	.340	.031	.07	1.76
		Fentanyl	.914*	.340	.031	.07	1.76
2 hour	Bupivacaine	Fentanyl	.829	.377	.094	-.11	1.76
		Ketamine	-.257	.377	.793	-1.19	.68
	Fentanyl	Bupivacaine	-.829	.377	.094	-1.76	.11
		Ketamine	-1.086*	.377	.019	-2.02	-.15
	Ketamine	Bupivacaine	.257	.377	.793	-.68	1.19
		Fentanyl	.0886*	.0331	.031	.006	.171

4.8.5 Floor SPO2

Table (44) showed that there was no significant different between the three group (Bupivacaine, Fentanyl, and Ketamine) in the measure of SPO2 at the 0.05 level (p>0.05).

Table 44: Floor SPO^{2}at among the three groups (Bupivacaine, Fentanyl, &ketamine).

	Group							
	Bupivacaine		Fentanyl		Ketamine			
Floor SPO^{2}at:	Mean	SD	Mean	SD	Mean	SD	F	Sig.
30 min	99.37	.731	99.20	.719	99.37	.731	.648	.525
1 hr.	99.23	.731	99.23	.646	99.31	.718	.175	.839
2 hr.	98.89	.758	98.80	.759	98.86	.692	.123	.885
3 hr.	98.83	.954	98.71	.860	98.57	.948	.684	.507
4 hr.	98.74	.919	98.83	.664	98.63	.877	.515	.599

4.8.6 Duration of Sensory, Motor, and Analgesia at floor

4.8.6.1 Duration of sensory block

Table (45) indicates that there were significant differences related to the duration of sensory blockade by minutes at the level ($p \leq 0.05$) in comparison between, bupivacaine 212.2 (±69.6), fentanyl 275.2 (±85.0) and ketamine 212.7(±75.1) ($p = 0.001$).These results mean that patients in the fentanyl group have a longer duration of sensory block with minutes compared to the other groups.

4.8.6.2 Duration of motor block

Table (45) indicates that there were significant differences related to the duration of motor blockade by minutes at the level ($p \leq 0.05$) in comparison between, bupivacaine 143.8 ± (43.7), fentanyl 172.8 (±53.2)

and ketamine 138.6 (±40.3) (p = 0.005).These results mean that patients in the Fentanyl group havea longer duration of motor block with minutes compared to the othergroups.

4.8.6.3 Duration of analgesia

Table (45) indicates that there were significant differences related to the duration of analgesia by minutes at the level ($p \leq 0.05$) in comparison between, bupivacaine 205.3 (±65.4), fentanyl 273.7 (±85.4) and ketamine 207.7 (±74.6) (p = 0.000).These findings indicate that patients in the Fentanyl group have a longer duration of analgesia in terms of minutes than patients in the other groups.

Table 45: Duration Sensory, Motor, and Analgesia by minute's comparison between the three groups (Bupivacaine, Fentanyl, &ketamine) Data is presented by Mean.

	Group							
	Bupivacaine		Fentanyl		Ketamine			
Duration:	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**F**	**Sig.**
Sensory(min)	212.2	69.6	275.2	85.0	212.7	75.1	7.782	.001
Motor(min)	143.8	43.7	172.8	53.2	138.6	40.3	5.595	.005
Analgesia(min)	205.3	65.4	273.7	85.4	207.7	74.6	9.221	.000

Table (46) the post hoc multiple comparisons revealed that, fentanyl group was statistically significant (p value < 0.05) and had a longer duration than the Bupivacaine and ketamine groups of sensory, motor, and analgesia.

Table 46: post hoc multiple comparisons for duration of sensory, motor, and analgesia comparison between the three groups (Bupivacaine, Fentanyl, &ketamine).

Dependent Variable	(I) participant group	(J) participant group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Duration Sensory(min)	Bupivacaine	Fentanyl	-63.000*	18.360	.004	-108.61	-17.39
		Ketamine	-.543	18.360	1.000	-46.15	45.07
	Fentanyl	Bupivacaine	63.000*	18.360	.004	17.39	108.61
		Ketamine	62.457*	18.360	.004	16.85	108.07
	Ketamine	Bupivacaine	.543	18.360	1.000	-45.07	46.15
		Fentanyl	-62.457*	18.360	.004	-108.07	-16.85
Duration Motor(min)	Bupivacaine	Fentanyl	-29.000*	11.013	.035	-56.36	-1.64
		Ketamine	5.171	11.013	.896	-22.19	32.53
	Fentanyl	Bupivacaine	29.000*	11.013	.035	1.64	56.36
		Ketamine	34.171*	11.013	.010	6.81	61.53
	Ketamine	Bupivacaine	-5.171	11.013	.896	-32.53	22.19
		Fentanyl	-34.171*	11.013	.010	-61.53	-6.81
Duration analgesia(min)	Bupivacaine	Fentanyl	-68.371*	18.070	.001	-113.26	-23.48
		Ketamine	-2.400	18.070	.991	-47.29	42.49
	Fentanyl	Bupivacaine	68.371*	18.070	.001	23.48	113.26
		Ketamine	65.971*	18.070	.002	21.08	110.86
	Ketamine	Bupivacaine	2.400	18.070	.991	-42.49	47.29
		Fentanyl	-65.971*	18.070	.002	-110.86	-21.08

* The mean difference is significant at the 0.05 level.

