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Comparison of Intrathecal tramadol and fentanyl as adjuvant in abdominal and lower limb surgeries: A randomized clinical study

[1] Sanjul Dandona, [2] Neha Batra, [3] Surendra Singh

[1] Assistant professor, Department of Anesthesia, Veer Chandra Singh Garhwali Government Medical Sciences & Research Institute, Srinagar, Pauri Garhwal, Uttarakhand, India

[2] Assistant professor, Department of Pathology, Veer Chandra Singh Garhwali Government Medical Sciences & Research Institute, Srinagar, Pauri Garhwal, Uttarakhand, India

[3] Associate professor, Department of Anesthesia, Veer Chandra Singh Garhwali Government Medical Sciences & Research Institute, Srinagar, Pauri Garhwal, Uttarakhand, India

Abstract

Introduction: This prospective, randomized, double-blind study compares the effect of intrathecal fentanyl-bupivacaine and tramadol-bupivacaine on the onset and duration of sensory and motor blockade, as well as postoperative analgesia in lower abdominal surgeries and limb surgeries.

Materials and methods: Patients of either sex, aged 40 to 60 years, American Society of Anesthesiologists (ASA) grade I/II undergoing lower abdominal surgeries like hydrocele, appendicectomy, inguinal hernia repair surgery and lower limb surgeries, were administered either 2.5 mL of 0.5% bupivacaine +0.5 mL (25 µg) of fentanyl citrate (group a) or 2.5 mL of 0.5% bupivacaine +0.5 mL (25 mg) of tramadol (group b) intrathecally. Monitoring of the vital parameters, onset and duration of sensory and motor block, duration of postoperative analgesia, visual analog scale (VAS) score, sedation score, and any side effects were noted at periodic intervals.

Results: fifty patients were randomized to the group a (n=25) and group b (n=25). The duration of sensory blockade was significantly prolonged in group a(280.00 ± 19.88 min) compared to group b(200 ±19. 34)Similarly, dura-tion of motor blockade was longer in group a(200.10±20.4)minutes) compared to group b(145±17.9). The total duration of analgesia was significantly prolonged ($p<0.001$) in group a (420±42)compared to group b(310±33.2301 minutes).Hemodynamic parameters, such as pulse, systolic blood pressure, diastolic blood pressure and oxygen saturation were comparable in both the groups. Visual analog scores were significantly lower in the group b patients as compared to the group a patients. The group a patients had got significantly higher sedation scores as compared to Group b patients.

Conclusion: Fentanyl seems to be a better alternative to tramadol as an adjuvant to spinal bupivacaine in surgical procedures as it provides prolonged duration of the sensory block, longer duration of postoperative analgesia and lesser number of doses of rescue analgesia are required.

Keywords: tramadol, bupivacaine, fentanyl, adjuvant

Introduction

Over the last two decades, there has been considerable revival of interest in the use of regional anesthesia techniques for surgery and pain management [1]. Narcotic analgesics are commonly used as adjuncts to local anesthetics (LA) in epidural anesthesia. They produce a synergistic effect by acting directly on opioid receptors in the spinal cord they hasten the onset, improve the quality of the block as well as prolong the duration of analgesia. Also dose of local anesthetics like bupivacaine can be reduced, thereby reducing its side effects like myocardial depression, hypotension, bradycardia, heart block, and ventricular arrhythmias. A wide variety of drugs have been used which are both non-opioids and opioids such as epinephrine, α_2-adrenoceptor agonists (clonidine and dexmedetomidine), acetylcholine esterase inhibitors (neostigmine), adenosine, ketorolac, midazolam, sodium bicarbonate and hyaluronidase, and opiods being hydrophilic (morphine) and lipophilic (fentanyl and sufentanyl), although very few drugs are actually in clinical use [2].

Fentanyl, a short-acting lipophilic opioid stimulates µ1 and µ2 receptors. It potentiates the afferent sensory blockade and facilitates reduction in the dose of local anesthetics without intensifying the motor block or prolonging recovery. Fentanyl provides good quality of intraoperative analgesia, hemodynamic stability, minimal side effects, and excellent quality of postoperative analgesia [3].

Tramadol, a synthetic 4-phenyl-piperidine analog of codeine, is a racemic mixture of two enantiomers, with synergistic anti-nociceptive interaction. The (+) enantiomer has moderate affinity for the opioids µ receptor and inhibits serotonin uptake, and the (−) enantiomer is a potent norepinephrine synaptic release inhibitor. It too has a potential to provide effective post effective analgesia [4]. Therefore keeping in mind cost effectiveness and the side effects, we have decided to compare both the drugs to find better adjuvant in all respects.

