Original Article

Comparison of intrathecal bupivacaine-fentanyl and bupivacaine-butorphanol combinations for joint replacement surgeries

Aakriti Sharma, Anita Kumari[1], Ruchi Gupta[1], Shubhdeep Kaur[1], Deepika Arora, Keerat Kaur

Department of Anaesthesia, PGI Chandigarh, [1]Department of Anaesthesia, Sri Guru Ram Das Institute of Medical Sciences and Research, Punjab, India

Abstract

Background and Aims: The objective of the study was to compare duration of analgesia of fentanyl versus butorphanol as adjuvants to bupivacaine in spinal anesthesia.

Material and Methods: A prospective, randomized, double-blinded study conducted in 80 patients of 18–75 years age group and American Society of Anesthesiologists Grades I and II undergoing joint replacement surgeries. A total of 40 patients in each Group A and Group B received 0.5% bupivacaine 3 ml with 25 mcg fentanyl and 25 mcg butorphanol respectively, in a total volume of 3.5 ml made with saline. Duration of analgesia, number of rescue analgesia, sensory, and motor block characteristics were compared between the two groups. Statistical analysis was done using t test and Chi-square test with SPSS 19.0 software.

Results: Mean duration of analgesia was found more in Group B in comparison to Group A ($P < 0.05$). A number of doses of analgesic required postoperatively were more in Group A compared to Group B ($P < 0.001$). Time required for onset of sensory and motor block was comparable in both the groups. However, two segment regression of sensory block was slower in Group B compared to Group A ($P < 0.05$).

Conclusion: We conclude that addition of butorphanol 25 μg as an adjuvant to 0.5% hyperbaric bupivacaine provided prolonged duration of analgesia compared to 25 μg fentanyl.

Keywords: Adjuvants, bupivacaine, butorphanol, fentanyl

Introduction

The increase in the proportion of elderly population has led to a large number of patients presenting for joint replacement surgery. One of the prime concerns for patients undergoing arthroplasty is postoperative pain. Our main objective is to provide effective analgesic techniques that give optimal pain relief along with minimizing side effects such as sedation, postoperative nausea and vomiting, hypotension, and motor block to reduce the patient's suffering to a minimum.[1] Good postoperative analgesia is associated with early mobilization, resumption of oral nutrition, and decreased hospital stay.[2] Intrathecal bupivacaine is often found to be inadequate for surgeries of longer duration.[3] Use of adjuvants can potentiate the effect of local anesthetic, prolong intraoperative anesthesia, and the duration of postoperative analgesia. The administration of intrathecal opioids with local anesthetics has shown promising results to this effect.[4,5]

Analgesia is produced principally through interaction with μ receptors at supra spinal sites by fentanyl. Fentanyl also

Address for correspondence: Dr. Anita Kumari,
Department of Anaesthesia, Sri Guru Ram Das Institute of Medical Sciences and Research, Punjab, India.
E-mail: kumarianitadr1@gmail.com

Access this article online

Quick Response Code:

Website:
www.joacp.org

binds to κ receptors causing spinal analgesia, sedation, and anesthesia. It is preferred as an adjuvant in spinal anesthesia because of its rapid onset and lesser incidence of respiratory depression in comparison to other opioids.[4] Butorphanol exhibits partial agonist and antagonist activity at the mu-opioid receptor, as well as competitive antagonist and partial agonist activity at the kappa receptors.[5] The available data regarding intrathecal use of butorphanol are limited and due to the advent of a variety of adjuvants, there is an ongoing debate on the choice, amount and concentrations of drugs to be used. Hence, the present study was conducted to evaluate and compare the efficacy of intrathecal butorphanol and fentanyl in combination with hyperbaric bupivacaine for knee replacement surgery in terms of postoperative duration of analgesia. The characteristics of sensory and motor block, postoperative analgesic requirements, and any associated complications were also studied.

