

ORIGINAL ARTICLE

Intrathecal tramadol versus intrathecal fentanyl for visceral pain control during bupivacaine subarachnoid block for open appendicectomy

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Abstract

Context: Profound side-effects following intrathecal use of local anesthetics as the sole drugs of choice make spinal anesthesia for open appendicectomy uncommon.

Aim: The aim of this study was to evaluate the effectiveness of intra-operative analgesia produced by intrathecal tramadol and fentanyl during bupivacaine spinal anesthesia for open appendicectomy.

Settings and Design: A prospective randomized study was performed.

Materials and Methods: A total of 186 American Society of Anesthesiologists 1 or 11 patients scheduled for emergency open appendicectomy were analyzed. Group FB ($n = 62$) received intrathecal fentanyl 25 μg plus 3 ml of 0.5% hyperbaric bupivacaine, Group SB ($n = 62$) received 0.5 ml normal saline plus 3 ml of 0.5% hyperbaric bupivacaine and Group TB ($n = 62$) received intrathecal tramadol 25 mg plus 3 ml of 0.5% hyperbaric bupivacaine. Visual analog scale scores and frequency of subjective symptoms among patients in the three groups formed the primary outcome measure of this study.

Results: Effective intraoperative sensory block was achieved in 100% of patients in group FB and TB while 29 (46.8%) patients in group SB had ineffective sensory block ($P = 0.0001$). The pain free period was significantly longer in patients in Group FB than Group SB and TB. Mean time for Group FB with regard to first analgesic request was 304.73 ± 67.91 min, Group SB was 146.59 ± 36.62 and Group TB was 238.39 ± 61.28 min. Incidence of complications were comparable among the three groups.

Conclusion: This study showed that intrathecal tramadol (25 mg) can safely replace intrathecal fentanyl (25 μg) in the management of visceral pain and discomfort during subarachnoid block for appendicectomy.

Key words: Analgesia, appendicectomy, intrathecal opioid, spinal anaesthesia

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Introduction

Open appendicectomy is commonly performed under general anesthesia world-wide.^[1] Attempts at using appropriate safe dose of local anesthetic agent intrathecally without additive while managing pain associated with appendicectomy had proved abortive in the past.^[1] Techanivate *et al.*,^[2] reported that bupivacaine spinal anesthesia with intrathecal fentanyl was able to mitigate visceral pain during appendicectomy

in Thailand. The use of intrathecal tramadol, an atypical opioid, to mitigate this visceral pain and discomfort during appendicectomy has not been studied. There is general paucity of reports on intrathecal opioids as adjuvants to local anesthetic agents during management of visceral pain of appendicectomy in Africa in general and in Nigeria in particular.

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Materials and Methods

This was a prospective, randomized, placebo-controlled clinical study, comparing intrathecal tramadol with intrathecal fentanyl and a normal saline placebo-controlled protocol for visceral pain control during bupivacaine subarachnoid block for open appendicectomy. Patients were drawn from those scheduled for emergency open appendicectomy requiring subarachnoid block. Ethical clearance and approval were obtained from the institution's ethical committee. Informed consent of every participating patient was obtained before the study was commenced.

A total of 195 American Society of Anesthesiologists (ASA) I or II patients scheduled for emergency appendicectomy, aged between 18 years and 60 years were recruited for the study. Exclusion criteria included patients unable to understand written or verbal information, patients with appendicular mass, rupture or any co-existing surgical procedure. Patients for elective appendicectomy were excluded because their overnight fast could affect incidence of nausea and vomiting. Patients with a history of hypersensitivity to local anesthetic agent and opioids that were used were excluded. Patients with peripheral neuropathy or having contraindications to regional anesthesia or patients who could not attain a minimum height block of T6 at 4 min following injection of spinal solution were also excluded.

All eligible patients were randomly assigned into three groups of 65 each by opening unmarked envelop indicating the type of coded spinal solution package to be used. A second anesthetist who was not involved in the study prepared the spinal solutions. The anesthetist performing the block was blinded to the spinal solution administered. Each of the spinal solutions was coded FB, SB or TC.

Pre-operative assessment of the patients, including history with detailed systemic review and examination of all systems, was carried out. Routine investigations such as hemoglobin concentration, urinalysis, serum electrolytes and urea were done for every patient. Visual analogue scale [VAS] score for pain assessment, consisting of 100 mm line with 0 = no pain and 100 = worst pain, was explained to all the patients during the pre-operative visit. They were all informed that VAS between 1 mm and 39 mm indicated a mild pain; between 40 mm and 69 mm indicated a moderate pain, 70 mm and above indicated severe pain. They were all educated on the use of VAS scores.