4.8.7 Floor complications among the three groups (Bupivacaine, Fentanyl, and ketamine)

4.8.7.1 Pruritus

During the floor period, 3 out of 35 cases (8.6%) in fentanyl group and no cases in the other two groups were complicated by Pruritus. There was significant difference regarding the Pruritus between the groups (P<0.046). Thus, fentanyl have highly incidence of Pruritus during the floor period (table; 47).

4.8.7.2 Nausea

During the floor period, 1 out of 35 cases (2.9%) in ketamine group, and no cases in the other two group were complicated by nausea. And thus there was no difference between the groups (P = 0.36table; 47).

4.8.7.3 Vomiting

There were no cases complicated with vomiting during the floorperiod, and thus there was no difference between the groups *(P*>0.05; Table47).

4.8.7.4 Shivering

During the floor period, 1 out of 35 cases (2.9%) in ketaminegroup, 3 out of35 cases in fentanyl group (8.6%)were complicated by shivering. The fentanyl group had more intense floor shivering compared to other group. And thus there was no difference between the groups (P = 0.19; Table 47).

4.8.7.5 Ramsy sedation scale in the floor

During the floor period, 2 out of 35 cases(5.7%) in ketamine group, however no any cases in bupivacaine and fentanyl group. There was no significant difference regarding the ramsy sedation scale between the groups(*P*=0.130; table 47).

4.8.7.6 Amnesia

There were no cases complicated with Amnesia during the floor period,and thus there was no difference between the groups *(P*>0.05; Table47).

4.8.7.7 Agitation

There were no cases complicated with agitation during the floor period, and thus there was no difference between the groups *(P*>0.05; Table 47).

4.8.7.8 Dissociative analgesia

There were no cases complicated with dissociative analgesia during the floorperiod, and thus there was no difference between the groups *(P*>0.05Table 47).

Table 47: Floor complications among the three groups (Bupivacaine, Fentanyl, &ketamine)

			Group				
Floor		**Total**	**Bupivacaine**	**Fentanyl**	**Ketamine**	X^2	**Sig.**
Pruritus	No	102(97.1%)	35(100.0%)	32(91.4%)	35(100.0%)	6.176	.046
	Yes	3(2.9%)	0(0.0%)	3(8.6%)	0(0.0%)		
N&V	No	104(99.0%)	35(100.0%)	35(100.0%)	34(97.1%)	2.019	.364
	Mild	1(1.0%)	0(0.0%)	0(0.0%)	1(2.9%)		
Shivering	No	102(97.1%)	35(100.0%)	33(94.3%)	34(97.1%)	6.05	.195
	3*	1(1.0%)	0(0.0%)	0(0.0%)	1(2.9%)		
	4*	2(1.9%)	0(0.0%)	2(5.7%)	0(0.0%)		
Sedation	2*	103(98.1%)	35(100.0%)	35(100.0%)	33(94.3%)	4.07	.130
	3*	2(1.9%)	0(0.0%)	0(0.0%)	2(5.7%)		
Amnesia	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	NA
Agitation	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	NA
Dissociative analgesia	No	105(100.0%)	35(100.0%)	35(100.0%)	35(100.0%)	-	NA

N&V: nausea and vomiting; **Shivering 3***: Muscular activity in more than one muscle group but not generalized shivering, **4*** Shivering involved the whole body.

Sedation 2*: Cooperative, tranquil, oriented, **3***: Drowsy but responsive to verbal commands.

Table (48) showed that there was a study statistically significantrelated to total analgesia consumption in 24 hours at level ($p<0.05$) in comparison between three group, Bupivacaine 3.68 (.471), Fentanyl 2.17 (.382), Ketamine 2.65 (.481). ($p=0.001$) .Thus, fentanyl has an effect in reduce total analgesia consumption on postoperative.

Table 48: total analgesia consumption in 24 hour.

