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Original Research Article

Effect on Postoperative Analgesia Following Spinal Anaesthesia with Bupivacaine and Fentanyl Vs. Bupivacaine and Clonidine in Lower Limb Orthopaedic Surgeries

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ABSTRACT

Background

Spinal Anaesthesia with Bupivacaine is administered routinely for lower limb orthopedic surgeries. Adding an adjuvant drug will increase the efficacy of neuraxial block including postoperative analgesia. A number of adjuvants has been tried e.g., Morphine, Fentanyl, Sufentanil and Tramadol. Clonidine, Ketamine, Neostigmine has been introduced recently.

Objective

To compare post-operative analgesia following spinal anaesthesia with Fentanyl or clonidine as adjuvant to 0.5% Hyperbaric bupivacaine.

Materials and methods

This study was done among patients of age group 18 to 65 years scheduled for Elective lower limb orthopedic surgeries under Spinal Anesthesia for one year in Department of Anaesthesiology, Government TDMC, Alappuzha. Patients were categorized based on inclusion and exclusion criteria into two groups of 37 each with total sample size of 74. Group A: patients who received Bupivacaine 0.5% 2.5ml along with Fentanyl 25mcg (0.5ml).Group B: patients who received Bupivacaine 0.5% 2.5ml along with Clonidine 50mcg(0.5ml). Both groups were observed for duration of post operative analgesia, time taken to attain sensory block at T10, highest level of sensory blockade, time taken for two segment regression of sensory level, side effects and total number of doses of post operative analgesic required in 24 hours.

Results

Data analyzed using IBM statistics SPSS Version 21.0. In this study the mean duration of post operative analgesia in fentanyl group was 308.65 ± 22.69 minutes and in clonidine group was 512.57± 18.21 minutes. A statistical significant difference was seen in two groups with more duration of analgesia in clonidine group. The mean time for onset of sensory block at T10 in Group A was 2.94 ± 0.92 minutes and in Group B was 4.38 ± 1.18. A statistical significant difference was seen between two groups ($t = 5.676$; $p < 0.001$) ,with

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more time for onset of blockade for clonidine. No statistical significant difference was seen between the highest level of sensory blockade attained in two groups. (χ^2=1.770; df=1; p>0.05) In the present study, the mean duration of two segment regression of sensory block in Group A was 78.38 ± 9.81 minutes and in Group B was 141.24 ± 9.71 minutes. A significant difference was seen between two groups. (t = 27.690; p < 0.001) ,with more time for regression of blockade in clonidine group. In this study, it was found that ,there was no statistical significant difference in the incidence of adverse effects between two groups.

Conclusion

Post operative analgesia following Spinal Anaesthesia with Bupivacaine and Clonidine was longer compared to Bupivacaine and Fentanyl with no statistically significant difference in the incidence of side effects between the two groups.

Keywords: Bupivacaine, Fentanyl, Clonidine, Adjuvant, Neuraxial block.

INTRODUCTION

Postoperative pain, especially when poorly controlled, results in harmful acute effects like adverse physiologic responses and chronic effects like delayed long term recovery and chronic pain. Recent applications have focused on postoperative analgesia rather than intraoperative anesthesia to improve patient comfort and to assist in rehabilitation and hospital dismissal.(1)

Local anesthetics applied to the neuraxis in subanesthetic doses can provide potent long lasting analgesia for a variety of indications, including intraoperative analgesia, acute post surgical pain, and severe chronic pain associated with malignancy.(1)

Bupivacaine is a highly protein bound amide local anesthetic with a slow onset because of its relatively high pKa. Bupivacaine is available as 0.25%, 0.5% and 0.75% clear isobaric solutions and also as a hyperbaric 0.5% and 0.75% solution containing 80mg/ml glucose. Hyperbaric Solutions of 0.5% and 0.75% are used to provide surgical anaesthesia.(1)
Prolongation of postoperative analgesia can be achieved by using adjuvants to local anesthetic agents such as midazolam, neostigmine, clonidine and opioids. (2)

Most commonly used opioid in regional Anesthesia is Fentanyl citrate which is a μ1 and μ2 receptor agonist. It is a highly potent drug because of its high lipophilicity. However pruritus, nausea, vomiting respiratory depression and urinary retention are common side effects. (3)

Clonidine an alpha 2 receptor agonist, has beneficial effects such as antiemesis, reduced post operative shivering, anxiolysis, sedation and Clonidine does not have unwanted opioid related side effects like pruritis and respiratory depression.(3)

OBJECTIVES

Primary objective: To compare post-operative analgesia following spinal anaesthesia with Fentanyl or clonidine as adjuvant to 0.5% Hyperbaric bupivacaine.

