

# Comparative Study of Low Dose Bupivacaine-Fentanyl versus Conventional Dose of Bupivacaine in Spinal Anesthesia for Orthopedic Procedures in Elderly Patients: A Prospective Randomised Double Blind Study

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**Abstract:** **Background:** Perioperative hypotension may affect postoperative recovery and increases risk of ischemia. Opioids and local anaesthetics administered together intrathecally have potent synergistic analgesic effect, enhancing the sensory blockade without altering the degree of sympathetic blockade ensuring better hemodynamic stability. **Objective:** To compare the low dose of Bupivacaine-Fentanyl and conventional dose of Bupivacaine in spinal anesthesia for orthopedic procedures in elderly patients. **Methodology:** After institutional ethics committee approval & written informed consent, 60 patients of both sex, age >50 years; with American Society of Anesthesiologists (ASA) physical status I, II & III, who are undergoing Elective lower limb orthopaedic surgeries were taken into study. They are divided into 2 groups (n=30). Group A - Received Bupivacaine 15mg (3ml). Group B - Received Bupivacaine 10mg (2ml) +25mcg Fentanyl made to 3ml by adding normal saline. Parameters like time of onset of adequate level of analgesia, duration of motor block, duration of sensory block, hemodynamic parameters blood pressure, heart rate, incidence of complications were noted in both groups. **Result:** Groups were comparable for Demographic data (Age, Weight, duration of surgery. Statistical analysis was done with Student test, p-value of <0.05 are considered to be significant. Duration of sensory block & motor block was slightly more for group A. Low pulse rates and less fall in blood pressure was noted in group B. Incidence of hypotension and use of vasopressors was much higher in group A. **Conclusion:** Subarachnoid block with 10mg Bupivacaine 0.5% & 25mcg Fentanyl is more safer and better option in lower limb surgeries in terms of maintaining hemodynamic stability and lower incidence of complications in elderly patients.

**Keywords:** fentanyl, bupivacaine, spinal, orthopedic, elderly

## 1. Introduction

Anesthesia of choice for lower limb surgery is subarachnoid block producing less post-op confusion and delirium than general anesthesia. Perioperative hypotension may affect postoperative recovery and increases risk of ischemia, coronary disease secondary to hypotension. Vasopressor and IV fluids are used to treat or prevent hypotension.

Studies have established that Opioids and local anaesthetics administered together intrathecally have potent synergistic analgesic effect, enhancing the sensory blockade without altering the degree of sympathetic blockade ensuring better hemodynamic stability. (1, 2, 3)

**Bupivacaine:** It is the R-isomer, highly lipid soluble with pKa 8.1. It is mainly used for neuraxial blockade. It is (1-butyl-2,6-pipecoloxylidide hydrochloride). It obstructs the inward flow of the sodium ions through the nerve membrane, thus preventing the generation of an action potential. Competitive binding to calcium sites is postulated to occur in the external lipid layer of the nerve membrane with resultant secondary interference of mobile phosphate groups. Passage of sodium ion is blocked by preventing molecular membrane reconfiguration from the resting (sodium impermeable) to the active (sodium permeable) state.

**Fentanyl:** Fentanyl, N-(1-phenethyl-4-piperidyl)

propionanilide, is structurally related to meperidine. It has a molecular weight of 528.29 and a melting point of 148.5 to 150 degree centigrade. The octanol-water partition coefficient at physiologic pH is 816 for fentanyl compared with 1.4 for morphine. It is synthetic pure agonist at  $\mu$  receptor with pKa 8.4, highly lipid soluble. Opioids have multiple central and peripheral mechanism of analgesic action. Spinal administration of Opioids provide analgesia primarily by attenuating C fibre nociception. Co administration of Opioids with central neuraxial local anaesthetics results in synergistic analgesia.

## 2. Objective

To compare the low dose of Bupivacaine-Fentanyl and conventional dose of Bupivacaine in spinal anesthesia for orthopedic procedures in elderly patients

## 3. Methodology

After taking approval from ethical committee of our institute Rangaraya Medical College, study had been done in Department Of Anesthesia, Government General Hospital, Kakinada from June 2019 to September 2019 on 60 patients.

**Type of study:** This is a prospective randomized double blinded study

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Written informed consent for anaesthesia was taken and all patients were thoroughly examined on the previous day of surgery and routine investigations were carried out.

