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THE CLINICAL TRIAL OF THREE DIFFERENT DOSES OF 0.5% BUPIVICAINE-FENTANYL IN SPINAL ANAESTHESIA FOR CAESAREAN DELIVERY

Dr. Natiq D. Shaalan*

Bahrka St, Gulan City, Erbil, Iraq.

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***Corresponding Author: Dr. Natiq Shalan**

Bahrka St, Gulan City, Erbil, Iraq.

ABSTRACT

Background: The combination of local anesthetics (0.5%bupivacaine) and opioid (fentanyl) in spinal anesthesia for Caesarean delivery has been practiced worldwide as it is safe, effective and has less maternal complications. This study aims to examine the effictiveness of 3 different doses of mixed spinal 0.5% bupivacaine with fentanyl and their subsequent maternal effects. **Patients and Methods:** After the consent was obtained from the patients who were included in our study, the prospective clinical trial case control study was conducted with the approval of the scientific committee of Iraqi consult. This study was conducted at the Department of Anesthesiology & Intensive Care, in obstetrics and gynecology hospital in Erbil from September to October 2015. Around 90 candidates of normotensive women with ASA I and II underwent elective Caesarean delivery under spinal anesthesia were randomly allocated into three groups of 30; group A received 10 mg (2ml) of 0.5% bupivacaine + 25 mcg fentanyl, group B received 12.5 mg (2.5ml) of 0.5% bupivacaine +25 mcg fentanyl, group C received 15 mg (3ml) of 0.5% bupivacaine +25 mcg fentanyl. In addition to the standard monitoring of vital signs, spo2 and ECG, monitoring of the anesthetic effects (onset of action, level of sensory block and muscle power (motor block)) were performed at 3 minutes interval after induction and preoperatively. Any complications that could occur during operation like nausea and vomiting were observed as well. **Results:** A total sample of 90 pregnant women underwent elective Caesarean delivery were selected in this study, with mean± S.D age of 27.36±6.126 years, and mean ±S. D weight of 72.69±10.24 kg. 60%, 73.3% and 80% for group A, group B and group C, respectively. Bolus dose of ephedrine was used for these cases. The heart rates of the patients among the study groups displayed significant difference between the study groups as the p-value was highly significant ($p<0.005$). Apparently, there was no significant difference in different doses of anesthetic drugs among the study groups regarding their onset of action, since the anesthetic agent of group C was the fastest to work by only 3.3 minutes while group A was slow to act with average of 4.4 minutes. However, the relationship between study groups and muscle power (motor block level) showed significant difference. The level of T10 dermatomal anesthesia reached in 99% of cases at 9^{th} min after anesthetic induction. **Conclusions:** The combination of 0.5% bupivacaine and fentanyl in spinal anesthesia for Caesarean delivery was highly effective with excellent level anesthesia , however in addition to its hemodynamic side effect of given doses, it would give unnecessary sensory blockade level that would change blood pressure and pulse rate.

KEYWORDS: Bupivacaine, Fentanyl, Spinal anesthesia and Caesarean delivery.

INTRODUCTION

For patients undergoing Caesarean delivery, spinal anesthesia offers them a fast and profound anesthesiaexperience that revolves on symmetrical sensory and motor block of excellent quality.[1,2] However, there are some adverse effects concerning the use of spinal anesthesia. Most commonly reported effect is hypotension that has incidence rate of 55-90%.[3] Therefore, several ways have been proposed to overcome this issue as hypotension possesses further detrimental effects on both maternal and neonatal. One of the strategies is to practice lateral urine displa-cement.[4] Besides, some health practitioners suggest the application of intravenous fluid preload, manipulation of gravity using Trendelenburg technique, devices compression on legs and prophylactic vasopressors to prevent hypotension during administration of spinal anesthesia.[1]