Secondary objectives:

1. Time taken to attain sensory block at T10
2. Highest level of Sensory blockade of dermatome attained.
3. Time of two segment regression of sensory blockade.
4. To study side effects like hypotension, bradycardia, sedation, vomiting and nausea.
5. Total number of doses of postoperative analgesics needed in 24 hours.

MATERIALS & METHODS

The present comparative observational study was conducted in the Department of

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Anesthesiology, Government TDMCH, Alappuzha from November 2021 to November 2022 after obtaining IRC clearance and IEC clearance.

Study subjects

Patiens of 18 to 65 years age group scheduled for elective lower limb orthopedic surgery under spinal anesthesia who were willing to participate in the study.

Inclusion criteria

1. Patients of 18 to 65 years age group scheduled for elective lower limb orthopedic surgery under spinal anesthesia who were willing to participate in the study.
2. ASA physical status Grade I and II.
3. Weight less than 80 kg.
4. Height between 145 cm to 175 cm.

Exclusion criteria

Patients with

1. Coagulopathies
2. Infection at the site of procedure.
3. Allergic to anesthetic drugs.
4. Patients on anti platelet drugs.

Sample size

In the study conducted by Dr. Baljit Singh Bajwa[4], et al titled, "comparison of intrathecal Clonidine and Fentanyl in hyperbaric Bupivacaine for spinal anaesthesia and postoperative analgesia" in lower limb orthopedic surgeries .

Mean difference obtained was 80.33 Alpha error – 5% Power – 80%

Using sample size calculation formula for difference of two means.

$$n = \frac{2Sp^2[z1\text{-}a/2 + z1\text{-}ß]^2}{[\mu1 - \mu2]^2}$$

SP = Pooled standard deviation µ1-µ2=Mean difference

Sample size obtained in one group is 37. So the total sample size in two groups was 74.

Sampling method

Consecutive sampling

Study variable

- Heart Rate, Systolic blood pressure, Diastolic blood pressure, MAP, Respiratory Rate was monitored till surgery was completed.
- Sensory dermatome level – tested by pinprick along mid clavicular line, bilaterally, every minute using a blunt 25 gauge needle, until the level is stabilized for two

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consecutive tests. Testing was done every 15 minutes until the point of two segment regression of sensory level.
- Assessment of post-operative analgesia.
- Total doses of post operative analgesics needed

Visual Analogue Score – Commonly used pain assessment score.

It is usually presented as a 100 mm horizontal line on which patient's pain intensity is represented by a point between the extremes of "no pain at all" to "worst pain imaginable"

Figure 1: Visual Analogue Scale

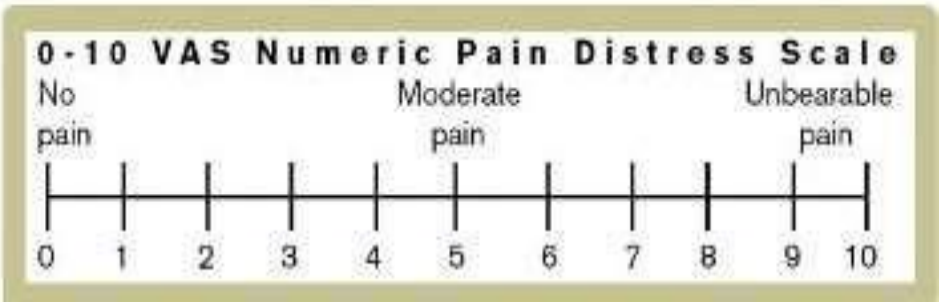

Table 1: RAMSAY SEDATION SCALE

SCORE	RESPONSE
1	Anxious or restless or both
2	Cooperative, oriented and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

Study materials

- Sterile tray with disposable syringes.
- 2 ml syringe plus 25 gauge needle with local anesthetic for skin infiltration.
- 5ml syringe containing Hyperbaric Bupivacaine 0.5% 2.5ml and Fentanyl 25mcg (0.5ml).
- 5ml syringe containing Hyperbaric Bupivacaine 0.5% 2.5ml and Clonidine 50mcg (0.5ml).
- 23 gauge Quincke spinal needle.