Material and Methods

A prospective, randomized, double blind study was conducted after obtaining approval from the institutional ethics committee/review board and registered with CTRI no CTRI/2018/04/012945. Patients between 18 and 75 years of age, belonging to American Society of Anesthesiologists (ASA) physical status I or II scheduled for unilateral knee or hip replacement surgery, were enrolled in the study after obtaining informed written consent. Patients in whom spinal anesthesia was contraindicated or those with known allergy to study drugs, peripheral neuropathy, spinal deformity, coagulation disorders, local site skin infection, impaired liver or renal functions, morbid obesity, hemodynamic instability, and patients with history of opioid intake were excluded.

A total of 80 patients were randomly allocated into two groups of 40 each based on computer generated random number slips. Group A received 3 ml of 0.5% hyperbaric bupivacaine with 25 μg fentanyl and Group B received 3 ml of 0.5% hyperbaric bupivacaine with 25 μg butorphanol. The adjuvants were diluted with 0.5 ml normal saline and a total volume of 3.5 ml was injected intrathecally. Total volume of drug was kept constant in both the groups to achieve blinding. The drug solution was prepared by an anesthesiologist not involved in the conduct of the case and recording the observations. Both the primary assessor and the patient were blinded to the study drug used.

All patients underwent a complete general physical and systemic examination along with relevant laboratory investigations, a day before surgery. The procedure was explained in detail and the visual analog scale (VAS) for pain was described in their own vernacular language during the preanesthetic check-up. Preoperatively, the patients were kept fasting for 6 h to solids and 2 h for clear fluids. Sedatives were avoided before as well as during surgery.

In the operation theater, routine monitoring was established and baseline values of heart rate (HR), systolic blood pressure, diastolic blood pressure, respiratory rate (RR), and peripheral arterial oxygen saturation (SpO2) were recorded. An intravenous (i.v.) line was established using 18 G cannula. Under all aseptic precautions, an 18 G Tuohy's epidural needle was introduced into the epidural space at L3–L4 level using the loss of resistance technique with air/saline or both. The test dose of 3 ml of 2% lignocaine with adrenaline was injected and the patient was observed for signs of any motor block or rise in HR. After confirming placement an epidural catheter was threaded 3–5 cm into the epidural space. The Tuohy's needle was withdrawn and the catheter secured. Spinal block was performed in the L3–L4 space using 25 G Quincke's spinal needle and 3.5 ml drug solution was given according to the group assigned. The patient was turned supine immediately. HR, NIBP, SpO_2, RR, and ECG were monitored continuously in the intraoperative period and recorded every 2 min for the first 10 min, every 5 min for the next 20 min, and thereafter at an interval of 15 min till the end of surgery. Hypotension (MAP <70 mm Hg) was treated with i.v. fluid bolus and mephentermine 6 mg i.v. increments if required. Bradycardia (HR <50 beats/min) was treated with atropine 0.6 mg i.v. Respiratory depression was defined as a respiratory rate <8 breaths/min or SpO_2 of <90% on room air. All the patients received O_2 via face mask at 6 L/min.

The onset of sensory block was assessed by pinprick test using a 20-G hypodermic needle in the midclavicular line bilaterally, every 2 min till the level of block was fixed for two/three consecutive readings. Sensory block was graded on a four point scale (normal pin prick sensation = 1, Pin prick felt as sharp/pointy but weaker compared to other areas = 2, pin prick recognized as touch with blunt object = 3, no perception of pin prick = 4). Grade 4 block was considered acceptable.[6] The highest level of sensory block achieved was recorded and the time taken to attain it from the time of the intrathecal injection was defined as onset of sensory block. Further sensory testing was performed at 20-min intervals till the sensory block regression of two dermatomal segments. The time taken from onset of block to 2 segment regression was taken as duration of anesthesia.

