Original Research Article

A study of safety and efficacy of analgesia and anaesthesia between intrathecal fentanyl and butorphanol as adjuvants with bupivacaine 0.5% heavy for lower limb orthopedic surgeries

Thati Ajith Kumar[1], P.Sreedevi[2*], Anjali Rajan[3], Pramod Parthasarathy[4]

[1]Senior resident, Department of Anaesthesia Gandhi Medical College and Hospital, Secunderabad, Telangana, India

[2]Associate professor, Department of Anaesthesia Gandhi Medical College and Hospital, Secunderabad, Telangana, India

[3]Senior resident, Department of Anaesthesia Gandhi Medical College and Hospital, Secunderabad, Telangana, India

[4]Senior resident, Department of Anaesthesia Gandhi Medical College and Hospital, Secunderabad, Telangana, India

Received: 20-08-2021 / Revised: 21-09-2021 / Accepted: 05-11-2021

Abstract

Aims: The aim of the study is to compare the safety and efficacy of anaesthesia and analgesia between intrathecal fentanyl and butorphanol as adjuvants with bupivacaine 0.5% heavy for lower limb orthopaedic procedures. **Materials and methods:** Eighty patients of ASA grade I and II of either sex in the age group of 18 to 50 years scheduled for elective lower limb orthopaedic procedures were allocated randomly into two groups of 40 each. Group A received intrathecal inj 0.5% heavy bupivacaine 2.5ml with 0.5ml inj fentanyl 25mcg while patients in group B received intrathecal inj 0.5% heavy bupivacaine 2.5ml with 0.5ml inj butorphanol 25mcg. Intra-operative hemodynamic parameters (HR, SBP, DBP,MAP, RR, SPO2) were noted. **Results**: There was no significant difference in the onset of sensory block .Time from injection to highest sensory block is significantly higher in butorphanol group. 25mcg of intrathecal butorphanol was found to provide a longer duration of two segment regression , longer duration of sensory regression to S2dermatome ,time to reach modified bromage grade 1 and prolonged time for first rescue analgesia as compared to 25mcg intrathecal fentanyl .Time for onset of modified bromage grade 3 is significantly higher in butorphanol group. **Conclusions**: Both 25mcg fentanyl and 25 mcg butorphanol given intrathecally along with 12.5 mg [2.5ml] of hyperbaric bupivacaine provide effective anaesthesia for lower limb surgeries. Intrathecal bupivacaine-butorphanol mixture provides longer duration of sensory, motor blockade and superior analgesia than intrathecal fentanyl- bupivacaine mixture.

Keywords: Butorphanol, Hyperbaric Bupivacaine, Fentanyl.

Introduction

Spinal anaesthesia with lignocaine was highly popular earlier for short surgical procedures as it had a predictable onset and provided dense sensory and motor blockade of moderate duration. Unfortunately, some reports of neurotoxicity had cast doubts on the intrathecal use of lignocaine. The phenomenon of 'transient neurological symptoms' may be associated with all local anesthetics; but it is 7-9 times more common with lignocaine than with bupivacaine[1]. In view of controversy and uncertainty surrounding the use of intrathecal lignocaine, hyperbaric bupivacaine (0.5%) has replaced lignocaine as the gold standard drug for the safe conduct of spinal anaesthesia in recent times.

*Correspondence
Dr. P. Sreedevi
Associate professor, Department of Anaesthesia Gandhi Medical College and Hospital, Secunderabad, Telangana, India.
E-mail: doctor.sreedevi@gmail.com

Postoperative pain relief is an unresolved issue. One of the methods of providing postoperative analgesia is by prolonging the duration of intrathecal hyperbaric bupivacaine (0.5%) by adding various adjuvant drugs such as Opioids, Clonidine, Ketamine , Neostigmine, Conotoxin ziconotide etc. However each drug has its own limitations and a need for alternative method or adjuvant drug always exists. Recently Conotoxin ziconotide gained registration for intrathecal use in specific pain conditions. Neuraxial opioids are widely used in conjunction with local anesthetics (LA) as they permit the use of lower dose of LA while providing adequate anaesthesia and analgesia[2].

First introduction of opioid adjuvant added to local anesthetic for spinal anaesthesia with intrathecal morphine into clinical practice as the forerunner. Neuraxial administration of opioids along with local anesthetics improves quality of intaoperative analgesia and also provides postoperative pain relief of longer duration. Animal studies have also demonstrated antinociceptive synergism between intrathecal opioids and local anesthetics during visceral and somatic nociception.

Fentanyl, a highly lipophilic opioid, has rapid onset of action following intrathecal administration. It does not tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally. It is associated with less side effects compared to morphine. It has become very popular additive to hyperbaric bupivacaine in recent times. However, fentanyl has side effects like pruritis, nausea and vomiting

and even a possible serotonin syndrome related to intrathecal fentanyl has been reported[2,3].