In the operating room, each patient had Edan multi-parameter monitor attached. Baseline pulse rate, non-invasive blood pressure, oxygen saturation and respiratory rate were obtained and recorded before induction of spinal anesthesia and subsequently during the procedure. A venous access was secured using 16 or 18 gauge cannula and the patient

was preloaded with normal saline (15 ml/kg) before the induction of spinal anesthesia. Aseptically, spinal anesthesia was carried out in a sitting position, using 25G Quincke spinal needle at $L_{2,3}$. Interspace was used in some cases where it was difficult to use $L_{3,4}$ interspace. After a free flow of cerebrospinal fluid was confirmed, each patient received one of the coded spinal solutions after randomization into Group FB, SB or TB. Patients in Group FB ($n = 65$) received intrathecal fentanyl 25 μg plus 3 ml of 0.5% hyperbaric bupivacaine, patients in Group SB ($n = 65$) received 0.5 mlb normal saline plus 3 ml of 0.5% hyperbaric bupivacaine and patients in Group TB ($n = 65$) received intrathecal tramadol 25 mg plus 3 ml of 0.5% hyperbaric bupivacaine.

Maximum sensory block height was assessed at 1 min, 2 min, 3 min and 4 min following injection of spinal solution, using loss of sensation to cold and gentle pin prick test. A minimum sensory block height of T6 at 4 min was the minimum desired level for commencement of surgery. Any patient who did not meet this minimum sensory block height was excluded from the study. The level of sensory analgesia defined as loss of sensation to pin prick test was recorded. Pulse rate, blood pressure, respiratory rate and oxygen saturation were also recorded every 3 min for the first eighteen minutes and then at interval of 5 min until the end of surgery. Time of skin incision was recorded. Following skin incision, VAS scores were recorded every 3 min for the first 18 min and then at interval of 5 min until the end of surgery.

Intraoperative complications such as hypotension (reduction in systolic blood pressure greater than 30% of the baseline), bradycardia (reduction in pulse rate greater than 30%), itching, paraesthesia, vomiting and shivering were identified and treated accordingly. Discomfort following visceral manipulation was recognized, recorded and treated accordingly. Discomfort such as dragging sensation, chest tightness, nausea, vomiting and retching were documented and treated appropriately. The time surgery ended was noted and duration of surgery in minutes was calculated and recorded.

Intra-operatively, patients who experienced pain, dragging sensation and chest tightness were managed with pentazocine, 30 mg intravenously as rescue analgesic. Nausea, vomiting or retching was treated with metochlopramide, 10 mg. Shivering was managed using warmed fluid, covering with more drapes. In addition, the air conditioner in the operating room was switched off, 100 mg tramadol was on stand by in case the shivering persisted despite the above mentioned management of shivering. Hypotension was treated with either rapid fluid infusion or aliquots of ephedrine, 3 mg intravenously and bradycardia was treated with atropine 0.6 mg intravenously. VAS scores were recorded post-operatively at 30 min interval for the first 1 h and then hourly for the next 12 h. Post-operative complications were assessed and recorded.

Time and VAS score of first analgesic requirement postoperatively were documented.

Duration of pain free period was defined as the period between time of injection of spinal solution and time of first rescue analgesic administered on demand or when VAS score was equal or greater than 40 mm. The effectiveness of analgesia produced by intrathecal fentanyl, tramadol or normal saline placebo intraoperatively was judged by presence or absence of pain and discomfort-dragging sensation, chest tightness, vomiting, nausea and retching-following abdominal manipulation. The effectiveness of post-operative analgesia produced by either intrathecal fentanyl, tramadol or normal saline placebo was assessed by the use of the duration of pain free period which was from time of injection of local anesthetic with or without opioid to time of first analgesic requirement in the post-operative period or when VAS score was greater or equal to 40 mm.

All data were presented as means and standard deviation; numbers and percentages; median and range except where specified. The data obtained were analyzed using statistical program for social sciences (SPSS) 16.0 software (Chicago Illinois, USA). All parametric data (continuous or discrete) obtained from age, height, weight and hemodynamic variations were analyzed using one-way ANOVA. Evaluation of non-parametric data (nominal or ordinal) obtained from sex, ASA, onset of block, pain free period, intestinal manipulation, intra-operative or post-operative complications and inadequate sensory block were analyzed using Chi-square, Fisher's exact, Kruskal-Wallis or Mann-Whitney test where applicable. $P < 0.05$ were considered to be significant.