All the 60 patients scheduled for surgeries were randomly divided into 2 groups by simple randomization using computer generated random numbers.

Each group contains 30 patients. Group A received Bupivacaine (15mg) 3ml. Group B received Bupivacaine (10mg)+Fentanyl (25mcg) made to 3ml

#### **Inclusion Criteria:**

ASA physical status I, II & III of either sex, Age >50 yrs  
Patients who were scheduled for elective lower limb orthopedic cases posted under Spinal Anesthesia

#### **Exclusion Criteria:**

ASA Grade IV, Patients who had history of allergy to local anesthetics, severe cardiac or respiratory diseases and uncontrolled hypertension were excluded.

Baseline vital parameters: heart rate, systolic arterial pressure (SAP), diastolic arterial pressure (DAP); mean arterial pressure (MAP) and oxygen saturation were recorded in the pre-operative ward. Patients were fasted 8-10 hours and in operation theatre, an IV line was secured with 18-G IV cannula and Ringer's lactate infusion (8 ml/kg) was started.

Routine standard monitors such as pulse oximetry, electrocardiography (ECG) and non-invasive blood pressure were monitored.

Under all aseptic and antiseptic precautions Lumbar Puncture was performed in sitting position in L3-L4 space by 23 Gauge Quincke point needle.

The patients were blinded to the treatment group and all recordings were performed by an anesthesiologist blinded to the group allocation, thus the study was made double-blinded.

The patients were randomly divided into two equal groups of 30 each.

#### **Group A**

Received Bupivacaine (15mg) intrathecally 3ml

#### **Group B**

Received Bupivacaine (10mg)+Fentanyl (25mcg) intrathecally made to 3ml

Pulse rate, blood pressure and SpO<sub>2</sub> were measured intraoperatively every 2 minutes for first 10 minutes and every 5 minutes for next 30 minutes and every 15 minutes thereafter till one hour postoperatively.

Hypotension was defined as SBP of < 90 mm of Hg or a decrease of more than 30% from baseline mean arterial pressure which was treated with an incremental IV bolus of mephentermine 6 mg.

Bradycardia (heart rate < 60 bpm) was treated with IV

atropine.

Time of onset of adequate level of analgesia, duration of motor block, duration of sensory block, incidence of complications like nausea, vomiting, pruritis, sedation, shivering were assessed in both groups.

#### **Motor block was assessed using modified Bromage scale.**

0- No paresis – full movements of lower limbs

1- Partial paresis – flex knees and ankles

2- Partial paresis – flex ankles

3- Partial paresis – flex toes only

4- Full paresis – no movement

#### **Sedation status was assessed using Ramsay sedation score**

0- Awake and alert

1- Respond to voice

2- Respond to painful stimuli

3- No response

#### **Statistical Analysis**

Data were compiled, analyzed, and presented as mean, standard deviation (SD), percentages, student unpaired t-test by using Microsoft Excel 2007 and were analysed using SPSS version 20 software. The P value was considered significant as shown below: P < 0.05 - Significant.

P < 0.01 - Highly significant P > 0.05 - Not significant

## **4. Results**

The demographic data (age, weight, sex & ASA grading) were comparable and statistically non significant (Table-1). Average duration of surgery was 120 to 150 minutes. Equal distribution of males and females in both groups was done and majority of them were ASA II.

- The time of onset of adequate level of sensory block (T<sub>10</sub>) was longer for group B (128 +/- 8.3sec) than group A (96±10.32) and was statistically significant (Table-2).
- Duration of motor block was longer in group A (160.5±7.5min) as compared to group B (128.4 +/- 9.9min) and was statistically significant. (P<0.05).
- Lower pulse rates and less fall in blood pressure was noted in group B than group A, thus there is better hemodynamic stability in group B (Graph-1).
- Incidence of hypotension and use of vasopressors was much higher in group A and was found to be statistically significant (Graph-2).
- Total duration of sensory block was slightly more for group A but was not found to be statistically significant.
- Sedation score was used to assess sedation intraoperative and postoperative.
- Incidence of bradycardia and pruritis was common in group B.
- None of the patients had nausea, vomiting and respiratory depression. (Graph-3)
- Shivering was higher in group A.

## **5. Discussion**

Maintenance of body physiology as near normal as possible in elderly patients during anesthesia is one of the primary

goal.

Marked hemodynamic derangements are often seen following subarachnoid block especially in trauma and elderly patients.

