An-Najah National University

Faculty of Graduate Study

Dose Response Study of Intrathecal Fentanyl Added to Bupivacaine in Patients Undergoing Elective Caesarean Section in Spinal Anesthesia

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This Thesis is submitted in Partial Fulfillment for the Requirements of a Master Degree in Anesthesia Nursing, Faculty of Graduate Studies, An-Najah National University, Nablus-Palestine.

2019

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Dedication

I dedicate this thesis to my dear mother, the memory of my father and all my family. I also dedicate this work to everyone who taught me in my life and also to all nurses, CRNA nurses, students and anesthesiologists.

Acknowledgement

I am grateful to God for the good health and well-being that was necessary to complete this thesis.

I would like to express my sincere gratitude to the advisors for Dr. Aida Alkaissi and Dr. Nouraldin Almasri for their continued support for my masters and related thesis, for their patience, motivation and immense knowledge. Their guidance helped me continuously in my research and writing of this thesis. I also want to thank all the participants in my study for their cooperation and confidence. I would also like to thank Anesthesia Department in Rafedia Hospital for their cooperation and for their spiritual support during the writing of this dissertation. Finally, I want to thank my family, my mother and my wife who have been supporting me all the time.

الإقرار

أنا الموقع أدناه، مقدم الرسالة التي تحمل العنوان:

Dose Response Study of Intrathecal Fentanyl Added to Bupivacaine in Patients Undergoing Elective Caesarean Section in Spinal Anesthesia

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.

Student`s name: **إسم الطالب:**

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Date: **التاريخ:**

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List of Abbreviations

ASA	American Society of Anesthesiologists
BP	Blood Pressure
LS	Lower segment
C-S	Cesarean section
LSCS	Lower segment Cesarean section
ECG	Electrocardiogram
T10	Thoracic vertebra number 10
T6	Thoracic vertebra number 6
LA	Local anesthesia
VAS	Visual analog scale
ERC	Ethics and research committee
HR	Heart rate
IV	Intravenous
IT	Intrathecal
Kg	Kilogram(s)
HIV	human immunodeficiency virus
Bpm	Beat per minutes
Cm	Centimeter
Min	Minute
Ml	Milliliter(s)
Mg	Milligram(s)
Spo2	Percentage of arterial oxygen saturation
µg	Microgram (s)
CRNA	Certified Registered Nurse Anesthetist
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
PACU	Post anesthesia care unit
CTZ	Chemoreceptor trigger Zone

Conceptual definition of the terms

Hypotension: defined as systolic blood pressure was lower than 100 mm Hg or 20% below the pre induction level. (Duck Hwan Choi, 2000).

Bradycardia: defined as Heart rate below 60 bpm, it was managed by 0.5 mg of atropine(Hwan Choi et al., 2000).

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

Apgar scores: on the first and fifth minutes for all newborns were determined and a score below eight was considered low(Chakrabarti et al., 2015) .

Onset of sensory blockade at T6: defined as the time from completion of spinal injection of solution until absence of pain at thoracic vertebra number 6 (Sowmya et al., 2016) .

Duration of surgery: defined as the time from the completion of injection of the study drug till end of closer of patient skin (hospital protocol).

Onset of sensory blockade at T10: defined as the time from completion of spinal injection of solution until absence of pain at thoracic vertebra number 10 (Sowmya et al., 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) .

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Abstract

Background

Applying spinal anesthesia for caesarean sections associated with a certain side effect such as hypotension caused by the dose of hyperbaric bupivacaine, additives of potent opioid such as fentanyl may reduce the dose of toxic local anesthesia which will be more hemodynamic stability and also enhance of adequate analgesia.

Aims

This study conducted in order to evaluate the side effects of four spinal solutions in purpose of finding best possible combinations of fentanyl and bupivacaine, comparing the efficiency and safety of this combinations by using different doses of fentanyl in spinal anesthesia in cesarean section, and assessing the side effects, duration of analgesia, hemodynamic parameters and neonatal outcomes by using an Apgar score.

Methods

One hundred sixty Patients randomized into four groups 40 of each : Group-I (F10): received 1.5ml (7.5mg) of 0.5% Bupivacaine heavy & 10μg Fentanyl .Group-II (F15): received 1.5ml (7.5mg) of 0.5% Bupivacaine heavy & 15μg Fentanyl .Group-III (F25): received 1.5ml (7.5mg) of 0.5% Bupivacaine heavy & 25μg Fentanyl and (control group). Group-IV (B10): received 2 ml (10mg) of 0.5% Bupivacaine heavy and saline containing no fentanyl. Side effects such as: nausea, vomiting, bradycardia, hypotension episodes, headache, pruritis, shivering, drowsiness, restlessness, dizziness, sedation, patients' satisfaction, analgesic requirements and duration of effective analgesia were evaluated. Moreover, onset and duration of sensory and motor block were measured.

Results

Similar distribution of age, height, weight and duration of surgery as evidenced by statistical analysis, The results show that there was significant differences at the level ($p \leq 0.05$) in comparison between B10 only and Fentanyl 10mcg, Fentanyl 15mcg and Fentanyl 25mcg related to the onset of sensory blockade to T10 and T6 and indicate fentanyl 25 mcg more fast onset of sensory block. Onset of motor block was earlier in bupivacaine 10 mg group in comparison with other three groups, which is statistically significant difference. According to bradycardia, there were no significant differences between groups. Hypotension episodes in bupivacaine 10mg more common mean (3.12), which is statistically significant difference

when compared to other three groups. Incidence of headache was decreased in fentanyl groups in comparison with B10 group but there were no significant differences between the groups. There were significant differences regarding the incidence of pruritis in fentanyl 25 mcg (9/40) and fentanyl 15 mcg (6/40) groups when compared to B10. Nausea and vomiting were observed in B10 group while decreased significantly in other three groups. According to Restlessness, sedation and respiratory depression, there were no significant differences between all groups. There were no significant differences in Apgar scores at 1 and 5 min. The duration of sensory block was prolonged significantly in fentanyl groups. Duration of motor blocked was decreased significantly with decrease Bupivacaine dose and early motor recovery was observed significantly in fentanyl groups compared to B10 group. Duration of effective analgesia increased as increased fentanyl dose which was statistically significant difference in all fentanyl groups compared to B10 group. Regarding to postoperative analgesic needed, significant differences were found in all fentanyl groups in comparison to control group, fentanyl 25 mcg more significant and less rescue analgesic requirements in post-operative period by mean (1.85) followed by fentanyl 15 (2.3) mcg then B10 (2.37) and fourthly fentanyl 10 mcg (2.42) .

Conclusion

Addition of Fentanyl was effective with minimal side effects; also it improves the quality of anesthesia, prolongs the duration of sensory block, faster onset of sensory block and significantly reduces post-operative rescue analgesic needed, also better hemodynamic stability. Where 0.5% bupivacaine 10 mg alone faster of onset of motor blocked and prolonged of duration of motor blocked. Finally we conclude and recommend of best combination in spinal anesthesia for elective cesarean section is fentanyl 25 mcg with 0.5% bupivacaine 7.5 mg because it was superior in duration of effective analgesia and less post-operative rescue analgesic needed also more patients' satisfaction, however may have less side effect in fentanyl 10 mcg and 15 mcg groups. In conclusion fentanyl 25 mcg with 0.5% bupivacaine 7.5 mg is more favorable.

Keywords

Intrathecal fentanyl; bupivacaine; spinal anesthesia; cesarean section.

Chapter One
Introduction

1. Introduction

Regional anesthesia has become more popular in Caesarean sections because most of the parts prefer to wake up during childbirth. In addition, it is safer than the General Anesthesia (Hwan Choi, Joo Ahn, & Hee Kim, 2000).

Applying spinal anesthesia for cesarean section is one of the most challenging tasks that can be handled by an anesthesiologist. The benefits of spinal anesthesia are economical procedures and are associated with rapid anesthesia and they improve the full analgesic effect, but it may have unwanted side effects such as hypotension. The quality of pain relief can be improved by adding a potent opioid such as fentanyl to hyperbaric bupivacaine (L.R. &Veena, 2017).

Bupivacaine, is the most common local anesthesia (LA) intrathecally for cesarean section. It is well known that the dose of the drug affects the duration of sensory as well as motor blockage and has a significant effect on the degree of hypotension (Liu, Ware, Allen, Neal, & Pollock, 1996). Many patients need supplemental painkillers to relieve pain associated with exteriorization of the uterus and abdominal traction (Russell &Holmqvist, 1987). Accordingly, adjuvants such as opioids (Fentanyl) can be added to reduce the dose of LA, improve the quality of intraoperative anesthesia, and extend the duration of postoperative analgesia.

The parturients prefer being awake during childbirth. So, most popular method in caesarean deliveries is regional anaesthesia , its more safe than general anaesthesia because when you use small amounts of local anesthetics, it makes fetal uptake and placental transfer of drug negligible if it compared with regional anaesthesia (Rao Annavarapu, Kumar SongaMD, & SravanthiK, 2015).

To obtain favorable outcomes such as reducing systemic toxicity of local anesthesia, prolonging the duration of local anesthesia, increasing block strength and thereby increasing the reliability of the block. Common additions include used fentanyl, neostigmine, ketamine and buprenorphine. Intrathecal opioids appear to selectively modulate C- and A- fibers with minimal impact on dorsal root axons. Intrathecal and epidural opioids provide effective analgesia without motor or sensory blockade (L.R & Veena, 2017).

Studies conducted on hemodynamic changes in spinal anesthesia showed that hypotension after spinal anesthesia is due to the sympathetic blocks. Among local anesthetics, the most commonly used is hyperbaric bupivacaine which is the preferred local anesthetics. It has preferred properties which are slow work (5-8 minutes) and longer duration and higher strength. Also, studies have shown that of adding isobaric bupivacaine and fentanyl produces less hypotension. Studies have also shown that in caesarean section, the quality of surgical analgesia is enhanced when adding intrathecal opioids to bupivacaine(Venkata, Porika, Talari, Pasupuleti, & Pabba, 2015).

During caesarean section, you have to remove the visceral pain that caused by traction on peritoneum and intraperitoneal organs and associated with bradycardia, nausea, vomiting, hypotension and shorter duration of action. So, will require larger doses of local anesthetics and early postoperative analgesics(Chakrabarti, Debroy, & Ray, 2015).

Reducing the dose of bupivacaine is important while increasing adequate surgical anesthesia. So, we can use the neuro axial opioids to increase the analgesia produced by local anesthetics via direct binding with specific spinal receptors and could be minimize the associated side effects such as nausea, vomiting, pruritis and adverse neonatal effects by using smallest effective dose of opioid(Chakrabarti et al., 2015).

The opioids if administered intrathecally improves the analgesic potency of local anesthetics, fentanyl's lipophilic opioid short-acting. It is well known to improve quality of spinal block(Hwan Choi et al., 2000) .

Background

Definition of cesarean section:

Cesarean delivery is a surgical procedure includes incision opening abdominal layers and the uterus to terminate pregnancy and remove fetus from the uterus. There are many indications for elective cesarean among them genital herpes in the mother, previous cesarean section and fetal mal-presentation. Also, pregnant with twins, mother with HIV and fetal mal-presentation, The most common complications of cesarean section include

injury to another organ such as the bladder, nausea and vomiting, heavy blood loss, wound infection In addition to neonatal tachypnea (Sami & Ussbah, 2016) .

Regional anesthesia:

Regional anesthesia expands to become alternative method to general anesthesia when appropriate. Regional anesthesia may be used afterward for postoperative analgesia. Currently, spinal and epidural anesthesia had a great impact in obstetrics and widely used for analgesia in women in labor and cesarean delivery. Cesarean section can be performed by epidural or spinal anesthesia. Both of them had advantages, mother stay awake to experience the birth of her 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) .

Bupivacaine:

Bupivacaine is widely use in spinal anaesthesia for parturients undergoing elective Lower segment Cesarean section (LSCS), most popular local anaesthetic, it's amide local anaesthetic and long acting with duration of action of 90-120 minutes, its available for use as racemic mixture of the S(-) and R(+) stereoisomers. where is R(+) component contributes to toxicity(Prabha, Shreyavathi, S, & Rao, 2014).

Fentanyl:

Fentanyl , an opioid can be administered intrathecally to enhance the quality and duration of post-operative analgesia to a significant extent .Also, it is used to improves the quality of sensory blockade intraoperatively without significant side effects on the neonate nor increasing sympathetic or motor blockade(Prabha et al., 2014).

Fentanyl is lipophilic opioids which has rapid onset of action more than morphine and it moves from the cerebrospinal fluids into the spinal cord more rapidly than the hydrophilic opioids .Also, fentanyl doesn't cause delayed respiratory depression(L.R & Veena, 2017).

Spinal anesthesia:

Spinal anesthesia one is the preferred and widely used technique for situations like cesarean section. It is easy to administer and rapid onset of action in order to provide analgesia and muscular relaxation. If compared with epidural anesthesia, it is more reliable sensory and motor blockade but, the lack of long lasting postoperative analgesia stay the main disadvantage in spinal anesthesia (Sun, Li, & Gan, 2015) .

