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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

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Abstract
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. Eighty patients of ASA grade I and II of either sex in the age group of 18 to 75 years scheduled for elective lower limb orthopaedic procedures were allocated randomly into two groups of 40 each. Group F received intrathecal inj 0.5% heavy bupivacaine2.5ml 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, RR, SPO_2) were noted. Results were compared among the groups using the student t test and chi square test. In all cases, $p < 0.05$ was considered statistically significant. The time taken to attain highest sensory level and time of onset of maximum bromage grade 3 motor blockade were comparable among the two groups. Significantly slower sensory block regression to S2 dermatome level was observed in the group receiving intrathecal butorphanol as compared to intrathecal fentanyl. A higher number of patients ingroup F requested for rescue analgesia during the postoperative period than in group B. It was concluded that Both 25mcg fentanyl and 25 mcg butorphanol given intrathecally along with12.5 mg of hyperbaric bupivacaine provide effective anaesthesia for lower limb surgeries. Intrathecal bupivacaine-butorphanol mixture provides longer duration of sensory blockade and superior analgesia than intrathecal fentanyl-bupivacaine mixture
Keywords: *Analgesia, Anaesthesia, Bupivacaine, Butorphanol, Fentanyl, Spinal.*

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.

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 drugs such as Opioids, Clonidine, Ketamine, Neostigmine, Conotoxin ziconotide etc. However each drug has its own limitations and a need for alternative method or 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].

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[3]. 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[4]. 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[5]. Butorphanol is a lipophilic opioid agonist-antagonist analgesic with a published affinity for opioid receptors in vitro of 1:4:25 (mu: delta: kappa)[6]. Abboud et al. have reported a dose-dependent increase in the duration of analgesia provided by epidural butorphanol for relief of post cesarean section pain[7].

The present study was undertaken to compare the safety and efficacy of anaesthesia and analgesia of intrathecal bupivacaine-butorphanol mixture with intrathecal bupivacaine-fentanyl mixture for lower limb orthopedic procedures. This study was conducted as only a limited numbers of studies have explored the use of intrathecal butorphanol in human subjects previously

Materials & Methods

To 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 procedures.

To assess the safety and side effects of intrathecal Fentanyl versus Butorphanol as adjuvants along with 0.5% heavy Bupivacaine for lower limb orthopaedic procedures in terms of Hypotension, Bradycardia. Nausea & Vomiting, Pruritis and Urinary retention.

This is hospital based prospective randomized study. The study is conducted at Kamineni academy of Medical Sciences and Research Centre, Hyderabad on patients admitted for elective lower limb orthopaedic surgeries, from January 2015 to may 2016. After obtaining institutional ethical and scientific committee approval, patients were thoroughly explained regarding the nature of study and informed written consent is taken from patients in both groups. 80 patients, aged 18 years to 75 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 0.5% bupivacaine heavy intrathecally. The butorphanol was diluted using distilled sterile water to obtain 25 mcg in 0.5 ml. The 25 mcg butorphanol was then added to 2.5 ml of0.5% hyperbaric bupivacaine to make a total volume of 3 ml to be given intrathecally to patients in Group B. Group F- Received inj

fentanyl 0.5ml of 25mcg with 2.5ml 0.5% bupivacaine heavy intrathecally

Patients in whom spinal anaesthesia or the study drugs are contraindicated, Patients with neurological disease, spinal deformities, local skin infection or mental disorders; obese, hemodynamic unstable or having coagulation disorders, liver disease, impaired renal functions were excluded from study. 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. Routine laboratory examinations were done. Patients were kept fasting for 6 hours to solids and 2 hours to clear fluids preoperatively and They were pre medicated with tab. Alprazolam 0.25 mg and tab. ranitidine 150 mg orally 12 hours before giving spinal anaesthesia.

In the operation theatre, an intra venous line was established. Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (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 SpO_2were recorded at 5 minutes (min) intervals for the first 15 min from the time of injection of spinal solution and there after every15 min for the complete period of surgery.

Hypotension (MAP <70 mmHg) was treated with fluid boluses and 6 mg intravenous (IV) boluses of ephedrine, 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 O_2 via face mask at 6l/min if the SpO_2 decreased below 90%.