Yet, no methods have achieved satisfactory outcomes. The administration of spinal analgesic drugs (spinal opioid) in combination (mixing) with local anaesthetic has become widespread since the combination has been shown to be synergistic. Since the opioid thought to bind to opioid receptors in the substantia gelatinosa of spinal cord modu -lating pain pathways, and ability to provide analgesia distant to the level of injection. A segmental effect has been reported, i,e. Maximal analgesia corresponding to the level of injection.[5]

Review of spinal anesthesia

Spinal anesthesia is one of the local anesthesia that involves injection of regional anesthetic into the interval space of arachnoid membrane and pia mater. This technique is also known as spinal block, spinal analgesia or sub-arachnoid block. It is generally administered through a fine, 9 cm long needle. Longer needles (>12.7 cm) are available for obese and extremely obese patients.

Injected substances

Bupivacaine (marcaine) is the most commonly used local anesthetic, although others may also be an option such as levobupivicaine, cinchocaine, lidocaine, tetracaine, ropivacaine, procaine, and procaine. Usually, opioids such as morphine, fentanyl, diamorphine or orbuprenorphine are being added to improve the numbing effect. They also serve as post-operation pain relief. In addition, non-opioids, for instance, clonidine may also be used together to extend the analgesia duration. It is noteworthy that hypotension might occur as a result of the side effect from clonidine. Meanwhile, The National Institute for Health and Care Excellence (NICE) suggests coupling of spinal anesthesia with intrathecal diamorphine for Caesarean section surgery. This combination acts as the modal form of anesthesia in that country. However, different legality of diamorphine (heroin) in different countries means that this cannot be practiced elsewhere without certain authorization.

Baricity is the comparison of density difference between any particular substances with respect to human cerebral spinal fluid. It is applicable to predict the spread behavior of a specific drug passing the routes of intrathecal space. Usually, hyperbaric drug, for instance, bupivacaine is selected because its spread can be effectively predicted and controlled by the anesthesiologist or nurse anesthetist. Hyperbaric solutions are prepared by adding glucose into the mixture. Apparently, adding solute into a solvent to create dissolution effect has direct impact on the spread of the drug. Particularly in tetracaine spinal anesthesia, it is reported that the onset rate of numbness is faster to reach maximum level when 10% glucose solution is used for spinal anesthetic solution rather than 5% glucose. Moreover, lesser amount of ephedrine is required when the patients receive 10% glucose solution rather than 5% glucose solution.[7]

Mechanism

Irrespective of the anesthetic agents, the aim is to ensure that the signals form afferent nerve are not transmissible from the peripheral nociceptors. In doing so, the pain will be eliminated by creating numbness.

Apparently, the degree of neuronal blockade can be influenced by a number of factors, specifically, the dose amount of local anesthetic and the axon properties. At first, pain sensory nerve that is thin, unmyelinated C-fibers.

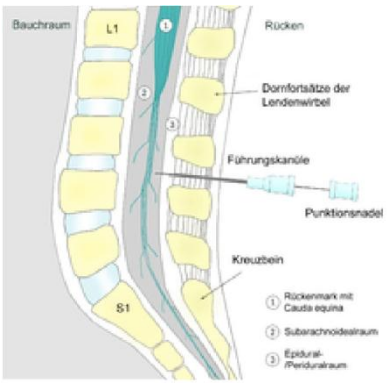

Figure 1: (Schematic drawing of the spinal anesthesia principles).

will be blocked. Meanwhile, thick, heavily myelinated A-alpha motor neurons are blocked moderately. As a result, the site area will achieve numbness. Nevertheless, pressure sensation can still occur when the thicker A-beta mechanoreceptors are not blocked completely. Consequently, surgical procedures can be accomplished without inflicting painful sensation upon the patient. Sedation is often given to aid relaxation for the patient during this procedure. Remarkably, with this efficacious spinal anesthetic, the patient can be wide awake while the surgery is ongoing.[7]

Indication

Spinal anesthesia can be conducted by its own or combined with sedation/general anesthesia. It is a common anesthetic technique to be practiced for surgeries such as leg surgeries, aneurysm repair, nephrectomy, cystectomy, prostate surgery, laparoscopy, hernia, hysterectomies and others.