Data collection tool

A profoma was used to collect the data which includes patient's particulars, indication for surgery, anesthetic details, intra operative monitoring, side effects, duration of postoperative analgesics.

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Study procedure

After getting clearance from the IRC and IEC, patients were selected as per the inclusion and exclusion criteria.

Detailed preanesthetic evaluation was done. Age, gender, height and weight of participating patients were recorded. Physical examination including vitals, airway assessment, respiratory system, CVS, Spine and neck movements was done. Informed and written consent was taken.

In preanesthetic evaluation, patients were given instructions to use visual analogue scale (VAS) with 0 indicating no pain and 10 indicating the worst imaginable pain.

Routine blood investigations, ABO blood grouping, Rh typing, screening for viral markers, RTPCR testing for covid-19 were done 48hours prior to surgery.Resuscitation equipments and drugs were kept ready.

Patient premedicated with Tab. Pantoprazole 40 mg and Tab. Ondansetron 4 mg on preoperative day at 10.00 pm and on the day of surgery at 6 am with sips of clear fluids.

Patient reassessed in premedication room on the day of surgery, peripheral IV Cannulation done using an 18G IV cannula.

Patient was shifted to the operation theatre and standard monitors like ECG, pulse oximeter, non-invasive blood pressure cuff were attached. 500 ml of Normal saline or Ringer lactate was coloaded. Preoperative heart rate, blood pressure, oxygen saturation noted. No sedatives or anxiolytics given. Drugs prepared by an Anesthesiologist who was not involved in study. Sterile normal saline was added to Clonidine 50 mcg to make it 0.5 ml, so as to make the study drugs identical in volume. Patient placed in right lateral decubitus position and under strict aseptic precaution L3 – L4 space was palpated and marked. After giving local infiltration with 2% lignocaine, subarachnoid block was performed through midline approach using 23G Quincke Babcock spinal needle, drug given only after confirming clear and free flow of CSF through spinal needle.

The time of administration of drug intrathecally taken as zero hour. After the subarachnoid block, patient was turned to supine position. Oxygen was given through simple face mask.

Sensory block and vital signs monitored. Sensory assessed by pin prick in midline every minute. Time of reaching sensory level T10 noted, highest level of sensory block of dermatome attained noted and surgery allowed to start. Every 10 minutes sensory level was reassessed till two segment regression of sensory blockade was noted. Pulse rate, blood pressure, respiratory rate and oxygen saturation checked every 2 minutes till first fifteen minutes and then every 5 minutes till completion of surgery. Normal saline was used as maintenance fluid.

Bradycardia (Heart rate < 50/min) treated with Inj. Atropine 0.6mg IV as needed. Hypotension (20% of fall in MAP from baseline) treated with Inj. Mephentaramine 6mg IV and rapid infusion of normal saline. Incidence of vomiting, nausea, shivering and respiratory depression noted. Respiratory depression was taken as respiratory rate less than 10 per minute. Patients with nausea treated with Inj. Ondansetron 4mg IV. Patient with shivering was managed with warm IV fluids and warm drapes. Patients categorized into two study groups of 37 each.

Group A: patients who received Bupivacaine 0.5% 2.5ml along with Fentanyl 25mcg [0.5ml] Group B: patients who received Bupivacaine 0.5% 2.5ml along with Clonidine 50mcg [0.5ml] During the Post-operative period, pain assessed initially every 1 hour for 2 hours, then every 2 hours for next 8 hours, then after every 4 hours till 24 hours with VAS. Side effects like hypotension, bradycardia, nausea, vomiting, pruritus and sedation assessed and monitored for 24 hours and recorded. Sedation graded according to Ramsay sedation score. During post operative period, if the VAS greater than or equal to 5, Inj. Tramadol

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50mg IV given along with Inj. Ondansetron 4mg IV and time was noted as duration of postoperative analgesia. If patient again complained of pain Inj. Paracetamol 1gm IV given and was repeated as needed. Total doses of Inj. Tramadol 50mg and Inj. Paracetamol 1gm given to the patient in 24 hours was noted.