Duration of the effect of intrathecal fentanyl is dose dependent. In spinal anaesthesia, hyperbaric bupivacaine combined with fentanyl 6.25 micrograms or more facilitates precise peri operative analgesia. Butorphanol is a lipophilic opioid agonist-antagonist analgesic with a published affinity for opioid receptors in vitro of 1:4:25 (mu: delta: kappa). We assess the safety and efficacy of anaesthesia and analgesia between intrathecal fentanyl and butorphanol as adjuvants with 0.5% heavy bupivacaine for lower limb orthopedic surgeries.

Materials and methods

Hospital based prospective randomized study conducted at Gandhi Medical College and Hospital, Secunderabad on patients admitted for elective lower limb orthopaedic surgeries from January 2018 to may july2019. Following institutional ethical and scientific committee approval, patients were thoroughly explained regarding the nature of study. The study was conducted after informed written consent is taken from patients in both groups under senior anaesthesia consultant guidance in the hospital.

80 patients, aged 18 years to 50 years, belonging to ASA physical status 1 & 2, of either sex, posted for elective lower limb surgeries under spinal anaesthesia were included in the study. Using computer generated randomization technique these patients were divided into two groups of 40 patients each.

Group B - Received inj butorphanol 0.5ml of 25 mcg with 2.5ml of 0.5% bupivacaine (12.5mg) heavy intrathecally (BUTORPHANOL group). The butorphanol was diluted using distilled sterile water to obtain 25 mcg in 0.5 ml.

Group A- Received inj fentanyl 0.5ml of 25mcg with 2.5ml 0.5% bupivacaine heavy intrathecally (FENTANYL group).

Inclusion Criteria

Patients belonging to ASA physical status I and II, between 18 to 50 years scheduled for elective lower limb orthopedic surgery.

Exclusion Criteria

Patients in whom spinal anaesthesia or the study drugs are contraindicated, neurological disease, spinal deformities, local skin infection or mental disorders; those that are morbidly obese, hemodynamic unstable or having coagulation disorders. Patients with liver disease, impaired renal functions

Pre anaesthetic check up was carried out with a detailed history, general physical examination and systemic examination. Airway assessment and examination of spine were done. The all basic investigation were done.

Preoperatively patient's informed consent was taken. Patients were kept fasting for minimum 6 hours to solids and 2 hours to clear fluids preoperatively and

The procedure of spinal anaesthesia was explained and the patient was informed to communicate to the anaesthesiologist about perception of any pain or discomfort during surgery.

In the operation theatre, an intravenous line was secured. Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratoryrate (RR) and peripheral arterial oxygen saturation (SPO2) were recorded for all subjects. All patients received 10ml/kg of lactated ringer's solution as preload within 20- 30 minutes. Subarachnoid block was performed under strict aseptic conditions in the lateral position at the level of L 3-4 or L 4-5 inter vertebral space using 25 G quincke's spinal needle. The midline approach was used to perform the spinal blocks after infiltrating the skin with 1 ml of 2% lidocaine. The test drug was injected over 15 seconds. Following the subarachnoid block, the patient was put in supine position. Intraoperatively, HR, SBP, DBP, RR and SpO2 were recorded at 3 minutes (min) intervals for the first 45 min from the time of injection of spinal solution and there after every5 min till 90 min there after every 15 min for the complete period of surgery.

Hypotension (MAP <60 mmHg) was treated with fluid boluses and 5 mg intravenous (IV) boluses of Mephenteramine, while bradycardia (HR <50bpm) was treated with 0.6 mg IV atropine. Respiratory depression was defined as a respiratory rate <8 breaths/min or a spo2 of <90% on room air. All patients were given supplemental O2 via face mask at 6l/min if the SpO2 decreased below 90%.

Post Operative Analgesia

The quality of postoperative analgesia was assessed using LVAS at 15 min, 30 min and there after every 30 min, till 2 hours postoperatively; and then every hour, till 4 hours postoperative duration .The patient was asked to mark on a 10 cm horizontal scale with no pain corresponding to 0 at one end and the worst pain to 10 at the other end. This was explained to the patient in his/her vernacular language. The patient's mark of severity of pain on the line was measured.

The duration of effective analgesia (the time from subarachnoid injection to the first dose of rescue analgesic) will be recorded. Injection diclofenac sodium 1.0 mg / kg intramuscular was the rescue analgesic given if LVAS score was found to be 4 or more.

Linear Visual Analogue Scale

VAS Score	Intensity of pain
0-1	No pain to slight pain
1-3	Mild pain
4-6	Moderate pain
7-10	Severe pain

Side effects such as hypotension, bradycardia, nausea, vomiting, pruritis and time to voiding were also recorded.