Spinal anesthesia is recommended for Caesarean section surgery as it does not use general anesthetics to reduce the risk of failed intubation that can occur approximately 1 in every 250 pregnant woman. In addition, during the procedure, the mother is awake and the partner is allowed to be present. This is a great news for patients with severe respiratory diseases e.g. COPD and anatomical abnormalities to avoid intubation and ventilation as well as minimizing the risk of endotracheal intubation.

Contraindications

- Performed without patient's consent.
- Potential local infection or sepsis at the lumbar puncture site.
- Might be risky for patients with bleeding disorders, thrombocytopaenia, or systemic anticoagulation (secondary to an increased risk of a spinal epidural hematoma).
- Space occupying lesions of the brain.
- Anatomical disorders of the spine.
- Hypovolemia following massive hemorrhage, including in obstetric patients.

Complications

Can be broadly classified as:

*Immediate – on the operating table, or

*Late – in the ward or in the post-anesthesia care unit, (P.A.C.U.)

- Hypertension (Spinal shock)
- Due to sympathetic nervous system blockade. It is common but usually easily treated with intravenous fluid and sympathomimetic drugs such as ephedrine, phenylephrine or metaraminol.
- Post dural puncture headache (PDPH) or post spinal head ache that is always associated with the size and type of spinal needle used.[8]
- Cauda equina injury - very rare, due to the insertion site being too high
- Cardiac arrest - very rare, usually related to the underlying medical condition of the patient.
- Spinal canal hematoma, with or without subsequent neurological sequelae due to compression of the spinal nerves. Urgent CT/MRI to confirm the diagnosis followed by urgent surgical decompression to avoid permanent neurological damage
- Epidural abscess, again with potential permanent neurological damage. May present as meningitis or an abscess with back pain, fever, lower limb neurological impairment and loss of bladder/bowel function. Urgent CT/MRI confirms the diagnosis followed by antibiotics and urgent surgical drainage.[6,7]

Currently, spinal anesthesia is offered as one of the options to relieve pain during labor. As opposed to epidural, this procedure is quicker, easier, cost effective and more comfortable with lower complication rates.[9] It is noted that the spinal block will cause maternal hypotension as a direct result of peripheral vasodilation and venous pooling. The incident is most likely to occur at high chances of 80-100% without prophylactic measures.

This remains as the major concern even though thorough precautions and investigations have been made. It is called "Holy Grail" of obstetric anesthesia as the negative effects of the hypotension will implicate both mother and child. The mother would feel nauseous, vomiting and dizziness.[10] Meanwhile, fetal hypoxia and acidosis are the potential risks to occur as a result from reduced uterine and intervillous blood flow due to hypotension. Therefore, proper treatments and prevention of hypotension have been the subjects of many investigations and also controversies.

Prophylactic measures can be done through a number of ways, namely tilting at left lateral, preloading fluid, application of vasopressors, and administering low dose of spinal anesthesia. Lateral tilt at 15° left is applied regularly during Caesarean section to prevent the compression of aorto-caval. However, it cannot act as the main solution. Left uterine displacement is achieved by tilting the operating table or by placing a wedge under the patient's hip.[10]

Bupivacaine

Bupivacaine is a type of drug that contains amino amide group. Generally, it is known by several trade names including vivacaine, marcaine, marcain and sensorcaine. It is formulated for local infiltration and acts to block retrobulbar, epidural, caudal, peripheral nerve and sympathetic nerve with retrobulbar blockade employs the most concentrated formulation (0.75%). This type of drug is widely using in local anesthetic especially for labor and management of postoperative pain. Occasionally, it is combined with epinephrine to extend the action interval. The combination also aims to prevent systemic absorption.[11]

Contraindications

Bupivacaine can be contraindicated for several patient's conditions. First, it should not be used on patients with known hypersensitivity reactions to bupivacaine or amino-amide anesthetics. It is also contraindicated in obstetrical paracervical blocks and intravenous regional anesthesia (Bier block) protocols. It bears potential risk of tourniquet failure, systemic absorption of the drug and subsequent cardiac arrest. In addition, the 0.75% formulation is contraindicated in epidural anesthesia during labor due to its association with refractory cardiac arrest.[11]