Variable	Group	N	Mean	SD	Min	Max	F	Sig.
total analgesia consumption in 24 hour (frequency)	Bupivacaine	35	3.68	.471	3.00	4.00	104.6	<.001
	Fentanyl	35	2.17	.382	2.00	3.00		
	Ketamine	35	2.65	.481	2.00	3.00		
	Total	105	2.83	.773	2.00	4.00		

Table (49) showed that there was a study statistically significantrelated to numeric rating scale in 24 hour at level ($p<0.05$) in comparison between three group, Bupivacaine 7.37 (.546), Fentanyl 4.34 (.481), Ketamine 5.94 (.639). ($p=0.001$). Thus, fentanyl has an effect on postoperative pain management (pain intensity).

Table 49: Numeric Rating Scale (NRS) in 24 hour (pain intensity).

Variable	Group	N	Mean	SD	Min	Max	F	Sig.
Numeric Rating Scale (NRS) in 24 hour	Bupivacaine	35	7.37	.546	6.00	8.00	256.55	<.001
	Fentanyl	35	4.34	.481	4.00	5.00		
	Ketamine	35	5.94	.639	5.00	7.00		
	Total	105	5.88	1.360	4.00	8.00		

Chapter Five
Discussion

5.1 Discussion

Spinal anesthesia is a fantastic anesthesia technique and is largely used due to it has many benefits over general anesthesia, such as a lower response to stress, less blood loss, inexpensive, and a lower rate of morbidity and death in high-risk patients. (Gaiser RR., 1997).Can be performed cesarean section under general anesthesia or regional anesthesia. Due to the smaller impact on the airway in the cesarean section, the regional C/S anesthesia is better than the time-based tribute anesthesia. It reduces the risk of aspiration and greater recognition during the entire operation and reduces. Weak uterine contractions are a dangerous complication (Wong CA, 2010). In addition, it is considered a safe and efficient modality for a wide range of operative procedures, although it is not free of risks (Ghani et al., 2015). We also evaluated the length of sensory, motor, and analgesic blockade, as well as the incidence of intraoperative adverse effects...

To our knowledge, this study was the first performed in Palestine to assess the effects of the ketamine plus bupivacaine, fentanyl plus bupivacaine, and bupivacaine alone on Hemodynamic parameters, length of sensory, motor, and analgesic blockade. The remaining 105 patients were included in the research and assigned to one of three groups at random. There were no variations in demographics across the groups. ($P > 0.05$; Table 2). Numerous hemodynamic parameters and other observations were recorded

every 3 min in the first15min then every 5min during the intraoperative period

5.2 Onset of sensory block

The period between the finish of the intrathecal anesthetic injection and the absence of pain at the T10 dermatome was considered the onset of sensory block. (Khezri, Ghasemi and, Mohammadi. 2013) As a result, the current study found statistically significant (p-value< 0.05) differences between the three groups (Bupivacaine, Fentanyl, and Ketamine). And our study revealed that the Fentanyl group had the lowest time in the onset of sensory blocks, made the statistically significant differences in comparing with Bupivacaine and Ketamine groups.The present study's findings are consistent with the findings of the Bogra study, (2005) & Unlugenc et al., (2006), who showed that administering fentanyl in combination with bupivacaine, resulted in a rapid sensory block onset. In addition, Khezri et al. (2013) revealed that combining bupivacaine with ketamine intrathecal delayed the sensory block onset. The result of the current study is in disagreement with Kamal et al., (2014) in day-case surgery showed that when adding ketamine to Bupivacaine The start period of sensory block was shorter in the ketamine group. Moreover, the result of the current study, contrary to Shrestha, Bhattarai, and Shah, (2013), showed that once the addition of preservative-free ketamine leads to rapid sensory block onset.

5.3 Onset of motor block

Onset of motor block: is a time of an injection of study drug till patient unable to flex lower limbs at the hip joint (Sowmya et al., 2016). When compared to the current study results, which showed that the Fentanyl group had the significant lowest mean onset motor block compared to the Bupivacaine and Ketamine groups, these findings do not agree with the findings of Kamal et al. (2014), Who found that ketamine used in combination with hyperbaric bupivacaine in spinal anesthetic reduces the time it takes for a motor block to begin.

5.4 Bradycardia

Bradycardia: defined as heart rate below 50 bpm (Khezri, Ghasemi and, Mohammadi in 2013). In the current study we noted 2 cases of bradycardia, one in ketamine group and one in fentanyl group intraoperative and no any case in postoperative period. Our results are consistent with, Ila Patel et al., (2011) result showed that the incidence of bradycardia are much less after adding ketamine to intrathecal bupivacaine. And with Archana et al., (2017) who concluded that the incidence of bradycardia was reduced when mixing fentanyl plus bupivacaine. In addition, Bogra et al., (2005), which found no significant different in each group in the incidence of bradycardia. The current study showed no significant different regarding the incidence of intra and postoperative bradycardia between groups.