Spinal anesthesia is an invasive procedure includes injection of local anesthetic such as Bupivacaine into the subarachnoid space by insertion of a spinal needle between lumbar vertebrae (3-4 or 4-5).It leads to sympathetic block out flow and block sensory and motor nerves from fourth thoracic to fourth sacral dermatomes, but it may be associated by complication like hypotension (Sami & Ussbah, 2016).

Statement of Problem

Spinal anesthesia is often used in elective cesarean sections. One of the disadvantages associated with spinal anesthesia using bupivacaine alone is that its duration is relatively short, which requires the need for painkillers after the operation. Another disadvantage is nausea occurs during manipulation of the uterus and Peritoneal closure(Hunt, 1989) .

Fentanyl, a lipophilic opioid, has rapid effect after intrathecal administration since it does not tend to migrate to the 4th ventricle in sufficient concentrations to cause delayed respiratory depression (Etches, Sandler, & Daley, 1989). Following intrathecal (IT) administration, Fentanyl diffuses into epidural space and then into plasma, indicating that it appears not only through spinal opioid receptors but also systemically. Twenty five microgram of Fentanyl added to low dose Bupivacaine gives intrathecally better surgical anesthesia and increased reliability of the block than only intrathecal Bupivacaine or Fentanyl 7.5 or 10 μg(Bogra, Arora, & Srivastava, 2005) . Due to the availability of minimal data when comparing different doses of fentanyl with a fixed dose of local anesthesia, we design this study as a dose response study of intrathecal Fentanyl (25 μg, and 15 μg, and 10μg) added to low dose 0.5% hyperbaric bupivacaine 7.5 mg (1.5 ml) for spinal anesthesia.

Obstetric patients need accurate and strict calculations of local anesthesia that is given through spinal anesthesia because they are more susceptible to hormonal and mechanical changes and any lack of anesthesia doses leads to insufficient anesthesia and analgesia(Venkata et al., 2015) .

This study can be implicated to select the best possible combination of local anesthetics and fentanyl that can be used in spinal anesthesia in cesarean section to improve quality of spinal anesthesia and decrease dose of local anesthesia that will be use.

Significance of the Study

The incidence of caesarean section increased significantly, as spinal anesthesia is the most common method(Abdul-Rahim, Abu-Rmeileh, & Wick, 2009). However, in Palestinian hospitals there is no study on the effect of fentanyl added to intrathecal hyperbaric bupivacaine in caesarean sections, which should be given a certain meaning.

The body of research is still growing in Palestine, and new studies are recommended to be introduced in general, and new studies are still needed for the quality of care improvement at Palestinian Hospitals.

In Palestine, there are different approach 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 of caesarean section.

Several studies have compared different drugs added to hyperbaric bupivacaine and its effect on mother and child in addition to the period of anesthesia and the need for post-operative painkillers. However, experimental data are rather controversial and there is no general agreement on spinal anesthesia composition in cesarean sections.

Aims of the study

This study is conducted in order to find best possible combination of fentanyl and bupivacaine in order to compare the efficiency and safety of this combination by using different doses of fentanyl in spinal anesthesia in cesarean section, Also, it is conducted to assess duration of analgesia, hemodynamic parameters and neonatal outcomes by using an Apgor score.

Objectives of the Study

The study will achieve the following objectives, among them are:

- Determining the hemodynamic parameters in patients undergoing elective cesarean section in spinal anesthesia in four groups.

- Assessing the duration of sensory block and extending analgesia in early postoperative period in patients undergoing elective caesarean sections in spinal anesthesia in four groups.

- Evaluating the neonatal outcomes by using an Apgar score in patients undergoing elective cesarean section in spinal anesthesia in three groups.

Hypothesis

The following hypothesis are to be tested:

1- There is a significant difference at 0.05 level related to intraoperative hemodynamic stability (blood pressure, heart rate, vasopressor needed) between groups of patients.

2- There is a significant difference at a level 0.05 related to duration of effective analgesia between groups of patients.

3- There is a significant difference at 0.05 level of related to the incidence and intensity of pain and analgesic consumption between patient groups.

4- There is a significant difference at 0.05 level related to the neonatal outcomes measured by using an Apgar score between patient groups.

5- There is a significant difference at 0.05 level related to the intra-operative and post- operative adverse effects that are nausea, vomiting, drowsiness, shivering and Pruritis between patient groups.

Chapter Two
Literature review

This chapter will introduce previous studies which clarify the effect of merger of fentanyl and bupivacaine in spinal anesthesia in females undergoing cesarean section, and to investigate effect and adverse effects of this combination and favorite dose of each that used to promote efficiency and safety to mothers and newborns.

Sowmya et al, (2016) performed a prospective randomized comparative trial to correlate intrathecal Fentanyl in various doses (10µg and15µg) with Hyperbaric Bupivacaine (10mg) for Caesarean Section. The objective of the trial was to investigate effect and adverse effects of enumerating fentanyl to 0.5% Bupivacaine in 2 different doses and to obtain lengthened analgesia and quicker outset of analgesia left out side effects in caesarian section. Participants appointed for planned caesarean section inconstantly prorated into two groups; Group A: obtained conservative free Fentanyl 10mcg, and Bupivacaine 10mg and Group B:obtained preservative free Fentanyl 15µg and Bupivacaine 10mg , the authors were evaluated the hemodynamic cohesion, grade of motor blockade, trait of analgesia, sedation, shaking and further adverse effects, The study was delineated that Mean of HR, SBP and DBP was greater in group A than in Group B and this divergence was statistically significant. Mean commencement of Motor and Sensory blockade was significantly greater in Group A than in Group B. The extension of analgesia after operation was significantly diminished in Group A than in Group B. As an

outcome, hemodynamic cohesion, quicker outset of sensory blockade and lengthened of analgesia after operation were realized when use 15µgof fentanyl and 10mg of bupivacaine correlated with 10µg of fentanyl and 10mg of bupivacaine. It demonstrates that 15µgof fentanyl and 10mg of bupivacaine promote hemodynamic cohesion, quicker outset of sensory blockade and lengthened of analgesia after operation

Rao et al., (2015) operated randomized controlled trial in order to assess the efficiency of low dose bupivacaine with fentanyl in spinal anesthesia for below segment caesarean section. This trial was operated to correlate the effect of fentanyl and hyperbaric Bupivacaine in women who are pregnant undergoing caesarean section in spinal anesthesia and to determine the effects of these drugs on hemodynamic and sensory and motor block and other adverse effects on participants. One hundred twenty participants were randomized and designated into four groups, thirty patients in every group. Group-1 obtained0.5% Bupivacaine 9mg +25µg Fentanyl, Group-2obtained 0.5% Bupivacaine 8mg +25µg Fentanyl, Group-3 obtained 0.5% Bupivacaine 7mg + 25µg Fentanyl and Group-4 obtained 0.5% Bupivacaine 6mg +25µg Fentanyl.Thetrialwas shown that quicker outset of sensory block to T6 dermatome when increment dose of Bupivacaine from 6mg to 9mg, Motor block and comprise time of analgesia were escalated in group one compared to other groups. There wasa significant deferred of pain after operation and sensory recovery when Fentanyl mixed with Bupivacaine. When Fentanyl 25µg wasconsolidatedto 0.5% hyperbaric Bupivacaine 6 mg, and 7 mg participants had more efficient analgesia and

less side effects, when utilized combinations of 8 mg and 9 mg 0.5% bupivacaine with fentanyl 25μg, patients derived longer-term of analgesia compared to6 mg and 7 mg bupivacaine, nonetheless, it had been associated with adverse effects such as lengthened duration of motor blocks that intrude with early ambulation.

Another randomized controlled prospective trial operated by Venkata et al, (2015). This trial was implemented to correlate the effect of small dose of 7.5 mg bupivacaine added to fentanyl to a traditional dose 10 mg of hyperbaric bupivacaine on the length of analgesia and the hemodynamic for cesarean section. Fifty participants enrolled for planned caesarean section were randomly prorated into two groups; experimental group received 7.5 mg of hyperbaric bupivacaine mixed to 25 μg fentanyl. Control group received 10 mg of hyperbaric bupivacaine, the study made comparison between the groups that were the length of analgesia and maternal hemodynamic and Apgar score of the newborn and sensory and motor block. The study showed that the time of effective analgesia was significantly lengthened in the experimental group than in the control group ($P < 0.001$), The blood pressure was significantly declined with >25% fall from the standard in a control group than in experimental group < 0.001. So, farther lengthened duration of analgesia and farther hemodynamic cohesion were concluded when utilized a small dose bupivacaine and fentanyl conform to bupivacaine only.

A Prospective double-blind comparative study was operated by Archana et al., (2017) in participants undergoing caesarean section to conform capacity and safety of intrathecal bupivacaine in consolidation with fentanyl and intrathecal bupivacaine only. Sixty participants were prorated into two groups, 30 patients in every group. Group I obtained 1.6 mL of 0.5% of bupivacaine added to 20mcg fentanyl, Group II obtained 2 mL of 0.5% of bupivacaine alone. Participants' hemodynamics was appraised and neonatal outcomes were checked out by Apgar score at 1 minute and 5 minutes. Complexity like nausea, bradycardia, vomiting, pruritis were deliberated. Time of request of rescue analgesia and the time of effective analgesia were documented. There were no adverse effects observed on the newborn in the two groups. The mean time of analgesia in the bupivacaine and fentanyl group was two hundreds and fourteen minutes, although in the bupivacaine only group was one hundred ninety five minutes ($p<0.5$). There was significantly quick outset of action in the bupivacaine (alone) group, decline in mean arterial pressure in the bupivacaine and fentanyl group, it was fifteen percentage while, in the bupivacaine (only) group was twenty three percentage ($p<0.001$). Remarkably in cesarean section under spinal anesthesia, inclusion of intrathecal20 µg of fentanyl to bupivacaine 8 mg, perpetuated the length of postoperative analgesia, enhanced the quality of intraoperative analgesia and introduced better hemodynamic stability without disturbing the newborn clinical condition.

A double-blinded, sequential, prospective study conducted by Choi, et al., (2000). The trial was conducted to decline the dose of bupivacaine to reach adequate surgical anesthesia by the addition of fentanyl to bupivacaine. One hundred twenty participants were admitted to planned caesarian section, there were sixty patients in every group, In group one, patients obtained intrathecal bupivacaine only, to determine the optimum dosage of hyperbaric Bupivacaine, In group two, patients obtained bupivacaine added to fentanyl, Intraoperative pain assessed by utilizing visual analogue scale (VAS),sensory and motor block was documented and side effects were also assessed, sensory and motor recovery were examined and the outset of pain in the post anesthesia care unit (PACU). The study findings illustrated that the dose of bupivacaine may be decreased from 12 mg to 8 mg as well. When the addition of fentanyl 10 micros to 8 mg of bupivacaine, it impeded the sensory recovery and the outset of pain postoperatively but no alter in motor recovery.

A study performed by Hemnath Babu, et al., (2016),in order to correlate effectiveness of subarachnoid block with bupivacaine only and small dose bupivacaine with fentanyl as ancillary in terms of outset and time of anesthesia and analgesia after operation. A prospective randomized case control trial was performed in sixty participants undergoing planned caesarean section. The participants were randomly prorated into two groups which included thirty participants in every group. Subarachnoid block was organized. Hemodynamic specifications, outstand time to sensory and motor blockade, analgesia request after operation and adverse effects were

correlated. It showed that outset of analgesia was earlier in Group BF in comparison to Group B ($p<0.05$). The time of two segment regression in Group BF was significantly lengthened than Group B ($p<0.05$). Time of sensory blockade in Group BF was significantly more than Group B ($p<0.05$). In Group BF, outset of motor blockade was decreased and period of motor blockade in comparison to Group B ($p>0.05$).Analgesia after operation in Group BF was significantly lengthened than Group B ($p<0.05$). The authors terminated that addition of fentanyl to bupivacaine emanated in quicker outset of action and efficient spinal anesthesia with a smaller dose of bupivacaine.

In the same purpose, atrial operated was conducted by Sergio &Belzarena (1992) in Brazil. The objectives of the trial was to determine the clinical effects of executed spinal, preservative-free fentanyl in one hundred twenty females undergoing caesarean section with 0.5% hyperbaric bupivacaine. Participants were prorated at random into four groups, thirty patients in every group. The first of which obtained 2 mL of saline encompassing no fentanyl (group 0); the second, 0.25 µg/kg (group 25); the third, 0.50µg/kg (group 50); and the fourth, 0.75, µg/kg (group 75) of fentanyl in a blinded manner. Surgical anesthesia was admirable in 100% of treated patients and in 87% of group 0. Respiratory rate reduced significantly in groups 50 and 75 and was documented as early as 4 minutes after the administration of the drug. Though, respiratory depression did not progress in any patient, and 40 minutes downstream all groups had an analogous respiratory rate. Recurrence of anesthesia to the T-12

dermatome took a lengthy time as the dose of fentanyl inclined, but all participants had recovered by 240 min after the injection. Efficient analgesia after operation stayed longer and significantly increased with the dose of fentanyl given. Neonatal rating was similar in all groups. Sedation and pruritus were the major adverse effects. The consolidation of bupivacaine and a small dose of fentanyl (0.25 µg /kg) affords distinguished surgical anesthesia with short-lasting analgesia after operation and very slight negative adverse effects. As the dose of fentanyl inclines to 0.5 or 0.75 µg/kg pain reliefs lasts longer after operation, but respiratory alterations occur and the incidence of adverse effects likewise inclined.