Data Analysis

Baseline data entered into Microsoft excel and analyzed. Qualitative variables summarized using proportions. Quantitative variables summarized using mean with standard deviation. Test of significance such as t test for quantitative variables and chi square for qualitative variables done. Data analyzed using IBM Statistics SPSS Version

RESULTS

Table 2: Comparison of post-op analgesia between two groups

Duration of Post-Op analgesia (minutes)	Group A (n=37)		Group B (n=37)
Mean	308.65		512.57
Standard deviation	22.69		18.21
t-value		42.630	
p-value		<0.001	

In the present study, the mean duration of post-op analgesia in Group A was 308.65 ± 22.69 minutes and in Group B was 512.57 ± 18.21 minutes. A statistical significant difference was seen between the mean duration of post operative analgesia of cases in two groups. ($t = 42.630$; $p < 0.001$)

Graph 1: **Comparison of post-operative analgesia between two groups**

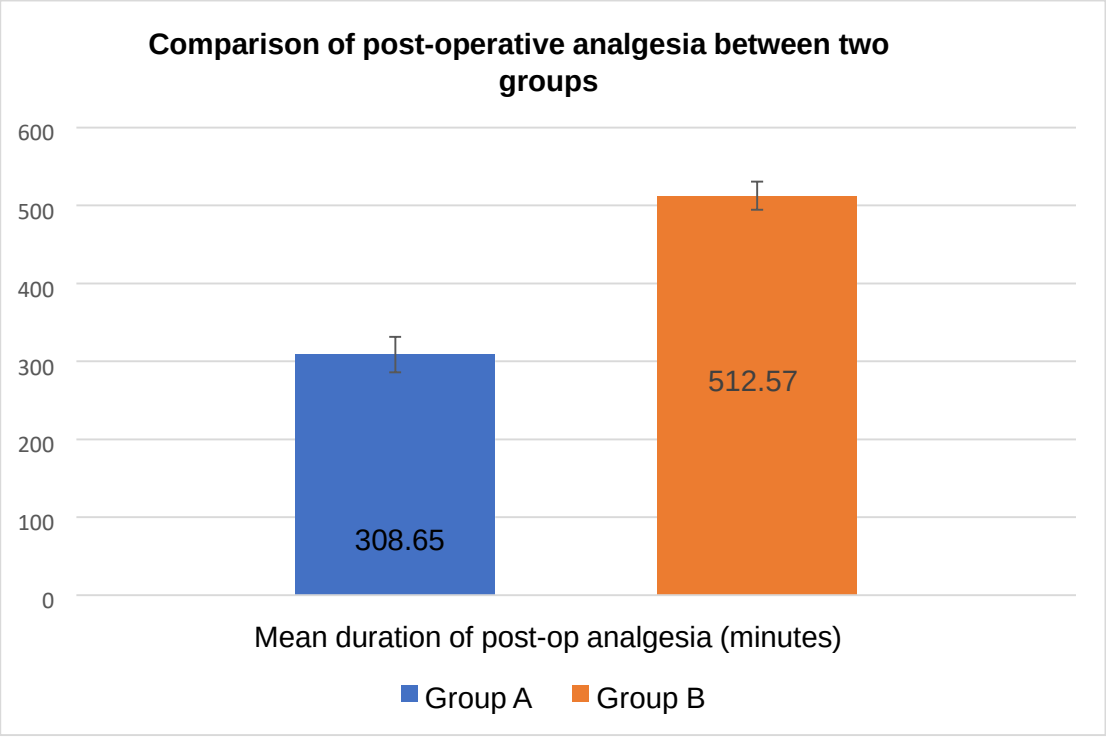

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Table 3: Comparison of time for onset of sensory block at T10 in two groups

Onset of sensory block at T10 (Minutes)	Group F (n=37)		Group C (n=37)
Mean	2.94		4.38
Standard deviation	0.92		1.187
t-value		5.676	
p-value		< 0.001	

In the present study, the mean duration of time for onset of sensory block at T10 in Group A was 2.94 ± 0.92 minutes and in Group B was 4.38 ± 1.18. A statistical significant difference was seen between the mean duration of time for onset of sensory block at T10 of two groups. ($t = 5.676$; $p < 0.001$)