Motor blockade was assessed using modified Bromage scale (MBS) (Grade 0 = no motor block, Grade 1 = unable

to raise extended legs, but able to flex knees and move feet, Grade 2 = unable to raise extended legs and flex knees, but able to move feet, Grade 3 = complete motor block). Onset of motor block was defined as the time from study drug injection to MBS Grade 3. Motor block was further assessed at the end of the surgery and then at 30 min intervals till regression to MBS Grade 0. The time from onset of motor block to MBS Grade 0 was defined as duration of motor block. A minimum dermatomal level of T10 with sensory block Grade 4 and motor block Grade 3 on MBS was considered acceptable for surgery to proceed. Blocks considered inadequate were supplemented with epidural bolus doses. In case of complete failure of block general anesthesia was administered to the patient. Both the patients receiving supplemental epidural and general anesthesia were included in our study but excluded from the statistical analysis.

At the end of the surgery, the patient was shifted to the recovery room. Postoperative pain was assessed using VAS (0–10 point scale) immediately, at 15 min, 30 min, 1 h and 2 h. Patients were shifted to the ward after 2 h and VAS assessed at 4, 8, 16, and 24 h postoperatively. The duration of analgesia was taken as the time from intrathecal drug administration to the first epidural top up. Epidural top ups of 0.125% bupivacaine 6 ml were given 6 hourly to patients reporting VAS score of ≥4. The minimum interval between two epidural doses was at least 2 h. The patients complaining of pain less than 2 h after administration of epidural top ups were given rescue analgesic in the form of injection diclofenac sodium 75 mg deep intramuscular injection. Total number of epidural top ups and rescue analgesic over 24 h was also noted. The study period for assessment of total analgesic requirements commenced at the time of injection of epidural bolus dose (time 0 min) till 24 h postoperatively. Patients were also observed for any adverse effects, such as nausea, vomiting, hypotension, bradycardia, shivering, pruritis, headache, urinary retention, sedation, and respiratory depression.

The primary objective of our study was to compare the duration of analgesia using bupivacaine fentanyl and bupivacaine butorphanol mixtures. The secondary outcome was assessed in terms of number of rescue analgesia, intraoperative sensory, and motor block characteristics.

By considering alpha error of 0.05 and power of study >80%, taking into consideration primary outcome which was duration of analgesia the sample size was calculated to be 74 based on a previous study by Reddy *et al.*[7] Then considering dropout rate of 10%, final number of 80 patients was selected. The data obtained were entered into a Microsoft Excel datasheet and analyzed using Statistical Package for the Social Sciences, SPSS 19.0. Categorical variables were represented as number

and percentage and continuous variables as mean ± standard deviation. Qualitative variables were analyzed using Chi-square test/Fisher's exact test and quantitative variables using *t*-test. $P < 0.05$ was considered statistically significant.

Results

The demographic profile of patients was comparable with respect to age, weight, ASA physical status, and mean duration of surgery in both the groups [Table 1 and Figure 1]. Mean duration of analgesia was longer in Group B (201.47 ± 37.75) compared to Group A (189.63 ± 39.29) ($P < 0.05$) [Table 2]. Although mean VAS score over 24 h postoperative was higher in Group A, it was found to be statistically insignificant between the groups ($P > 0.05$) [Figure 1]. The number of epidural top ups required postoperatively was more in Group A compared to Group B ($P < 0.001$) [Figure 2]. A total of 92.5% patients in Group B required four or less than four epidural top ups and none of the patients required more than five. However, in Group A 80% patients required five or more epidural top ups. In addition, mean requirement of rescue analgesia was more in Group A than Group B which was statistically significant ($P < 0.001$) [Figure 3]. In Group B only 22.5% of patients required rescue analgesia in the form of injection diclofenac sodium 75 mg IM (nine doses in nine patients), whereas in Group A 82.5% patients required rescue analgesia (64 doses in 33 patients).