A trial operated by Bogra, et al., (2005) in India purposed for potentiating the efficiency of intrathecal local anesthetics by enumerating of fentanyl in pursuit in order to decrease the dose of bupivacaine, through decreasing the adverse effects caused by greater doses of intrathecal bupivacaine in cesarean section. The trial was performed on hundred twenty cesarean section participants prorated into six groups, classified as B8, B10 and B 12.5. 8.10 and 12.5 mg of bupivacaine mg and FB8, FB10 and FB 12.5 received a merger of 12.5 µg intrathecal fentanyl correspondingly. The criterion that taken into deliberation were visceral pain, hemodynamic coherent, intraoperative sedation, intraoperative and postoperative shivering, and pain after operation. The results showed that outset of sensory block to T6 ensued quicker with rising bupivacaine doses in bupivacaine alone groups and bupivacaine-fentanyl combination groups.

Lower concentrations of bupivacaine only could not remove the visceral pain completely. Blood pressure decreased with the rising concentration of Bupivacaine and Fentanyl. Occurrence of nausea and shivering declined significantly granting all this, pain relief after operation and hemodynamics coherent increased by adding fentanyl. Pruritis, maternal respiratory depression and changes in Apgar score of babies did not develop with fentanyl. The authors demonstrated that spinal anesthesia among obstetric patient's demands thorough dose calculations because minimal dose alteration can displayed to complexity and side effects derive. Here the symbiotic, potentiating effect of fentanyl (an opioid) on bupivacaine (a local anesthetic) in spinal anesthesia for caesarian section is conferred. Fentanyl was capable to decline the dose of bupivacaine and hence its annoying effects.

Ng et al (1990) performed a trial in which subarachnoid fentanyl 20 micrograms were assessed to investigate its efficiency for postoperative analgesia, its conceivable side effects and its effects on the newborn. Sixty ASA class I or II at-term pregnant women undergoing elective cesarean section were randomly prorated into two groups. In the experimental group, fentanyl 20 micrograms with 0.5% heavy Marcaine 2.0 ml was given intrathecally and in the control group only 0.5% heavy Marcaine 2.0 ml was given intrathecally. The average time for participants in the fentanyl group to demand the first dose of opioids for pain was 6.8 +/- 3.2 h and in the control group it was 3.9 +/- 1.1 h. The occurrence of nausea and vomiting after operation were greater in the fentanyl group than in the

control group. Pruritus was apart launched in the fentanyl group and extended to 50%. Early or late respiratory distress was not launched in the fentanyl group. Neonatal status as stead fasted by 1-min and 5-min Apgar score was satisfactory and displayed no significant difference in both groups. Investigation on neurobehavioral and reflexes performed at the baby demonstrated no irregularity in both groups.

Gauchan, et al (2014) operated a trial to compare the effects of addition of fentanyl to intrathecal bupivacaine on the outset and period of spinal anesthesia and its effect on mother and neonate. Seventy participants with singleton pregnancy in connection with elective cesarean section were randomly designated to obtain subarachnoid block with 0.5% bupivacaine heavy 2.4 ml (Group A) or fentanyl 20 microgram (0.4 ml) added to 0.5% bupivacaine heavy 2ml (Group B). Blood pressure, heart rate, respiratory rate, oxygen saturation, along with character of spinal block was appraised at full length the surgery and in the postoperative ward until the patient requested analgesia. It was displayed that duration of sensory block was lengthened in fentanyl group ($p<0.05$). Duration of comprehensive analgesia (97 ± 8.23 minutes in group (A) vs 153 ± 7 minutes in group (B); p value= 0.00) and adequate analgesia (134 ± 5.6 minutes in group (A) vs 164 ± 9 in group (B); p value= 0.00) were also found to be lengthened in Group B. There were no variations in the incidence of adverse effects in both groups. The authors wrapped up that the addition of fentanyl to intrathecal bupivacaine for cesarean section inclined the time of postoperative analgesia request without rising maternal or neonatal adverse effects.

A double blind randomized controlled trial performed by Chakrabarti et al., (2015) to determine of hemodynamic specifications and neonatal results devote to spinal anesthesia with small dose of hyperbaric Bupivacaine with and without Fentanyl in Participants undergoing planned caesarean section by mixing of local anesthetic and opioid to empower use of lower dose of spinal anesthetic and in clines benefit of anesthesia. Hundred full term pregnant women for planned caesarean section, randomly designated in to two groups: Group BF: Study group-50 participants. Group B: Control group- 50 participants. Group BF: obtained fentanyl 12.5mcg (0.25ml) added to 8 mg hyperbaric bupivacaine (0.5%) and Group B: received 0.25ml of normal saline added to 8 mg hyperbaric bupivacaine (0.5%) intrathecally, the study noted intraoperative trait of anesthesia, outset of sensory block, total period of analgesia, grade of motor block and maternal and fetal side effects. The trial showed the outset of motor blockade in Group BF was (230.00 ± 6.639) seconds, which was significantly earlier compared to Group B (235.30±7.229) seconds. The outset of sensory blockade in seconds in group BF was (154.58±5.17), which was significantly earlier correlated to group B (158.64±6.226) seconds, The quality of anaesthesia was distinguished in all patients in group BF in comparison to 82% in group B (Statistically significant). Sensory recovery was lengthened in Group BF to (149.40±1.784) minutes compared to Group B (84.26±5.91) minutes, and this was statistically significant. In the two groups, Apgar score at 1 minute and 5 minutes was not statistically significant difference between the groups. Motor recovery was lengthened in Group BF to (147.10±1.843) minutes in comparison to Group B

(81.78±6.136) minutes (Statistically significant), in conclusion, the function of 0.5 % hyperbaric bupivacaine 8 mg added to 12.5mcg fentanyl in spinal anesthesia in caesarian section enhanced the quality of anesthesia and lengthened the period of sensory block and inclined analgesia in early post-operative time without any significant adverse effects on mother and new-born.

Chapter Three
Methodology

Methodology

This chapter introduces synopsis of the research methodology utilized for this trial. It comprise: study design, study sample (study population, sample size, and sampling process), setting, ethical consideration, study instruments, data collection, and data analysis procedures.

Study Design:

A prospective, controlled randomized, double-blind study**.**

Study Population

The target population is full-term pregnant women with aged 18 to 45 years old and programmed for planned cesarean delivery with. American Society of Anesthesiologists (ASA) Classification I & II.

Study Setting

The study was implemented in specialized gynecological department at hospital in North of Palestine.

Participants

One hundred and sixty parturient participants, ranging age from 18-45years old, with American Society of Anesthesiologists (ASA) physical

status I or II who were programmed for elective cesarean delivery under spinal anesthesia.

Sample and sampling

A formula (i.e.Pocock's sample size formula) was used. Sample size was predesigned by power analysis collaborated by the probability that the decision rule would edge to the denouement that the pain developed in the control group (these data were extracted from the previous study) (Hemnath Babu, Somani, Somani, & Vm, 2016) .

The error (a) was steadfast to 0.05 which is the risk of making Type I errors, and (b) Power (1-type II error) was set to 0.80. Minimum standard error = 1. According to the efficacy analysis, 40 patients were recommended in each group**.**

A formula (i.e. Pocock's sample size formula) that can be specifically adept for correlation of proportions P_1 and P_2 in two uniformly sized groups:

$$n = \frac{[P_1 (1-P_1) + P_2 (1-P_2)]}{(P_1-P_2)^2} (Z_{\alpha/2} + Z_{\beta})^2$$

Where:

n: needed sample size

P_1: anticipated percentage of study result in the experimental group (i.e. combination therapy) (P_1 = 0.40).

P_2: anticipated percentage of study result in the control group (placebo therapy) ($P_2 = 0.70$).

α: level of statistical significance

$Z_{\alpha/2:}$ outturn the desired level of statistical significance (typically 1.96 for α = 0.05)

$Z_{\beta:}$ outturn the desired power (typically 0.84 for 80% power)

$$n = \frac{[0.40(1-0.40) + 0.70\ (1-0.70)]}{(0.40-0.70)^2} (1.96+ 0.84)^2$$

$$n = \frac{[0.40\ (0.60) + 0.70(0.30)]}{(0.30)^2} (2.8)^2$$

$$n = \frac{[0.24 + 0.21]}{0.09} (7.84)$$

$$n = \frac{[0.45]}{0.09} (7.84)$$

$n \approx 39$ patients

A total of 160 patients (40 for each group) should be performed for recruitment into the study.

Pre-recruitment assessment

All the participants' involved in the trial were clinically examined by the physician to find out any chronic and acute illness that may affect the patient's life.

Regular laboratory tests were completed, a complete blood count to control hemoglobin levels and platelet counts to find out any patient that had a low platelet count (less than 100 x 10^3), any patients anguishing from coagulation disorders were precluded.

Randomization

Randomization consummated through opaque and well-sealed envelopes. The sequence generation was performed with a computer by using random allotment software 1.0. The number is stamped on envelopes and the group type is recorded on the card in alliance with the sequential number. When the patients reached, envelopes were opened to see the group to be designated. In this prospective double-blind comparative study, 160 women were designated into four groups of 40 each.

Blindness

The patients, health care providers comprehended in the patient care, the person who gathered, inspected and interpreted data, and the outcome arbitrators were unconcerned of the treatment group appropriation.

Study period

From July 2018 to October 2019.

Inclusion criteria

- Assigned for planned caesarean section.
- All the participants taken for this trial resided to American Society of Anesthesiology (ASA) grade 1 or II.
- The age group is from 18 to 45 years.

None of the participants had any discrepancy for spinal anesthesia.

- Singleton pregnancy with full term gestation.

Exclusion criteria

- Rejection to enlist in the study.
- Patient rejecting spinal anesthesia.
- Allergy to bupivacaine/fentanyl.
- Patients younger than 18 years of age.
- Convoluted pregnancies such as multiple pregnancies, pregnancy induced hypertension and placenta Previa.
- The antenatal women with acute fetal distress.

- Women with co-morbid situation like anemia, diabetes mellitus, asthma, hypertension, cardiac diseases and other systemic problems.

- Women affinity to ASA class III and above.

- Women with Pregnancy-convinced hypertension (PIH), eclampsia, multiple gestation.

- Women who has a heart rate <60 beats per minute and > 120 beat per minute.

Study Measures(Variables)

(a) Dependent variables:

Time of analgesia, hemodynamic parameters (systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, peripheral capillary oxygen saturation (SpO2), Pain, the duration of sensory block and extending analgesia in early postoperative period, nausea, vomiting, shivering, purities, sedation, headache, backache, bradycardia and hypotension, neonatal effects measuring by using Apgar Score.

(b) Independent variables: hyperbaric bupivacaine, fentanyl, Spinal anesthesia.

Follow up with patients

All participants accomplished the study and prorated into groups were pursued attentively during the operation. Monitor of blood pressure and heart rate and any occasion that can occurred during operation were

recorded. Pursue the patients after the operation in post-anesthesia care unit (PACU) and the participants overruled on surgical ward. Vital sign measured by nurses every 15 minutes and recorded in patients file.

Procedure

Prior starting with spinal anesthesia, fasting of the participants entrenched. All equipment and supplies were processed, went through and ensured they were gird to use. The anesthesia machine tested and devoted size tracheal tubes and two work laryngoscopes examined, the emergency trolley and the devices are equipped with suction and emergency medicine together with naloxone being completed.

Pre-anesthetic oversee done to exclude associated medical conditions and complications of pregnancy and to evaluate the respiratory and spine.

Routine tests such as hemoglobin, bleeding time, clotting time, blood grouping and typing, urine testing achieved. Intravenous (IV) line was inserted with 18-gauge I.V. cannula and preloading with sodium chloride 0.9 % 1000 cc over 40 mints. The women brought into the operating theater replaced in the left side position to avoid aortocaval confining and placed on the operating table in supine post with a 20-degree inclination to the left by installing a wedge under the right hip. The sphygmomanometer cuff is linked to the upper arm and criterion blood pressure was measured. The pulse oximeter linked and saturation recorded. Prior anesthesia commences, women were briefed on the method of

sensory and motor evaluation. All safety precautions were succumbed for cardiovascular and pulmonary resuscitation.