Graph 2: Comparison of time for onset of sensory block at T10 in two groups

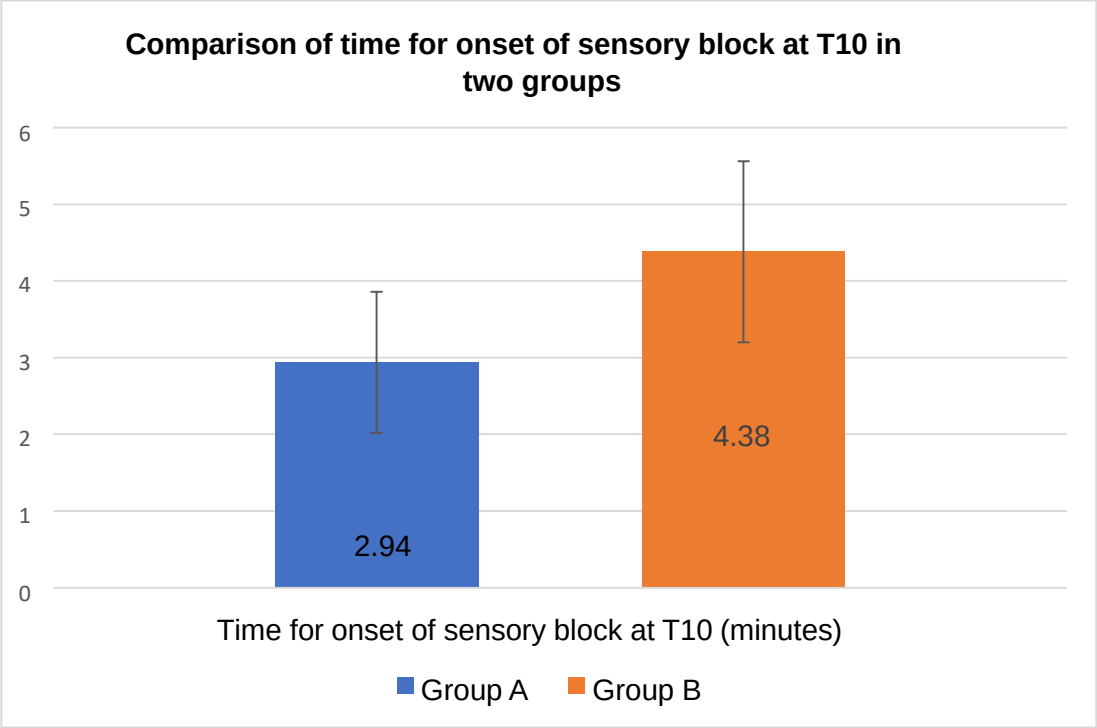

Table 4: Comparison of highest level of sensory blockade attained in two groups

Highest level of sensory blockade attained	Group A (n=37)		Group B (n=37)
T4	25 (67.6%)		30 (81.1%)
T6	12 (32.4%)		7 (18.9%)
Total	37 (100%)		37 (100%)
χ^2-value		1.770	
p value		0.183	

In the present study, highest level of sensory blockade attained in group A was, T4 in 25 (67.6%) and T6 in 12 (32.4%). The highest level of sensory blockade attained in group B was, T4 in 30 (81.1%) and T6 in 7 (18.9%). No statistical significant difference was seen

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between the highest level of sensory blockade attained in two groups. (χ^2=1.770; df=1; p>0.05)

