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Comparison of Analgesic Effect of Intrathecal Fentanyl & Clonidine with Hyperbaric Bupivacaine in Lower Limb Surgeries

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Abstract

Background: Smooth and rapid induction, optimal operating conditions, and rapid recovery with minimal side effects such as nausea, vomiting, bleeding, and postoperative pain are the characteristics of ideal anesthetic. *Objectives:* To compare the effect of sub-arachnoid fentanyl and clonidine on onset & duration of sensory & motor block, post-operative pain relief, complications, side effects and hemodynamic status. *Materials and Methods:* This was a randomize controlled study conducted from July to November 2018. A total of 60 adult patients of American Society of Anaesthesiologists (ASA) physical status grade I or II, aged between 20-50 years, of either sex, posted for lower limb orthopedic surgery included after informed consent. All the patients were randomly allocated into one of the two groups using computer generated random number table. Group BF received induction with Fentanyl while group BC was induced Clonidine. *Results:* The baseline demographic analysis showed that the two groups did not differ significantly in age, weight, sex, ASA grade and operative times. Duration of motor, sensory & analgesia was higher in BC group. During the course of surgery, Heart Rate (HR) & Blood Pressure (BP) was significantly low in group BC at 15,30,40 & 45 minutes than in group BF and RR was also low in BF group at 30 minutes of post-operative period. Adverse effects and VAS score was low in BC group than BF group. *Conclusion:* Clonidine has significantly better hemodynamic stability, post-operative recovery and less post-operative complications compared to fentanyl.

Keywords: Analgesia; Bupivacaine; Intrathecal clonidine; Orthopedic lower limb surgery; Subarachnoid fentanyl.

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Introduction

Spinal anesthesia used since 1898 in clinical practice and very famous technique for lower limb orthopedic surgery [1]. Spinal anesthesia have many advantages like less intraoperative blood loss, decreased incidence of deep venous thrombosis, and continued postoperative analgesia over general anesthesia for lower limb orthopedic surgery [2]. Additives who have quality like optimal adjuvant, increase the quality of analgesia and lengthen the duration of spinal anesthesia with minimum side effects [3,4].

Bupivacaine usually used as local anesthetic for spinal anesthesia, but it has some disadvantages

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like short duration of spinal anesthesia and larger doses require for analgesics in the postoperative period. Higher doses of bupivacaine which again can produce cardiac toxicity. According to one of the study research, duration of analgesia due to bupivacaine in spinal anesthesia can be increased by using adjuvants such as midazolam, opioids, neostigmine, dexmedetomidine, and clonidine [5].

Intrathecal fentanyl citrate which is a μ1 - and μ2 -receptor agonist is used frequently as opioid in regional anesthesia. Fentanyl citrate has characteristic like hugely potent, high lipophilicity, rapid onset and short duration of action, minimal cephalic spread but it has also some side effects like pruritus, nausea, vomiting, respiratory depression, and urinary retention. Intrathecal clonidine, an α2-receptor agonist, increase the duration of sensory and motor block in spinal anesthesia and cater the delayed postoperative analgesia [6,7,8].

Clonidine has characteristic like antiemesis, decreased postspinal shivering, anxiolysis, and sedation, less unwanted opioid-related side effects such as pruritus and respiratory depression [9,10]. So, this study was carried out with the objectives to compare the effect of sub-arachnoid fentanyl and clonidine on onset & duration of sensory & motor block, post-operative pain relief, complications, side effects and hemodynamic status.

Material and Methods

Study setting and duration

This study was conducted in department of Anesthesiology within the premises of Banas Medical College and Research Institute, Civil Hospital, Palanpur from July to November 2018.

Study design and study population

This randomized controlled study was carried out, after obtaining approval from the Hospital Ethics Committee and written informed consent from the patients. Sixty (60) patients of the American Society of Anesthesiologists Classes I or II of either sex and of age 20–50 years of age posted for lower limb surgery included after informed consent. Patients who did not provide consent not included in the study or patients with correlated cardiovascular, pulmonary, neuropsychiatry illness, renal disease or history of hypersensitivity to halogenated anesthetic agents, emergency surgery cases, ASA 3,4,5 physical statues, patient on beta blocker therapy, bleeding or clotting disorders, superficial back site infection, history of alcoholism & drug abuse and weight >100 kg were excluded from the study. All the patients were randomly allocated into one of the two groups using computer generated random number table. Hence each group contained a total of 30 patients.