The woman was located in the left side position. The skin above the back was attentively prepared disinfectant and draped with a sterile towel. A 25G Quincke needle was keenly inserted into the L3-L4 spaces in the center line until it grasped the subarachnoid space. The needle position was proven by free flow of CSF, after that the test drug was injected intrathecally, for 30 seconds with the bevel operated cephalic.

Patients were randomized into four groups 40 of each

(**F10**): was obtained 1.5ml (7.5mg) of 0.5% Bupivacaine heavy & 10μg Fentanyl.

(**F15**): was obtained 1.5ml (7.5mg) of 0.5% Bupivacaine heavy & 15μg Fentanyl.

(**F25**): was obtained 1.5ml (7.5mg) of 0.5% Bupivacaine heavy & 25μg Fentanyl.

(**B 10**): was obtained 2 ml (10mg) of 0.5% Bupivacaine heavy and saline containing no fentanyl.

Preservatives-free normal saline solution supplemental to 10, 15 or 25 μg of fentanyl to generate a total of 2ml, which injected after free-flowing cerebrospinal fluid (CSF) achieved. The fentanyl solution processed by anesthesiologist, not involved in data collection. The dose of fentanyl chosen in a randomized demeanor. Immediately after that a dose of bupivacaine was given. The sum of injected fentanyl is unfamiliar to the

anesthetist who injected the drug and assessed the participant's feedback.

The needle was taken out after proceeding the drug and the patient was situated in the back end position with the left ramp by installing a wedge under the right hip. Oxygen through face mask (at a rate of 6 liter / min) was united to the woman till the end of operation. Heart and respiratory parameters were monitored and the assessment of the level of sensory and motor blockade was performed on a regular basis. 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. Hypotension was treated with intravenous bolus of Ringers Lactate, 40 μg Neo-Synephrine iv and maternal bradycardia, treated with 0.5 mg I V Atropine. Assessment of sedation is done using Ramsay sedation score (Appendix 5).

Dermatomal sensory block was tested with pin prick sensation at the center of the clavicular line on both sides with a blunt27G needle every 15 seconds until the block attained the T6 dermatome. Subsequent, the level was controlled every two minutes until the maximum sensor block was obtained.

Surgical incision was acquiesced when sensor level is ≥ T6 dermatome and motor blocking is satisfactory. The height of the blocks was assessed frequently until complete amended of the block function. The highest level of sensory analgesia was the maximum sensory level obtained.

Time for two segments sensory regression is the time from maximum sensory block attainment to blocked regression of two segments. Sum duration of analgesia was the time from drug injection to first demand for analgesics. The degree of motor blockade in the lower limbs was assessed independently by asking the patient to move the lower extremities and was recorded conferred to the Bromage scale (Appendix 4). The degree of motor blockade in the lower limbs was assessed by utilizing Bromage Scale (Appendix 4).

Intraoperative, incidence of visceral pain, drowsiness, shivering was recorded with operate questioning and regular observation and disburse treatment were documented. Delivery time of the baby was recorded. Newborn evaluation was done using Apgar score at 1 min and 5 min. The birth weight was recorded.

The extent of efficient analgesia was noted. The adverse effects were assessed that were hypotension, bradycardia, pruritis, drowsiness, nausea and vomiting, shivering, patients 'satisfaction and respiratory depression. They attained as follows 0 as not present, 1 as present, no treatment is required and 2 as present and treatment was given. Intravenous Metoclopramide 10 mg, utilized to treat nausea when the patient specified the intensity of nausea ≥3 on the lickert scale 0-6 (0=no nausea, 1=very mild, 2= mild, 3= moderate, 4= severe, 5= very severe, 6= intolerable) or/and vomiting frequency twice or more. The incidence of side effects and opioid needs during the first 24 hours were documented.

After operation, participants transported to the recovery room where arterial blood pressure, heart rate and respiratory rate were deliberated every 15 minutes for 2 hours and then at 6, 12 and 24 hours in the obstetric ward. Sensory and motor components were noted repeatedly for complete reconstituted of sensory and motor function. Time for first utilization for analgesic is registered. Morphine 2.5 mg I.V was given when the patient got pain ≥4 on VAS. All scrutiny was executed by the nurse who did not familiar of the study groups.

The time for two segment regressions of the sensory blockade was recorded, Apgar score of newborn was noted at 1 min and 5 min. The pain was also assessed in the post anesthesia care unit (PACU). All these parameters were evaluated from the beginning of the spinal injection.

Rescue medication for hypotension

Hypotension was described systolic blood pressure was lower than 100 mm Hg or 20% below the pre induction level, 12.5 to 60 mic neosynephrine intravenously (IV) was given and treated with intravenous boluses of Ringers Lactate.

Rescue medication for bradycardia

bradycardia (heart rate <60 beats/min) ,Atropine was given in 0.5 mg increments (Sami & Ussbah, 2016).

Data Collection

Data were gathered in a designed data sheet (appendix 1)

Data Analysis Plan

SPSS Version 20 was performed for data analysis. Descriptive statistics (frequency, percentage, mean and standard deviation) were utilized. The student t-test for continuous data, Mann-Whitney test for ordinal data, and Chi-square test for nominal data were performed to analyze the results and chi square test to investigate a significant in one or more categories and post hock test also used. A $p < 0.05$ is considered significant.

Ethical Considerations

The study was performed in accordance with the Helsinki Declaration and approved by the Institutional Review Board of An-Najah National University (IRB) and was approved by the research ethical committee of Palestinian Ministry of Health. Consent forms were taken from the women before participation. As the research is on human participants, it is necessary to follow scrutiny ethical principles. The participants were demanding to dedicate their consent, and they were guaranteed that participation or information provided will not be utilized against them. They were likewise guaranteed of their right to confidentiality and anonymity. Anonymity was obtained by coding the women and by ruining the names connected to the numbers.

Privacy:

Confidentiality was guaranteed by managing against unjustified entrance to the data. All the women participating in the trial were adequate informed of the aims, methodology, risks and benefits of the research and guaranteed that their anonymity would be cultivated during analysis and reporting of the results. The women were ensured that the manifestation of the data will not accompanied with any names to protect the patient's anonymity and confidentiality.

Refusal to participate \ withdraws from the study:

All patients were informed about the aim and design of the study and were informed that they will voluntarily free to disengage from the trial on any occasion.

Harm:

No harm will happen to the women from participating, and women` name will at no time be voiced to anyone.

Possible benefits of the study

- The consolidation of bupivacaine and fentanyl administers admirable surgical anesthesia with short-lasting postoperative analgesia and little negative adverse effects(Belzarena, 1992) .

- The increments in efficient analgesia intraoperative and postoperative with the incorporation of Fentanyl to bupivacaine(Bogra et al., 2005).

- The outset of analgesia is earlier in groups of Bupivacaine and fentanyl(Bogra et al., 2005).

- Period of two segments regression in groups of Bupivacaine and fentanyl is significantly protracted than Group Bupivacaine alone (Hemnath Babu et al., 2016).

- Bupivacaine alone could not unify detached the visceral pain (Bogra et al., 2005)

- Changes of Apgar score of babies do not endure with Fentanyl (L.R & Veena, 2017) .

Possible risks of the study and how they can be minimized.

Follow-up of the patient conferred to the protocol organized for the study work in the early disclosure of changes in vital signs or any diversity.

The anesthesiologists at assigned hospital and other hospitals in Palestine implemented spinal anesthesia adopting bupivacaine and fentanyl, conceding to the anesthesiologist's assessment. The vital signs were deliberate every two minutes at the onset of spinal anesthesia and every five minutes until the edge of the surgery. Patients maintained to be monitored for vital signs, in PACU and obstetric ward. Sensory block and motor block were monitored. The patient were observed for possible adverse effects such as nausea, vomiting, shivering, and drowsiness. The patient advanced to have 6liter / min oxygen by mask during operation and after operation. Hypotension was treated as the target hospital regular by

administering Ringer Lactate and if needed phenylephrine 40ug IV. Bradycardia is treated as the target hospital regular by administering atropine 0.5 mg I.V.

Assessment of sedation was performed utilizing Ramsay sedation scale.

Conceivable adverse effects were treated in all groups if happened like nausea and vomiting were treated as hospital regular with Metoclopramide 10mg I.V. None the less fentanyl which is highly lipophilic do not endure free in the cerebrospinal fluid long enough when given in the subarachnoid space at the lumbar level to attain Chemoreceptor trigger Zone (CTZ) in adequate concentration to generate vomiting. Hitherto, it adequately amplifies local anesthesia mediated block to decrease nociceptive stimulation which occurs during manipulation like peritoneal traction and thus decreases nausea and vomiting (Hejazi, Lavenbarg, Foran, & McCallum, 2010) .

Pruritus can be treated with I.V. Naloxon as hospital regular. No increment in the pain score was noted following Naloxon in the earlier study (Hunt, et al. 1989).

Chapter Four

Results

Results:

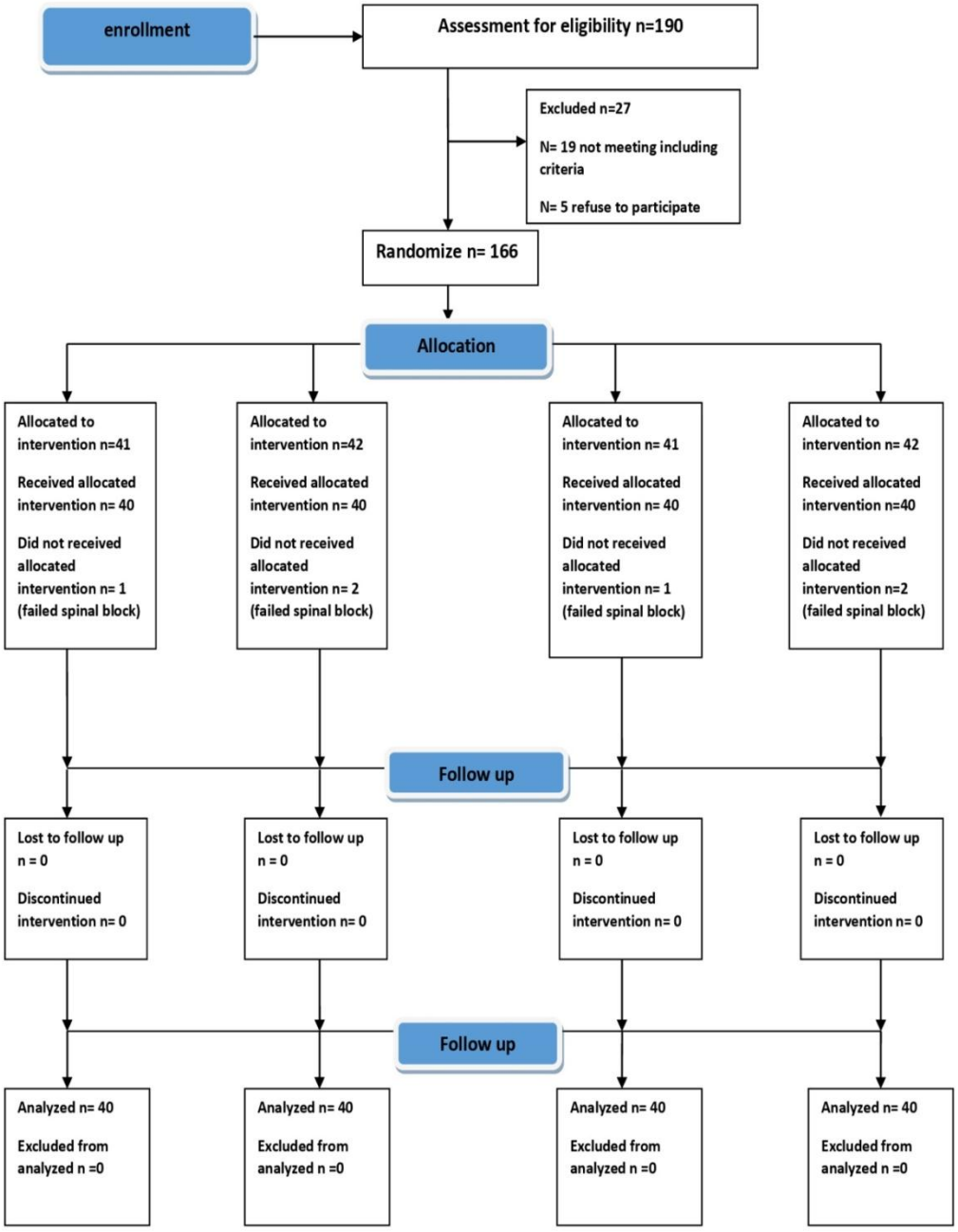

Table 1.Demographic variables and duration of anesthesia of the four groups are presented as Mean ±

Variable		F10	F15	F25	f value	p value
Age in years	Mean	29.6000	29.4625	30.7875	2.859	0.061
	Std. Deviation	5.26416	4.52823	5.57729		
Weight in Kg	Mean	66.8500	68.6500	70.3125	2.396	0.096
	Std. Deviation	7.31238	13.36356	12.36225		
Height in Cm	Mean	160.8750	159.7500	160.9375	0.961	0.385
	Std. Deviation	4.18670	10.08759	5.16155		
Duration of Surgery	Mean	38.613	39.179	38.188	2.014	.1380
	Std. Deviation	3.1522	4.6031	3.7857		

*. The mean difference is significant at the 0.05 level. Table (1) shows study groups are compared with respect to age, height and weight of the patients and duration of surgery.