Graph 3: Comparison of highest level of sensory blockade attained in two groups

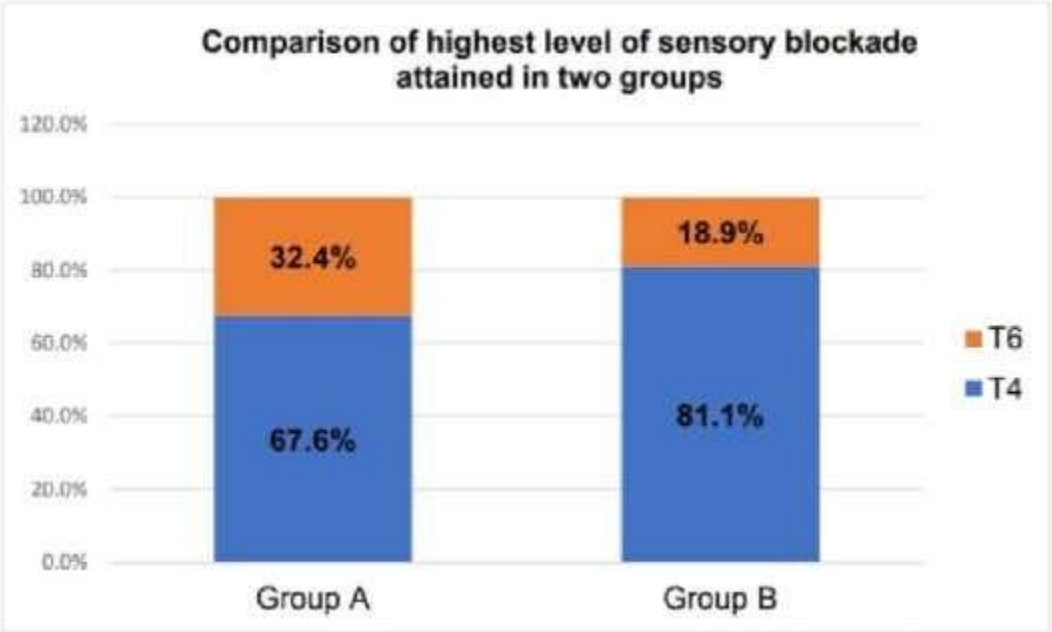

Table 5: Comparison of two segment regression of sensory block in two groups

Two segment regression of sensory block (Minutes)	Group A (n=37)		Group B (n=37)
Mean	78.38		141.24
Standard deviation	9.81		9.71
t-value		27.690	
p-value		<0.001	

In the present study, the mean duration of two segment regression of sensory block in Group A was 78.38 ± 9.81 minutes and in Group B was 141.24 ± 9.71 minutes. A statistical significant difference was seen between the mean duration of two segment regression of sensory block of two groups. (t = 27.690; p < 0.001)

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Graph 4: Comparison of two segment regression of sensory blockade in two groups

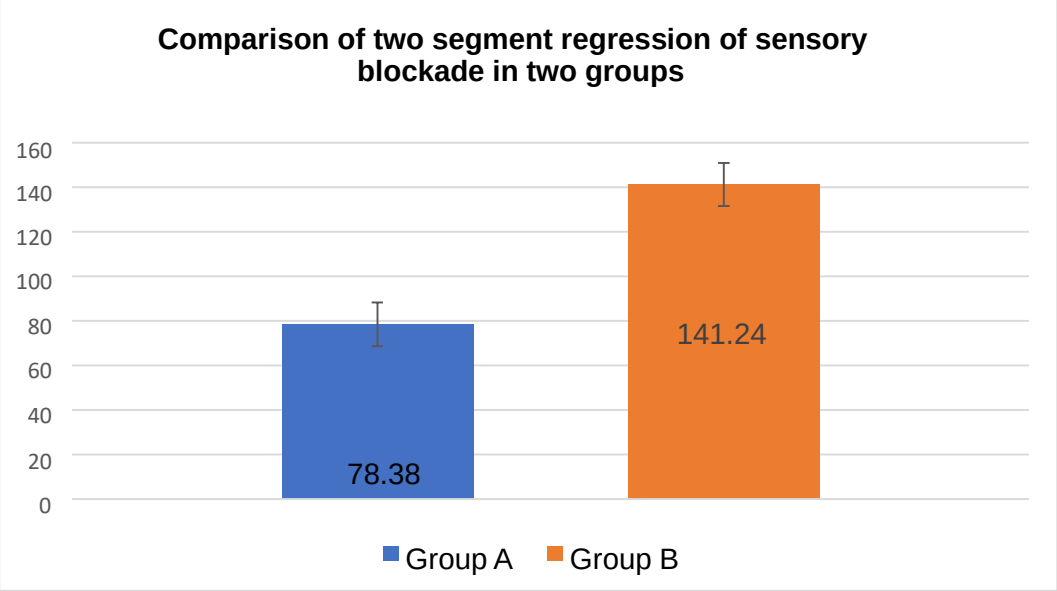
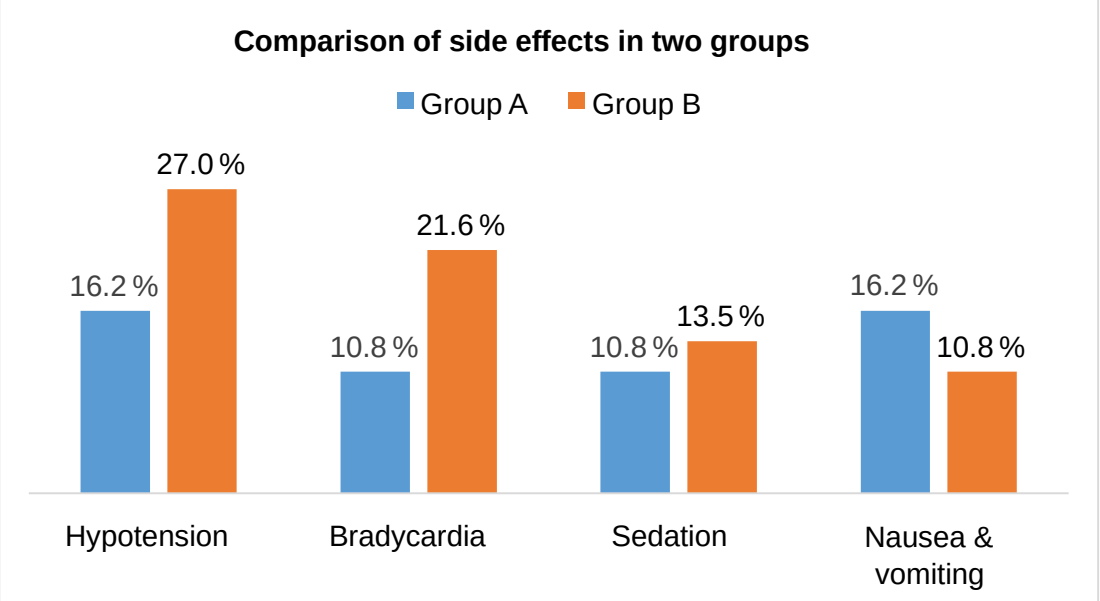