Group

Group BF: Inj. Bupivacaine 0.5% heavy 3 ml + Inj. Fentanyl 25 μg (0.5 cc)

Group BC: Inj. Bupivacaine 0.5% heavy 3 ml + Inj. Clonidine 30 μg (0.2 cc) and normal saline

Anaesthesia technique: induction, maintenance and recovery

Total volume of study drug was 3 ml. Preanesthetic checkup was done, and visual analog scale (VAS) was explained to all patients. All the patients were kept nil orally for 6h before surgery. After shifting the patients to Operation Theater, intravenous (IV) cannula was inserted, and preloading was done with Ringer solution (10 ml/kg).

Pre anesthetic checkup was performed the day before and on the day of surgery. Basic routine investigations like hemoglobin, renal function tests, serum electrolytes, random blood sugar and chest X-ray PA view were done and recorded. In the operating room, all standard monitors like non-invasive blood pressure (NIBP), pulseoximetry (SpO_2), electrocardiogram (ECG) were attached and vital parameters of the patient recorded. Sensory and motor block was monitored at 2, 4, 6, 8, 10, 15 min, and after that at 15 min interval. Sensory block was tested by pinprick method. The motor block was assessed according to the Modifid Bromage Scale:

Bromage 0: Patients able to move hip, knee, and ankle,

Bromage 1: Patients unable to move hip but able to move the knee and ankle,

Bromage 2: Patient unable to move hip and knee but able to move the ankle,

Bromage 3: Patient unable to move hip, knee, and ankle [8]

The onset of sensory block was taken from the time of intrathecal injection till loss of pin prick sensation at T10. Duration of sensory block was taken as time from maximum height of block till regression to L1. The onset of motor block was defied as time from intrathecal injection to motor blockade Level 2 in Bromage scale. Duration of motor blockade was taken as time from intrathecal injection till no motor weakness (Bromage 0). Any side effects such as nausea, vomiting, pain,

shivering, pruritus, sedation, hypotension, bradycardia, and respiratory discomfort were noted. Postoperatively, the pain score was recorded by using VAS between 0 and 10 (0 = no pain, 10 = severe pain) [9]. Injection paracetamol (1 gm) was given intravenously as rescue analgesic when VAS was >5. Time of administering the first dose of rescue analgesia was noted.

Measurement tools

The heart rate, non-invasive blood pressure, oxygen saturation (SpO_2) and respiratory rate recorded pre-operatively. After Spinal Anaesthesia vitals recorded at 5, 10, 15 and 30 minutes then every hourly till first six hours and then every four hourly till 24 hours. Anesthesia time and operative time were also recorded. Postoperative follow up for complications like nausea, vomiting and general discomfort was done for 24 hours.

Data analysis

Qualitative data were expressed as percentages and proportions. Quantitative data were expressed as mean and standard deviation. The differences between two groups with respect to continuous variables were analysed using unpaired t-test while categorical variables were analysed using chi-square test. All the statistical tests were performed in Epi Info 3.5.1 software by CDC, USA [6]. p value < 0.05 was considered as statistically significant while p value<0.01 was considered as statistically highly significant.

Results

Table 1: Baseline variables of study participants (N=60)

Characteristic		BF Group (n=30)	BC Group (n=30)	P value
Mean Age ± SD (years)		51.5 ± 11.5	53.9 ± 11.0	>0.05
Mean Weight ± SD (kg)		61.5 ± 9.1	59.5 ± 11.2	>0.05
Mean Height ± SD (in min)		157.5 ±5.4	156.3 ± 11.2	>0.05
Sex	Male	16	19	0.6
	Female	14	11	
ASA grade	Grade I	9	12	0.58
	Grade II	21	18	
Operative time (min)		110.3 ± 45.5	113.9 ± 43.5	>0.05