5.5 Hypotension episode

Hypotension was defined as a systolic blood pressure less than 90 mm Hg or 20% lower than the pre-induction level. (Khezri, Ghasemi, and Mohammadi, 2013).The incidence of hypotension is higher in the ketamine 30 patient, 29 in the fentanyl, and 21 in the bupivacaine group intraoperative, postoperatively one patient in the bupivacaine in fentanyl, and one in the ketamine group. That was in contrary to Ila Patel et al., (2011) stated that the incidence of hypotension is much less after adding ketamine to intrathecal bupivacaine. In addition, Srivastava et al., (2004) showed that systolic blood pressure was considerably decreased in the bupivacaine group. The current study found no statistically significant differences in the occurrence of during surgery and after surgery hypotension across groups. Siddik-Sayyed et al., (2002)showed that individuals who got intrathecal fentanyl had a significantly reduced occurrence of hypotension.

5.6 Pruritus

In this research, no incidence of pruritus intraoperative and postoperative in each group, although the current result correlated with Archana et al. (2017), showed no patients in the bupivacaine group developed pruritus. However, one patient in the bupivacaine plus fentanyl group did. Moreover, the study by Bogra et al. (2005) observed no incidence of pruritus. And disagreement with Balzarena et al. (1992), the study found that individuals who got bupivacaine alone less in the occurrence of

pruritus than those who obtained bupivacaine with fentanyl. In addition, Himabindu et al ., (2015) showed that in the fentanyl group, one patient complained of noticed mild itching, possibly due to fentanyl adverse effects., and in contrary with Ali et al., (2018) result that Patients who received 25mic fentanyl had a higher incidence of pruritus. Also, Shrestha et al .,(2013) The occurrence of pruritus was significantly higher in the hyperbaric bupivacaine 0.5 percent with twenty-five microgram fentanyl than in the hyperbaric bupivacaine 0.5 percent combined to twenty-five milligram preservative-free ketamine.

5.7 Shivering

In the present study no significant difference regarding the incidence of shivering intraoperative and postoperative in each group. These findings are consistent with Himabindu et al., in (2015 & Kang et al.,(1998), study which stated lower incidences of shivering was observed in group fentanyl combined with bupivacaine or bupivacaine alone. In addition in the same direction with Bogra et al., (2005) which found that the incidence of shivering reduces considerably in bupivacaine and fentanyl group.

5.8 Nausea and vomiting

The current study showed eight patients were nauseated in the Bupivacaine group, five in the fentanyl group, two in the ketamine group, which consider mild, and two cases, one in bupivacaine, one in ketamine, were considered moderate, however. No patient was vomited in the three groups. However, in correlation with Archana & Veena (2017), they observed that

nausea and vomiting were reported in two patients in the bupivacaine plus fentanyl group, whereas similar symptoms were observed in one patient, the bupivacaine alone group, with no statistical difference between groups**.** Bogra et al. (2005) and Dahlgren et al. (1997) found that when combined bupivacaine plus fentanyl, the occurrence of nausea and vomit were reduced. In contrast with Himabindu et al. (2015), no patients complained of nausea and vomiting. And to Ila Patel et al. (2011), the ketamine group has a higher occurrence of nausea and vomiting.

5.9 Headache

There was no intraoperative or postoperative headache in any group in the current research. The current result isin correlation with Khezri et al. (2016) and Unlugenc et al. (2006) result stated that there were no significant differences regarding headaches.

5.10 Sedation

Sedation as side effect was recorded in ketamine group. The Ramsay Sedation Scale was used in the current study to assess the degree of sedation .It was shown that there were significant different between group, this result was in accordance with the study results conducted by Shrestha et al., (2013)& Gunastý., (2007) which conduct sedation rating was greater in group ketamine; in addition Ila Patel et al. (2011) incidence of sedation is more in theketaminegroup.

5.11 Respiratory depression

In the present study, no significant difference regarding the incidence of respiratory depression intraoperative and postoperative between the groups that contained five participants (three in bupivacaine, one in ketamine, and one in fentanyl). Our results are consistent with Bogra et al., (2005), result who stated that respiratory depression did not occur with fentanyl. Himabindu et al., (2015), Showed that there were no significant occurrences of respiratory distress in any group (bupivacaine, fentanyl combined bupivacaine), which was consistent with the results of (Kang et al., 1998).

5.12 Duration of sensory block

The duration of the sensory blockade is the time it takes from the beginning of sensory blockage to sensory recovery, at thoracic 10 (Sowmya, Ravi, Sujatha, Dinesh, & Kavya, 2016).The period of sensory block significantly longer there in the fentanyl group than in the ketamine & bupivacaine groups. When compared to the Bupivacaine and Ketamine groups, the Fentanyl group showed the longest sensory block duration. Ali et al., (2018), a result which who stated that patients who received 25 mics of fentanyl plus bupivacaine extended sensory block. In addition, with Kamal & El-Fawy., (2014), the study showed that ketamine administered in conjunction with hyperbaric bupivacaine in regional anesthesia led to a lower length of the blockage. However, contrary to Khezri, (2013), which

concluded that ketamine combined with bupivacaine had a long time of sensory block than bupivacaine alone.