Table 6: Comparison of side effects in two groups

Side effects	Group A (n=37)	Group B (n=37)	p value
Hypotension	6 (16.2%)	10 (27%)	0.259
Bradycardia	4 (10.8%)	8 (21.6%)	0.207
Sedation	4 (10.8%)	5 (13.5%)	0.722
Nausea & vomiting	6 (16.2%)	4 (10.8%)	0.496

In the present study, 6 (16.2%) patients in Group A and 10 (27%) patients in Group B had hypotension. 4 (10.8%) patients in Group A and 8 (21.6%) patients in Group B had bradycardia. 4 (10.8%) patients in Group A and 5(13.5%) patients in Group B had sedation. 6 (16.2%) patients in Group A and 4 (10.8%) patients in Group B had nausea and vomiting. There was no statistical significant difference in the incidence of adverse effects between two groups.

Graph 5: Comparison of side effects in two groups



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DISCUSSION

Adequate and prolonged post operative analgesia increases patient satisfaction, early mobilisation, decreases post operative morbidity, shortens hospital stay and reduces hospital cost. Spinal anaesthesia is the most widely used anaesthetic technique for lower limb orthopaedic surgeries. Use of adjuvants to local anaesthetics provides prolonged adequate post operative analgesia. A wide variety of additives have been used routinely along with bupivacaine in spinal anaesthesia. Fentanyl, Clonidine, Buprenorphine, Dexmedetomidine are the most commonly used additives

Fentanyl is a μ1 and μ2 receptor agonist. It is highly potent opioid because of its high lipophilicity The major advantage of "selective" blockade of pain by fentanyl lies in the absence of sympathetic blockade and postural hypotension potentially allowing early ambulation of the patient and avoidance of the major complications of the spinal anaesthetic blockade. Pruritis, nausea, vomiting, respiratory depression and urinary retention are common side effects associated with fentanyl.

Clonidine is a selective partial agonist for Alpha-2-adrenoreceptor. It is known to potentiate both sensory and motor block of local anaesthetics. Mechanisms involves suppression of the activity of wide dynamic range neurones and release of substance P, norepinephrine and acetylcholine in spinal cord dorsal horn and direct inhibition of impulse conduction is A delta and especially C fibres by increasing potassium conductance.

Intrathecal clonidine might result in intraoperative hypotension and bradycardia. Beneficial effects of clonidine include antiemesis, reduced post operative shivering, anxiolysis and sedation.

There are so many previous studies comparing Fentanyl and clonidine as additives, but on extensive research it was found that only few studies are there comparing Fentanyl and Clonidine as additives in spinal Anaesthesia for lower limb orthopaedic surgeries. So I did my study to compare the efficacy of these two drugs in postoperative analgesia following spinal anaesthesia in lower limb orthopaedic surgeries. In the present study 74 patients undergoing elective lower limb orthopaedic surgeries were included as per inclusion and exclusion criteria.

Patients categorized into two study groups of 37 each, patients who received Bupivacaine 0.5% 2.5ml along with Fentanyl 25mcg 0.5ml as group A and patients who received Bupivacaine 0.5% 2.5ml along with Clonidine 50mcg 0.5ml as group B. The demographic data in terms of Age, Gender, Height, Weight, Duration of surgery, Highest level of sensory blockade of dermatome attained was comparable in both groups.