Adverse effects

When compared with other local anesthetics, bupivacaine is evidently cardiotoxic. Nevertheless, adverse drug reactions (ADRs) are rare to happen when it is administered correctly. Most ADRs are initiated by quick absorption from the injection site, unintentional intravascular injection or slow metabolic degradation. Notably, allergic reactions are less likely to occur.[12]

As a result of bupivacaine systemic absorption, the adverse events are clinically significant that incriminate the central nervous system (CNS). Typically, the CNS effects will transpire when the blood plasma concentrations are low. Selective pathways of cortical inhibitory are blocked to manifest the signs of neuronal excitation. When the plasma concentrations are getting higher, both inhibitory and excitatory pathways will be blocked, leading to depression of CNS depression and

possibly comatose. This condition can also impact the cardiovascular system though alarmingly, cardiovascular failure might occur at low plasma concentrations.[16] Apparently, the CNS effects signify imminent cardiotoxicity. Thus, these changes should be carefully monitored.[11]

- CNS effects: circumoral numbness, facial tingling, vertigo, tinnitus, restlessness, anxiety, dizziness, seizure, coma.
- Cardiovascular: hypotension, arrhythmia, bradycardia, heart block, cardiac arrest.

Toxicity is possible to occur during application of subarachnoid injection when performing spinal anesthesia at high concentration. The toxicity effects that might transpire are apnea, hypoventilation, fecal incontinence paresthesia, paralysis and urinary incontinence. Furthermore, chondrolysis might manifest after continuous infusion into a joint space. Unfortunately, it has been reported that bupivacaine has caused several deaths when the epidural anesthesia is administered intravenously by accident.[11]

Treatment of overdose

Intralipid, a common intravenous lipid emulsion is effective to treat cardiotoxicity caused by local anesthetic overdose. Successful treatment for human case has been reported extensively.[13]

Pregnancy and lactation

Bupivacaine is able to cross the placenta, hence it is being categorized as category C drug for pregnant patients. Animal reproduction studies have demonstrated some adverse effects imposed on the fetus. Despite those potential risks, the potential benefits of the drug have permitted its use in pregnant women even though the well-control studies in humans are still limited. It is approved to be used at term as obstetrical anesthesia. The fact that bupivacaine is excreted in breast milk, all risks concerning to discontinuing breast feeding versus discontinuing bupivacaine should be discussed with the patient.

Mechanism of action

sFirstly, bupivacaine will bind to the intracellular portion of voltage-gated sodium channels. This will block sodium influx into nerve cells which prevents depolarization. As a result, no initiation or conduction of pain signal arises.[11]

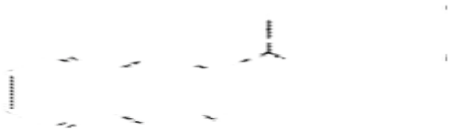

Figure 2: chemical structure of Bupivacaine.

Usual Adult Dose for Local Anesthesia

A single dose of bupivacaine for an adult is prescribed up to 175 mg. However, any increment or reduction of the dose may be used to cater individualize dose. Recurring doses are up to once every 3 hours. Notably, the maximum dose is 40.0 mg within 24 hours. For local infiltration, about 0.25% concentration is given as injection is up to the maximum dose.

Epidural block

For epidural block, different concentrations demand different injection doses as tabulated in Table 1.

Table 1: Injection dose based on drug concentration.

Concentration, %	Injection dose, mg	Remark(s)
0.75	75-150	Complete motor block, not applicable for obstetrical anesthesia
0.5	50-100	Moderate-to-complete motor block
0.25	25-50	Partial-to-moderate motor block, repeat dose will increase the motor block degree

The concentrations of epidural anesthesia in the range of 0.5-0.75% must be administered by 3-5 mL increment with adequate time between doses. This approach is commendable to distinguish toxicity that might arise from accidental injection into intravascular or intrathecal. Meanwhile, in obstetrics, only 0.5% and 0.25% concentrations of epidural should be used. Maximum 0.5% solution can be administered by 3-5 mL increment that is not exceeding 50 to 100 mg at any dosing interval. Notably, repeat dose should be accompanied with epinephrine that if they are not contraindicated, preservative-free products can be used.