Neuraxial opioids predominantly act at the  $\mu$ - receptors present in Substantia gelatinosa of Spinal cord to exert its synergistic analgesic effect more specifically for visceral pain.

Geriatric patients show an increased responsiveness to analgesics. The reported enhanced sensitivity to systemic opioids seems to be related to pharmacokinetic or dynamic factors and/or physiological changes that occur in the central nervous system during the process of aging.

Regional anaesthesia is well tolerated by geriatric patients undergoing orthopedic surgery, producing less postoperative confusion and delirium than general anaesthesia. In the nongeriatric population, the association of fentanyl and local anesthetics improves the sensory block induced by the spinal administration of local anesthetics in the intra- and postoperative period.<sup>(4)</sup>

The recommended level of regional anesthesia for lower limb surgery is T 10.

In our present study, we have added 25mcg Fentanyl a highly lipophilic opioid to lower doses of 0.5 % hyperbaric Bupivacaine. There was significant increase in time for onset of adequate block in Group B as compared to Group A (p-value <0.001). Addition of Fentanyl reduces the pH of hyperbaric Bupivacaine. This may be the reason for delay in onset of adequate block.

Total duration of sensory block was slightly more for group A in our study. The differences between two groups were statistically insignificant. (p-value 0.0778).

Fernandez-Galinski, Diana et al<sup>(4)</sup> compared 3.5ml of hyperbaric bupivacaine with same dose of bupivacaine with 25 micrograms of fentanyl, both onset and duration of sensory block were decreased in the fentanyl group, the differences were not statistically significant.

In our study the dose of bupivacaine in fentanyl group is much lower which can be the reason for slightly lower duration of sensory block.

Duration of motor blockade is significant higher for group A than Group B (p value 0.001).

In our study 12 patients of Group A developed Hypotension, and needed vasopressors compared to 3 patients of Group B.

Regarding haemodynamics, no significant difference was observed which is consistent with studies by Ben-David *et al.*<sup>(5)</sup> and Atallah *et al.*<sup>(6)</sup> where fentanyl was used.

In Ayderen T, Arslan M, *et al* study where the same dose like our study (fentanyl group) was used for ambulatory arthroscopic knee surgery, no incidence of significant hypotension and HR changes were reported.<sup>(7)</sup>

Ben-David *et al.*<sup>(8)</sup> found that fentanyl 20  $\mu$ g with 4 mg bupivacaine provided complete and satisfactory spinal anaesthesia with dramatically less hypotension.

Kim *et al.*<sup>(9)</sup> observed that fentanyl beyond 25  $\mu$ g intrathecally produced no benefit in regard to the duration of analgesia. However, fentanyl 25  $\mu$ g intrathecally with low dose bupivacaine improves post-operative analgesia and haemodynamic stability.<sup>(10)</sup>

Incidence of bradycardia was more in group B. Shivering was higher in group A than group B.

Sympathetic denervation causes heat loss from periphery, leading to hypothermia, compensatory vasoconstriction in the non anesthetised regions above the block occurs makes the patient shiver.

Fentanyl abolishes shivering by central mechanism in Group B. Opioids treat shivering via the  $\mu$  or  $\kappa$  opioid receptors and exert their antishivering effects via decreasing the shivering threshold.

Pruritus is the most common side effect of intrathecal opioid. In our group 3 among 30 in group B had pruritus.

Pruritus, a subjective unpleasant and irritating sensation that provokes an urge to scratch and the symptoms typically start at the trunk, nose, around the eyes and is usually localized to facial areas, innervated by the trigeminal nerve. The spinal nucleus of the trigeminal nerve is rich in opioid receptors and is continuous with the substantia gelatinosa and Lissauer tract at C3-C4. The ophthalmic division of the spinal sensory nucleus of the trigeminal nerve is most inferior; thus, supporting the observation that the pruritus following neuraxial opioid administration is typically in the nose and upper part of the face.

Pain and pruritus are transmitted by the same population of sensory neurons, namely small un-myelinated nerve fibers (C-fibers) and the release of prostaglandins (PGE1 and PGE2) enhance C-fiber transmission to the central nervous system, which potentiates pruritus.

The spinal trigeminal nucleus located superficially in the medulla is an integrative center for sensory input from the face and an area known as the "itch center." The Cephalic migration of neuraxial opioids toward this "itch center and activation of 5-HT<sub>3</sub> receptors by opioids may play a role in the generation of neuraxial opioid-induced pruritus.

