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Comparison between Fentanyl as an adjuvant to Bupivacaine versus Bupivacaine alone among patients undergoing lower abdominal surgeries under sub arachnoid block

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ABSTRACT

Background and Aims: Postoperative pain management is one of the key issues among patients undergoing lower abdominal surgery under subarachnoid block. We decided to study the effect of intrathecal addition of 25 µg fentanyl to 0.5% bupivacaine in terms of quality of blocks and post-operative analgesia. **Methods:** A total of 80 ASA Grade I/II patients aged >18 years were enrolled in the study and were randomized to two groups: Group I (n=40) received 0.5% hyperbaric bupivacaine (3ml) with fentanyl 25 µg (0.5 ml) intrathecally whereas Group II (n=40) received 0.5% hyperbaric bupivacaine (3ml) diluted with 0.5 ml Normal Saline only. Hemodynamics, sensory block level, onset time and duration of motor/sensory block, adverse effects and Time for first rescue analgesic were noted. Data was compared using SPSS 21.0. **Results:** Both the groups were comparable demographically and for baseline hemodynamic parameters. No hemodynamic event took place in either of two groups. Median block level achieved was higher in Group I (T6) as compared to Group II (T8) ($p<0.001$). No significant difference between two groups was observed with respect to mean time taken for onset of sensory and motor blocks ($p>0.05$). However, mean duration of sensory and motor block was longer in Group I (229.50±56.16 and 163.38±35.15 min) as compared to that in Group II (158.50±50.93 and 116.05±37.66 min) ($p<0.001$). Time taken to first request for postoperative analgesia was also longer in Group I (288.0±90.37 min) as compared to that in Group II (196.25±59.21 min) ($p<0.001$). No significant difference in adverse effects was observed ($p>0.05$). **Conclusion:** Intrathecal adjuvant use of fentanyl potentiated the post-operative analgesic effect and prolong sensory blockade without affecting motor block.

Key words: Bupivacaine, fentanyl, intrathecal, lower abdominal surgery, subarachnoid block

INTRODUCTION

Lower abdominal surgeries may be performed under local, regional (spinal or epidural) or general anaesthesia, but neuraxial blockade is the preferred mode of anaesthesia. Neuraxial block may reduce the incidence of venous thrombosis and pulmonary embolism. It may also allow earlier return of gastro-intestinal function following surgery. It is the first choice because of its rapid onset, superior blockade, low risk of infection as from catheter in situ, less failure rates and cost-effectiveness. However, postoperative pain control is a major problem because

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spinal anaesthesia using only local anaesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed in the postoperative period. A number of adjuvants have been studied to prolong the effect of spinal anaesthesia[1,2].

Bupivacaine has been used extensively in regional analgesia because it offers the advantage of providing a long duration of action and a favourable ratio of sensory to motor neural block. Bupivacaine can be used appropriately for the procedures lasting for 2 to 2.5 hours[3]. Despite its popularity bupivacaine suffers from the issue of post-operative pain control[4].

In recent years, use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anaesthesia and faster recovery. Adequate pain management is essential to facilitate rehabilitation and accelerate functional recovery, enabling patients to return to their normal activity more quickly. The quality of the spinal anaesthesia has been reported to be improved by the addition of opioids (such as morphine, fentanyl and sufentanyl) and other drugs [such as Dexmedetomidine (DXM), clonidine, Magnesium sulfate (Mg), neostigmine, ketamine and midazolam], but no drug to inhibit nociception is without associated adverse effects[5–7].

Adjuvant use of opioids like fentanyl to bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block[8]. Low dose fentanyl added to Bupivacaine provided sub-arachnoid block for lower abdomen surgeries with less hypotension, vasopressor requirements, and nausea[9].

Although addition of opioids to local anaesthetic solution have their own disadvantages, such as pruritus and respiratory depression[10-11]. However, these side effects have been shown to be dose-dependent and some recent studies using variable dose combinations of fentanyl have shown that these side effects could be controlled to a great extent and has been reported to provide a stable haemodynamics, early and prolonged anaesthesia as compared to other adjuvants[12-16]. These studies have shown that fentanyl could be safely used as an adjuvant to bupivacaine for lower abdominal surgeries while getting the required analgesic and anaesthetic effect.