Statistic Analysis

The raw data was entered into a Microsoft excel spreadsheet. Appropriate statistical tests were done using SPSS 17A and openepi.com to compare between qualitative data and quantitative data. The qualitative data were presented in the form of number and percentage and the quantitative data were presented in the form of mean and standard deviation. T-tests were used to analyze differences between two groups. Chi square test used to analyze hypotension, bradycardia, pruritis, nausea, vomiting and urinary retention. Consideration of p values: <0.05 = significant and >0.05 = Not significant.

Results

Table 1: Tabular presentation of age of patients in two groups

Age of the patients (years)	Mean	Std Dev
Butarphanol group	32.85	8.79
Fentanyl group	32.575	9.6
P value	0.903	
Height between two groups		
Butarphanol group	168.35	5.126
Fentanyl group	169.15	5.56
P value	0.505	
Weight of the patients (Kgs)		
Butarphanol group	71	10.96

Fentanyl group	71.35	9.58
P value	0.87954	
Duration of surgery		
Butarphanol group	144.95	3.77542662
Fentanyl group	143.125	4.81550647
P value	0.06319077	

No significant difference between demographic distribution between both the groups.

Table 2: Highest level of sensory block

Highest sensory block	Butarphanol group	Fentanyl group
T4	5 (12.5%)	10 (25%)
T6	34 (85%)	27 (67.5%)
T8	1 (2.5%)	3 (7.5%)

Table 3: Details in sensory block

Time of onset of sensory block (Seconds)	Mean	Std Dev
Butarphanol group	112.55	3.046
Fentanyl group	112.275	3.464
P value	0.70718	
Inference	No significant difference between two groups for onset of sensory block.	
Time from injection to highest sensory block (Min)		
Butarphanol group	8.675	0.526
Fentanyl group	8.4	0.591
P value	0.03081	
Inference	Significant difference between two groups from injection to highest sensory block	
Time for sensory regression to S2 Dermatome from highest sensory level (in minutes)		
Butarphanol group	154.025	7.959
Fentanyl group	149.55	2.062
P value*	0.00127	
Inference	Time for sensory regression to S2 Dermatome from highest sensory level (in minutes) is significantly higher in Butarphanol group	

The present study concludes that there was no significant difference in the onset of sensory block. Time from injection to highest sensory block is significantly higher in butorphanol group

25mcg of intrathecal butorphanol was found to provide a longer duration of two segment regression , longer duration of sensory regression to S2 dermatome as compared to 25mcg intrathecal fentanyl.

Table 4: Time for onset of modified bromage Grade 3 and 1(in minutes)

Time for onset of modified BROMAGE Grade 3 (in minutes)	Mean	Std Dev
Butarphanol group	8.85	0.769615289
Fentanyl group	8.5	0.506369684
P value	0.01902847	
Inference	Time for onset of modified BROMAGE Grade 3 (in minutes) is significantly higher in Butarphanol group.	
Time to reach modified BROMAGE Grade 1 (in minutes)		
Butarphanol group	170.025	10.0268
Fentanyl group	162.975	3.78
P value*	0.00012513	
Inference	Time to reach modified BROMAGE Grade 1 (in minutes) is significantly higher in Butarphanol group	

25mcg of intrathecal butorphanol was found thst time to reach modified bromage grade 1 as compared to 25mcg intrathecal fentanyl .Time for onset of modified bromage grade 3 is significantly higher in butorphanol group.

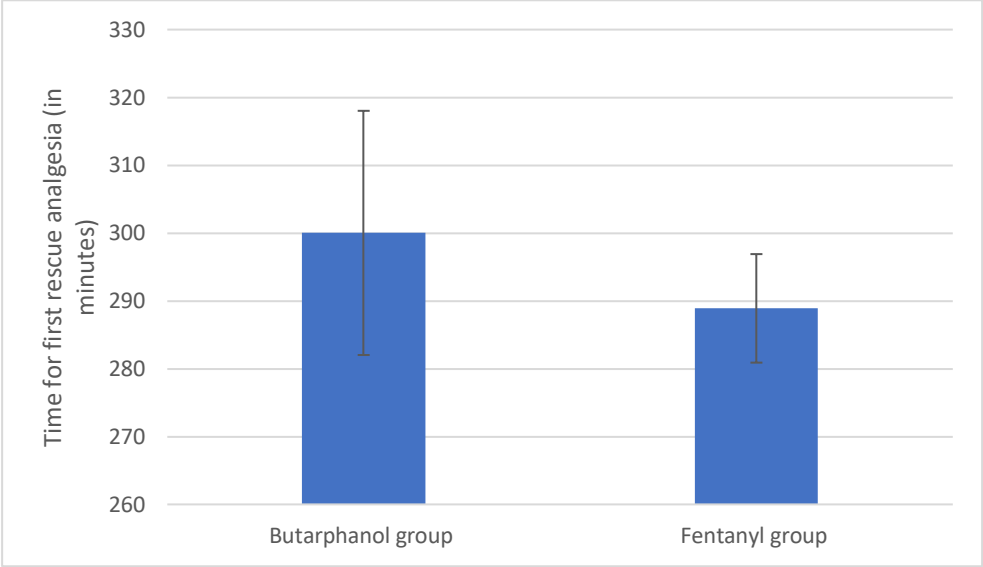

Fig 1: Time for first rescue analgesia (in minutes)