Material and methods

The prospective randomized, double-blind study was

conducted after approval of ethical committee of the institution. Written informed consent was obtained from all patients.

Sample size-50 patients

Inclusion criteria

- American Society of Anesthesiologists (ASA) physical status I or II,
- Either sex,
- Age 40–60 years,
- Scheduled for lower abdominal surgeries and limb surgeries.

Exclusion criteria

- Patient allergic to drug,
- Heart block/dysrrhythmia,
- Use of pain modifying drugs
- Gross spinal deformity
- History of peripheral neuropathy

A day before surgery, a detailed pre-anesthetic check-up was carried out and visual analog score for pain was explained to the patientsand they were given diazepam 0.2 mg/kg orally, the night before surgery. The patients were preloaded with Lactated Ringer's solution 20 mL/kg. They were monitored with automated noninvasive blood pressure, pulse oximetry, and electrocardiogram. 25G QUENCKE spinal needles were introduced through L3–L4 interspaces in sitting position using aseptic precautions. Patients were randomly divided into the following groups: Group A—to receive 2.5 mL volume of 0.5% hyperbaric bupivacaine with 25 μg FENTANYL and Group B—to receive 2.5 mL volume of 0.5% hyperbaric bupivacaine with 25 μg intrathecal TRAMADOL. Intrathecal injection was given over approximately 10–15 s. immediately after completion of the injection patients were made to lie supine.

Oxygen (2 L/min) was administered via a mask if the pulse oximeter reading decreased below 90%. Hypotension, defined as a decrease of systolic blood pressure by more than 30% from baseline or a fall below 90 mmHg, was treated with incremental IV doses of ephedrine 5 mg and IV fluid as required. Bradycardia, defined as heart rate < 50 bpm, was treated with IV atropine 0.3–0.6 mg. The incidence of adverse effects, such as nausea, vomiting, shivering, pruritus, respiratory depression, sedation, and hypotension were recorded. Sensory testing was assessed by loss of pinprick sensation to 23G hypodermic needle and dermatomes levels were tested every 2 min until the highest level had stabilized by consecutive tests. On achieving T7 sensory blockade level, surgery was allowed. Testing was then conducted every 10 min until the point of two segment regression of the block was observed. Further testing was performed at 20-min intervals until the recovery of S2 dermatome. The surgeon, patient, and the observing anesthesiologist were blinded to the patient group. Data regarding the highest dermatome level of sensory blockade, the time to reach this level from the time of injection, time to S1 level sensory regression, time to urination, and incidence of side effects were recorded. Sedation was assessed by a modified Ramsay sedation scale. The motor block level with a modified Bromage scale.

Table 1: Modified Bromage scale

Score	Response
0	Full flexion of knee and free movement of feet
1	Just able to flex knees and free movement of feet
2	Able to move feet only
3	Unable to move feet or knees

Modified Ramsay sedation scale

1. Anxious, agitated, restless.
2. Cooperative, oriented, tranquil.
3. Responds to commands only.
4. Brisk response to light glabellar tap or loud noise.
5. Sluggish response to light glabellar tap or loud noise
6. No response.

Postoperatively, the pain score was recorded by using visual analog pain scale (VAS) between 0 and 10 (0 = no pain, 10 = most severe pain), initially every 1 h for 2 h, then every 2 h for the next 8 h and then after every 4 h till 24 h. Diclofenac was given intramuscularly as rescue analgesia when VAS was >4. A follow-up was carried out 1 week postoperatively by the blinded anesthesiologist, who asked about postoperative headache as well as postoperative pain and dysesthesia in the buttock, thighs, or lower limbs.

Statistical analysis was done using the Statistical Package for Social Science (SPSS15.0 Evaluation version). To calculate the sample size, a power analysis of α=0.05 and α=0.90, showed that 25 patients per study group were needed. Data are expressed as either mean and standard deviation or numbers and percentages. Continuous covariates were compared using analysis of variance (ANOVA). Paired and unpaired *t*-tests were used for statistical calculations. The comparison was studied using the Chi-square test or Fisher's exact test as appropriate, with the P value reported at the 95% confidence interval. P<0.05 was considered statistically significant.