Bupivacaine in dextrose injection

For lower extremity and perineal procedures such as prostate transurethral resection and hysterectomy of vagina, 7.5 mg (1 mL) of spinal anesthesia is used. Meanwhile, procedures for lower abdominal parts, e.g. abdominal hysterectomy, tubal ligation and appendectomy, 12 mg (1.6 mL) is used whilst 6 mg dose is used for vaginal delivery.[14]

Treatment of overdose

Animal model studies demonstrate that intralipid can be effective to treat severe cardiotoxicity that transpires due to local anesthetic overdose. Successful strategy is achieved in human case studies.[15]

Pharmacokinetics

In general, the rate of systemic absorption for bupivacaine and other local anesthetics is heavily influenced by the drug dosage, the concentration of drug administered, the administration route, the administration site vascularity and the availability of epinephrine during

the preparation.[12] The pharmacokintetics of bupivacaine are listed in Table 2.

Table 2: Pharmacokinetics of bupivacaine.

Pharmacokinetics	Details
Onset of action	1-17 min (route and dose dependent)
Hal life	8.1 h (neonates), 2.7 h (adults)
Time to peak plasma concentration	30-45 min
Protein binding	~95%
Type of metabolism	Hepatic
Site of excretion	Renal (6% unchanged)

Chemical structure

Similar with lidocaine, bupivacaine is an amino-amide anesthetic. It contains aromatic head and hydrocarbon chains that are linked by amide bond rather than ester group in earlier local anesthetics. As a result, the amino-amide anesthetics are more stable and less likely to cause allergic reactions. Unlike lidocaine, the terminal amino portion of bupivacaine (as well as mepivacaine, ropivacaine, and levobupivacaine) is located within piperidine rings, known as pipecholyl xylidines.[12]

Fentanyl Citrate

Fentanyl citrate is a synthetic opioid that is derived from pethidine. The manufacturing of this analgesic drug began in 1960s that exhibits 100 time analgesic potent as morphine. It is widely used preoperatively as an analgesic, for sedation (e.g.in ICU) and in chronic pain. Onset of action is within 4-5 min. Duration of action is about 20 min.,terminated by redistribution, initially as plasma clearance is less than morphine, but fentanyl is more highly lipid- soluble than morphine, thus cross the CSF and bind to the spinal cord more rapidly. Opioids are often mixed with local anesthetics since combination has been shown to be synergistic (e.g. bupivacaine plus fentanyl or diamorphine). Fentanyl is widely used in the UK for bolus and infusion in labour.

Postoperative respiratory depression is possible side effect if large doses are used, especially in combination with opioid premedication and other depressant drugs. Causes minimal histamine release or cardiovascular change, although may cause bradycardia.[20]

Dosage:

- To obtund the pressure response to laryngoscopy: 7-10 mcg/kg i.v.
- As a co-induction agent/ during anesthesia: 1-3 mcg/kg i.v. with spontaneous ventilation: 5-10 mcg/kg with IPPV. Up to 100 mcg/kg is used for cardiac surgery.

Muscular rigidity and hypotension are more common after high dosage.

Has been used in neuroleptanaesthesia.