Hence, the present study was carried out to assess the degree of sensory and motor blockade along with postoperative analgesia using 25 µgm fentanyl admixed with bupivacaine as compared to bupivacaine alone in patients undergoing lower abdominal surgeries under Sub Arachnoid Block

METHODS

This prospective single blinded, as patient's didn't know about the treatment, randomized study was carried out at Department of Anaesthesiology, Era's Lucknow Medical College, Lucknow on 80 adult patients, under ASA-I and II, patients of either sex aged above 18 years, scheduled for elective surgeries of lower abdomen under sub arachnoid block and expected to have a post-operative stay of at least 24 hours after obtaining clearance from Institutional Ethical Committee and getting informed consent from the participating patients. Patients with significant cardiovascular disease, renal failure, hepatic dysfunction or chronic pulmonary disease (ASA Grade 3 and 4), those having Neuromuscular disorders, Obesity (BMI≥30 kg/m^2), Coagulation disorders (Platelet count < 50,000/mm^3), Infections, History of allergy or sensitivity to any of the study drugs, patchy blockade, multiple attempts, Diabetes Mellitus and those in whom surgery exceeded 2 hrs were excluded.

The sample size was calculated at a targeted mean difference in first analgesic need of 47.4 min between fentanyl augmented group as compared to non-augmented group with a pooled standard deviation of 30 min and keeping Type I error at 5% and Type II error at 10% with a targeted 90% power of study. The calculated sample size was 36 for each group. However after making contingency provisions, the sample size was kept at 40 for each group.

After selecting the patients, they were randomly allocated to one of the two groups, Group 1 (n=40) Bupivacaine 0.5% (Heavy) 3.0 ml with fentanyl 25 µgm (0.5 ml). Group 2 (n=40) Bupivacaine 0.5% (Heavy) 3.0 ml diluted with 0.5 ml Normal Saline to make a total volume of 3.5 ml. Randomization was done through computer generated numbers.

The patients were visited a day prior to surgery for pre-anaesthetic review. They were kept nil per oral from midnight before surgery. Patients were administered with Tab Diazepam 5mg and Tab Ranitidine 150 mg on the night before surgery. Written and informed consent was obtained from the patients.

On arrival of patients in the operation theatre, Intravenous line was initiated with 18G cannula. All patients were preloaded with 20ml/kg of Ringer's Lactate. Patients were

connected to the monitors and Baseline parameters shall be recorded. Heart rate (HR), Non-Invasive Blood Pressure (NIBP), Respiratory Rate (RR) and peripheral oxygen saturation (SpO_2) was monitored throughout the surgery. The monitoring was done at following time intervals:

- T0 → Before administration of the drug
- T1 → Just after administration of the drug
- T2 → 5 min after administration of the drug
- T3 to T30 → Every 5 min thereafter for 145 min

Under strict aseptic precautions, a 25 G spinal needle was introduced between L_3-L_4 space intrathecally. After confirmation of free flow of CSF, Group 1 patients received Inj. Bupivacaine 0.5% (heavy) 3.0 ml + Fentanyl 25 µgm (0.5 ml) and Group 2 shall receive Inj Bupivacaine 0.5 % (heavy) 3.0 ml+ 0.5 ml Normal Saline. Post-operative pain was measured by 10 point Visual Analogue Scale (VAS) with calibrations from 0-10. Patients with a VAS of 4 or more were administered an IV infusion of Inj. Paracetamol 1gm.Primary objective i.e. Sensory blockade was assessed using pinprick and cold sensation using alcohol swabs in mid-axillary line bilaterally. Recovery time for sensory blockade was defined as 2 dermatome regression of anaesthesia from the maximum level. Motor block was assessed immediately after sensory block assessment using Modified Bromage score. Motor block duration was defined as the time for return to Bromage scale score of '0'.Sensory and motor blocks were assessed every 2 mins for first 10 mins and thereafter every 10 mins during surgery and post-operatively till the duration of block. The highest sensory block level and recovery time of both sensory and motor block were recorded. Adverse effects: Sedation, Nausea/Vomiting, Respiratory Depression, Urinary Retention and Pruritus were observed and managed symptomatically. Heart Rate (HR), Non-Invasive Blood Pressure (NIBP), Respiratory rate (RR) and peripheral oxygen saturation (SpO_2) were recorded and corrected. Hypotension (was defined by a decrease in MAP below 20% of baseline or SBP< 90 mmHg) was treated by Inj. Mephentermine 6 mg IV Stat. Fluids like crystalloids and colloids can also be given, as a volume expanders. Bradycardia (HR< 50 bpm) was treated by Inj Atropine 0.6 mg IV stat.Respiratory depression (RR < 8 breaths per min or SpO_2< 95%) was proposed to be managed by oxygen supplementation and respiratory support if required. Time to first "analgesic dose "i.e., requirement was noted.