The highest level of sensory block was determined in the mid clavicular line bilaterally, by pinprick test using a 20-G hypodermic needle every 2 min till the level had stabilized for four consecutive tests. The highest level of sensory block and the time taken to attain it from the time of intrathecal injection was recorded. Further sensory testing was performed at 20 min intervals till the recovery of S2 dermatome.

Time taken for onset of maximum bromage grade 3 motor blockade from the time of intrathecal injection and the time taken to reach bromage grade 1 was noted. It was assessed by straight leg raising while lying supine and was graded according to Bromage scale[8].

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

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, and

urinary retention. Consideration of p values: <0.05 = significant and >0.05 = Not significant

Results

This study is conducted at Kamineni hospitals. There is no significant difference between the demographic data of two groups. The mean duration of surgery was 133.2±5.2,and 131.6±5.6 in fentanyl and Butorphanol respectively.

Table.1: Sensory characters

Parameters	Fentanyl (n=40)	Butorphanol (n=40)
Highest level(median)	T 7	T 7
Time from injection to highest sensory level(min)	8.10 ±0 .744	8.08 ±0.82
Time for sensory regression to S_2 dermatome (min)	152.78± 8.350	166.63 ±13.05

Comparison between times from injection to highest sensory level among two groups is statistically insignificant. Comparison between time for sensory regression to S_2 dermatome among two groups is statistically significant as p is <0.05.Comparison between time to onset of maximum bromage grade 3 among two groups is statistically in significant. Comparison between time to reach bromage grade 1 among two groups is statistically insignificant.

Table 2: Motor block characteristics

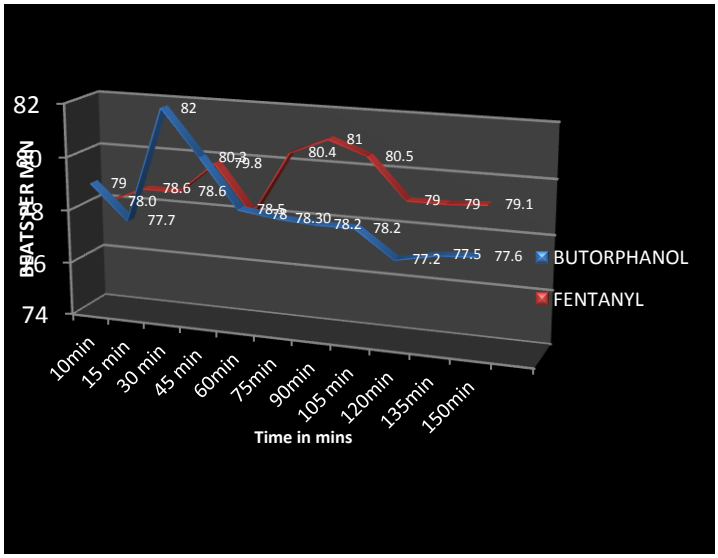
parameters	Fentanyl group(n=40)	Butorphanol group(n=40)
Time from injection to onset of maximum bromage grade 3(min)	9.28±0.9	10.0±0.9
Time to reach bromage grade 1(min)	176.0± 6.2	183.6± 8.1*

Time for first rescue analgesia (min) was 307±14 and 365±15.1 in fentanyl and Butorphanol respectively.

Table.3: Comparison of post op LVAS score (mean±SD)

Time	Fentanyl group	Butorphanol group	p value
15 min	0	0	0.00
30 min	1.30±0.5	1.10±0.3	0.00
60 min	1.80±0.5	1.55±0.6	0.033#
90 min	4.60±0.5	2.83±0.8	0.039#
120min	5.90±0.5	4.10±0.7	0.349
180 min	6.30±0.5	5.25±0.4	0.325
240 min	6.73± 0.6	6.10±0.5	0.015

Fig1: Comparison of mean pulse rates among two groups



The mean systolic pressure in this study was com sturdily maintained in butorphanol group, mean diastolic pressure was high compared to fentanyl group and mean systolic pressure and mean diastolic pressure were shown in fig 2&3.The mean respiratory rates were given in fig 4 and comparable in both groups. The side effects observed in this study were hypotension, brady cardia and pruritis were also comparable in both groups.