Block tables:

Table (2):The onset of sensory blockade to T10 by seconds. Comparison between B10, F10, F15 and F25. Data is presented as Mean±

Group	Mean Seconds	Standard Division	t value	p value
B10	182.1250	11.31187		
F10	157.9000	6.57033	11.712	***0.000**
F15	142.7500	11.49749	15.440	***0.000**
F25	126.4000	13.04588	20.411	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (2) indicates that there were significant differences at($p < 0.05$) level of onset of sensory block to T10 by second in comparison between B10 M (SD) 182.12 (11.31) and F10 157.90 (6.57) ($p = 0.000$), F15 142.75 (11.49) ($p = 0.000$), and F25 126.40 (13.04) ($p = 0.000$).There was also a significant difference in the onset of sensory blockage between F10 157.90 (6.57) and F25 126.40 (13.04) P <0.0001 and F15 142.75 (11.49) P <0.0001 in favor of F25.These results indicate that the time to onset of sensory block in the F25 group is significantly shorter than the F10 and F15 groups. This means that the F25 was the best.

Table (3): The onset of sensory blockade to T6 by seconds – Comparison between B10, F10, F15 and F25. Data is presented as Mean ±.

Group	Mean	Standard Division	t value	p value
B10	279.3750	6.73181		
F10	267.2750	8.34815	7.136	***0.000**
F15	251.5500	6.02112	19.485	***0.000**
F25	225.8500	17.13528	18.388	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (3) indicates that there were significant differences at ($p \leq 0.05$) level of onset of sensory block to T6 by second in comparison betweenB10 279.37 (6.73) andF10 267.27 (8.34) (p=**0.000)**, F15 251.55 (6.02) **(p=0.000)** and F25225.85 (17.13) **(p=0.000)**. There was also a significant difference in the onset of sensory blockage to T6 by second between F10 267.27(8.34) and F25 225.85 (17.13) P <0.0001 and F15 251.55(6.02) and F25 225.85 (17.13) P <0.0001 tin favor of F25.These results indicate that

the time to onset of sensory blockage to T6 by second in the F25 group is significantly shorter than the F10 and F15 groups. This means that the F25 was the best.

Table (4): The onset of motor blockade by seconds – Comparison between B10, F10, F15 and F25.Data is presented as Mean ±

Group	Mean	Standard Division	t value	p value
B10	252.9750	5.25009		
F10	381.8718	6.17371	-100.057-	***0.000**
F15	363.8750	6.32126	-85.357-	***0.000**
F25	348.4750	5.23787	-81.444-	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (4) indicates that there were significant differences at ($a \leq 0.05$) level of the onset of motor blockade by seconds in comparison between B10 252.97 (5.25) (p=0.000) andF10 381.87 (6.17), F15 363.87 (6.32) ((p=0.000) and F25 348.47 (5.23) (p=0.000) respectively. There was also a significant difference in the onset of motor blockade by second between F10 381.8718 (8.34) and F25 348.47(5.23) P <0.0001 and F15 363.87(6.32) and F25 348.47(5.23) P <0.0001 in favor of F25.These results indicate that the time to onset of motor blockade by second in the F25 group is significantly shorter than the F10 and F15 groups. This means that the F25 was the best.

Side effects:

Table (5): The incidence of Bradycardia by frequency (%) – Comparison between B10, F10, F15 and F25.Using Pearson Chi-Square.

Bradycardia						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	5	0	0	2
		% of Total	6.2%	0.0%	0.0%	2.5%
	NO	Count	35	40	40	38
		% of Total	43.8%	50.0%	50.0%	47.5%
Pearson Chi-Square				5.33	5.33	1.40
p value				***0.021**	***0.021**	**0.235**

*. The mean difference is significant at the 0.05 level.

Table (5) indicates that there were significant differences at ($p \leq 0.05$) level regarding the incidence of bradycardia when compared between B105 (6.2%) and F10 (0.0%) (p=0.021), B10 and F15 (0.0%), p= (p=0.021). And there were no significant differences at ($p \leq 0.05$) level in comparison between B10 5(6.2%) andF25 2(2.5%) (P = 0.4202). The results indicate that patients in B10 group had significantly more bradycardia incidence than F10 and F15 groups.

Post hoc test:

Side effect table: Bradycardia.

Table (6): The incidence of Bradycardia – Comparison between B10, F10, F15 and F25 groups. Post Hoc Multiple Comparisons were used.

Post Hoc Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Bradycardia	**bupivacaine 10mg**	**fent10**	-.12500-*	.04485	**0.030***	-.2415-	-.0085-
		fent15	-.12500-*	.04485	**0.030***	-.2415-	-.0085-
		fent25	-.07500-	.04485	**0.342**	-.1915-	.0415
*. The mean difference is significant at the 0.05 level.							

Table (24) shows that the differences are significant between B10 and (F10), p=0**.030** in favor of F10, and between B10 andF15, p=**.030** in favor of F15.The results indicate that the incidence of bradycardia is significantly more in B10 group.

Table (7): The incidence of vasopressor needed by frequency (%) – Comparison between B10, F10, F15 and F25. Data is presented as Mean ±.

Group	Mean	Standard Division	t	p value
B10	3.1250	.56330		
F10	1.9000	.59052	9.493	***0.000**
F15	2.1000	.74421	6.946	***0.000**
F25	2.2000	.75786	6.195	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (6) indicates that there were significant differences at ($p \leq 0.05$) level related to the incidence of vasopressor needed presented by frequency (%) in comparison between B10 M (SD) 3.12 (.563) and F10 1.90 (.590) p= 0.000, F15 2.10 (.744) p= 0.000 and F252.20 (.757), p= 0.000 respectively. The results indicate that patients in B10 group were needed significantly more vasopressor than patients in the other three groups.

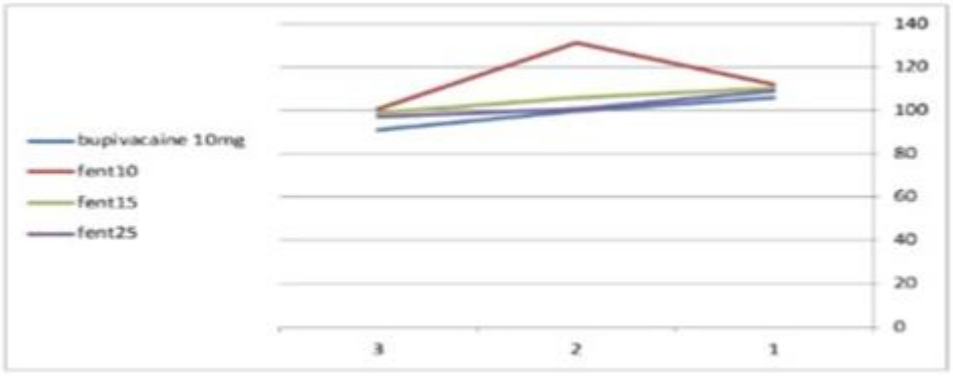

Figure 1: Systolic blood pressure at 2 and 4 and 6 mints during caesarian section.

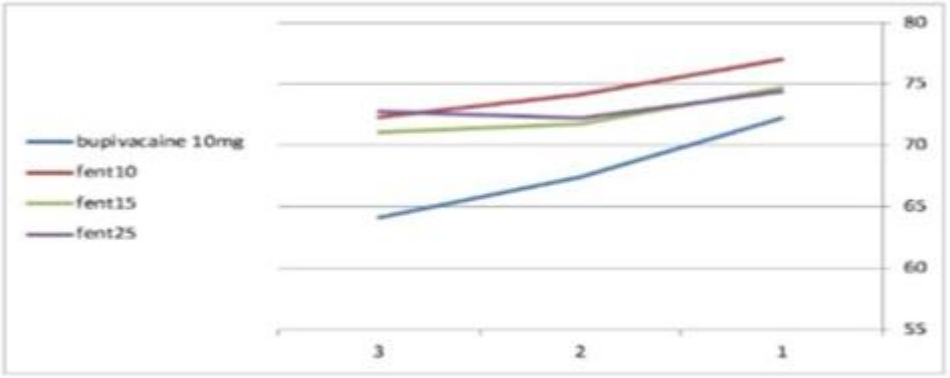

Figure 2: Heart rate at 2 and 4 and 6 mints.

Table (8): The incidence of headache by frequency (%)– Comparison between B10, F10,F15 and F25.By using Pearson Chi-Square.

Headache						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	9	3	4	3
		% of Total	11.2%	3.8%	5.0%	3.8%
	NO	Count	31	37	36	36
		% of Total	38.8%	46.2%	45.0%	45.6%
Pearson Chi-Square				3.529	2.296	3.361
p value				**0.060**	**0.130**	**0.060**

*. The mean difference is significant at the 0.05 level.

Table (8) indicates that there were no significant differences at ($p \leq 0.05$) level related to the incidence of headache by frequency (%) in comparison between B10 (9(11.2%)) and F10 (3(3.8%)), F15 (4 (5.0%)), F25 (3(3.8%) respectively, $p > 0.05$.

Post hoc test:

Side effect table: headache.

Table (9): The incidence of headache – Comparison between B10, F10, F15 and F25. Multiple comparison by using Tukey HSD.

Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Headache	**bupivacaine 10mg**	**fent10**	-.15000-	.07211	**0.164**	-.3373-	.0373
		fent15	-.12500-	.07211	**0.310**	-.3123-	.0623
		fent25	-.14808-	.07257	**0.178**	-.3366-	.0404
*. The mean difference is significant at the 0.05 level.							

Table (9) shows that there were no significant differences between all groups when multiple comparison by using Tukey HSD was used.

Table (10): The incidence of Pruritis by frequency (%) – Comparison between B10, F10, F15 and F25. By using Pearson Chi-Square.

Pruritis						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	1	2	6	9
		% of Total	1.2%	2.5%	7.5%	11.2%
	NO	Count	39	38	34	31
		% of Total	48.8%	47.5%	42.5%	38.8%
Pearson Chi-Square				0.34	3.91	7.31
p value				**0.556**	***0.048**	***0.007**

*. The mean difference is significant at the 0.05 level.

Table (9) indicates that there were significant differences regarding the incidence of pruritis at ($p \leq 0.05$) level when compared between B10 (1(1.2%)) and F15 (6(7.5%)) ($p = 0.048$), F25 9 (11.2%) ($p = 0.007$) respectively. And there were no significant differences at ($p \leq 0.05$) level in comparison between B10 (1(1.2%)) and F10 (2(2.5%), p=0.556.

Post hoc test:

Side effect table: Pruritis.

Table (11): The incidence of Pruritis – Comparison between B10, F10, F15 and F25.Post Hoc Multiple Comparisons- Tukey HSD test was used

Post Hoc Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Pruritus	**bupivacaine 10mg**	**fent10**	.02500	.06922	**0.984**	-.1548-	.2048
		fent15	.12500	.06922	**0.275**	-.0548-	.3048
		fent25	.20000*	.06922	**0.023***	.0202	.3798
*. The mean difference is significant at the 0.05 level.							

Table (11) shows that the differences between the incidence of pruritis in B10 group and F25 group in favor of P10 (p=0. 23).The results indicate that patients who received 25 µg of fentanyl had significantly more pruritis compared to the patients in B10 group.

Table (12): The incidence of Shivering by frequency (%) – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Shivering						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	7	1	2	2
		% of Total	8.8%	1.2%	2.5%	2.5%
	NO	Count	33	39	38	38
		% of Total	41.2%	48.8%	47.5%	47.5%
Pearson Chi-Square				5	3.13	3.13
p value				***0.025**	**0.077**	**0.077**

*. The mean difference is significant at the 0.05 level.

Table (12) indicates that there were significant differences at ($p \leq 0.05$) level related to the incidence of shivering in comparison between B10 f (%) (7(8.8%) and F10 (1(1.2%)) ($p = 0.025$).And there were no significant differences at ($p \leq 0.05$) level in comparison between B10 andF15 (2(2.5%), F25 (2(2.5%)) respectively. The result indicates that the patients in B10 group had significantly more shivering than the patients in F10 group.

Post hoc test:

Side effect table: Shivering.

Table (13): The incidence of Shivering – Comparison between B10, F10, F15 and F25.

Post Hoc Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Shivering	**bupivacaine 10mg**	**fent10**	-.15000-	.05815	**0.052**	-.3010-	.0010
		fent15	-.12500-	.05815	**0.142**	-.2760-	.0260
		fent25	-.12500-	.05815	**0.142**	-.2760-	.0260
*. The mean difference is significant at the 0.05 level.							

Table (13) shows that there were no significant differences between all groups regarding shivering.