- By infusion: 1-5 mcg/kg/hr., e.g. for sedation. For patient-controlled analgesia: 20-100 mcg bolus with 3-5 min. Lockout.
- 25, 50, 75 or 100 mcg/hr. Transdermal patch placed on the chest or upper arm and replaced (using a different sites) every 72 hr. A patch employing iontophoresis has been developed for postoperative patient-controlled analgesia, but is not currently marketed.
- 100-800 mcg sublingual lozenges for break through cancer pain or short painful procedures (e.g.burns dressing change).[20]

PATIENTS AND METHODS

(Study design): A non-randomized controlled clinical trial case control study used as per approval of the scientific committee of Iraqi consult.Normotensive women with ASA of I&II (n=90) were randomly divided into three groups of 30, lablled as group A, B and C. They received 25mcg fentanyl mixed with the following doses of 0.5% bupivacaine that was given in each group as follows; 10 mg, 12.5 mg and 15mg for group A, B and C, respectively. They were injected intrathecally at the level of L3-L4 in sitting position. Cold sensation test was used to determine the dermatomal level of sensory block. Next, Two Peripheral venous canulat were done for each patient, one on each hand dorsum or forearm with cannula gauge 18 or 20. Spinal needle gauge 22 was used for injection in all cases.All patients had been given 1000 ml. Crystelloid preoperatively; 500 ml (0.9% normal saline) + 500 ml. (5% glucose and 0.9% normal saline) as the patient lying in the left lateral tilt position and continue i.v. fluid intraoperative according to need and vital signs measurement.In addition to the standard monitoring of vital sings, spo2 and ECG at pre and perioperative. In addition to that period were performed at 3 minutes interval post induction and continued perioperatively and also monitoring for complications that could be occur during operation like hypotension, nausea and vomiting was performed.

Study population: The patients considered for inclusion were adult female indicated for elective caesarean section. Study was carried out at Erbil Obstetrics and Gynecology Hospital. The study period was from 1st of December 2014 to 30 october 2015.

The study sample was 90 healthy pregnant women without fetal compromise of ASA I and II who would undergo elective Caesarean section under spinal anesthesia were included in the research.

Inclusion criteria

1- Women advised for elective CS with term single gestation pregnancy
2- of 39-41 weeks of single gestation.
3- Age between 18-39 years.
4- Weight between 60-80 kg.
5- Hight between 155-170 cm.
6- Women belonging to ASA I and II category.

Exclusion criteria

1- Patients refused to participate in the study
2- Parturient with obstetric complications, with ASA III or more like
3- PIH, pre-existing uncontrolled hypertention and Obesity.
4- Women with evidence of fetal anomalies and fetal compromise.
5- Patients who are contraindicated for spinal anaesthesia.
6- Any allergy for drugs used.
7- Patients who developed labor pains before induction of spinal anesthesia

Statistical analysis.

*Data were collected using standardized data collection form/ Chi square and ANOVA test using SPSS statistical software ver16 were used for data analysis.

*ANOVA test at p-value < 0.05 level of significance was the measure for statistical significance.

RESULTS

1: Demographic data: A 90 pregnant women undergoing spinal anesthesia for elective cesarean delivery were enrolled this study, with mean± S.D age of 27.36±6.126 years, and mean ±S.D weight of 72.69±10.24.

Table 1: Demographic data of cases.

	Minimum	maximum	Mean	S.D
Age in years	18	39	27.36	6.126
Weight in Kg	60	80	70.803	10.24

2: Hemodynamic monitoring

- Systolic blood pressure (SBP).

The data from Table (2) show significant difference in SBP among the study groups over the course of operations, except for the beginning and 21 minutes. ANOVA- test was done to compare between them.

- Diastolic blood pressure (DBP).

The analyzed findings from Table (3) illustrate that there was a significant difference in DBP among the study groups in all times during the surgery except for the beginning of the operation in which all groups had approximate readings. ANOVA- test was performed to compare between the average DBPs of the three groups.

- Heart rate.

The data of Table (4) prove that there was significant difference among study groups in regarding heart rates of the patients. ANOVA test was performed to find the relationship and P – values were highly significant and in all conditions less than 0.05.

Table 2: Systolic blood pressure (SBP) difference among study groups.