There was no difference in the highest level of sensory block achieved (T10 and T8) in both the groups ($P > 0.05$). Time of onset of sensory block was also comparable in both the
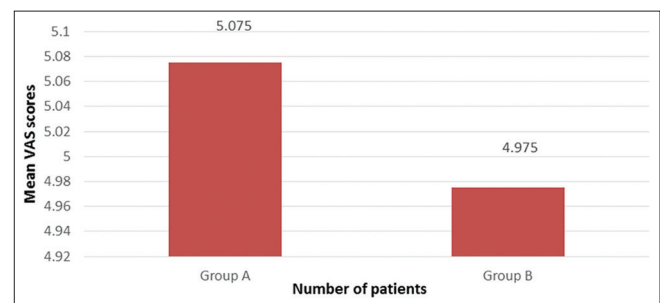

Figure 1: Comparison of mean VAS scores postoperatively till 24 h in study groups

Table 1: Demographic data

Parameters	Group A (n=40)	Group B (n=40)	P
Age (years)	55.8±9.8	58.1±10.7	0.342
Weight (kg)	69.2±11.1	58±15.2	0.751
ASA Grade (I:II)	26: 14	24 : 16	0.818
Duration of surgery (minutes)	153.1±35	160.5±28.4	0.304

Data presented as mean±standard deviation

Table 2: Characteristics of sensory and motor block

Parameter	Group A (*n*=40)	Group B (*n*=40)	*P*
Highest sensory level achieved T*	T10 (6-10)	T8 (6-8)	
Onset of sensory block (min)	4.9±1.6	5.6±1.9	0.088
Duration of anesthesia (min)	86±12.4	110.75±15.8	0.000**
Duration of analgesia (min)	189.63±39.29	201.47±37.75	0.018*
Grade 3:Onset of motor block	4.12±1.09	4.47±1.03	0.145
Grade 2:Motor block regression to MBS 2	79.80±7.14	81.15±7.41	0.409
Grade 1:Motor block regression to MBS 1	119.75±5.76	121.50±6.22	0.196
Grade 0:Duration of Motor block	162.87±6.39	163.87±6.55	0.492

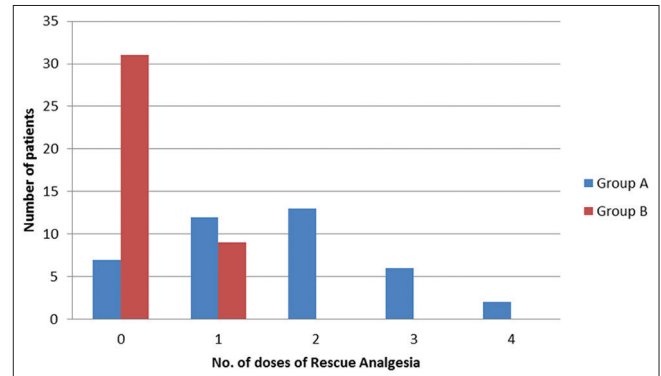*Data presented as mean±standard deviation. **P<0.001=highly significant. Data presented as median (range)**
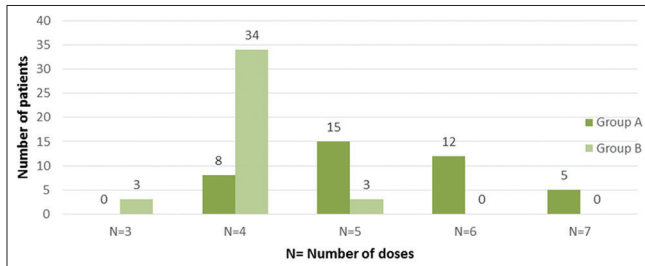
Figure 2: Mean epidural analgesic top ups in study groups over 24 h

Figure 3: Mean rescue analgesic requirement over 24 h postoperatively

groups ($P > 0.05$). However, duration of sensory block was significantly longer in Group B (110.75 ± 15.75 min) compared to Group A (86 ± 12.41 min) ($P < 0.001$) [Table 2]. There was no statistically significant difference in onset of motor block in both the groups ($P > 0.05$). Further, the time taken for motor block to regress to Bromage score of 2, 1, and 0 was also comparable between Group A and Group B ($P > 0.05$) [Table 2].