Results

Out of 195 patients who were recruited into the study, nine of them were however disqualified. The reasons for the disqualification were inappropriate documentation for two patients. One patient had appendectomy with ovarian cystectomy. Three patients had minimum sensory block height below T6 at 4 min. One patient had appendicular mass, two others had high grade fever. As a result, only one hundred and eighty six patients in the three groups were analyzed.

Table 1 shows patient's characteristics. There was no statistically significant difference amongst the three groups with regard to age, height and weight ($P = 0.54, 0.17$ and 0.56 ; respectively).

As shown in Table 2, at 4 min, which was the cut-off point, majority of patients in Group FB and TB had attained T₄ as the maximum height of sensory block ($P = 0.002$). Despite this high height of sensory block, none of the patients studied had oxygen saturation less than 95%.

Table 3 shows intra-operative pain score. Patients in Groups FB and TB did not experience any pain intra-operatively, whereas 55 patients (88.7%) in Group SB reported no pain ($P = 0.001$).

No patient in both Groups FB and TB had any form of discomfort following intestinal manipulation as shown in Table 4. In Group SB, three patients (4.8%) had episode of intra-operative vomiting ($P = 0.108$), 3 patients (4.8%) reported nausea ($P = 0.108$) and 3 patients (4.8%) complained of retching ($P = 0.108$).

However, 8 patients (12.9%) had dragging sensation in group SB ($P = 0.0001$). Seven patients (11.3%) in Group SB had chest tightness ($P = 0.001$).

Table 1: Patient's characteristics

Parameter	Mean \pm SD			P value
	Group FB (n=62)	Group SB (n=62)	Group TB (n=62)	
Age (years)	28.58 \pm 1.37	28.79 \pm 1.34	28.55 \pm 1.23	0.54
Height (m)	1.65 \pm 0.01	1.64 \pm 0.01	1.65 \pm 0.01	0.17
Weight (kg)	69.34 \pm 1.25	67.32 \pm 1.48	68.84 \pm 1.71	0.56
Sex distribution (n [%])				
Male	23 (37.1)	25 (40.3)	22 (35.5)	0.85
Female	39 (62.9)	37 (59.7)	40 (64.5)	
ASA status (n [%])				
I	56 (91.5)	57 (91.9)	55 (88.3)	0.83
II	6 (8.5)	5 (8.1)	7 (11.7)	

ASA=American society of anesthesiologists, SD=Standard deviation, FB=Fentanyl group, TB=Tramadol group, SB=Saline group

Table 2: Sensory level attained after spinal block

Time	No. (%) median (range)			P value
	Group FB (n=62)	Group SB (n=62)	Group TB (n=62)	
1 min	T ₉ (T ₇ -T ₁₁)	T ₁₀ (T ₈ -T ₁₁)	T ₁₀ (T ₈ -T ₁₀)	0.470
2 min	T ₅ (T ₄ -T ₈)	T ₇ (T ₆ -T ₉)	T ₈ (T ₅ -T ₁₀)	0.065
3 min	T ₄ (T ₂ -T ₆)	T ₆ (T ₅ -T ₈)	T ₆ (T ₄ -T ₇)	0.059
4 min	T ₄ (T ₂ -T ₆)	T ₆ (T ₄ -T ₆)	T ₄ (T ₂ -T ₆)	0.002

FB=Fentanyl group, TB=Tramadol group, SB=Saline group

Table 3: Intra-operative pain score

Classification of pain (VAS score)	No. (%)			P value
	Group FB (n=62)	Group SB (n=62)	Group TB (n=62)	
No pain (0)	62 (100.0)	55 (88.7)	62 (100.0)	0.001
Mild pain (1-39)	0 (0.0)	2 (3.2)	0 (0.0)	0.330
Moderate (40-69)	0 (0.0)	4 (6.5)	0 (0.0)	0.035
Severe pain (70 and above)	0 (0.0)	1 (1.6)	0 (0.0)	1.000

VAS=Visual analogue scale, FB=Fentanyl group, TB=Tramadol group, SB=Saline group

Intra-operative symptoms of inadequate block were shown in Table 5. This signified that 29 patients (46.8%) in Group SB significantly ($P = 0.0001$) had inadequate anesthesia, whereas no patient (0.0%) in Groups FB and TB had inadequate anesthesia.