Results

The maximum sensory level achieved was T6 in both the groups. The mean time to onset of sensory block to T10 dermatome and the time to achieve maximum sensory block level was comparable in both the groups. The mean time for regression of sensory blockade to L5 dermatome was prolonged in the fentanyl group (280.00 ± 19.88 min) as compared to tramadol group (200 ± 19.34 min), which was highly significant, P < 0.001. The maximum motor block level achieved and the time to achieve maximum motor block level was comparable in both the groups. The mean total duration of motor block in the fentanyl group (200.10 ± 20.4 min) was more than the tramadol group (145.0 ± 17.9min) (table-3)and the difference was highly significant, P < 0.001. The time of request of the first analgesia in fentanyl group was 420.00 ± 42.99 min, which was significantly more than the tramadol group in which it was 310.20 ± 33.20 min, P < 0.001, indicating superior analgesia. The number of injections of rescue analgesia in fentanyl group was 3.16± 0.48 and in tramadol group was 3. 00 ± 0.60. The difference in the two groups was highly significant (P < 0.001). The quality of surgical anesthesia was excellent in both the groups in the intraoperative period.

Baseline hemodynamic parameters were comparable in the two groups, $P > 0.05$(table-2). The mean heart rate, systolic and diastolic blood pressures were comparable in both the groups preoperatively, intraoperatively, and postoperatively.

Hypotension was not observed in any of the groups. Bradycardia was seen in two (6%) patients in tramadol group and one (2%) patient in fentanyl group, which was statistically nonsignificant ($P > 0.05$).

Sedation score in the intraoperative period was nonsignificant in between the two groups. There was no incidence of pruritus in tramadol group whereas two patients had pruritus in fentanyl group. (Table-4) The difference between two groups was statistically not significant ($P < 0.05$). Nausea/vomiting was seen in 11 patients in fentanyl group and 14(16%) patients in tramadol group and the difference was statistically nonsignificant ($P > 0.05$).

Discussion

Spinal analgesia offers superior pain relief and early mobilization especially when local anesthetic dose is combined with the adjuvant. The demographic profile in the present study was comparable to similar other studies and did not show any significant difference on statistical comparison. with an adjuvant as compared to LA used alone [5]. fentanyl is a powerful synthetic opioid analgesic that is similar to morphine but is 50 to 100 times more potent Fentanyl is 800 times more lipid soluble than morphine and rapidly is absorbed from the epidural space and CSF. Because of the reduced cephalic spread the side effects are theoretically less [3] In the present study, an attempt was made to compare the analgesic effects and side-effects of tramadol and fentanyl for lower abdominal surgery when used as an adjuvant with bupivacaine in patients undergoing lower abdominal surgery. For this a comparative study was carried out in which a total of 50 patients undergoing abdominal lsurgery under spinal anesthesia using bupivacaine were enrolled. Of these 50 patients, 25 (50%) each were randomly allocated to two study groups – Group a, patients managed with spinal bupivacaine with tramadol as adjuvant and Group b, patients managed with bupivacaine and fentanyl as adjuvant. The two groups were matched demographically, hemodynamically, biochemically and for surgical complexity at baseline, to rule out any confounding effect. Nishikawa *et al* [6] evaluated the effects of adding 100 mg of fentanyl to lidocaine for axillary BPB in 66 patients scheduled for hand and forearm surgery. The duration of sensory blockade was significantly increased in the fentanyl group (323 ±96 min) compared to the control group (250 ± 79 min). In another RCT, Karakaya *et al*. [7] also found similar benefits in terms of prolonged analgesia and sensory blockade, when fentanyl (2.5 mg/ml) was added to 40 ml of 0.25% bupivacaine for axillary block. Fentanyl did not result in significant bradycardia. Subedi *et al* [8] demonstrated that for cesarean section under subarachnoid block with hyperbaric bupivacaine, intrathecal tramadol 10 mg produces a longer duration of pain relief with a lower incidence of shivering compared to intrathecal fentanyl 10 mg. Afolayan *et al* [9] demonstrated that intrathecal tramadol 25 mg is equipotent with 25 μg of intrathecal fentanyl during bupivacaine subarachnoid block for appendisectomy. Singh [10] compared bupivacaine with bupivacaine- tramadol and bupivacaine-fentanyl and found that duration of analgesia is prolonged with both tramadol and fentanyl, but is more prolonged with fentanyl. Worldwide, many studies have been conducted on the intrathecal use of either fentanyl or tramadol in combination with local anesthetic agents, but there is not a single study available which has compared the intrathecal use of these two opioids in terms of efficacy and safety. So, this study was conducted to compare the two opioids, fentanyl and tramadol, when combined intrathecally with hyperbaric bupivacaine for postoperative analgesia. Hemodynamic parameters, such as pulse rate and oxygen saturation were comparable in both the groups. The difference of the systolic and diastolic blood pressure between fentanyl group and tramadol groups was not significant. In both the groups, the systolic and diastolic blood pressures dropped till 40 to 50 minutes and then it steadily increased over the time. No episode of hypotension occurred. The patients did well throughout the observation period. No patient required injection ephedrine for the treatment of hypotension. All the patients were calm, sleeping comfortably, and responding to verbal commands. Patients from fentanyl group were more sedated than the patients from tramadol group. No patient had any evidence of delayed respiration or hypoxia in both the groups. Biswas *et al* [11] in their study found that there was no respiratory depression or hypoxia in the patients receiving intrathecal fentanyl and intrathecal bupivacaine alone. Chakraborty *et al* [4] found that there was no consequent respiratory depression in the patients receiving intrathecal tramadol and bupivacaine alone.