Fig 2: Comparison of mean systolic blood pressures among two groups

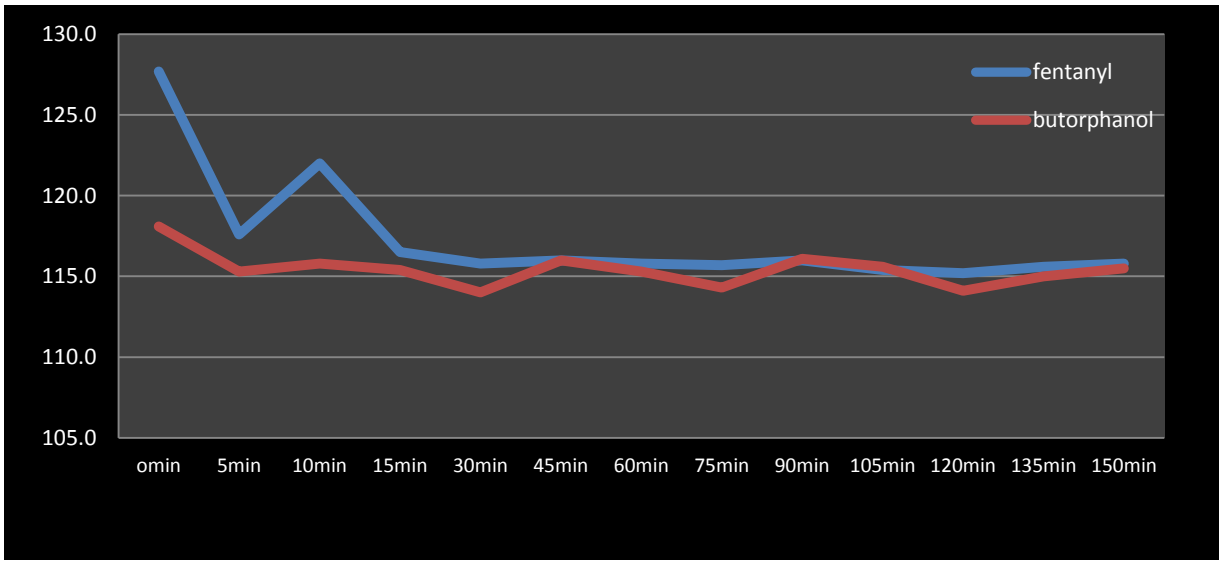


Fig 3 : Comparison of mean diastolic blood pressures among two groups

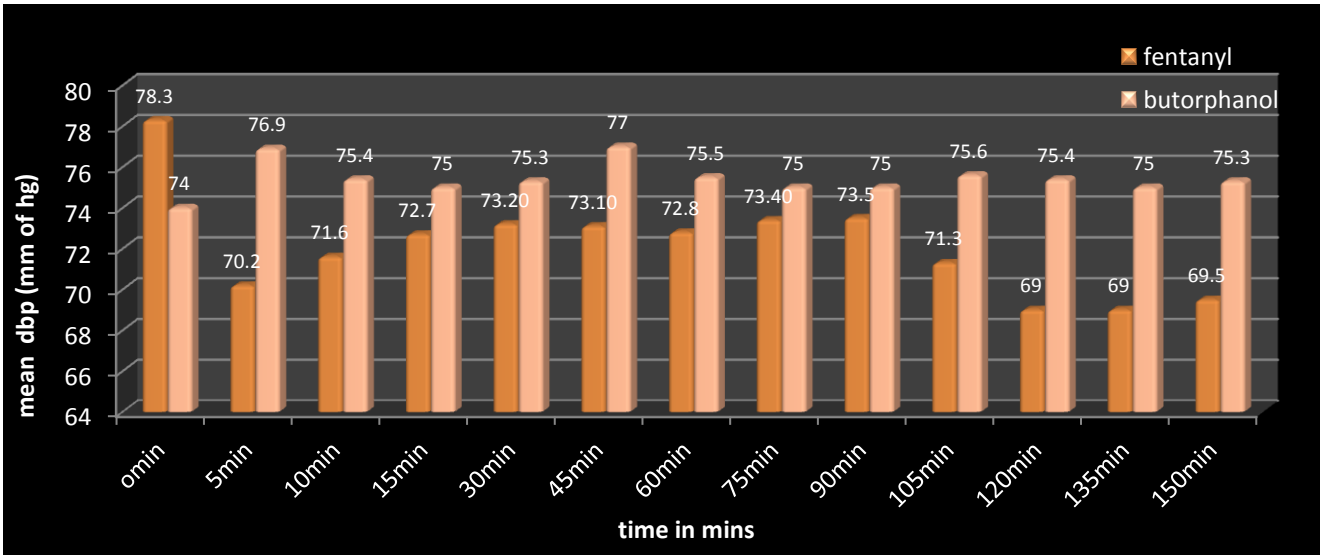


Fig 4: Comparison of mean respiratory rates among two groups

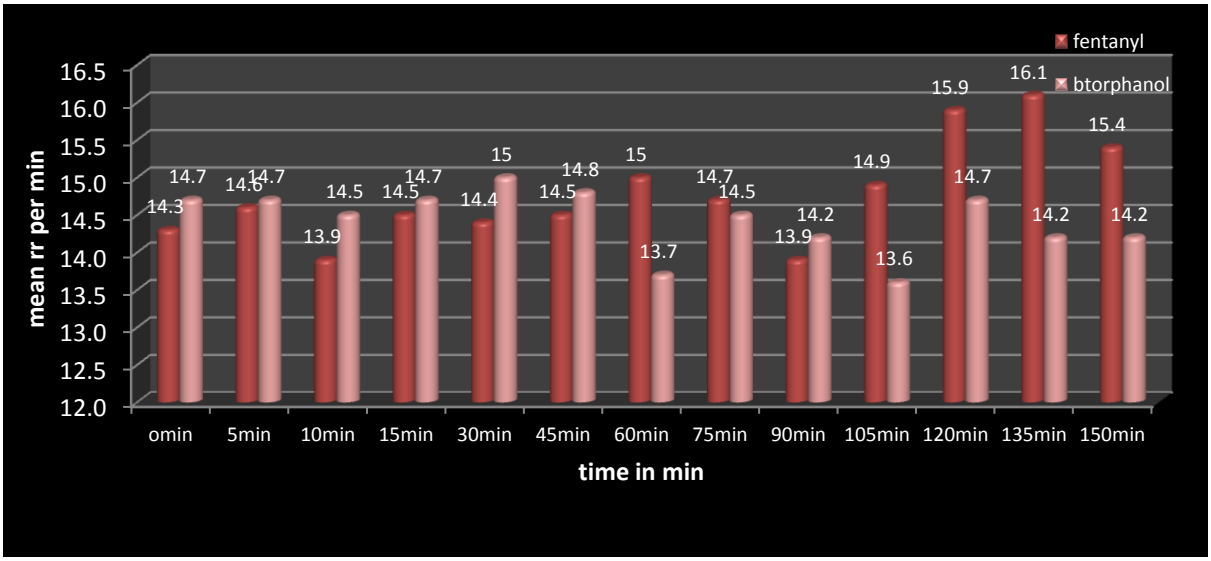


Table 4: Side effects between two groups

Side effects	Fentanyl Group (n=40)	Butorphanol Group (n=40)
Hypotension	6 (15%)	3(7.5%)
Bradycardia	2 (5%)	2 (5%)
Pruritis	5 (12.5%)	0 (0%)
Urinary retention	5 (12.5%)	3 (7%)
Nausea	0 (0%)	0 (0%)
Vomiting	0 (0%)	0 (0%)

Discussion

Among all available local anesthetic agents administered intrathecally, 0.5% hyperbaric injection bupivacaine has become increasingly popular as it provides good sensory and motor blockade for longer duration[4]. 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[9]. Highly hydrophilic opioids such as morphine, though provides very good intra and postoperative analgesia, its use becomes limited because of delayed respiratory depression that it causes due to rostral spread in intrathecal space.

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[10]. It is associated with fewer side effects compared to morphine. Based on "Combination Wisdom," fentanyl was used widely with mini dose bupivacaine in many studies[10]. However, fentanyl has side effects like pruritis, nausea and vomiting and even a possible serotonin syndrome related to intrathecal fentanyl has been reported.

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)[11]. Abboud et al[12] have reported a dose-dependent increase in the duration of analgesia provided by epidural butorphanol for relief of post-cesarean section pain. Butorphanol is used in epidural analgesia and in animal studies[11], but there are very few studies in the literature on the clinical characteristics of intrathecal butorphanol. We therefore conducted the present study to evaluate the efficacy of intrathecal fentanyl and butorphanol as adjuvants to bupivacaine in various lower limb surgical procedures.