Table (14): The incidence of Nausea by frequency (%) – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Nausea						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	8	1	3	6
		% of Total	10.0%	1.2%	3.8%	7.5%
	NO	Count	32	39	37	34
		% of Total	40.0%	48.8%	46.2%	42.5%
Pearson Chi-Square				6.135	2.635	.346
p value				***0.013**	**0.105**	**0.55**

*. The mean difference is significant at the 0.05 level.

Table (14) indicates that there were significant differences related to ($p \leq 0.05$) incidence of nausea at the level in comparison between B10 f (%) (8 (10.0%)) and F10 (1(1.2%)) (p= 0.013). And there were no significant differences related to the incidence of nausea at ($p \leq 0.05$) level in comparison between B10 andF15 (3.8%)), F25 (6(7.5%) respectively.

Post hoc test:

Side effect table: Nausea.

Table (15): The incidence of Nausea – Comparison between B10, F10, F15 and F25.

Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Nausea	**bupivacaine 10mg**	**fent10**	-.17500-	.06991	**0.063**	-.3566-	.0066
		fent15	-.12500-	.06991	**0.283**	-.3066-	.0566
		fent25	-.05000-	.06991	**0.891**	-.2316-	.1316
*. The mean difference is significant at the 0.05 level.							

Table (15) shows that there were significant differences between all groups $p<0.05$ regarding nausea.

Table (16): The incidence of vomiting by frequency (%) – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Vomiting						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	5	0	0	0
		% of Total	6.2%	0.0%	0.0%	0.0%
	NO	Count	35	40	40	40
		% of Total	43.8%	50.0%	50.0%	50.0%
Pearson Chi-Square				5.33	5.33	5.33
p value				***0.021**	***0.021**	***0.021**

Table (16) indicates that there were significant differences related to the incidence of vomiting by f (%) at the level ($p\leq 0.05$) in comparison between B10 (5 (6.2%)) andF10 (0.0%), F15 (0.0%), F25 (0.0%), p=0.021 respectively. The results indicate that the percentage of patients who were vomited was significantly higher in B10 group compared with the other three groups.

Post hoc test:

Side effect table: Vomiting.

Table (17): The incidence of Vomiting – Comparison between Bupivacaine Only, F10, F15 and F25.Post Hoc Multiple Comparisons-Tukey HSD was used.

Post Hoc Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Vomiting	**bupivacaine 10mg**	**fent10**	-.12500-*	.03745	**0.006***	-.2222-	-.0278-
		fent15	-.12500-*	.03745	**0.006***	-.2222-	-.0278-
		fent25	-.12500-*	.03745	**0.006***	-.2222-	-.0278-
*. The mean difference is significant at the 0.05 level.							

Table (17) shows that there were significant differences regarding the incidence of vomiting between B10 and (F10) in favor of F10, and between B10 and F15 in favor of F15 and between B10 and F 25) in favor of F25, p=0.006.

Table (18): The incidence of Restlessness by frequency (%) – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Restlessness						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	0	0	0	0
		% of Total	0%	0%	0%	0%
	NO	Count	40	40	40	40
		% of Total	50.0%	50.0%	50.0%	50.0%
Pearson Chi-Square				--------	----	--------
p value				--------	----	--------

Table (18) shows that there were no significant differences regarding the incidence of restlessness between the four groups.

Table (19): The incidence of Ramsay Sedation Scale – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Ramsay Sedation Scale						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	0	0	0	0
		% of Total	0%	0%	0%	0%
	NO	Count	40	40	40	40
		% of Total	50.0%	50.0%	50.0%	50.0%
Pearson Chi-Square				--------	-----	--------
p value				--------	-----	--------

Table (19) shows that there were no significant differences regarding the incidence of Ramsay Sedation Scale between the four groups.

Table (20): The incidence of Respiratory Depression by frequency (%) – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Respiratory Depression						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	0	0	0	0
		% of Total	0%	0%	0%	0%
	NO	Count	40	40	40	40
		% of Total	50.0%	50.0%	50.0%	50.0%
Pearson Chi-Square				--------	-----	--------
p value				--------	----	--------

Table (20) shows that there were no significant differences regarding the incidence of respiratory depression between the four groups.

Table (21): The incidence of Dizziness by frequency (%) – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Dizziness						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	0	0	0	0
		% of Total	0%	0%	0%	0%
	NO	Count	40	40	40	40
		% of Total	50.0%	50.0%	50.0%	50.0%
Pearson Chi-Square				--------	----	--------
p value				--------	----	--------

Table (21) shows that there were no significant differences regarding the incidence of dizziness between the four groups.

Table (22): The incidence of drowsiness by frequency – Comparison between B10, F10, F15 and F25.By using Pearson Chi-Square.

Drowsiness						
			Spinal solution			
			B10	F10	F15	F25
	YES	Count	1	0	0	0
		% of Total	1.2%	0.0%	0.0%	0.0%
	NO	Count	39	40	40	40
		% of Total	48.8%	50.0%	50.0%	50.0%
Pearson Chi-Square				1.01	1.01	1.01
p value				**0.314**	**0.314**	**0.314**

Table (22) indicates that there were no significant differences related to the incidence of drowsiness at the level ($p \leq 0.05$) in comparison between B10 and F10, F15, F25.

Post hoc test:

Side effect table: Drowsiness.

Table (23): The incidence of Drowsiness – Comparison between Bupivacaine Only, F10, F15 and F25.

Post Hoc Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Drowsiness	**bupivacaine 10mg**	**fent10**	-.02500-	.01768	**.492**	-.0709-	.0209
		fent15	-.02500-	.01768	**.492**	-.0709-	.0209
		fent25	-.02500-	.01768	**.492**	-.0709-	.0209
*. The mean difference is significant at the 0.05 level.							

Table (23) shows that there were no significant differences between all groups related to the incidence of drowsiness, p=**.492**.

Apgar score table:

Table (24): The Apgar score at 1min – Comparison between B10, F10, F15 and F25.Data is presented by Mean±.

Group	Mean	Standard Division	t value	p value
B10	7.9000	.30382		
F10	7.9750	.15811	-1.385-	**0.171**
F15	7.9500	.22072	-.842-	**0.402**
F25	7.9000	.30382	.000	**1.000**

*. The mean difference is significant at the 0.05 level.

Table (24) indicates that there were no significant differences related to the Apgar score at 1min at the level ($p \leq 0.05$) in comparison between B10 andF10, F15 and F25.

Table (25): The Apgar score at 5min – Comparison between B10, F10, F15 and F25.Data is presented by Mean±.

Group	Mean	Standard Division	t value	p value
B10	9.1250	0.33493		
F10	9.0750	.266750	0.739	**0.462**
F15	9.0250	.158110	1.708	**0.093**
F25	9.0000	.226460	1.356	**0.179**

Table (25) indicates that there were no significant differences at the level ($p \leq 0.05$) related to the Apgar score at 5min in comparison between B10 andF10, F15 and F25.

Block table: Postoperative

Table (26): The duration of sensory blockade by minutes– Comparison between B10, F10, F15 and F25.Data is presented by Mean±.

Group	Mean	Standard Division	t value	p value
B10	102.0250	2.73146		
F10	109.4750	3.71406	-10.220-	***0.000**
F15	118.6250	4.69417	-19.331-	***0.000**
F25	129.9750	3.48247	-39.940-	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (26) 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 B10 M (SD) (102.02 (2.73)) and F10 (109.47 (3.714)), p0.000=F15 (118.62(4.69417)), p=0.000 and F25 (129.97 (3.482), p=0.000 respectively. There were also significant differences between F10 (109.47 (3.714)) and F25 (129.97 (3.482), $P< 0.0001$ as well as F15 (118.62(4.69417)) and F25 (129.97 (3.482), $P < 0.0001$. These results mean that patients in the F25 group have a longer duration of sensory block with minutes compared to the other groups.

Table (27): The duration of motor blockade by minutes – Comparison between B10, F10, F15 and F25.Data is presented by Mean±.

Group	Mean	Standard Division	t value	p value
B10	93.7750	5.08133		
F10	59.1250	5.71632	28.653	***0.000**
F15	61.3750	5.41928	27.584	***0.000**
F25	72.2750	10.58782	11.578	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (27) 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 B10M (SD) (93.77 (5.081)) andF10 (59.12(5.716), p=0.000, F15 (61.37 (5.419), p=0.000and F25 (72.27(10.587), p=0.000. The results indicate that patients in group F10 had significantly less duration to motor blockade by minutes followed by F15, F25 and then B10.

Table (28): The duration of analgesia in minutes – Comparison between B10, F10, F15 and F25. Data is presented by Mean±.

Group	Mean	Standard Division	t value	p value
B10	157.5250	3.45660		
F10	165.9750	7.33620	-6.590-	***0.000**
F15	179.8974	8.36281	-15.468-	***0.000**
F25	205.0500	6.61758	-40.259-	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (28) indicates that there were significant differences related to the duration of analgesia in minutes at the level ($p \leq 0.05$) in comparison between B10M (SD) (157.52 (3.456)) andF10 (165.97 (7.336), p= 0.000, F15 (179.89(8.362)), p= 0.000and F25 (205.05 (6.617).The results indicate

that combination of bupivacaine with fentanyl increased significantly duration of analgesia. There were a significant different related to the duration of analgesia in minutes between F10 (165.97 (7.336) and F25 (205.05 (6.617), P< 0.0001 and F15 (179.89(8.362)) and F25 (205.05 (6.617), P < 0.0001. The results indicate that patients in group F25 had longer duration of analgesia in minutes followed by F15.

Table (29): The level of patients' satisfaction – Comparison between B10, F10, F15 and F25 groups. Data is presented by frequency (%). Pearson Chi-Square is used.

Satisfaction						
			Spinal solution			
			Bupivacaine only	F10	F15	F25
	Satisfied	Count	32	27	23	5
		% of Total	40.0%	33.8%	28.8%	6.2%
	Very satisfied	Count	8	13	17	35
		% of Total	10.0%	16.2%	21.2%	43.8%
Pearson Chi-Square				1.614	4.713	36.656
p value				**0.204**	***0.030**	***0.000**

*. The mean difference is significant at the 0.05 level. Table (29) indicates that there were significant differences related to the level of satisfaction (satisfied and very satisfied) at the level ($p \leq 0.05$) in comparison between B10 f (%) 8 (10.0%) and F15 17 (21.2%) ($p = 0.030$) andF25 35(43.8%) ($p = 0.000$) respectively.

Post hoc test: Satisfaction

Table (30): The level of satisfaction – Comparison between B10, F10, F15 and F25.Multiple Comparisons- Tukey HSD

Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) spinal solution**	**(J) spinal solution**	Mean Difference (I-J)	Std. Error	**Sig.**	95% Confidence Interval	
						Lower Bound	Upper Bound
Satisfaction	**bupivacaine 10mg**	**fent10**	-.12500-	.09695	**.571**	-.3768-	.1268
		fent15	-.22500-	.09695	**.098**	-.4768-	.0268
		fent25	-.67500-*	.09695	**.000**	-.9268-	-.4232-
*. The mean difference is significant at the 0.05 level.							

Table (30) shows that the differences between B10 and F25 in favor of F25 group.

Analgesia:

Table (31): Rescue analgesia times given Comparison between B10, F10, F15 and F25 groups by frequency (%). Data is presented as Mean±.

Group	Mean	Standard Division	t value	p value
B10	2.3750	0.49029		
F10	2.4250	0.50064	-.451-	**0.653**
F15	2.3250	0.47434	0.464	**0.644**
F25	1.8500	0.42667	5.109	***0.000**

*. The mean difference is significant at the 0.05 level.

Table (31) indicates there were no significant differences related to rescue analgesia times given at ($p \leq 0.05$) level in comparison between B10 and F10, F15. And there were a significant differences at ($p \leq 0.05$) level in comparison between B10 M (SD)(2.3750 (0.490) and F25(1.8500 (0.426) **(p = 0.000)**. there were also significant differences between F10 (2.4250 (0.500) and F25(1.8500 (0.426), $P < 0.0001$, F15 (2.3250 (0.474) and F25(1.8500 (0.426), $P < 0.0001$. these results indicate that F25 reduces significantly most the rescue analgesia times given requirements.