25mcg of intrathecal butorphanol was found have prolonged the time for first rescue analgesia as compared to 25mcg intrathecal fentanyl

Table 5: Comparison of Post operative LVAS

Post op LVAS	Mean Butarphanol group	Mean Fentanyl group	p value	Inference
15 min	0.025±0.1581	0.025±0.1581	1	Non significant
30 min	1±0.5547	1.075±0.4743	0.51771	Non significant
60 min	1.375±0.58561	1.475±0.554122	0.43515	Non significant
90 min	2±0.50637	2.25±0.5883	0.04513	Significantly lesser in Butarphanol group
120 min	2.6±0.4961	4.075±0.2667	0.00052	Significantly lesser in Butarphanol group*
180 min	4.225±0.479	4.475±0.750641	0.08051	Non significant
240 min	5.575±0.747	5.75±0.543021	0.2348	Non significant

Post operative LVAS was increased significantly at 90 and 120 mins in fentanyl group.

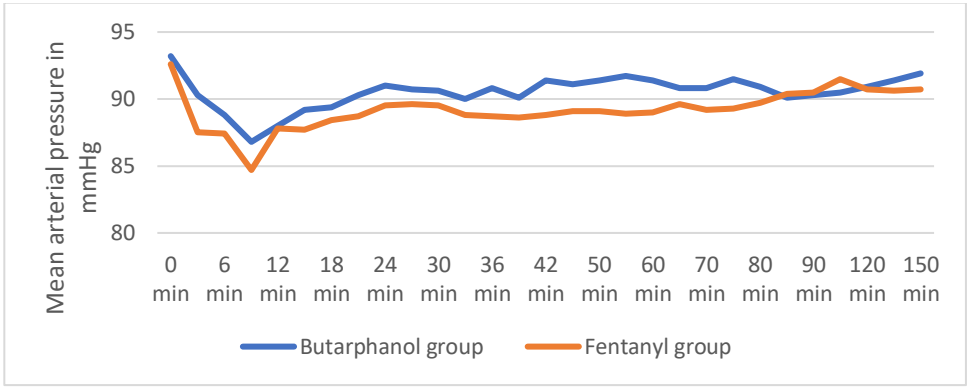

Fig 2: Mean arterial pressure in both groups

Mean arterial pressure recordings when compared to fentanyl group were high in butorphanol group at 36min, 42 min, 55 min, 60 min, 65 min after subarachnoid block. There is no significant difference in heart rate, respiratory rate, peripheral oxygen saturation during intraoperative period between both groups

Table-6: Adverse events in the different groups

Adverse event	Butarphanol	Fentanyl	P value	Inference
HYPOTENSION	3 (7.5%)	6 (15%)	0.2885	No significant difference
BRADYCARDIA	2 (5%)	2 (5%)	1	No significant difference
PRURITIS	0 (0%)	5(12.5%)	0.01152	Significantly higher in Fentanyl group
URINARY RETENTION	3 (7.5%)	5(12.5%)	0.4561	No significant difference
NAUSEA	0 (0%)	0 (0%)	1	No significant difference
VOMITING	0 (0%)	0 (0%)	1	No significant difference
Total	8(20%)	18(45%)	<0.05	Significantly higher in Fentanyl group

There was no significant difference between the two groups with respect to the occurrence of side effects except for pruritis which was developed in 12.5% of patients in fentanyl group [Group-A].where as none in butorphanol group [Group-B] developed it, which is statistically significant as p value is less than 0.05(p = 0.0115]

Discussion

Subarachnoid block with bupivacaine has been most extensively used for lower abdominal and lower limb surgeries because of its simplicity, speed, reliability, profound sensory and motor blockade and minimal exposure to depressant drugs. However, a single intrathecal injection of bupivacaine provides analgesia for only 2-2.5 hours. Most patients require further analgesia during post operative period. Also disadvantages of subarachnoid block due to sympathetic blockade like hypotension, bradycardia, and decreased cardiac output are generally proportional to the level of sympathetic blockade.

Among all available local anesthetic agents administered intrathecally, injection 0.5% hyperbaric bupivacaine has become increasingly popular as it provides good sensory and motor blockade for longer duration[3]. Baricity, i.e. specific gravity, plays an important role in determining the extent to which local anaesthetic agents spread within the CSF during subarachnoid block, and thus influences the extent of spinal anaesthesia[4]. Dextrose solution is the adjunct usually added to local anaesthetics to alter their baricity, making them hyperbaric. When dextrose 8% is added to bupivacaine 0.5% it forms 'heavy bupivacaine', which is specifically marketed for intrathecal use. However, the use of heavy bupivacaine is reported to cause an increased incidence of hypotension during subarachnoid block[4].