5.13 Duration of motor block

The duration of motor block in the fentanyl group has the highest time than the ketamine and bupivacaine group. And our study revealed that the Fentanyl group had the highest duration of motor block in comparison with Bupivacaine and Ketamine groups. That in correlation with Ali et al., (2018), who found that Patients received 25 mics of fentanyl plus bupivacaine extended motor block. In addition, Kamal and El-Fawy., (2014) concluded that ketamine given with bupivacaine in spinal anesthesia resulted in a reduced time period of blockage and a lower time to complete motor power. However, in contrast with Khezri et al., (2013), the result found the injection of intrathecal ketamine plus spinal bupivacaine extended the period time of the block in the motor. And Govindan et al., (2001), in lower abdominal surgery, showed extended in the motor block by intrathecal ketamine.

5.14 Duration of analgesia

Duration of analgesia: is a time from spinal solution injection till first complain of pain ≥4 in VAS score and need for analgesic drugs (Venkata et al., 2015), in our study show an increased duration of analgesia in the fentanyl group than the ketamine and bupivacaine group. This finding is in agreement with Khezri et al., (2016) result, which states that the request analgesic was once higher in group ketamine as compared to Fentanyl and

bupivacaine groups. Also, our study corresponds with Shrestha et al., (2013) & Unlugenc et al., (2006); it was shown that the period of analgesia was higher in the Fentanyl group compared to the ketamine group. Moreover, Weigl et al.,(2016) result found that administer intrathecal fentanyl with spinal anesthesia provides powerful intraoperative analgesia and decreases opioid intake, and increase the duration of analgesia call after C/S, Archana et al., (2017) concluded that intrathecal fentanyl plus bupivacaine increased duration of postoperative analgesia and improved intraoperative analgesia. However, in contrast with Khezri et al., (2013), the study shows that in managed elective cesarean birth, ketamine intrathecally combined with bupivacaine extended time to the primary analgesic request compared to bupivacaine alone.

5.15 Rescue analgesia needed

Regarding postoperative rescue analgesics needed, we found significant differences in all groups. Fentanyl is effective and fewer analgesic requirements in the postoperative period. The result of the current study is in correlation with the study results conducted by Weigl, (2016); the present study's findings are consistent with those of Weigl (2016), who showed that adding fentanyl intrathecally to bupivacaine reduced analgesic intake in the fentanyl group compared to the placebo group with bupivacaine. In addition, Idowu OA et al. (2011) found that combining fentanyl with bupivacaine intrathecally for elective cesarean delivery decreased analgesic need in the early postoperative period. However, In

contrast to Khezriet al. (2013), total analgesic consumption in the 24 hours following operative procedure reduced in the ketamine institution compared to the bupivacaine group.

5.16 pain intensity (NRS)

Regarding postoperative pain intensity (NRS), we found significant differences in all groups. Fentanyl is effective and less pain score in the postoperative period. The result of the current study is in correlation with the study results conducted by Bogra, (2005), which showed that postoperative pain relief by way of adding fentanyl. In addition, Idowu OA et al, in (2011), showed that when add fentanyl to bupivacaine intrathecally for elective cesarean section will reduce pain intensity in postoperative period.

5.17 Conclusion

In spinal anesthesia for the elective cesarean segment, 25 mic fentanyl to 10mg bupivacaine showed faster onset of sensory and motor block and better hemodynamic stability with minimal side effects, longer sensory and motor block duration, and duration of analgesia, decreased total analgesic consumption and reduce pain intensity in the post-operative period.and higher patient satisfaction. Furthermore, the incidence of sedation is higher in the ketamine group.

5.18 Recommendation

We recommend that if a future study on ketamine for CS patients under spinal anesthesia is conducted, the Apgar score be used to demonstrate whether ketamine has an effect on the newborn baby.

5.19 Limitation

- Not all anesthesiologist accepted to use ketamine in spinal anesthesia

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Appendix

Appendix 1

Consent form

نموذج طلب موافقة على المشاركة في بحث علمي

اسم الباحث: محمد احمد سليمان جوري طالب ماجستير تمريض تخدير – جامعة النجاح الوطنية

د.عايدة القيسي– عميد كليه التمريض والقباله – منسق برنامج ماجستير تمريض تخدير – جامعه النجاح الوطنية

د. توفيق ابو عيشة –أخصائي تخدير وعناية مكثفة

مكان إجراء البحث: مستشفى العربي التخصصي / نابلس

أنا الموقع أدناها: ... ...