Summary of block values:

Characteristics	Group	P value	Group	P value	Group	P value	Group	P value
	Mean		Mean		Mean		Mean	
onset of sensory blockade to T10	F25	**0.00**	F15	**0.00**	F10	**0.00**	B10	
	126± 13 second		143± 11 second		158± 7 second		182±11 second	
onset of sensory blockade to T6	F25	**0.00**	F15	**0.00**	F10	**0.00**	B10	
	226 ± 17 second		252 ± 6 second		267± 8 second		279± 7 second	
onset of grade 2 motor blockade	B10		F25	**0.00**	F15	**0.00**	F10	0.00
	253± 5 second		348± 5 second		364±6 second		382± 6 second	
duration of sensory blockade	F25	**0.00**	F15	**0.00**	F10	**0.00**	B10	
	130± 3 mints		119±5 mints		109±4 mints		102± 3 mints	
duration of motor blockade	B10		F25	**0.00**	F15	**0.00**	F10	**0.00**
	94± 5 mints		72± 11 mints		61± 5 mints		59± 6 mints	

Summary of side effects:

Characteristics	Group	P value						
	Incident	Percentage						
Bradycardia	F10	**0.021**	F15	**0.021**	F25	**0.235**	B10	
	(0\40)	0.0%	(0\40)	0.0%	(2\40)	2.5%	(5\40)	6.2%
Hypotension episodes	F10	**0.00**	F15	**0.00**	F25	**0.00**	B10	
	Mean (1.9)		**Mean** (2.1)		**Mean**(2.2)		**Mean**(3.12)	
Headache	F10	**0.060**	F25	**0.060**	F15	**0.130**	B10	
	(3\40)	3.8 %	(3\40)	3.8 %	(4\40)	5 %	(9\40)	11.2 %
Pruritis	B 10		F10	**0.556**	F15	**0.048**	F25	**.007**
	(1\40)	1.2%	(2\40)	2.5%	(6\40)	7.5 %	(9\40)	11.2 %
Shivering	F10	**0.025**	F15	**0.077**	F25	**0.077**	B10	
	(1\40)	1.2 %	(2\40)	2.5 %	(2\40)	2.5 %	(7\40)	8.8 %
Nausea	F10	**0.013**	F15	**0.105**	F25	**0.55**	B10	
	(1\40)	1.2 %	(3\40)	3.8 %	(6\40)	7.5 %	(8\40)	10 %
Vomiting	F10	**0.021**	F15	**0.021**	F25	**0.021**	B10	
	(0\40)	0.0 %	(0\40)	0.0 %	(0\40)	0.0 %	(5\40)	6.2 %
Drowsiness	F10	**0.314**	F15	**0.314**	F25	**0.314**	B10	
	(0\40)	0.0 %	(0\40)	0.0 %	(0\40)	0.0 %	(1\40)	1.2 %

Other side effects:

Characteristics	Group	P value						
	Incident	Percentage						
Restlessness	F10	----	F25	-----	F15	----	B10	
	(0\40)	0.0%	(0\40)	0.0%	(0\40)	0 %	(0\40)	0 %
Dizziness	F10	----	F25	----	F15	---	B10	
	(0\40)	0.0%	(0\40)	0.0%	(0\40)	0.0%	(0\40)	0.0%
Sedation	F10	----	F25	----	F15	----	B10	
	(0\40)	0 %	(0\40)	0 %	(0\40	0 %	(0\40)	0 %

Apgar score summary:

	Group	P value						
	Mean							
Apgar score at 1 minute	F10	**0.171**	F15	**0.402**	F25	**1.00**	B10	
	Mean (7.97)		**Mean** (7.95)		**Mean**(7.9)		**Mean**(7.9)	
Apgar score at 5 minutes	F10	**0.462**	F15	**0.093**	F25	**0.179**	B10	
	Mean (9.07)		**Mean** (9.02)		**Mean**(9.00)		**Mean**(9.12)	

Satisfaction and analgesia summary:

	Group	**P value**						
	Mean \ Incident							
Satisfaction	F25	**0.000**	F15	**0.030**	F10	**0.204**	B10	
	(35\40)	43.8%	(17\40)	21.2%	(13\40)	16.2%	(8\40)	10.0%
Analgesic requirements	F25	**0.000**	F15	**0.644**	B10		F10	**0.653**
	(1.85) times		(2.32) times		**(**2.37) times		**(**2.42) times	
duration of effective analgesia	F25	**0.000**	F15	**0.000**	F10	**0.000**	B10	
	(205) mints		(180) mints		(166) mints		(158) mints	

Chapter Five
Discussion

Discussion:

The current study has been conducted to find the best possible combination of fentanyl and bupivacaine and compare the efficacy and safety of this combination by using different doses of fentanyl in the spinal anesthesia in cesarean section. Also, it aims to assess the variances of painkillers, hemodynamic parameters and newborns and mothers outcomes.

In the current study, it was shown that fentanyl improves the quality of intraoperative analgesia and reduces intrathecal doses of local anesthetic toxicity, also fentanyl has a faster effect and it improves postoperative pain relief with less postoperative side effects. However, there are some risks associated with regional anesthesia that were shown by Gauchan et al., (2014) in the form of the risk of higher block levels.

Onset of sensory block to T 10:

Local anesthetic and fentanyl have a synergistic effect in central neuraxial blocks, thus prolonging postoperative analgesia, improving intraoperative analgesia, and faster onset of sensory block to T10 and T6 at increased dose of fentanyl (Rao Annavarapu et al., 2015). So, in our study it has been indicated that there were significant differences at level ($p < 0.05$) in comparison between B10only and Fentanyl 10 µg, Fentanyl 15 µg and Fentanyl 25 µg associated with onset of sensory block to T10. The

current study result indicates that fentanyl 25 micrograms had a fastest onset of sensory action block, this result is in accordance with the study results conducted by Sowmya, et al (2016).

Onset of sensory block to T 6:

Regarding the faster onset of sensory block into T6, it was faster in fentanyl 25 mcg and statistically significant in all groups compared to only B10. These results are in alignment with the study results conducted by Venkata, et al (2015).On the other hand, it differs from Randalls et al (1991) who showed that the onset of sensory block into T6 was faster when increasing the bupivacaine dose alone.

Onset of motor block:

Onset of motor block was earlier in bupivacaine 10 mg group in comparison with other three groups , which is in accordance with Rao Annavarapu et al, (2015) that noted earlier motor blocked when increased Bupivacaine dose. On other hand Gauchan et al, (2014)compared 0.5% bupivacaine heavy 2.4 ml to fentanyl 20 mcgrogram 0.4 ml added to 0.5% bupivacaine heavy 2ml and they didn't found any significant difference regarding onset of motor blocked .

Bradycardia:

We noted five cases of bradycardia in B10 group and 2 cases in F25 group , which was statistically insignificant when compared to B10 that correlate with Rao Annavarapu et al., (2015) and Gauchan et al, (2014). On the

other side no case of bradycardia in fentanyl 10 mcg and fentanyl 15 mcg which statistically significant when compared to B10.

Vasopressor needed \ hypotension episodes:

More hemodynamic stability was found when reduce dose of bupivacaine to 7.5 mg because. Hypotension episodes in bupivacaine 10mg was common and more vasopressor needed when compared with the other three groups. It might mostly be due to higher doses of bupivacaine that lead to more sympathetic blockade. Similar results was found in Rao Annavarapu et al., (2015) and shawagfeh et al , (2011).

Headache:

In our study incidence of headache was decreased in fentanyl groups in comparison with B10group but the differences were not significant which is correspond with Shim et al, (2018)

Pruritis:

In the present study, one patient had pruritis in B10 where nine were in fentanyl 25 mcg and 6 in fentanyl 15 mcg, these differences were statistically significant in favor of B10.This result correlates with the results of the studies conducted by Belzarena, (1992) and Weigl et al, (2016).On other hand Archana& Veena, 2017compared 1.6 mL of 0.5% of bupivacaine with 0.4 mL of fentanyl 20 mcg (Group I) and 2 mL of 0.5% of bupivacaine (Group II)but they did not find significant difference .

However, in the current study, two patients in the fentanyl group F10 were complained of pruritis, which is not statistically significant, it may be because a low dose of fentanyl was used.

Shivering:

In the current study, according to shivering two patients were complained of shivering in fentanyl 25 mcg group and two patients in fentanyl 15 mcg and seven patients in the B10 group, and this was statistically not significant. These results were in alignment with the study's results conducted by Hwan Choiet al.,(2000) , where is in fentanyl 10 mcg just one patient was complained from shivering and that statistically significant.

Nausea and vomiting:

Five patients were vomited in B10group, where no any patient was vomited in the other three groups, this difference was statistically significant. As a result, we can conclude that combine (bupivacaine + fentanyl) reduces vomiting. these results is in accordance with the study results conducted by Dahlgrenet al., (1997)that found when combine (bupivacaine + fentanyl), the incidence of nausea and vomiting were decreased. In a study conducted by Langevinet al, (1999) was shown that alfentanil compared with equipotent doses of fentanyl and sufentanil, was associated with a lower incidence of PONV. Higher doses of some opioids may actually reduce nausea and vomiting by interacting with mu opioid receptors in the

vomiting center rather than the CTZ (Scotto di Fazano, et al2002) .In contrast Archana& Veena, 2017 compared 10 mg of 0.5% of bupivacaine and 8 mg of bupivacaine with 20 mcg fentanyl in their study, they found that no statistically significant difference between the two groups.

Sedation:

Sedation as a side effect can be recorded as it increases with the fentanyl dose(Belzarena, 1992).The Ramsay Sedation Scale was used in the current study to assess the degree of sedation. It was shown that there were no significant differences between groups, none of the patients were sedated. This result was in accordance with the study results conducted by Weigl et al, (2016) and did not agree with the study results conducted by Belzarena, (1992), it may be because different assessment scale was used.

Respiratory Depression:

In the present study, no episodes of respiratory depression were noted in all groups. This result was in line with the study results conducted by Singh, et al (1995); Gauchan et al., (2014) and Belzarena, (1992)

Apgar scores:

We found similar neonatal conditions in all groups evaluated by Apgar scores at 1 and 5 min, that Corresponds with Belzarena, (1992)and Archana& Veena, (2017) .

Duration of sensory block:

The duration of sensory block was extended in fentanyl groups as well as with increasing fentanyl dose. These results were in agreement with the study results conducted by Hemnath Babu et al, (2016) and Belzarena, (1992) who found the same results. And the present study also agreed with Singh et al. (1995) comparing two groups, 13.5 mg hyperbaric bupivacaine 0.75% was added 25 mcg fentanyl and 13.5 mg hyperbaric bupivacaine 0.75% was added to 0.5 ml Cerebrospinal fluid and find long-lasting sensory blocked in fentanyl group.

Duration of motor block:

In the present study, the duration of the motor block decreased with decreased Bupivacaine dose and it was noted that early motor recovery was occurred in fentanyl groups. These results corresponded to Hwan Choi et al., (2000) and RaoAnnavarapu et al., (2015), who noted early motor recovery when reduced dose of Bupivacaine. In contrast, Gauchan et al.,(2014) compared 0.5% bupivacaine 2.4 ml (Group 1) with 2 ml 0.5% bupivacaine 2 ml with 20 micrograms of fentanyl (group2) and found no significant differences between two groups according to length of the motor block as well as Singh et al, (1995).

Duration of effective analgesia:

In the current study, we aimed to achieve maximum analgesia using different doses of fentanyl 10, 15, 25 mcg and reduced 0.5% heavy Bupivacaine to 7.5 mg. The results were shown that increased duration of effective analgesia by increasing the fentanyl dose and the 25 mcg group was the best group to note effective analgesia. The same results were found by Sowmya et al, (2016) who used 10 mcg or 15 mcg of fentanyl added to 10 mg of Bupivacaine and showed significant improvements in postoperative analgesia in the 15 mcg fentanyl group.

Also our study corresponds with Randalls et al, (1991)that used 12.5 mg of hyperbaric bupivacaine with or without 10 mcg of fentanyl and noted a longer time until first request for analgesia in fentanyl groups .

moreover, Weigl et al, (2016) compared fentanyl 25 mcg(study group) and normal saline (control group) and noted reduced analgesic consumption in fentanyl 25mcg group .

another study conducted byHemnath Babu et al, (2016) that used 10mg of 0.5% heavy Bupivacaine in group one and 7.5 mg of 0.5% heavy Bupivacaine with 25 mcg Fentanyl in group two and found significant prolonged of post-operative analgesia .

Consistent with our study , Hwan Choi et al, (2000)used different doses of 0.5 hyperbaric bupivacaine (8,10,12 mg) with or without fentanyl 10 mcg and found a significant delayed of onset of postoperative pain when added fentanyl 10 mcg .

Rescue analgesia needed

Regarding to postoperative rescue analgesic needed we found significant differences in all groups in comparison to control group that was bupivacaine only. Fentanyl 25 mcg more significant and less analgesic requirements in post-operative period , which that correspond with Weigl et al, (2016) used 25 mcg fentanyl added to Bupivacaine compared to group placebo with Bupivacaine and found less analgesic consumption in fentanyl 25 mcg group

Conclusion:

In the current trial we studied dose response of four spinal solutions by addition of Fentanyl 25 mcg, 15 mcg and 10 mcg with reduced dose of 0.5% bupivacaine 7.5mg compared to conventional dose 0.5% bupivacaine 10 mg alone. Addition of Fentanyl to bupivacaine was effective with minimal side effects, prolonged the duration of sensory block, faster onset of sensory block and significantly reduced post-operative rescue analgesic needed and better hemodynamic stability. Where10 mg was in 0.5% bupivacaine alone gave faster of onset of motor block and prolonged of duration of motor block.