Spinal opiates have been of much interest in recent times as they potentiate the effect of local anesthetic agent and provide long lasting post- operative analgesia. Neuraxial administration of opioids in conjunction with local anesthetics improves the quality of intra-operative analgesia and prolongs the duration of post-operative analgesia. A combination of these agents allows for a reduction in the dose of both the classes of drugs, lessening the likelihood of side-effects attributable to each, which is particularly beneficial in geriatric patients[5].

Fentanyl, a highly lipophilic, pure μ-agonist opioid, has rapid onset of action and short duration of action, has been used with various local anesthetics for a wide variety of surgical procedures. It is associated with fewer side effects compared to morphine. Based on "Combination Wisdom," fentanyl was used widely with minidose bupivacaine in many studies. However, fentanyl has side effects like pruritis, nausea and vomiting and even a possible serotonin syndrome related to intrathecal fentanyl has been reported[6].

Butorphanol is a synthetic lipophilic opioid agonist-antagonist analgesic with a published affinity for opioid receptors in vitro of 1:4:25 (mu: delta: kappa). Abboud et al[7] have reported a dose-dependent increase in the duration of analgesia provided by epidural butorphanol for relief of post-cesarean section pain.

This randomized prospective study was done in 80 patients belonging to the age group of 18-75 years of both sexes of ASA physical status classification 84 class I & II scheduled for elective lower limb surgeries and compared the effects between fentanyl 25 mcg and butorphanol 25mcg as additives to 0.5% hyperbaric bupivacaine 12.5 mg for spinal anaesthesia.

Patients belonging to group A received 2.5 ml of 0.5% hyperbaric bupivacaine (12.5mg) + 0.5 ml (25mcg) of fentanyl. Patients of group B received 2.5ml of 0.5% hyperbaric bupivacaine (12.5mg) + 0.5 ml (25 mcg) of butorphanol. The two groups were comparable with regards to age, weight, height and duration of surgery. The mean onset to highest sensory blockade in Fentanyl group was 8.4 min and in Butorphanol group it was 8.675 min and this is statistically significant in my study. Similar values were obtained with regard to onset of highest sensory blockade in Kumar et al[8] study, where as it was 7.0 ± 2.1min in Fentanyl group and 7.2 ± 1.8min in Butorphanol group in Singh V et al[8] study. According to study of vikas kumar et al[9]the mean onset to highest sensory blockade in fentanyl group was 7.2 min and in butorphanol group it was 7 min and it is statistically insignificant.

The mean age in Singh V et al[10] study was 50 ± 12yrs in group A and 53 ± 10yrs in group B as compared to 32.57±9.6 yrs and 32.85 ± 8.79 yrs in group A and group B respectively in the present study. As patient ages there are small but significant increases in rate of onset of block and cardiovascular instability, regardless of the solution used. It is probable that these are secondary to age-related changes in spinal anatomy, nerve physiology and cardiovascular reflexes.

In Singh V et al[10] study, the spinal needle used was Pencil point needle with cephalad directed bevel. In the present study Quinke needle was used with cephalad directed bevel. Studies have shown that type of needle and direction of a pencil point needle affects the rate of sensory blockade with cephalad directed bevel giving faster onset of sensory block. Also in Singh V et al study the solution used was different from the present study. In Singh V et al study the diluent added was CSF and in the present study it was distilled water to make the volume 3ml. So compared to the solution used in present study the solution used in Singh V et al study was slightly hyperbaric. As onset of sensory blockade is faster with hyperbaric local anesthetic solution, it might also have influenced the onset of sensory blockade in Singh V et al study which is faster in both the groups compared to the present study. The age of study population, spinal needle and local anesthetic solution used in Kumar et al were same as the present study. It explains the comparable onset times in both the studies. Though the onset was slower than in Singh V et al[10] study there was no significant difference between both the groups of the present study in which it agrees with the previous studies.

The mean duration of two segment sensory regression in group A was 99 min and in group B was 107.5 min. There was significant difference between the two groups with p value is 0.00101. According to the study of V singh et al the mean duration of two segment regression in fentanyl group is 85 min, in butorphanol group 106 min and p value is <0.001 [significant].

In the study conducted by vikas kumar et al[9] the mean duration of two segment regression in fentanyl group is 85 min ,in butorphanol group 106 min. There was statistical significant difference between both groups with p value < 0.001.

Two segment regression was not included in the study conducted by kumar et al[8]. The mean duration of sensory regression to S2 in group A was 149.55 min and in group B was 154.025 min. There was significant difference between the two groups with respect to the duration of sensory blockade as P value is <0.05. In the study of vikas kumar et al[9]the mean duration of sensory regression to S2 in fentanyl group was 135 min and in butorphanol group was 158 min. There was significant difference between the two groups.