اقر انه تم شرح طلب المشاركة في مشروع البحث العلمي بعنوان (المقارنة ما بين دواء الكيتامين مع البوفاكين والفينتانيل مع البوفكين في التخدير النصفي عند النساء الخاضعات لعمليات الولادة القيصرية)

لقد أعطيت نسخة من توجيهات الطلب / المشروع واقبل المشاركة في المشروع. لقد تلقيت معلومات شفهية وخطية عن الدراسة، وأنا أدرك أن مشاركتي طوعية. وأنا على علم بأنه في أي وقت، دون الحاجة إلى شرح، يمكنني أن انسحب من الدراسة إذا كنت ارغب في ذلك. إذا لزم الأمر يمكنني الاتصال لمقابلة جديدة أو توضيح ..

توقيع المشترك .....

التاريخ

Appendix 2

Data collection Sheet

AN-NAJAH NATIONAL UNIVERSITY

MASTER OF ANESTHESIOLOGY

RESEARCHER :

Date and time: _____ **Participant # ON LIST: ----------**

1. Patient profile (Demographic data)	
Age (years)	
Weight (Kg)	
Parity	
Gravida	
Gestational age	
ASA	
History of spinal C/S	

Parameter	Time \min
Time from spinal blockade\ Incision (after assuring block)	
Onset time of motor block	
Onset time of sensory block	

2. Intraoperative hemodynamic						
Time	**BP+(MAP)**	**HR**	**RR**	**SPO2**	**ECG**	**T°-**
Baseline V/S	/ ( )					
Induction time	/ ( )					
3 min after	/ ( )					
6 min after	/ ( )					
9 min after	/ ( )					
15 min after	/ ( )					
20 min after	/ ( )					
25 min after	/ ( )					
30 min after	/ ( )					
35 min after	/ ( )					
40 min after	/ ( )					
45 min after	/ ( )					

3. Intraoperative Side effect table				
Parameter	**Yes**	**No**	**Frequency or value**	**Required treatment**
Bradycardia heart rate < 50 will treated by 0.5 mg atropine.				
Hypotension SBP<90 mm HG Will treat by and 50-100 mic neosynephrine heart rate ≥ 70 bpm) or ephedrine 5–10 mg (heart rate < 70 bpm).				
Pain scale (0-10)				
Pruritus				
Shivering (0-4)				
Severity of Nausea |Likert-type scale (0 no nausea, 6 intolerable) none, mild (1-2), moderate (3-4) or severe (5-6)≥3 will treated by 10 mg metoclopramide iv, if no response will give Ondansetron 4mg				
Vomiting Vomiting ≥2 times will be treated by 10 mg metoclopramide iv if no response will give Ondansetron 4mg				
Respiratory depression, respiratory rate < 10.				
Ramsay Sedation Scale (1-6)				

PACU v/s	BP+(MAP)	HR	RR	SPO2	ECG	TEMP
1 min	/ ( )					
5 min	/ ( )					
10 min	/ ( )					
15 min	/ ( )					

4. Post-operative Side effect: In PACU

Parameter	Yes	No	Frequency or value	Required treatment
Bradycardia heart rate < 50 will treated by 0.5 mg atropine.				
Hypotension SBP<90mm HG Will treat by and 50-100 mic neosynephrine heart rate ≥ 70 bpm) or ephedrine 5–10 mg (heart rate < 70 bpm).				
Headache				
Pain scale (0-10) Morphine 2.5 mg I.V will give when the patient got pain ≥4 on NRS				
Pruritus				
Shivering (**0–4 scale)**				
Use of IV meperidine to treat PAS				
Nausea Likert-type scale (0 no nausea, 6 intolerable).				
Vomiting : ≥ 2 times				
Respiratory Depression, RR < 10.				
Satisfaction: Likert-type scale (0-4) 0:Very unsatisfied 4: Very satisfied				
Need of Post op. intravenous fluids				

4- hemodynamic in the floor					
Time	**HR**	**RR**	**SPO_2**	**ECG**	**Bpm-**
30 min after					
1hr after					
2hr after					
3hr after					
4hr after					

Block table: Post-operative:

Parameters	**Time**
Sensory recovery	
Motor recovery	
duration of sensory blockade **time from sensory onset to sensory recovery**	
duration of motor blockade **time from motor onset to motor recovery**	
Time to First rescue of analgesia	
Duration on analgesia **Time from successful spinal puncture to first rescue of analgesia**	

5- side effect of spinal block after cs in the floor					
Side effect	**Yes**	**No**	**Frequency**	**Required Treatment**	**Time**
Itching					
Nausea ,vomiting					
Shivering					
Ramsay Sedation					
Amnesia					
Agitation					
Dissociative analgesia					