Table 6 shows incidence of intra-operative complications. Fifteen (24.2%), 13 (20.9%) and 15 (24.5%) patients respectively in Groups FB, SB and TB had hypotension ($P = 0.886$). Itching was significantly higher in Group FB ($P = 0.035$). The incidence of post-operative vomiting was significant statistically ($P = 0.016$), as shown in Table 7.

Figure 1 shows duration of pain free period in minutes. Mean and standard deviation time for Group FB with

Table 4: Discomfort following intestinal manipulation				
Parameter	No. (%)			P value
	Group FB (n=62)	Group SB (n=62)	Group TB (n=62)	
Vomiting	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Nausea	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Retching	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Dragging sensation	0 (0.0)	8 (12.9)	0 (0.0)	0.0001
Chest tightness	0 (0.0)	7 (11.3)	0 (0.0)	0.001

FB=Fentanyl group, TB=Tramadol group, SB=Saline group

Table 5: Intra-operative symptoms of inadequate block				
Parameter	No. (%)			P value
	Group FB (n=62)	Group SB (n=62)	Group TB (n=62)	
Pain	0 (0.0)	5 (8.1)	0 (0.0)	0.011
Chest tightness	0 (0.0)	7 (11.3)	0 (0.0)	0.001
Dragging sensation	0 (0.0)	8 (12.9)	0 (0.0)	0.0001
Vomiting	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Retching	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Nausea	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Incomplete block	0 (0.0)	29 (46.8)	0 (0.0)	0.0001

FB=Fentanyl group, TB=Tramadol group, SB=Saline group

Table 6: Intra-operative complications				
Complication	No. (%)			P value
	Group FB (n=62)	Group SB (n=62)	Group TB (n=62)	
Pain	0 (0.0)	5 (8.1)	0 (0.0)	0.011
Chest tightness	0 (0.0)	7 (11.3)	0 (0.0)	0.001
Vomiting	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Retching	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Nausea	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Bradycardia	0 (0.0)	1 (1.6)	0 (0.0)	1.000
Hypotension	15 (24.2)	13 (20.9)	15 (24.2)	0.886
Shivering	0 (0.0)	3 (4.8)	0 (0.0)	0.108
Itching	4 (6.5)	0 (0.0)	0 (0.0)	0.035
Paraesthesia	1 (1.6)	0 (0.0)	0 (0.0)	1.000

FB=Fentanyl group, TB=Tramadol group, SB=Saline group

regard to first analgesic request was 304 ± 67.91 min, Group SB was 146.59 ± 36.62 min and Group TB was 238.39 ± 61.28 min. The difference in the duration of pain relief was highly significant when comparing duration of pain relief in Groups SB and TB ($P = 0.001$); Group FB and Group TB ($P = 0.001$) or FB and Group SB ($P = 0.001$). This signified that the longest duration of pain relief was observed in Group FB when compared with Group TB and Group SB. However, Group TB had significant longer duration of pain free period than Group SB.

Discussion

The study showed that the addition of intrathecal fentanyl and intrathecal tramadol to hyperbaric bupivacaine for spinal anesthesia in patients who underwent open appendicectomy significantly improved the quality of intra-operative analgesia without increasing the side effects such as respiratory depression, nausea, hypotension, bradycardia or shivering. Peritoneum and intestine have innervations as high as T_4 therefore any level of sensory block below T_4 may result in visceral pain and discomfort.^[3] In some of the cases, a maximum height of sensory block (T_4) for appendicectomy may not be attained if intrathecal 0.5% hyperbaric bupivacaine is used alone,^[1] hence the need to add intrathecal opioid to bupivacaine for management of visceral pain and discomfort that are manifested during appendicectomy

Experimental studies have shown that addition of opioids to local anesthetic agent intrathecally was able to relieve visceral pain and discomfort.^[4,5] Apart from the works of Parthasarathy and Ravishkar,^[6] Chakraborty