No significant perturbation in hemodynamic parameters, such as HR, blood pressure, SPO_2, and RR were observed intraoperatively. In the present study, hypotension was observed in six patients in Group A and eight patients in Group B and was treated with mephenteramine bolus 6 mg i.v. Bradycardia was observed in only one patient in Group A and was treated with i.v. atropine 6 mg. No other complications, such as nausea, vomiting, shivering, pruritis and urinary retention, were seen in both the groups. Sedation was observed in four patients in Group B and none of the patients had sedation in Group A. However respiratory depression was not seen in any patients in both the groups [Table 3].

Discussion

In lower limb joint surgeries, adjuvants along with longer acting local anesthetics, such as bupivacaine, are the most common modalities employed for prolonging the duration of anesthesia and analgesia. The synergistic administration of intrathecal local anesthetics and opioids has been described for management of acute pain. Both butorphanol and fentanyl exert their action by opening K^+ channels and reducing the Ca^{++} influx, resulting

in inhibition of transmitter release. A combination of these effects may explain the observed synergism between bupivacaine and butorphanol/fentanyl. The synergism is characterized by enhanced somatic analgesia without an effect on the degree of level of local anesthetic-induced sympathetic or motor blockade.[8]

Our analysis showed that intrathecal butorphanol 25 μg as an adjuvant to 3 ml of 0.5% hyperbaric bupivacaine significantly prolonged the duration of analgesia (201.47 ± 37.75 min) as compared to 25 mcg fentanyl (189.63 + 39.29 min). Similar results were concluded by Bhatia *et al.*[9] and Pratibhan[10] who observed that co-administering opioids and local anesthetics intrathecally have a potent synergistic effect, thereby improving the quality of intraoperative and postoperative analgesia.

The postoperative VAS scores were higher in the fentanyl group throughout 24 h observation period. In fentanyl group, an average number of five or more epidural bolus doses were required in the 24-h postoperative period, whereas majority of the patients receiving butorphanol needed up to four epidural top ups. Inferring that butorphanol with bupivacaine led to more analgesic effect extending to postoperative period. The requirement of rescue analgesia was also considerably less in butorphanol group. Our results are in concordance with Kumar *et al.*[11] who observed in their study that patients receiving butorphanol had lower VAS scores and requested rescue analgesia earlier than patients in butorphanol group.

Table 3: Comparison of perioperative side-effects

Complications	Group A (*n*=40)	Group B (*n*=40)
Hypotension	6 (15%)	8 (20%)
Bradycardia	1	0
Nausea	0	0
Vomiting	0	0
Shivering	0	0
Pruritis	0	0
Urinary retention	0	0
Sedation	6 (15%)	0
Respiratory depression	0	0

n=number of patients

The results of the present study suggest that time to onset of sensory and motor block was comparable between both the groups. Similar results were obtained by other investigators who compared both fentanyl and butorphanol in dosages of 25 mcg each in 3 ml of 0.5% bupivacaine for lower limb surgeries.[12] The results were in concordance with a study by Reddy *et al*. who found that 20 mcg fentanyl and 200 mcg butorphanol when used in combination with low dose hyperbaric bupivacaine were equally efficacious in terms of onset and spread of sensory block.[7] However, the time taken for regression of motor block to Grades 3, 2, and 1 was similar in both the groups. This implies that addition of intrathecal adjuvants like butorphanol and fentanyl provides longer duration of sensory but not motor block when used in the same dosage of 25 mcg. Similar results were obtained by Singh *et al*.[13] and Kumar *et al*.[11] who found that time to two segment regression of sensory block was significantly higher in butorphanol group compared to fentanyl group however, the duration of Grades 3, 2, and 1 motor block was similar in the butorphanol and fentanyl group when used in the dosage of 25 μg with 0.5% intrathecal bupivacaine. In our study, hypotension was observed in 15% of patients in Group A compared to 20% patients in Group B. Our results are in concordance with the findings of Singh *et al*. [13] who have reported the incidence of hypotension in 20% patients in fentanyl (25 μg) group and 17% patients in butorphanol (25 μg) group. Sedation is also a reported side effect after neuraxial administration of opioids.[14] In our study sedation was observed in 15% of patients in Group B, but all the patients were arousable and no respiratory depression was observed in any patients. Our findings are in consistence with the findings of Singh *et al*. [13] who reported a 20% incidence of sedation in butorphanol group.