Variables	Study groups	N	Mean	P-value	ANOVA test
	A	30	127.40		
SBP0min	B	30	127.83	0.52	Non-difference
	C	30	129.17		
	Total	90	128.13		
	A	30	122.00		
SBP3min	B	30	118.93	0.046	difference
	C	30	114.17		
	Total	90	118.37		
	A	30	108.40		
SBP6min	B	30	105.63	0.006	difference
	C	30	97.57		
	Total	90	103.87		
	A	30	98.00		
SBP9min	B	30	96.10	0.02	
	C	30	90.47		difference
	Total	90	94.86		
	A	30	96.47		

SBP12min	B	30	94.20	0.004	difference
	C	30	89.93		
	Total	90	93.53		
	A	30	103.13		
SBP15min	B	30	95.67	0.0001	difference
	C	30	90.57		
	Total	90	96.46		
	A	30	108.53		
SBP18min	B	30	102.70	0.0001	difference
	C	30	99.43		
	Total	90	103.56		
	A	30	111.00		
SBP21min	B	30	110.73	0.067	Non- difference
	C	30	108.13		
	Total	90	109.96		

Table 3: Diastolic blood pressure (DBP) difference among study groups.

Variables	Study groups	N	Mean	P-value	ANOVA test
	A	30	80.97		
DBP0min	B	30	79.80	0.10	N0n- difference
	C	30	81.97		
	Total	90	80.91		
	A	30	77.17		
DBP3min	B	30	72.73	0.010	
	C	30	70.00		difference
	Total	90	73.30		
	A	30	65.20		
DBP6min	B	30	60.47	0.006	
	C	30	56.00		difference
	Total	90	60.56		
	A	30	55.20		
DBP9min	B	30	51.17	0.043	difference
	C	30	49.87		
	Total	90	52.08		
	A	30	51.40		
DBP12min	B	30	49.57	0.0001	difference
	C	30	46.63		
	Total	90	49.20		
	A	30	56.97		
DBP15min	B	30	51.00		
	C	30	45.23	0.0003	difference
	Total	90	51.07		
	A	30	63.73		
DBP18min	B	30	58.33		
	C	30	55.13	0.0002	difference

	Total	90	59.07		
	A	30	62.90		
DBP21min	B	30	62.13		
	C	30	61.80	0.0001	difference
	Total	90	62.94		

Table 4: Heart rate difference among the study groups.

Variables	Study groups	N	Mean	P-value	ANOVA test
	A	30	88.30		
HR0min	B	30	88.30	0.016	Non- difference
	C	30	91.57		
	Total	90	89.39		
	A	30	93.27		
HR3min	B	30	89.57	0.0001	difference
	C	30	99.37		
	Total	90	94.07		
	A	30	100.33		
HR6min	B	30	98.00	0.0004	difference
	C	30	107.70		
	Total	90	102.01		
	A	30	107.27		
HR9min	B	30	102.20	0.002	difference
	C	30	112.17		
	Total	90	107.21		
	A	30	112.03		
HR12min	B	30	105.63	0.003	difference
	C	30	110.37		
	Total	90	109.34		
	A	30	112.30		
HR15min	B	30	108.77	0.0012	difference
	C	30	107.00		
	Total	90	109.36		
	A	30	107.80		
HR18min	B	30	103.40	0.005	difference
	C	30	101.57		
	Total	90	104.26		
	A	30	105.77		
HR21min	B	30	100.97		
	C	30	100.33	0.0004	difference
	Total	90	102.36		

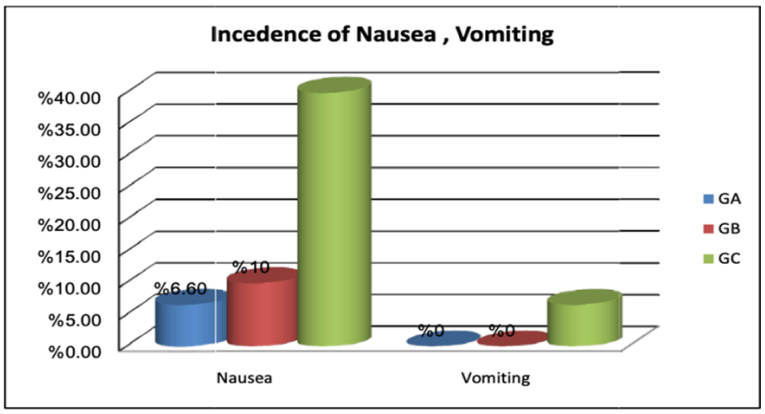

Figure 2: Ince dence frequency of nausea, vomiting among the study groups.