In their study in 2013, Kumar et al also found out that there was significant difference in the duration of sensory regression to S2 dermatome when fentanyl (156.0 ±18.4mins) and butorphanol (167.0±23.8mins) were administered as adjuvants to intrathecal hyperbaric bupivacaine. Study conducted by Singh V et al[8] in 2006 also found out that there was significant difference in the duration of sensory regression between the two groups (135 ± 35mins versus 158 ± 22mins 90 in Fentanyl and Butorphanol groups respectively).

The duration of blockade produced by hyperbaric solution was shorter compared to hypobaric or plain bupivacaine in previous studies[11]. This could be due to greater spread of solutions allowing most rapid uptake into the blood from the anesthetized nervous tissue. This might explain the early regression of blockade observed in Singh V et al study.

Also, whereas distilled water used as diluent in the present study which was at room temperature, the CSF used in Singh V et al study was at 37degree C i.e. body temperature making the temperature of the local anesthetic mixture slightly higher than in the present study. As the temperature of the local anesthetic solution increases, the time taken for block regression decreases[12]. This also explains the lesser

time taken for the regression of sensory level to S2 in Singh V et al study[10].

Age of the patient doesn't affect the time take for the regression of block[13].The present study finding is in accordance with the study conducted by Kumar et al[44] and Singh V et al[8] that adding 25mcg Butorphanol to Bupivacaine significantly increases the duration of sensory block compared to adding 25mcg Fentanyl.

The mean time to onset of maximum bromage grade 3 group A was 8.5 min and in butorphanol group was 8.85 min. There is statistically significant difference with P value 0.01902. In study conducted by Kumar et al[8] in 2013 and in the study of vikas kumar et al[9] there was no significant difference in both groups as p value>0.05. It was earlier in Singh V et al study as it was 8.2 min in fentanyl group and 8.0 min in butorphanol group. There was no significant difference between the two groups as p value >0.05.

The mean age in Singh V et al[10]study was 50 ± 12yrs in group A and 53 ± 10yrs in group B as compared to 32.57 ± 9.6yrs and 32.85 ± 8.79yrs in group A and group B respectively in the present study. As the age increases the rate of onset of motor blockade increases, thereby decreasing the time taken reach maximum motor block, regardless of the solution used. his might explain the earlier onset of maximum motor blockade in Singh V et al study compared to the present study.

The time taken to reach Bromage grade 1 was 162 min in fentanyl group and in butorphanol group it was 170.025 min. It was a significant difference as the P value obtained was 0.000125. In the study conducted by Kumar et al[8] (176.4 min for fentanyl group and 183.8 min for butorphanol group) there was no significant difference between groups. Though it was earlier in Singh V et al study as it was 162 min in fentanyl group and 165 min in butorphanol group when compared Kumar et al study and present study, it was not significantly different between the groups of the study. As was explained before the baricity of the solution used in Singh V et al study was slightly higher compared to that used in Kumar et al and the present study. It could be the reason for the early regression of motor blockade in Singh V et al study[10].

In the study conducted by vikas kumar et[9] al time taken to reach modified bromage grade 1 in fentanyl group is 162 min and in butorphanol group is 165 min and p value is <0.001 [statistically significant.] The mean time for first rescue analgesia in group A was 288.9 min and in group B, mean time for first rescue analgesia was 300.025 min. There was significant difference between the two groups with respect to the duration of effective analgesia as P value obtained 0.00106. Present study shows that the time for first request of rescue analgesia was found to be significantly longer in the butorphanol group as compared to the fentanyl group. Similar values were obtained with regard to the time for first rescue analgesia in butorphanol group in the studies conducted by Kumar et al in 2013 than in fentanyl Group. Singh V et al[10] have also reported that lesser number of patients receiving intrathecal butorphanol requested for rescue analgesia as compared to those receiving intrathecal fentanyl.

Kim et al[14] study compared intrathecal fentanyl and sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy and reported the duration of analgesia of approximately 7 hours after the use of 4 mg bupivacaine with 25 mcg fentanyl. Hamber EA, Viscomi CM[15] report the duration of analgesia with intrathecal fentanyl ranging from one to four hours. Chari et al[16]in their study comparing butorphanol and normal saline as an adjuvant to local anesthetic agent in subarachnoid block observed that the time to rescue analgesia was significantly delayed ($p < 0.005$) in the butorphanol group (227 min ± 13.18 min), compared with the normal saline group (149.07 ± 8.19 min). They concluded that addition of butorphanol gives longer duration of post- operative analgesia without serious side effects. Philip BK, Scott DA, Freiberger D, Gibbs RR, Hunt C, Murray E[17]. Butorphanol compared with fentanyl in general anaesthesia for ambulatory laparoscopy have reported the equi-analgesic doses as 1 mcg/kg and 20 mcg/kg for fentanyl and butorphanol, respectively. We studied the 25 mcg dose of intrathecal fentanyl and butorphanol based on earlier studies.