The data was analysed using Statistical Package for Social Sciences version 21.0. Data has been represented as mean±SD and numbers and percentages. Chi-square, Independent samples and Mann-Whitney U 't' tests were used to compare the data. A 'p' value less than 0.05 was considered to indicate a significant difference.

RESULTS

Majority of patients in both the groups were within 40 years of age and were females. Mean BMI of patients was 21.25±4.04 and 21.06±6.20 kg/m^2. In Group I, majority of patients were ASA Grade II (55%) whereas in Group II, majority were Grade I (55%). Statistically there was no significant difference between two groups with respect to age, gender, BMI and ASA grade.

At baseline mean heart rate, arterial pressure, respiratory rate and oxygen saturation values were 87.23±13.56 bpm, 98.75±11.33 mmHg, 14.33±1.76/min and 99.55±0.98% respectively in Group I and 84.23±20.07 bpm, 96.25±10.04 mmHg, 14.25±1.45/min and 99.30±1.04% respectively in Group II. Statistically, there was no significant difference in baseline hemodynamic parameters between two groups.

Intraoperatively, both the groups were comparable hemodynamically for mean arterial pressure and respiratory rate. However, for heart rate a significant difference between two groups was observed between two groups from T23 to T27 when mean value was significantly higher in Group II as compared to that in Group I (Figures 1-3). Mean oxygen saturation remained above 99% in both the groups throughout the study period.

Median block was significantly higher in Group I (T6) as compared to that in Group II (T8) ($p<0.001$). No significant difference in mean duration of surgery was observed between two groups ($p=0.827$) Although mean time taken for onset of motor and sensory block was lower in Group I (6.65±2.05 and 8.68±2.09 min respectively) as compared to that in Group II (6.93±2.03 and 8.88±2.57 min respectively) yet there was no significant difference between two groups ($p=0.548$ and 0.704). However, mean time taken for regression of motor block to Bromage score 0 and for sensory regression of first two dermatomes was significantly longer in Group I (229.50±56.16 and 163.38±35.15 min respectively) as compared to that in Group II (158.50±50.93 and 116.05±37.66 min

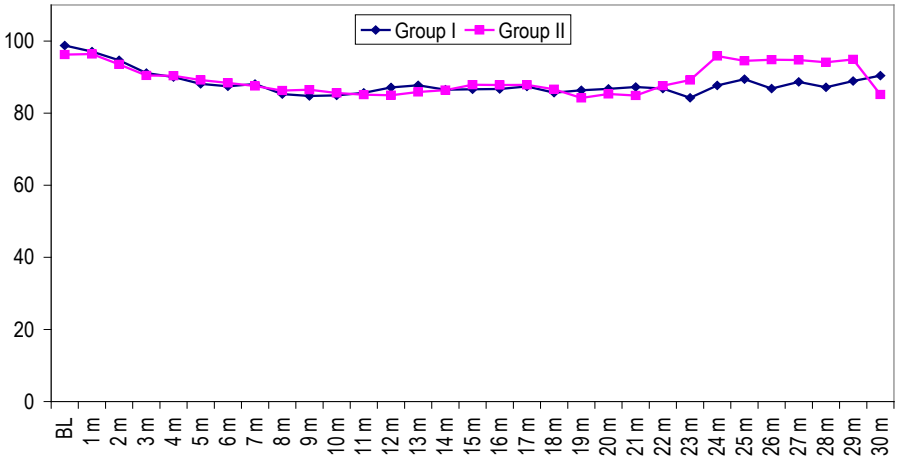

Figure 1. Between group comparison of mean arterial pressure (mm Hg) at different time intervals.