There is significant rel ation ship between study groups and incidence frequency of nausea. P-Values were significant and less than 0.001.

Table 5: association between study groups and incidence frequency of nausea and vomiting.

	G.A	G.B	G.C	P-Value
Nausea	6.6%	10%	%40	<0.001
Vomiting	0 %	0%	6.6%	0.462

Table 6: difference i n used doses of ephedrine among the study groups.

ephedrine used (mg)	Group-A (%) N	Group-B (%) N	Group-C (%) N
no	19(63.4 %)	17 (56.7 %)	13 (43.3 %)
5	7(23.3 %)	9 (30%)	3(10%)
10	4(13.3 %)	4(13.3 %)	3(10%)
20	-	-	11(33.7%)
total	30(100 %)	30 (100%)	30(100 %)

DISCUSSION

Even though spinal anesthesia for Caesarean section has been practiced for a long time and well-established, hypotension remains to be a problem as it is the most common complication reported. It is very frequent, accounting 55-90% of prevalence if not prevented.[3]

In this study, it was found that the BP was reduced (hypotension is regarded if systolic arterial blood pressure is below 100 mmHg or if its fall in systolic arterial blood pressure is more than 20% below baseline) as the dose of bupivacaine was increased in spinal anesthesia (about 36.6% of group A, 43.3% of Group B and 53.7% of Group C). Note that the bolus dose of ephedrine was used for these cases.

Based on a study conducted by Moya and Smith (1962), they found that after spinal anesthesia, the blood pressure was lowered by 10%, 20% and 30% in 68%, 46% and 23% of different groups of mothers, respectively.[18]

Carvalho B et al., 2005 demonstrated that reduced dose of bupivacaine might lead to decreased hypotension.[19] Ben- David B et.al reported a three-time decrease in the occurrence of hypotension and nearly ten-time reduction of ephedrine amount required in those patients who received lower dose spinal anesthetics when they decreased the bupivacaine dose from 12 mg to 4.5 mg.

In the present the incidence frequency of nausea in Group A was 6.6%, 10% in Group B and 40% in Group C. Vomiting was recorded with low incidence only in group C (6.6%), and these mostly occur due to hypotension, hypoxemia to the vomiting center and sometimes following excessive elevation of blood pressure due to administration of vasopressors. Bruce Ben- David studied 32 women who underwent Caesarean section under spinal anesthesia. His study revealed that amini dose of 5 mg of 5% bupivacaine in combination with 20 mcg of fentanyl yielded successful spinal anesthesia and less hypotension, less vasopressor requirement and decrease incidence of nausea.[17]

However, notable spread increase was observed when the volume was increased from 2 to 3 mL. Therefore, they concluded that the spinal anesthesia could be further spread and prolong by manipulating its volume. According to that, in our study, a statistical difference between groups A, B and C were suggested due to the difference in anesthetic doses and/or volume.

CONCLUSIONS

This Study demonstrated that the combination of 12.5 mg (2.5cc) of 0.5% bupivacaine and 25 mcg (0.5cc) fentanyl as spinal anesthesia was highly effective for Caesarean delivery with excellent level anesthetic and analgesic satisfaction. Less hemodynamic side effect of the given dose were managed to achieve.

Recommendation

The study recommend that the patients undergoing spinal anesthesia for Caesarean delivery is better to receive low dose (12.5mg) of 0.5%Bupivacaine(2.5cc) mixed with 25 mcg (0.5cc) of Fentanyl, since they provide satisfactory level of anesthesia and analgesia with less hemodynamic side effect as hypotension, nausea, vomiting ...etc.

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