Appendix 3

ASA physical status classification system for assessing a patient before surgery

I. Normal healthy patient.

II. Patient with mild systemic disease.

III. Patient with sever systemic disease.

IV. Patient with severe systemic that is a constant threat to life.

V. Mori bund patient who is not expected to survive without the operation.

VI. Patient declared brain dead who see organs are to be harvested for donor purposes.

Appendix 4

The randomization list

The randomization list											
N	**Group**	**N**	**Group**	**N**	**Group**	**N**	**Group**	**N**	**Group**	**N**	**Group**
1	B	**21**	K	**41**	B	**61**	F	**81**	B	**101**	K
2	K	**22**	K	**42**	K	**62**	B	**82**	K	**102**	K
3	F	**23**	F	**43**	K	**63**	B	**83**	B	**103**	B
4	F	**24**	F	**44**	B	**64**	B	**84**	B	**104**	F
5	K	**25**	F	**45**	B	**65**	B	**85**	K	**105**	K
6	K	**26**	F	**46**	B	**66**	B	**86**	B		
7	F	**27**	F	**47**	F	**67**	F	**87**	K		
8	K	**28**	K	**48**	F	**68**	F	**88**	K		
9	F	**29**	F	**49**	B	**69**	F	**89**	B		
10	B	**30**	K	**50**	B	**70**	F	**90**	B		
11	F	**31**	F	**51**	K	**71**	F	**91**	K		
12	K	**32**	F	**52**	F	**72**	F	**92**	K		
13	K	**33**	F	**53**	B	**73**	B	**93**	B		
14	B	**34**	F	**54**	K	**74**	B	**94**	B		
15	F	**35**	F	**55**	B	**75**	K	**95**	K		
16	K	**36**	B	**56**	B	**76**	B	**96**	B		
17	F	**37**	B	**57**	K	**77**	B	**97**	B		
18	K	**38**	K	**58**	F	**78**	K	**98**	K		
19	K	**39**	F	**59**	F	**79**	K	**99**	K		
20	K	**40**	F	**60**	F	**80**	B	**100**	K		

Appendix 5

Bromage Scale

Grade	Criteria	Degree of block
0	Free movement of legs and feet	Nil (0%)
I	Just able to flex knees with free movement of feet	Partial (33%)
II	Unable to flex knees, but with free movement of feet	Almost complete (66%)
III	Unable to move legs or feet	Complete (100%)

Appendix 6

Ramsay sedation score

No.	Description
1	Anxious, agitated
2	Cooperative, tranquil, oriented
3	Drowsy but responsive to verbal commands
4	Asleep, brisk response to stimulus
5	Asleep, sluggish response to stimulus
6	No response

Appendix 7

IRB approval Letter

An-Najah
National University
Health Faculty of medicine&
Sciences
IRB

جامعة النجاح
الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref : Mas , May /20/14

IRB Approval Letter

Study Title:

"Comparative Study of Hyperbaric Bupivacaine Plus Ketamine vs Bupivacaine Plus Fentanyl for Spinal Anaesthesia During Caeserean Section. A prospective, randomized, double-blind, controlled study"

Submitted by:
Mohammed Ahmad Joori

Supervisor:
Dr. Aidah Alkaissi, Dr. Tawfiq Abu Aisha

Date Approved:
28th May 2020

Your Study Title **"Comparative Study of Hyperbaric Bupivacaine Plus Ketamine vs Bupivacaine Plus Fentanyl for Spinal Anaesthesia During Caeserean Section. A prospective, randomized, double-blind, controlled study"** was reviewed by An-Najah National University IRB committee and was approved on **28th May 2020.**

Hasan Fitian, MD

IRB Committee Chairman

An-Najah National University

IRB

جامعة النجاح الوطنية

كلية الدراسات العليا

المقارنة ما بين دواء الكيتامين مع البوفاكين والفينتانيل مع البوفاكين في التخدير النصفي عند النساء الخاضعات لعمليات الولادة القيصرية: دراسة عشوائية مراقبة مزدوجة التعمية

إعداد

محمد أحمد جوري

إشراف

د. عايدة القيسي

د. توفيق أبو عيشة

قدمت هذه الرسالة استكمالاً لمتطلبات الحصول على درجة الماجستير في برنامج تمريض التخدير، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس– فلسطين.