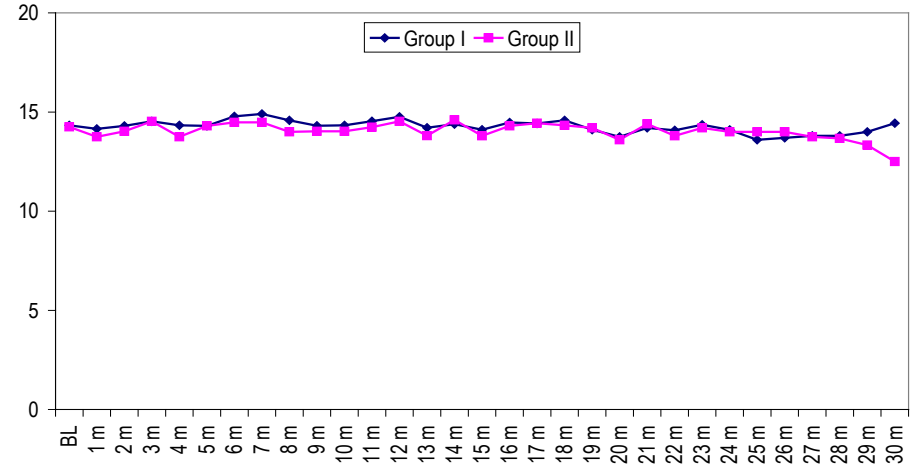

Figure 2. Between group comparison of respiratory rate (per min) at different time intervals.

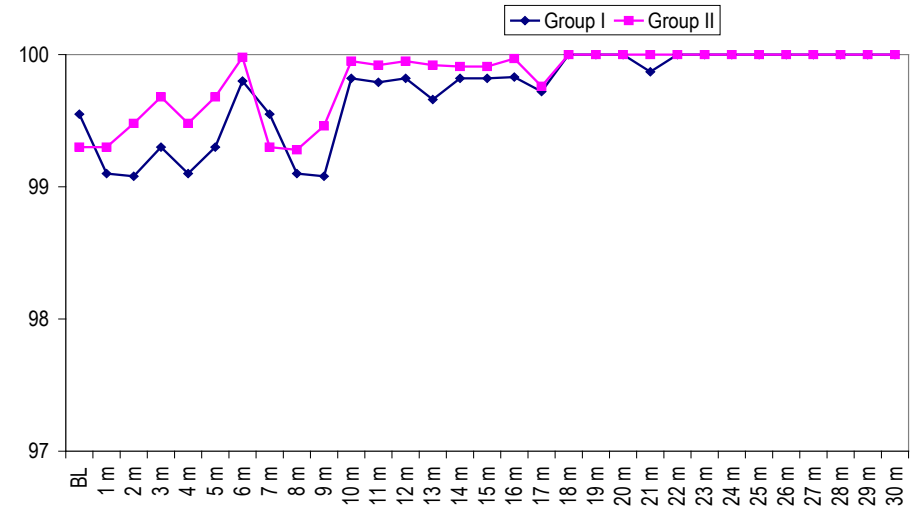

Figure 3. Between group comparison of oxygen saturation (%) at different time intervals.

Table 1: Demographic profile and baseline characteristics			
	Group I (n=40)	Group II (n=40)	'p'
Age Group (Years)			
≤40 Yrs	21 (52.5%)	27 (67.5%)	0.171
>40 Yrs	19 (47.5%)	13 (32.5%)	
Gender			
Male	19 (47.50%)	16 (40.0%)	0.499
Female	21 (52.50%)	24 (60.0%)	
Mean BMI±SD (kg/m^2)	21.25±4.04	21.06±6.20	0.870
ASA			
I	18 (45%)	22 (55%)	0.371
II	22 (55%)	18 (45%)	
Mean Heart rate±SD (bpm)	87.23±13.56	84.23±20.07	0.436
Mean MAP±SD (mmHg)	98.75±11.33	96.25±10.04	0.299
Mean RR±SD (/min)	14.33±1.76	14.25±1.45	0.836
Mean SpO_2±SD (%)	99.55±0.78	99.30±1.04	0.229

respectively) (p<0.001). Time taken to first request for postoperative analgesia was also longer in Group I (288.0±90.37 min) as compared to that in Group II (196.25±59.21 min) (p<0.001) (Table 2).