5-HT<sub>3</sub> receptors are abundant in the dorsal horn of the spinal cord and the spinal tract of the trigeminal nerve in the medulla. The interaction between opioids and 5-HT<sub>3</sub> receptors may play a role in the generation of neuraxial opioid-induced pruritus. 5-HT<sub>3</sub> antagonists Ondansetron, has been used to prevent the neuraxial opioid-induced pruritus. There was no incidence of sedation or respiratory depression in 2 groups.

## 6. Conclusion

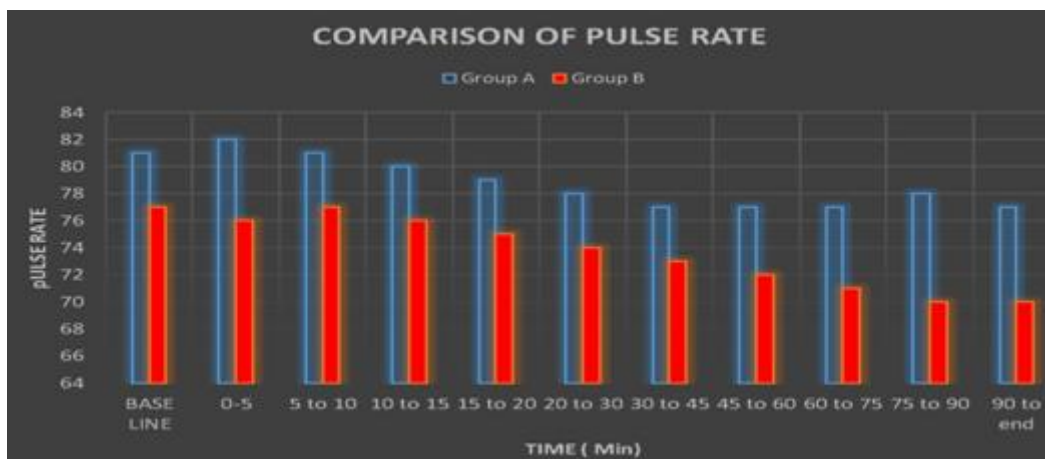
Subarachnoid block with 10mg Bupivacaine 0.5% & 25mcg Fentanyl is more safer and better option in lower limb surgeries in terms of maintaining hemodynamic stability and lower incidence of complications in elderly patients undergoing orthopedic lower limb surgeries. Bupivacaine with fentanyl can be a safer alternative for elderly patients, who may have more hypotension after conventional dose of bupivacaine, which can be reduce after adding fentanyl in low dose bupivacaine.

## References

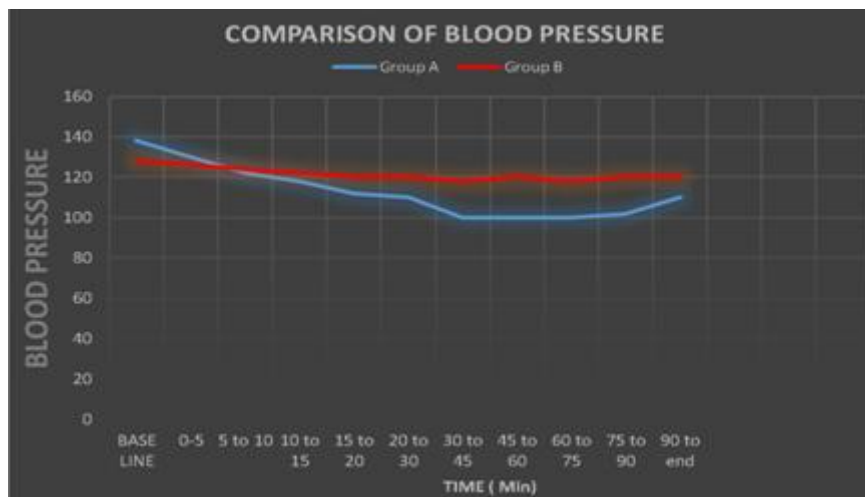
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**Table 1: Demographic Data**

Variables	Group A	Group B	p Value
Age (years)	63.3 ± 2.42	63.6 ± 2.8	0.728
Height	161.3 ± 2.17	161.1 ± 2.60	0.914
Sex (Male: Female)	19: 11	19: 11	
ASA status II: III	19: 11	18: 12	
Duration of Surgery (min)	130 ± 30.6	121.8 ± 32.4	>0.05