2021

المقارنة ما بين دواء الكيتامين مع البوفاكين والفينتانيل مع البوفاكين في التخدير النصفي عند النساء الخاضعات لعمليات الولادة القيصرية: دراسة عشوائية مراقبة مزدوجة التعمية

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إشراف

د. عايدة القيسي

د. توفيق أبو عيشة

الملخص

الخلفية: التخدير النخاعي هو الطريقة المفضلة لتخدير الولادة القيصرية، ولكن إدارة الألم بعد الجراحة هي أولوية رئيسية للنساء اللواتي يخضعن للولادة القيصرية. يرتبط عدم كفاية إدارة الألم في فترة ما بعد الجراحة الحادة بالألم المستمر وزيادة استخدام المواد الأفيونية وتأخر الانتعاش الوظيفي وزيادة اكتئاب ما بعد الولادة. في هذه الدراسة، قمنا بتقييم فعالية الكيتامين داخل النخاع مقارنة بالفنتانيل داخل النخاع، على مدة استخدام التسكين لتقليل المواد الأفيونية بعد الجراحة في العملية القيصرية الاختيارية.

الطريقة: هذه الطريقة مزدوجهالتعميه، وتم توزيع 105 بشكل عشوائي الى ثلاث مجموعات المجموعة الاولى تلقت 10 ملغم من دواء البوبافكين ممزوج مع دواء الفينتانيل، المجموعة الثانية تلقت 10 ملغم من دواء البوبافكين لوحده وايضاً المجموعة الثالثة تلقت 10ملغم من دواء البوبافكين ممزوج مع 15 ملغم من دواء الكيتامين، تم تسجيل الاثار الجانبية لدراسة: من غثيان، وقئ، انخفاض النبض، هبوط الضغط، وجع بالرأس، حكة، رجة، ورضا المريض، تم قياس بداية والمدة الحسية والحركية ومده التسكين، والعلامات الحيوية قبل، اثناء وبعد عملية الولادة القيصرية التي اجريت تحت التخدير النصفي، تم التسجيل كل 5 دقائق أثناء العملية الجراحية وكل 5 دقائق لمدة 15 دقيقة في وحدة (العناية ما بعد التخدير).

النتائج: اظهرت الدراسة انه لا فرق في المعلومات الجغرافية بين المجموعات. كان المريض الذي تلقى الفنتانيل سريعًا في بداية الكتلة الحسية بمتوسط (1.57 دقيقة) عل (p <0.001)، وأسرع في بداية الكتلة الحركية بمتوسط (2.68 دقيقة) على (P <0.001)، وكان لديه إطالة ملحوظة في مدة الكتلة الحسية والحركية، في مجموعة الفنتانيل (P <0.05)، وكان لها استطالة في مدة تسكين الالم (P <0.000)، ولم يكن هناك فرق بين الثلاث مجموعات فيما يتعلق بـ: حدوث تباطؤ في دقات القلب أثناء العملية كان هناك 1/35 (2.9٪) في مجموعة الفنتانيل مقابل 1 \ 35 (2.9٪) في مجموعة الكيتامين، كان معدل حدوث انخفاض ضغط الدم أثناء العملية

25 \ 35 (71.4٪) في مجموعة بوبيفاكين مقابل 29 \ 35 (82.9٪) في مجموعة الفنتانيل و30 \ 35 (85.7٪) في مجموعة الكيتامين، كان حدوث الآثار الجانبية والمضاعفات أثناء العملية القيصرية قليلًا في المجموعات الثلاث، حيث لم يحدث الألم والحكة والقيء في أي من المشاركين ضمن المجموعات الثلاث.

بعد العملية الجراحية، كانت نسبة حدوث انخفاض ضغط الدم 1 \ 35 (2.9٪) في ثلاث مجموعات وحالات وشدة الارتعاش بعد العملية الجراحية حيث 1 \ 35 (2.9٪) في مجموعة بوبيفاكين، مقابل3\ 35 (8.6٪) في الفنتانيل، مقابل 2\ 35 (5.7٪) في الكيتامين (p>0.58). حدوث وشدة الغثيان بعد العملية الجراحية حيث 1\ 35 (2.9٪) في مجموعة بوبيفاكايين، (قيمة p> 0.36) ولا أحد في المجموعات الأخرى، حدوث آثار جانبية في فترة ما بعد الجراحة، مثل تباطؤ في دقات القلب، والصداع، والحكة، والرعشة، والغثيان والقيء والضيق التنفسي لم يحدث في أي من المشاركين ضمن المجموعات الثلاث.

الخلاصة: نستنتج من الدراسة ان عند اعطاء الفنتانيل مع البوفاكين، يعمل على تسريع في بداية الكتلة الحسية وبداية الكتلة الحركية، وعلى إطالة مدة الكتلة الحسية والحركية، وايضاً في مدة التسكين الالم، مقابل الكيتامين مع البوفاكين او البوفاكين لوحده لدى النساء الخاضعات للعمليات القيصرية تحت تأثير التخدير النصفي النخاعي.

الكلمات المفتاحية: الفينتانيل، الكيتامين، البوبفاكين، التخدير النخاعي، العمليه القيصرية.