The present study was a single-center, prospective, randomized, double-blind study. The patients were

Divided into two groups of 25 patients each. We have sought to compare the onset, duration, and analgesic effect of intrathecal fentanyl-bupivacaine with that of tramadol-bupivacaine. Group a received 2.5 mL of 0.5% hyperabaric bupivacaine with 0.5 mL (25 μg) of fentanyl while group b received 2.5 mL of 0.5% hyperbaric bupivacaine with 0.5 mL (25 mg) of tramadol. Mixing of these drugs did not show any physical changes like precipitation, turbidity, and changes in color.

In the present study, demographical parameters like age, sex, weight, height, and ratio of ASA were comparable between the fentanyl group and tramadol group. Likewise, duration of surgery and types of surgery in both the groups were comparable. The effect of intrathecal fentanyl and tramadol in combination with hyperbaric bupivacaine on sensory parameters including onset with time for peak sensory block and duration of sensory block was compared.

It was found that the patients receiving fentanyl and tramadol had nearly the same onset of sensory block but fentanyl group attained the peak sensory level earlier which is statistically significant. The duration of sensory blockade was found to be longer with intrathecal fentanyl than intrathecal tramadol.

Biswas *et al* and Ben-David *et al* [11] found that the duration of sensory blockade was longer in the patients who received intrathecal bupivacaine with fentanyl than the patients who received intrathecal bupivacaine alone. In our study, it was found that patients receiving fentanyl and tramadol had nearly the same onset of motor block and comparable time to achieve peak motor block the duration of motor block was longer in group F as compared to group T and was sta-tistically highly significant $p \leq 0.001$). It implies that the motor recovery and street fitness was delayed in fentanyl group as compared to the tramadol group. The duration of postoperative analgesia was found to be significantly prolonged in fentanyl group as

compared to the tramadol groups; p<0.001), this result was similar to that of singh *et al*. Clinically, it was also found that the patients from fentanyl group were more pain free and comfortable than the tramadol group. Similar results have been obtained by Biswas *et al* and Ben-David *et al*. According to Dahlgren *et al*, intrathecal fentanyl- bupivacaine and sufentanil-bupivacaine had prolonged duration of analgesia as compared to the patients receiving intrathecal bupivacaine alone [12]. Chakraborty *et al* found that the duration of postoperative analgesia was longer in the patients receiving intrathecal bupivacaine-tramadol than the patients receiving only bupivacaine.

Parthasarathy and Ravishankar [13] found that the duration of postoperative analgesia was significantly longer in intrathecal tramadol and intrathecal bupivacaine alone. Though fentanyl and tramadol act on μ receptors, as fentanyl is more lipophilic, it ascends higher than tramadol and causes more sedation. No patient experienced airway compromise or required airway assistance. All the patients were monitored in the intraoperative and postoperative period for opioid-related side effects. Seven patients from fentanyl group and 14 patients from tramadol group experienced nausea while 3 patients from fentanyl group and 11 patients from tramadol group experienced vomiting. Eleven out of 30 patients complained of Pruritus from the fentanyl group. There were no incidence of respiratory depression and headache intra operatively and postoperatively. No incidence of urinary retention could be identified as all patients were catheterized intraoperatively till postoperative period.

Conclusion

It is concluded from our study that bupivacaine when combined with tramadol or fentanyl provided adequate subarachnoid block for lower abdominal surgeries. Both the groups were effective in providing adequate surgical anesthesia and hemodynamic stability, but fentanyl seems to be a better alternative to tramadol as an adjuvant to spinal bupivacaine in surgical procedures. It provides good quality of intraoperative analgesia, hemodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia. Also found superior in these three terms-

1. Prolonged duration of the sensory block
2. Longer duration of postoperative analgesia
3. Lesser number of doses of rescue analgesia required.

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