It is concluded that the best combination in spinal anesthesia for elective cesarean section is fentanyl 25 mcg with 0.5% bupivacaine 7.5 mg because it was superior in duration of effective analgesia and less post-operative rescue analgesic needed also more patients' satisfaction .

Study limitations:

- Study time is long.
- Public culture and awareness among participants.
- The study required more human resources.

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Annexes

Appendix 1

Consent Form

موافقة الاشتراك في البحث العلمي

اسم الباحث : عاهد سميح عبد اللطيف يحيى طالب ماجستير تمريض تخدير – جامعه النجاح الوطنية

د.نور الدين المصري –أخصائي طب تخدير–أستاذ مساعد – جامعه النجاح الوطنية

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

أنا الموقع أدناها: ... ...

اقر انه تم شرح طلب المشاركة في مشرع البحث العلمي بعنوان (دراسة استجابة جرعه دواء الفنتانيل مضافة إلى دواء بوبيفاكين في المرضى الذين يخضعون لعملية قيصرية اختيارية في التخدير الشوكي النصفي)

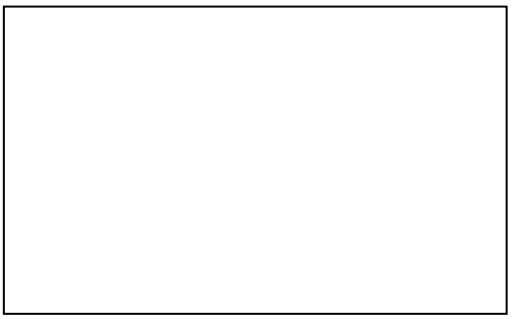
لقد أعطيت نسخة من توجيهات الطلب / المشروع واقبل المشاركة في المشروع. لقد تلقيت معلومات شفهية وخطية عن الدراسة، وأنا أدرك أن مشاركتي طوعية. وأنا على علم بأن في أي وقت، دون الحاجة إلى شرح، يمكنني أن انسحب من الدراسة إذا كنت ارغب في ذلك. إذا لزم الأمر يمكنني الاتصال لمقابلة جديدة أو توضيح ..

... ... توقيع المشترك

التاريخ

Appendix 2

Study – Data Sheet



Study data: (patient profile)

Age in years	
Weight in Kg	
Height in Cm	
Duration of Surgery	

Block table: Intraoperative:

Parameters	**Time**
Time of spinal puncture	
onset of sensory blockade to T10	
onset of sensory blockade to T6	
onset of motor blockade (measured by Bromberg scale)	

Pain table: intraoperative:

Pain location	Yes	No	Frequency	Intensity (vas).	Analgesia needed. (Vas > 4)
total analgesic times					

Side effect table:

Parameter	yes	No	Frequency or value	Required treatment
Bradycardia heart rate < 50 will treated by 0.5 mg atropine.				
Hypotension systolic blood pressure<100 mm HG Will treated by 12.5 to 60 mic neosynephrine.				
Headache				
Pruritus				
Shivering				
Nausea Likert type scale 0-6 (o no nausea, 6 intolerable), nausea ≥3 will treated by 10 mg metoclopramide iv.				
Vomiting: Vomiting ≥2 times will be treated by 10 mg metoclopramide iv.				
Restlessness				
Ramsay Sedation Scale (1-6)				
Respiratory Depression, respiratory rate < 10.				
Dizziness				
Drowsiness				

Apgor score table:

Apgar score	**At 1 minute** **(Value)**	**At 5 minutes** **(Value)**

Base line V/S: **BP**: **HR:** **RR:** **SPO2:** **T:** **ECG:**

Intraoperative hemodynamic					
Time	**BP**	**HR**	**RR**	**SPO2**	**ECG**
Immediate					
2 min					
4 min					
6 min					
8 min					
10min					
15 min					
20 min					
25 min					
30 min					
35 min					
40 min					
45 min					

Block table: Post-operative :(In PACU (0–2 hour postoperatively)

Parameters	**Time**
Sensory recovery to T10	
Motor recovery to B0	
duration of sensory blockade **time from sensory onset to sensory recovery to T 10**	
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**	

Post-operative hemodynamic: In PACU (0–2) hour postoperatively)					
Time	**BP**	**HR**	**RR**	**SPO_2**	**ECG**
Immediate post op					
15 min					
30 min					
45 min					
60 min					
2hrs					

In Ward (0-24 h postoperatively). Pain table:

Pain location	**Yes**	**No**	**Frequency**	**Intensity (vas).**	**Analgesia needed (Vas > 4)?**
total analgesic times					

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 severe systemic disease.

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

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

VI. Patient declared brain dead who see organs are to be harvested for do nor purposes.

Appendix 4

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 5

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 6

IRB approval Letter

Faculty of medicine
&Health Sciences
Department of Graduate
Studies

الوطنية
كلية الطب وعلوم الصحة
دائرة الدراسات العليا

IRB Approval Letter

Study Title:

"Dose response studyof intrathecal fentanyl added to bupivacaine in patients undergoing elective caesarean section in spinal anesthesia, A randomized, controlled,double-blind study"

Submitted by:

Ahed Sameeh,AbedAlateef Yahya, Dr. Aidah Alkaissi

Date Reviewed:

16th April 2018.

Date Approved:

3rd May 2018.

Your Study titled ***"Dose response studyof intrathecal fentanyl added to bupivacaine in patients undergoing elective caesarean section in spinal anesthesia, A randomized, controlled,double-blind study"*** with archived number (18) April 2018 was reviewed by An-Najah National University IRB committee and was approved on 3 May, 2018.

Hasan Fitian, MD

IRB

IRB Committee Chairman

An-Najah National University

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جـامــعة الــنجاح الــوطــنية

كليـــة الدراســات العليـا

دراسة استجابة جرعة من دواء الفنتانيل مضافة إلى دواء البوبيفاكايين في المرضى الذين يخضعون لعملية قيصرية اختيارية في التخدير الشوكي النصفي

إعداد

عاهد يحيى

إشراف

د. عايدة القيسي

د. نور الدين المصري

قدمت هذه الرسالة استكمالاً لمتطلبات الحصول على درجة الماجستير في تمريض التخدير، بكلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس- فلسطين.

2019

دراسة استجابة جرعة من دواء الفنتانيل مضافة إلى دواء البوبيفاكايين في المرضى الذين يخضعون لعملية قيصرية اختيارية في التخدير الشوكي النصفي

إعداد

عاهد يحيى

إشراف

د. عايدة القيسي

د. نور الدين المصري

الملخص

نبذه:

قد يؤدي التخدير النصفي الشوكي للعمليات القيصرية الى بعض الاثار الجانبية مثل انخفاض ضغط الدم الناجم عن جرعه دواء البوبيفاكايين، وعند اضافه أفيونيات قوية مثل دواء الفنتانيل، يمكننا من تقليل جرعة دواء البوبيفاكايين الزائدة المضرة، وهذا سيكون أكثر استقراراً لضغط الدم ويضمن تسكينا للالم بصوره جيده.

أهداف الدراسة:

أجريت هذه الدراسة لتقييم الآثار الجانبية للأربعة محاليل شوكية بغرض إيجاد أفضل توليفات ممكن من الفنتانيل والبوبيفاكايين ومقارنة كفاءة وسلامة هذه التوليفات باستخدام جرعات مختلفة من الفنتانيل في التخدير الشوكي في العملية القيصرية، ولتقييم الاثار الجانبية، ومدة تسكين الالم، ومدى استقرار الدورة الدموية ونتائج حديثي الولادة باستخدام مقياس أبغار.

أساليب الدراسة:

مائة وستون مريضاً تم اختيارهم بصورة عشوائية في أربع مجموعات، اربعين مريضاً في كل مجموعه:

المجموعة الأولى: (F10)

تلقت 1.5 مل (7.5 ملغ) من 0.5 ٪ بوبيفاكين ثقيل و 10 ميكروغرام من الفنتانيل.

المجموعة الثانية:(F15)

تلقت 1.5 مل (7.5 ملغ) من 0.5 ٪ بوبيفاكين ثقيل و 15 ميكروغرام من الفنتانيل.

المجموعة الثالثة:(F25)

تلقت 1.5 مل (7.5 ملغ) من 0.5 ٪ بوبيفاكين ثقيل و 25 ميكروغرام من الفنتانيل.

المجموعة الرابعة: (مجموعه المراقبة) (B10)

تلقت 2 مل (10 ملغ) من 0.5 ٪ بوبيفاكين ثقيل ومحلول ملحي لا يحتوي على الفنتانيل.

تم تقييم الآثار الجانبية: الغثيان، والقيء، وبطء دقات القلب، وحالات انخفاض ضغط الدم،والصداع، والحكة، والرعشة، والأرق، والدوخة، والتخدير، ورضا المرضى، ومتطلبات المسكن ومدة تسكين فعال. وعلاوة على ذلك، تم قياس بداية فقدان الاحساس ومدتها وايضا قياس بداية توقف الحركه ومدتها.

النتائج:

توزيع مماثل للعمر والطول والوزن ومدة العملية الجراحية كما يتضح من التحليل الإحصائي، كانت هناك فروق ذات دلالة إحصائية عند المستوى ($P \leq 0.05$) بالمقارنة بينB10 وF10 وF15 وF25 المتعلقة بفقدان الاحساس على مستوى الفقرة العاشرة T10 والفقرة السادسة T6 وتشير الدراسة ان مجموعه F25 هي الاسرع. لوحظ ان فقدان الحركة في وقت اسرع في مجموعه B10مقارنة مع الثلاث مجموعات أخرى ، وهو فرق ذو دلالة إحصائية. وفقاً لبطء دقات القلب لم تكن هناك اختلافات ذو دلاله إحصائية بين المجموعات. نوبات انخفاض ضغط الدم في مجموعه B10 أكثر شيوعًا (3.12)، وهو فرق ذو دلالة إحصائية عند مقارنته بالمجموعات الثلاث

الأخرى. انخفض معدل حدوث الصداع في مجموعات الفنتانيل (F10, F15, F25) مقارنة مع مجموعةB10 ولكن لم يكن هناك اختلافات ذو دلاله إحصائية.

كانت هناك فروق ذات دلالة إحصائية فيما يتعلق بحدوث الحكة في مجموعات F25 (40/9) وF15 (40/6) بالمقارنة معB10 وقد لوحظ الغثيان والقيء في المجموعةB10في حين انخفض بشكل ملحوظ في المجموعات الثلاث الأخرى. وفقاًللأرق والتخدير وفشل في الجهاز التنفسي لم تكن هناك أي اختلافات بين المجموعات. لم تكن هناك فروق ذات دلالة إحصائية في درجات أبغار في الدقيقة الاولى والخامسة. فتره فقدان الاحساس كانت اطول بشكل كبير في مجموعات الفنتانيل وكانت ذو دلاله إحصائية. انخفضت فتره فقدان الحركة بشكل كبير مع انخفاض جرعةالبوبيفيكايين ولوحظت بداية استعاده الحركة بشكل ملحوظ في مجموعات الفنتانيل مقارنة بمجموعة B10. زادت مدة التسكين الفعال مع زيادة جرعة الفنتانيل التي كانت فرقًا ذو دلالة إحصائية في جميع مجموعات الفنتانيل مقارنةً بمجموعة .B10 فيما يتعلق بمسكنات ما بعد الجراحة اللازمة ، وجدنا فروق ذات دلالة إحصائية في جميع مجموعات الفنتانيل مقارنةً بمجموعة المراقبةB10، مجموعهF25هي الاقل من حيث متطلبات مسكنات للألم بعد الجراحة بمتوسط (1.85) متبوعة بمجموعه F15 (2.3) ثم مجموعه B10 (2.37) واخيراً F10 (2.42).

الملخص:

كانت إضافة دواء الفينتانيل فعالة مع الحد الأدنى من الآثار الجانبية، كما يحسن من جودة التخدير ويطيل فتره فقدان الاحساس واستعاده الحركة بشكل مبكر ويقلل بشكل كبير من متطلبات تسكين الالم بعد العملية الجراحية، وكذلك اكثر استقرار للدورة الدموية، بينما استخدام دواء البوبيفكايين لوحده يسرع في فقدان الحركة ويطيل فتره فقدان الحركة. أخيرًا، نختتم ونوصي بأفضل مزيج في التخدير النصفي الشوكي للولادة القيصرية الاختيارية هو الفنتانيل 25 ميكروغرام مع 0.5٪ بوبيفاكايين 7.5 ميلي غرام لأنه كان متفوقًا في مدة تسكين فعال وأقل متطلبات لتسكين الالم بعد العملية الجراحية وهو ايضا الاكثر رضا للمرضى واقل تأثير جانبي من المجموعات الاخرى. في الختام فنتانيل 25 ميكروغرام مع 0.5 ٪ بوبيفاكايين 7.5 ملغ هو أكثر ملاءمة.

الكلمات الدالة:

الفنتانيل، البوبيفاكايين، التخدير الشوكي، العملية القيصرية.