As far as adverse effects were concerned, though incidence of nausea, vomiting, bradycardia, hypotension, respiratory distress and pruritus was higher in Group II as compared to Group I but this difference was not found to be statistically significant (Table 3).

DISCUSSION

The present study showed that both the interventions had almost similar haemodynamic control. There was no hemodynamic event needing intervention in either of two groups, thus the two groups had stable and comparable hemodynamic profile. Addition of fentanyl to bupivacaine at variable dosages, has shown not to affect the hemodynamic stability. Similar to our study Atallah *et al.* (2006) also found that addition of 10 µg of fentanyl

Table 2: Between group comparison of duration of surgery and block characteristics			
Parameter	Group I (n=40)	Group II (n=40)	'p'
Median sensory block	T6	T8	<0.001
Duration of Surgery (mins)	100.75±41.04	99.00±29.25	0.827
Onset of motor block (min)	6.65±2.05	6.93±2.03	0.548
Onset of sensory block (min)	8.68±2.09	8.88±2.57	0.704
Regression of Motor Block to Bromage 0 (min)	229.50±56.16	158.50±50.93	<0.001
Sensory Regression of 1st two Dermatomes (min)	163.38±35.13	116.05±37.66	<0.001
Time To 1st Request For Postop. Analgesia (min)	288.00±90.37	196.25±59.21	<0.001

Table 3: Between Group Comparison of adverse effects			
Adverse effects	Group I (n=40)	Group II (n=40)	'p'
Nausea	6 (15%)	8 (20%)	0.556
Vomiting	4 (10%)	7 (17.5%)	0.330
Bradycardia	5 (12.5%)	7 (17.5%)	0.531
Hypotension	5 (12.5%)	7 (17.5%)	0.531
Respiratory distress	4 (10%)	6 (15%)	0.499
Pruritus	4 (10%)	5 (12.5%)	0.723

to 7.5 mg of hyperbaric bupivacaine did not result in any significant alteration in haemodynamic profile[17]. Sawhney *et al.* (2015) also found that both 0.2% bupivacaine alone or 0.1% bupivacaine + 2 μg/ml fentanyl offer similar stable hemodynamic profile[18]. On the other hand Shah *et al.* (2016) found that addition of 25 μg of fentanyl to 10 mg of 0.5% bupivacaine ensures a better hemodynamic stability[19]. However, in present study, both the groups were hemodynamically stable throughout the procedure and no such deterioration or improvement in hemodynamic stability was observed with addition of 25 μgm Fentanyl to 0.5% (Heavy) 3.0 ml bupivacaine. Most of the studies reviewed by us also do not report any qualitative change in hemodynamic parameters by addition of fentanyl at variable dosage-combinations[13–15,17–19].

Although respiratory depression is one of the reported complications of fentanyl[10,11], however, as far as mean oxygen saturation levels were concerned, the two groups did not show a significant difference. No significant effect on mean oxygen saturation owing to addition of fentanyl at variable bupivacaine/fentanyl combinations has also been reported in different studies reviewed by us[13–15,17–19].

In present study, median block levels achieved were T6 and T8 respectively in bupivacaine alone and bupivacaine + fentanyl group respectively. Compared to this, the Gupta *et al.* (2011) showed median block level to be T6 in fentanyl added group whereas Jain *et al.* (2012) using various combinations of hyperbaric bupivacaine (4 mg to 7.5 mg) with 25 μg fentanyl showed achievement of median sensory block of T2 and T3[13,20]. In other studies too, addition of fentanyl has been shown to help in achievement of a higher level of sensory block[21,22]. A slight variability in height of sensory block in different studies is dependent on patient characteristic as well as dose-combination of bupivacaine and fentanyl.