In my study the mean duration of post operative analgesia in fentanyl group was 308.65 ± 22.69 minutes and in clonidine group was 512.57± 18.21 minutes. A statistical significant difference was seen between mean duration of post operative analgesia in two groups. ($t=42.630$; $p<0.001$), **Baljit Singh Bajwa, et al[4]** did similar study and found that duration of analgesia was significantly higher in clonidine group [497.20± 139.78 minutes] than in fentanyl group [416.87± 105.67] [$P<0.05$] the findings are comparable with my study.

Sidharth Sraban Routray et al[5], did similar study in lower limb orthopaedic surgeries and found that duration of analgesia in clonidine group was 510.84± 24.1 minutes and fentanyl group was 434.95± 19.16 minutes. The results were comparable with my study in clonidine group but in fentanyl group the duration of analgesia was lower in my study.

In another similar Study did by **Bharat Choudhary et al[2]** found that postoperative analgesia in clonidine group was 492.32 +/-17.32 minutes and fentanyl group was 418.80 +/-19.68 minutes. In above cited studies comparing both drugs, clonidine group got prolonged duration of analgesia than fentanyl group which is similar to my study finding. But in my

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study patients who received fentanyl has got lesser duration of postoperative analgesia than previously mentioned studies.

In our study the mean duration for onset of sensory block at T10 in Group A was 2.94±0.92 minutes and in Group B 4.38±1.18 minutes. A statistically significant differences was seen between the mean duration for onset of sensory block at T10 of two groups. (t=18.461; p<0.01), **Abdul Hakkim et al[6]** compared intrathecal fentanyl and clonidine found that the onset of sensory blockade was earlier in fentanyl group(12.50+/- 1.30) than clonidine(9.10+/-1.40), which is similar to my study.

In our study the mean duration of two segment regression of sensory block (minutes) in Group A was 78.38± 9.81 minutes and in Group B was 141.24 ± 9.71 minutes which is statistically significant. (t=27.690; p < 0.01). Two segment sensory regression was slower in clonidine group than fentanyl group which is comparable with the study by **Abhishek Bhattacharjee et al[7],** who compared fentanyl and clonidine as additive in caesarean section. In the meta analysis done by **Fantahun Tarekegn et al[8]** , they got similar results.

In my study side effects such as bradycardia, hypotension, sedation, nausea, vomiting are minimal in clonidine group compared with fentanyl group, **Baljit Singh Bajwa et al[4]** found that systemic side effects such as bradycardia, hypotension, or sedation are usually not associated with small dose of intrathecal clonidine or fentanyl and hemodynamic stability observed in both groups, this results are similar to my study.

In the present study, the mean Total number of doses of post operative analgesics needed in 24hours in Group A was 2.73 ± 0.45 and in Group B was 1.68 ± 0.47. A statistically significant difference was seen between the mean total number of doses of post operative analgesics needed in 24 hours in two groups. (t = 9.801; p < 0.001], this correlates with study conducted by **Sites BD et al[9]** found that the combined administration of clonidine and bupivacaine decreases the post operative need for analgesics with compared with using bupivacaine alone. **Ravanjith singh et al[10]** found that 24 hour mean analgesic consumption was found to be lesser in clonidine group than fentanyl group.

Intraoperatively in group A, mean heart rate changes from 88.97 (±6.56) beats per minute to 69.62 (±3.36) beats per minute and in group B, the change was from 85.49 (±3.61) beats per minute to 58.11 (±3.72) beats per minute. The mean heart rate decreased more in group B than group A intra-operatively (p < 0.01), Intraoperatively in group A, mean arterial pressure changes from 89.57 (±3.57) to 85.22 (±3.64) and in group B mean arterial pressure changes from 89.14(±3.38) to 76.05 (±1.64). The mean arterial pressure decreased more in group B than with group A intra-operatively. There was statistical significant difference in variation in hemodynamic parameters such as heart rate and mean arterial pressure in my study groups. **Sidharth sraban routray et al[5]** found that there was no significant difference regarding hemodynamic parameters such as heart rate and mean arterial pressure.

CONCLUSION

From my study it was found that addition of clonidine 50ug as adjuvant to bupivacaine in spinal anaesthesia has prolonged duration of post operative analgesia compared with fentanyl 25ug. Also my study revealed that there was no statistically significant difference in the incidence of side effects between two groups.

Hence clonidine can be used as a better alternative than fentanyl as adjuvant to bupivacaine in spinal anesthesia for lower limb orthopedic surgeries

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