Conclusion

Thus to conclude, both fentanyl and butorphanol in a dose of 25 μg are effective as intrathecal adjuvants to 0.5% hyperbaric bupivacaine in lower limb joint replacement surgeries without any side effects; however, intrathecal bupivacaine and butorphanol combination is superior to bupivacaine and fentanyl combination in terms of duration of analgesia and postoperative analgesic requirement.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Cohen FL. Postsurgical pain relief: Patients' status and nurses' medication choices. Pain 1980;9:265-74.
2. Keith I. Anaesthesia and blood loss in total hip replacement. Anaesthesia 1997;32:444-50.
3. Arora R, Pandey V, Sodhi GS, Mohindra BK. A comparative study of intrathecal bupivacaine and bupivacaine with different doses of clonidine in lower limb surgeries. Anesth Essays Res 2018;12:412-6.
4. Upadya M, Neeta S, Manissery JJ, Kuriakose N, Singh RR. A randomized controlled study comparing intrathecal hyperbaric bupivacaine-fentanyl mixture and isobaric bupivacaine-fentanyl mixture in common urological procedures. Indian J Anaesth 2016;60:44-9.
5. Hamber EA, Viscomi CM. Intrathecal lipophilic opioids as adjuncts to surgical spinal anesthesia. Reg Anesth Pain Med 1999;24:255-63.
6. Sharma A, Jaswal S, Jaswal V, Pathania J. Effect of magnesium sulphate as an adjuvant to bupivacaine in interscalene brachial plexus block for postoperative analgesia. J Clin Diagn Res 2019;13:UC01-04.
7. Reddy NG NG, Manohar S, Supriya P, Himani A. Comparison of efficacy of butorphanol and fentanyl as intrathecal adjuvant to bupivacaine. J Evol Med Dent Sci 2015;4:5675-81.
8. Pope JE, Deer TR, Amirdelfan K, McRoberts WP, Azeem N. The pharmacology of spinal opioids and ziconotide for the treatment of non-cancer pain. Curr Neuropharmacol 2017;15:206-16.
9. Bhatia U, Patel N, Parikh N. Comparison of intrathecal adjuvants with bupivacaine using fentanyl 50 μg and butorphanol 25 μg. Natl J Integr Res Med 2017;8:41-8.
10. Pratibhan. Comparative study of postoperative analgesia provided by butorphanol and fentanyl as an adjunct to spinal levo-bupivacaine for lower limb orthopaedic surgeries. MedPulse Int J Anesthesiol 2020;13:87-91.
11. Kumar A, Kumar R, Verma VK, Prasad C, Kumar R, Kant S, *et al*. A randomized controlled study between fentanyl and Butorphanol with low dose intrathecal bupivacaine to facilitate early postoperative ambulation in urological procedures. Anesth Essays Res 2016;10:508-11.
12. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. J Anaesthesiol Clin Pharmacol 2011;27:339-43.
13. Singh V, Gupta LK, Singh GP. Comparison among intrathecal fentanyl and butorphanol in combination with bupivacaine for lower limb surgeries. J Anaesthesiol Clin Pharmacol 2006;22:371-5.
14. Singh H, Yang J, Thornton K, Giesecke AH. Intrathecal fentanyl prolongs sensory bupivacaine spinal block. Can J Anaesth 1995;42:987-91.