Thus, the results of our study are consistent with experimental evidence of synergistic interaction between spinal opioids and local anesthetics, which are characterized by enhanced somatic analgesia without effect on the degree or level of the local anesthetic induced sympathetic or motor blockade. The present study also supports the previous studies with regards to the duration of analgesia, which is prolonged more with Butorphanol than with Fentanyl when added to Bupivacaine for subarachnoid block thus decreasing the need for post operative analgesics.

Mean systolic blood pressure recordings when compared to fentanyl group were high in butorphanol group at 15 min ,55min,60 min after subarachnoid block Mean diastolic blood pressure (Table No. 20) recording when compared to fentanyl group was high in butorphanol group at 42 min after subarachnoid block. Mean arterial pressure (Table No. 21) recordings when compared to fentanyl group were high in butorphanol group at 36min,42 min, 55 min,60 min, 65 min after subarachnoid block. And there is no significant difference in remaining intraoperative period. There is no significant difference in heart rate, respiratory rate, oxygen saturation during intraoperative period between both groups. In the study conducted by vikas kumar et al, there is no significant difference in systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate between both fentanyl and butorphanol groups.

Six (15%) patients in the fentanyl group and three (7.5%) patients in the butorphanol group had hypotension in our study requiring treatment with 5mg of intravenous mephentermine in addition to crystalloid bolus. There is no statistical significance as p=0.288 Neuraxial administration of opioids has been reported to be associated with hypotension. Singh V et al, in comparison of 25 mcg intrathecal fentanyl and butorphanol with hyperbaric bupivacaine, have reported the instance of hypotension as 20% in the fentanyl group and 17% in the butorphanol group.

This increased incidence of hypotension in Singh V et al study may be due to increased age of the study population, slightly hyperbaric solution and using CSF at body temperature as diluent. 5% of people in both the groups developed bradycardia which is statistically insignificant. 5(12.5%) people in fentanyl group developed pruritis where as none in butorphanol group developed it, which is statistically significant as p value is less than 0.05(p=0.012).

Pruritis was mild and didn't require any treatment. Pruritis is the commonest side effect of intrathecal opioids. Nair GS et al,[18] have reported on spinal anaesthesia for ambulatory knee arthroscopy, the combination of bupivacaine with fentanyl was associated with an instance of pruritis ranging from 48 to 75% compared with the groups receiving bupivacaine alone . Ackerman et al[78] have also reported that opioids that stimulated κ- receptors following epidural administration exhibited significantly less pruritis than pure μ-receptor opioids administered similarly. Furthermore, investigators have reported that continuous epidural butorphanol relieves pruritis associated with epidural morphine infusions in children[19].

Urinary retention was developed in 12.5% (5) of people in fentanyl group where as 7.5% (3) of people developed in butorphanol, which is statistically insignificant as p value is more than 0.05. Kamphuis ET et al[20] have reported that intrathecal bupivacaine is associated with a clinically significant disturbance of bladder function and spontaneous voiding may not be expected until the sensory blockade has regressed to the S3 level.

There was no significant difference between the two groups with respect to the occurrence of nausea and vomiting as the P value obtained was > 0.05. None of the patients in our study had any post operative complications like lower limb weakness, PDPH or any other neurological deficits. Thus, the present study concludes that the highest sensory level achieved, onset of sensory and motor blockade were comparable between 25mcg Fentanyl and 25mcg Butorphanol when added to Bupivacaine for subarachnoid block.25mcg of intrathecal butorphanol was found to provide a longer duration of sensory regression to S2 dermatome, prolonged motor block and

prolonged the time for first rescue analgesia as compared to 25mcg intrathecal fentanyl. There was no significant difference between the two groups with respect to the occurrence of side effects except for pruritis with Fentanyl causing statistically significant number of pruritis compared to Butorphanol.

Conclusion

Despite advances in the knowledge of pathophysiology, pharmacology and the development of more effective techniques for the management of perioperative analgesia, many patients continue to experience distressing pain in the postoperative period. It is shown that relief of pain with neuraxial blockade with a local anesthetic like bupivacaine alone is limited to the initial postoperative period. When adjuvants like butorphanol and fentanyl are added to local anesthetic, pain relief can be extended well into the postoperative period. The present study demonstrated that time for onset of highest sensory and motor blockade was significantly high in butorphanol group (Group B) when compared to fentanyl group (Group A). Intrathecal butorphanol 25mcg was found to provide a significantly longer mean duration of sensory blockade, motor blockade and prolonged the time for first rescue analgesia as compared to 25 mcg fentanyl. There is no much significant difference in systolic blood pressure, diastolic blood pressure,mean arterial pressure, heart rate, respiratory rate, peripheral oxygen saturation during intraoperative period between both groups.