A total of 60 patients aged 20-50 years belonging to ASA grade I-II were included in the study in two equal random groups. The table 1 of baseline demographic analysis showed that mean age, weight, height & duration of surgery was 51.1 & 53.9 years, 61.5 & 59.5 kg, 157.5 & 156.3 minutes of BF & BC groups respectively but difference between this variables was statistically not significant (p>0.05). Study included 16 & 19 males and 14 & 11 females in BF & BC group and difference was statistically not significant (p>0.05). Study included 9 & 12 ASA I and 21 & 18 ASA II in BF & BC group and difference was statistically not significant (p>0.05). Mean time of surgery was 110.3 min with 45.5 SD & 113.9 min with 43.5 SD of BF & BC group respectively and difference was statistically not significant (p>0.05).

Table 2: Characteristics of spinal block (N=60)

Variables	BF Group (n=30) (Mean ± SD)	BC Group (n=30) (Mean ± SD)	P value
Duration of sensory block (min)	138.3 ± 16.8	187.4 ± 24.6	<0.05
Duration of motor block (min)	126.0 ± 13.2	141.7 ± 16.0	>0.05
Duration of analgesia (min)	241.6 ± 24.2	369.0 ± 38.0	<0.05

Table 2 shows mean duration of sensory block was 138.3 min with 16.8 SD & 187.4 min with 24.6 SD of BF & BC group respectively and difference was statistically significant (p<0.05). Duration of motor block was 126.0 min with 13.2 SD & 141.7 min with 16.0 SD of BF & BC group respectively and difference was statistically not significant (p>0.05). Duration of analgesia was 241.6 min with 24.2 SD & 369.0 min with 38.0 SD of BF & BC group respectively and difference was statistically significant (p<0.05).

Table 3 shows that nausea & vomiting, pruritus, urinary retention, bradycardia & hypotension was observed in 13.3% & 3.3%, 26.6% & 0.0%, 40.0% & 0.0, 3.3% & 33.3%, 3.3% & 26.6% in BF & BC group respectively.

Table 3: Complications among study participants (N=60)

Variables	BF Group (n=30)	BC Group (n=30)
Nausea & Vomiting	4 (13.3)	1 (3.3)
Pruritus	8 (26.6)	0 (0.0)
Anxiety	0 (0.0)	2 (6.6)
Respiratory Depression	1 (3.3)	0 (0.0)
Urinary Retention	12 (40.0)	0 (0.0)
Bradycardia	1 (3.3)	10 (33.3)
Hypotension	1 (3.3)	8 (26.6)

Figure 1 shows that heart rate was statistically significantly higher in BF group than BC group at 15, 30, 45, 60, 120, 180 and 240 minutes of post-operative measurement (p<0.05). Figure 2 shows that systolic BP was statistically significantly higher in BF group than BC group at 15, 30, 45, 60, 120 and 180 minutes of post-operative measurement

($p<0.05$). Figure 2 shows that diastolic BP was statistically significantly higher in BF group than BC group at 10, 15, 30, 45, 60 and 120 minutes of post-operative measurement ($p<0.05$). Figure 3 shows that respiratory rate was statistically significantly higher in BF group than BC group at 30 minutes of post-operative measurement ($p<0.05$). Figure 4 shows that SpO_2 level at different time duration of post-operative measurement but difference was statistically not significantly ($p>0.05$).