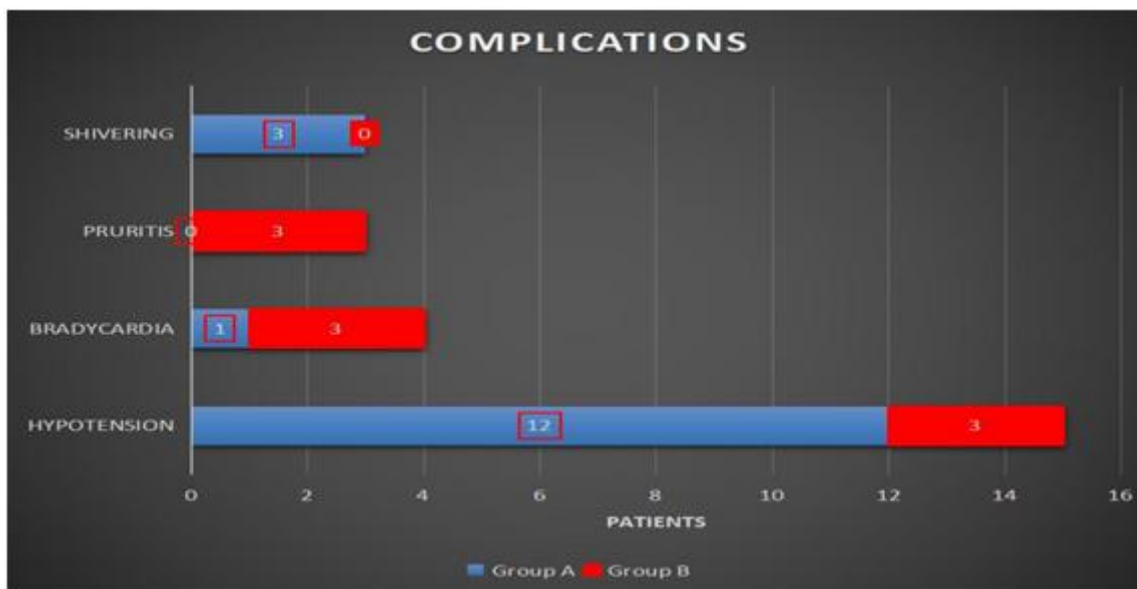
**Graph 1: Comparison of pulse rate**



Graph 2: Comparison of blood pressure

Table 2: Characteristics of Spinal Block

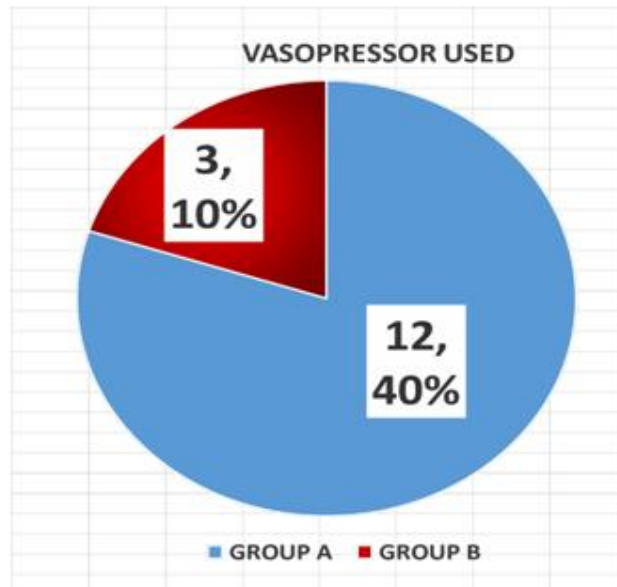
	Group A	Group B	p Value
Time of onset of adequate block-T10 (sec)	96±10.32	128±8	<0.001
Duration of motor block (min)	160.5±7.5	128.4±9.9	<0.001
Duration of sensory block (min)	225.4±7.8	222.5±9.5	0.0778



Graph 3: Complications

Table 3: Comparison of complications

	Group A	Group B
Hypotension	12 (40%)	3(10%)
Bradycardia	1	3
Pruritis	0	3
Sedation	0	0
Nausea & Vomiting	0	0
Shivering	3 (10%)	0
Respiratory	0	0
Depression		



Graph 4: Vasopressors used