Hence, we suggest that addition of 25 mcg intrathecal butorphanol is superior additive to 0.5% heavy bupivacaine combination in respect to the duration of sensory , motor blockade and requirement of rescue analgesia without any significant increase in adverse effects.

References

1. Srivastava U, Kumar A, Saxena S, Saxena R, Gandhi NK, Salar P. Spinal anaesthesia with lignocaine and fentanyl. Indian J Anaesth. 2004; 48(2): 121- 123.
2. Stocks GM, Hallworth SP, Fernando R, England AJ, Columb MO, Lyons G. Minimum local analgesic dose of intrathecal bupivacaine in labor and the effect of intrathecal fentanyl. Anaesthesiology 2001; 94:593-8.
3. Biswas BN, Rudra A, Bose BK, Nath S, Chakrabarty S, Bhattacharjee S. Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early postoperative period. Indian J. Anaesth. 2002; 46(6): 469-472.
4. Rushman GB, Davis NJ, Cashman JN. Spinal anaesthesia; intradural and extradural. In: Lee's Synopsis of Anaesthesia. 12th ed. Oxford: Butterworth Heinman; 1999. p. 506-7.
5. Ben-David B, Frankel R, Arzumonov T, Marchevsky Y, Volpin G. Minidose Bupivacaine- Fentanyl Spinal Anaesthesia for Surgical Repair of Hip fracture of aged. Anesthesiology 2000;92:6-10.
6. Kim SY, Cho JE, Hong JY, Koo BN, Kim JM, Kil HK. Comparison of intrathecal fentanyl And sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy. Br J Anaesth 2009; 103:750-4.
7. Abboud TK, Moore M, Zhu J, Murakawa K, Minehart M, Longhitano M, et al. Epidural Butorphanol or morphine for the relief of post-caesarean section pain: Ventilatory responses to carbon dioxide. Anesth Analg 1987; 66:887-93.
8. Kumar B, Williams A, Liddle D, Verghese M. Comparison of intrathecal bupivacaine- Fentanyl and bupivacaine-butorphanol mixtures for lower limb orthopedic procedures. Anesth Essays Res 2011;5:190-5.
9. Dr.vikas kumar gupta,dr.abhay raj yadav,dr.aditya agarwal – A Comparative study of intrathecal butorphanol and fentanyl as an adjuvant to bupivacaine(heavy) for lower limb orthopedic Surgeries, GJRA 2017;6[7]:21
10. Singh V, Gupta LK, Singh GP. Comparison among intrathecal fentanyl and butorphanol in combination with bupivacaine for lower limb surgeries. J Anaesth Clin Pharmacol. 2006; 22(4): 371-375.
11. Brown DT, Wildsmith JA, Covino BG, Scott DB. Effect of baricity on spinal anaesthesia with amethocaine. Br J Anaesth 1980; 52: 589–96.
12. Callesen T, Jarnvig I, Thage B, Krantz T, Christiansen C. Influence of temperature of bupivacaine on spread of spinal analgesia. Anaesthesia 1991; 46: 17–19
13. Veering BT, Burm AGL, Spierdijk J. Spinal anaesthesia with hyperbaric bupivacaine: effects of age on neural blockade and pharmacokinetics. Br J Anaesth 1980;60:187-194.
14. Kim SY, Cho JE, Hong JY, Koo BN, Kim JM, Kil HK. Comparison of intrathecal fentanyl And sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy. Br J Anaesth 2009; 103:750-4.
15. Hamber EA, Viscomi CM. Intrathecal lipophilic opioids as adjuncts to surgical spinal anaesthesia. Reg Anesth Pain Med 1999; 24:255-63.
16. Ranga Chari VR, Goyal AA, Singh V. A study of addition of Inj.Butorphanol to hyperbaric Inj.Bupivacaine given intrathecally to patients undergoing lower segment caesarean section: A randomized, controlled trial. Med J DY Patil Univ 2013;6:156-60.
17. Philip BK, Scott DA, Freiberger D, Gibbs RR, Hunt C, Murray E. Butorphanol compared with fentanyl in general anaesthesia for ambulatory laparoscopy. Can J Anaesth 1991; 38:183-6.
18. Nair GS, Abrishami A, Lermitte J, Chung F. Systematic review of spinal anaesthesia using bupivacaine for ambulatory knee arthroscopy. Br J Anaesth 2009; 102:307-15.
19. Ackerman WE, Juneja MM, Kaczorowski DM, Colclough GW. A comparison of Incidence of pruritis following epidural opioid administration in the parturient. Can J Anaesth 1989; 36:388-91.
20. Kamphuis ET, Ionesco TI, Kuipers PW, De Gier J, Van Venrooij GE, Boon TA. Recovery of storage and emptying functions of the urinary bladder after spinal anaesthesia with lidocaine and with bupivacaine in men. Anaesthesiology 1998; 88: 310-6.

Conflict of Interest: Nil Source of support: Nil