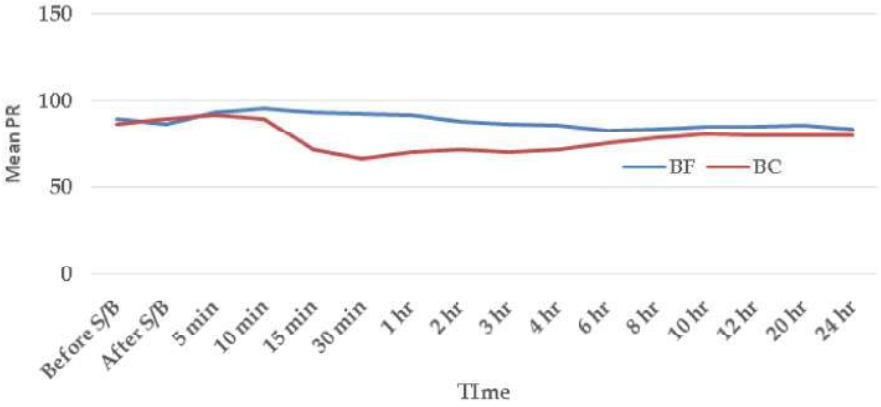

Fig. 1: Mean pulse rate (PR) (per min) at various intervals

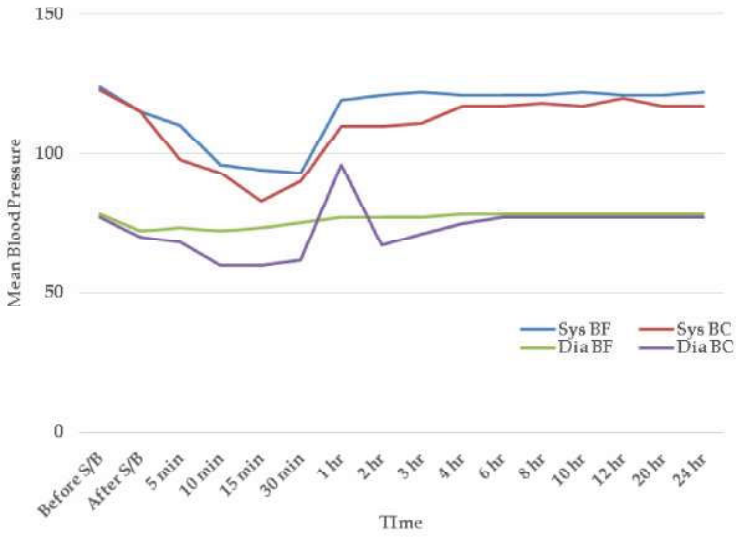

Fig. 2: Mean systolic and diastolic blood pressure (mmHg) at various intervals

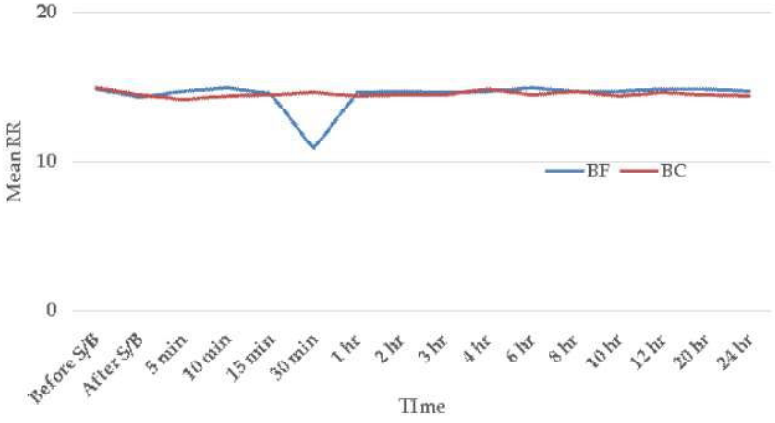

Fig. 3: Mean Respiratory rate (RR) (per min) at various intervals

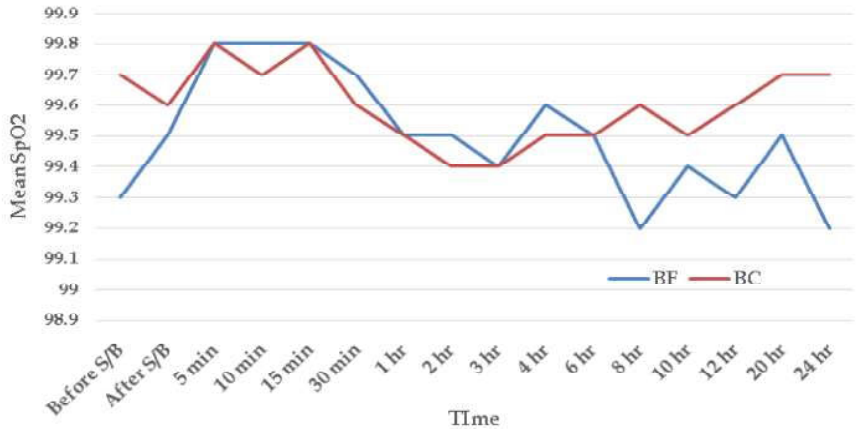

Fig. 4: Mean SpO_2 (per min) at various intervals

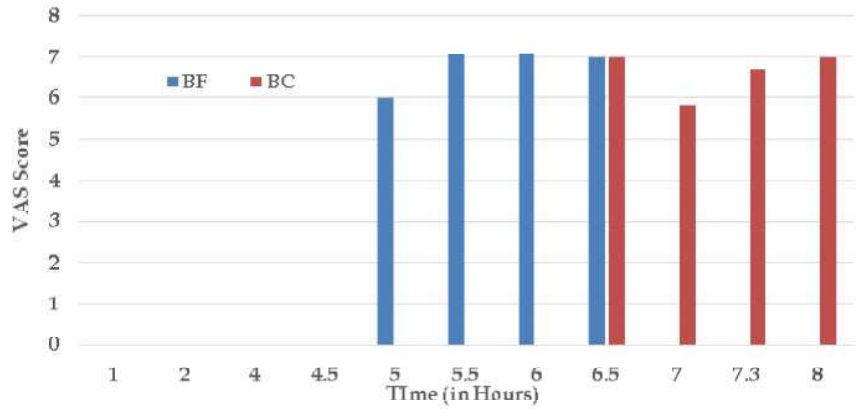

Fig. 5: Average post-operative Visual Analog Scale (VAS) among study groups (N=60)

Fig. 5 Shows that VAS score was statistically significantly higher in BF group than BC group at 5 hours of post-operative measurement ($p<0.05$) and higher in BC group at 7 & 8 hour of post-operative measurement ($p<0.05$).

Discussion

Due to lower dose requirement, clonidine and fentanyl are secure and extend the postoperative analgesia of intrathecal bupivacaine. In our study, we compared intrathecal clonidine and fentanyl in terms of safety and efficacy. Present study found the comparable difference between the demographic variables of both the groups. The total duration of operation was slightly higher in the clonidine group than the fentanyl group. Present study found that the significantly higher total duration of sensory block in clonidine group than the fentanyl group. Similar observation also found regarding total duration of analgesia. Our study also found the longer duration of motor block in clonidine group but it was statistically not significant. This finding is correlate with the similar study done by Singh R et al. [4], Routray SS et al. [10], Benhmou D et al. [11], Singh R et al. [12], Negi AS et al. [1] and Strebel S et al. [13]. But this finding is not correlate with the similar study done by Bajwa BS et al. [14]. Present study observed that clonidine has