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 class 1 & 2 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.

The median highest sensory levels achieved were same in both groups (T7). The mean onset to highest sensory blockade in Fentanyl group was 8.10min and in Butorphanol group it was 8.08min. Similar values were obtained with regard to onset of highest sensory blockade in Kumar et al[12] 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[4] study. There were no statistically significant differences between the two groups with respect to the onset of blockade.

The mean duration of sensory regression to S2 in group F was 152.78min and in group B was 166.63min. There was significant difference between the two groups with respect to the duration of sensory blockade as P value is <0.05. In their study in 2011, Kumar et al[12] 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[4] 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 in Fentanyl and Butorphanol groups respectively).

The mean time to onset of maximum bromage grade 3group F was 9.28min and in butorphanol group was 10.0 min. There is no statistically significant difference as P value >0.05. These were similar to other studies [4,12]. Present study

shows thatthe 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[12] than in fentanyl group. Hamber EA, Viscomi CM[14] report the duration of analgesia with intrathecal fentanyl ranging from one to four hours. Chari et al[14] 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.

Six (15%) patients in the fentanyl group and three (7.5%) patients in the butorphanol group had hypotension in our study requiring treatment with small doses of intravenous ephedrine (6 mg in 7 and 12 mg in 2 patients) in addition to crystalloid bolus. Nair GS et al [15], 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. Urinary retention was developed in 12.5% (5) of people in fentanyl groupwhereas7% (3) of people developed in butorphanol, which is statisticallyin significant as p value is more than 0.05. Kamphuis et al[16] have reported that intrathecal bupivacaineis 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.

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 post operative period.

The present study demonstrated that intrathecal administration of 25mcg of butorphanol or fentanyl to hyperbaric bupivacaine had similar time to onset of highest sensory and motor blockade. Intrathecal butorphanol 25mcg was found to provide a significantly longer mean duration of sensory blockade and prolonged the time for first rescue analgesia as compared to 25mcg fentanyl without significant prolonged motor blockade. Hence, we suggest that addition of 25mcg intrathecal butorphanol is superior additive to0.5% heavy bupivacaine combination in respect to the duration of sensory blockade and requirement of rescueanalgesia 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. 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.
5. Ozkardesler S, Gurpinar T, Akan M, Koca U, Sarikaya H, Olmez T et. al. A possible perianaesthetic serotonin syndrome related

to intrathecal fentanyl. J Clin Anaesth. 2008; 20(2): 143-145.
6. Commiskey S, Fan LW, Ho IK, Rockhold RW. Butorphanol: Effects of a prototypical Agonist-antagonist analgesic on kappa-opioid receptors. J Pharmacol Sci 2005;98:109-116.
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. Bromage PR. Epidural Analgesia. Philadelphia; WB Sanders; 1978; 144.
9. Brown DT, Wildsmith JA, Covino BG, Scott DB. Effect of baricity on spinal anaesthesia with amethocaine. British journal of anaesthesia 1980; 52: 589-95.
10. Kim SY, Cho JE, Hong JY, Koo BN, Kim JM, Kil HK. Comparison of intrathecalfentanyl Andsufentanil in low-dose dilute bupivacaine spinal anaesthesia fortransurethral prostatectomy. Br J Anaesth 2009; 103:750-4.
11. Wongchanapai W, Tsang BK, He Z, Ho IK. Relative involvement of spinal opioid receptors in physical dependence on intrathecal butorphanol and morphine. Pharmacol Biochem Behav1998;60:899-907
12. 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.
13. Hamber EA, Viscomi CM. Intrathecal lipophilic opioids as adjuncts to surgical spinal anaesthesia. Reg Anesth Pain Med 1999; 24:255-63.
14. Ranga Chari VR, GoyalAA, Singh V. A study of addition of Inj.Butorphanol to hyperbaric Inj. Bupivacaine given intrathecally to patients undergoing lower segmentcaesareansection: A randomized, controlled trial. Med J DY Patil Univ 2013;6:156-60
15. 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
16. Kamphuis ET, Ionesco TI, Kuipers PW, De Gier J, Van Venrooij GE, Boon TA.Recovery of storage and emptying functions of the urinary bladder afterspinal anaesthesia with lidocaine and with bupivacaine in men. Anaesthesiology1998; 88: 310-6.