Mean onset time for motor and sensory block was 6.65±2.05 and 8.68±2.09 min respectively in fentanyl+bupivacaine group as compared to 6.93±2.03 and 8.88±2.57 min respectively in bupivacaine alone group; however, the difference between two groups was not significant statistically. The onset time of sensory and motor blocks has been reported to vary substantially in different dose-combinations of bupivacaine and fentanyl. Using variable combinations of bupivacaine and fentanyl, different workers have reported the mean onset time to range from 4.75 and 5.8 to 12.73 and 9.7 min respectively for sensory and motor blocks in the fentanyl supplemented group[19,22–24]. There are two reasons for this huge variability in onset time for sensory and motor blocks- first is the dose-combination while second is difference in targeted block level. In present study, we targeted Bromage 2 as the criteria for onset of motor block and T_{10} as the targeted sensory block.

Despite these differences in onset times in different studies, most of the studies in literature have found no significant difference in mean onset times for sensory and motor blocks. However, there are certain studies that have shown a difference in achievement of onset of block between bupivacaine alone as compared to fentanyl supplemented group. For example, Motiani*et al.* (2011) in their study, reported onset time for sensory block to be earlier in fentanyl supplemented group (4.73 min) as compared to bupivacaine alone group (7.26 min) while Mehta *et al.* (2015) in their study reported mean onset time for sensory block to be longer in fentanyl supplemented group (128 sec) as compared to that in bupivacaine alone group (95 sec)[15,16]. However, Jaiswal and Thakare (2016) in their study, like our study found the onset time for sensory block to be little faster in fentanyl supplemented group (6.17±1.44 min) as compared to that in bupivacaine alone group (6.73±1.52)[24]. The findings in present study were similar to their study.

In present study mean duration of motor and sensory block was 229.5 and 163.38 minutes respectively in fentanyl supplemented group as compared to 158.5 and 116.05 minutes respectively in bupivacaine group and thus showed that the duration of both sensory as well as motor blocks was significantly longer in fentanyl supplemented groups as compared to bupivacaine alone group. Similar to our study, Motiani *et al.* (211.5 min) at Fentanyl 25μg (0.5ml) ± 15 mg of 0.5% hyperbaric bupivacaine (3.0 ml) [15]. In another study, Shah *et al.* reported the mean duration of motor and sensory block in fentanyl supplemented group to be 219.65min and163.75 min respectively[19].

In present study, duration of analgesic effect was significantly longer in fentanyl supplemented group (288.00±90.37 minutes) as compared to that in bupivacaine alone group (196.25±59.21 minutes). In different studies, the reported duration of analgesic effect has been reported to vary from as early as 166.83 min for hyperbaric Bupivacaine 15mg + Fentanyl 25 μg in 0.5 ml normal saline to 398 min for Bupivacaine 0.5% heavy (0.8 ml)+fentanyl 25 μg (0.5 ml) + normal saline 0.3 ml[22,25]. In present study, this duration was 288 min which is comparable to a number of studies that reported the duration of block to range from 276.23 min to 280 min[15,21,26]. A variability in duration of analgesic effect for same dosage combination in different studies could be attributed to the difference

in profile of patients, definition of analgesic effect (some studies have defined it as VAS targeted while some others have calculated it as the time at which rescue analgesia was given).

One of the major concerns while using fentanyl as an adjuvant to bupivacaine is the issue of respiratory depression and pruritus. In present study, none of the patients showed respiratory depression. Similar to present study, none of the studies reported respiratory depression as the side effect associated with intrathecal use of fentanyl as an adjuvant to bupivacaine. However, pruritus has been reported to be a side effect in a number of studies. Incidence of pruritus is reported to range from 3.3% to 26% in different studies [13,15,16,19,22,24]. However, most of these studies have reported it to be within 10% range[13,15,16,22]. In present study, this rate was 10% which is comparable to other studies.

In present study as well as in all the other studies except that of Shah *et al.* (2015) despite occurrence of pruritus mainly in fentanyl supplemented group only, it has not been recorded to cause a significant difference from non-supplemented group[19]. For other side effects too, in present study no significant difference between two groups was reported which is in accordance with the findings in literature.

CONCLUSION

Thus, findings of present study showed that adjuvant use of intrathecal fentanyl to bupivacaine for spinal anaesthesia among patients undergoing lower abdominal surgeries is a viable choice at the dose schedule used in present study and does not pose a significant risk of side effects or complications, however, it helped in prolonging the block duration and analgesic effect and endorses the current literature advocating its use as an adjuvant.

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