slightly better statistically significant stability at some post-operative duration than fentanyl regarding hemodynamic parameters like HR, BP and end SpO_2. These findings are correlate with the similar study done by Singh R et al. [12], Singh R et al. [4], Nazareth M et al. [15], Routray SS et al. [10] and Strebel S et al. [13].

Present study found post-operative complications like urinary retention, nausea, vomiting more among fentanyl group and bradycardia & hypotension observed more among clonidine group. These findings are correlate with the similar study done by Staikou C et al. [3] and Gabriel JS et al. [16], Routray SS et al. [10], Benhamou D et al. [11], Singh R et al. [4] and Gashi AG et al. [17]. But these findings are not comparable with the study done by Bhattacharjee A et al. [18] where higher incidence of adverse effects was observed in clonidine group. Present study observed lower

VAS score among BC group in early hours of and lower VAS score among BF group in late hours of post-operative period. This finding is corelate with the similar study done by Singh R et al. [4], Strebel S et al. [13], Benhalou D et al. [11] & Merivirta R et al. [19].

Conclusion

Intrathecal clonidine when added to bupivacaine in spinal anesthesia provides prolonged duration of postoperative analgesia than the fentanyl but with higher degree of sedation. Our study also observed prolong duration of motor and sensory block among clonidine group. Study also observed the better hemodynamic stability, less incidence of adverse effect and low VAS score among participants of clonidine group. Clonidine has longer duration of motor blocked, it is good option for long duration orthopedic surgery.

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Conflict of interest: Not Declared

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