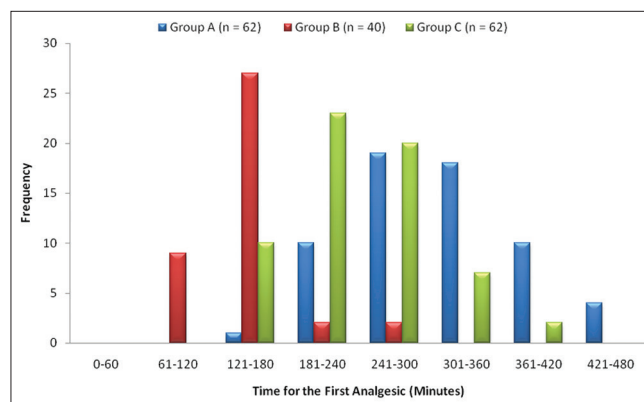


Figure 1: Time of first analgesic requirements (minutes)

Table 7: Post-operative complications				
Complication	No. (%)			P value
	Group FB (n=62)	Group SB (n=62)	Group TB (n=62)	
Headache	1 (1.6)	0 (0.0)	0 (0.0)	1.000
Vomiting	2 (3.2)	3 (4.8)	10 (16.1)	0.016

FB=Fentanyl group, TB=Tramadol group, SB=Saline group

et al.,^[7] Alhashemi and Kaki^[8] and Frikha *et al.*,^[9,10] many of the researches have not been carried out on intrathecal administration of tramadol especially for procedures such as appendicectomy. Tramadol is a synthetic 4-phenyl-piperidine analogue of codeine with a dual mechanism of action.^[11] It stimulates the μ -receptor and to a lesser extent δ - and κ -opioid receptors. Similar to tricyclic antidepressants, it activates spinal inhibition of pain by decreasing the reuptake of norepinephrine and serotonin. This produces a non-opioid basis of analgesia.^[12-14] A report suggesting that tramadol may have a direct serotonin-releasing action has been documented.^[13] Tramadol is presented in a sterile intravenous preparation with water for injection and sodium acetate. It does not contain preservative such as sodium metabisulphite, methylparaben or chlorocresol which is neurotoxic agent. It is usually prepared preservative-free.^[15]

A total of 25 mg of intrathecal tramadol was considered adequate for the study based on the work carried out by Alhashemi and Kaki^[8] where 25 mg of intrathecal tramadol was proven to be safe during the spinal anaesthesia. Although Frikha *et al.*,^[10] used 50 mg tramadol, Parthasarathy and Ravishkar^[6] used 10 mg and Chakraborty *et al.*,^[7] used 20 mg of tramadol in their studies, but 25 μ g of fentanyl is equipotent with 25 mg of tramadol according to report by Duthie.^[16] He also reported that tramadol has the same analgesic potency as pethidine, one fifth (1/5) that of nalbuphine, one-tenth (1/10) that of morphine and one-thousandth (1/1000) that of fentanyl.

One of the advantages of using intrathecal fentanyl is its rapid onset.^[5] This study demonstrated that intrathecal fentanyl and intrathecal tramadol had faster onset and higher level of block than placebo. This was in agreement with the study conducted by Singh *et al.*,^[17] where fentanyl mean onset time was found to be 2.72 ± 1.51 min. In another study, Cherng *et al.*,^[18] concluded that epidural injection of the mixture of 100 μ g fentanyl and 2% lidocaine solution accelerated the onset of sensory block. Bogra *et al.*,^[19] also found that onset time of sensory block to T₆ was faster with the group that received intrathecal fentanyl during spinal anaesthesia for Cesarean section. This was in agreement with the work of Motiani *et al.*,^[5] who demonstrated that intrathecal fentanyl 25 μ g as adjuvant led to an earlier onset compared with placebo.

The result of the present study differed from the observations of Techanivate *et al.*,^[2] and Singh *et al.*,^[20] who, in different studies, demonstrated that intrathecal fentanyl did not enhance onset of sensory block during bupivacaine subarachnoid block. The onset time to T₄ sensory block in this present study did not agree with that of Techanivate *et al.*,^[2] probably because a high volume dose (4 ml) of 0.5% bupivacaine was used as against 3 ml in this study. This high volume was enough to cause a rapid onset in

the three groups studied by them. It was documented by Bogra *et al.*,^[19] and Rousel *et al.*,^[21] in separate trials that the onset of sensory block to T₄ was faster with increasing bupivacaine doses.

Pain and discomfort are major problems during subarachnoid block for appendicectomy.^[2] In this present study, all patients who had intrathecal fentanyl and intrathecal tramadol had complete sensory block (no patient had any form of pain or discomfort), whereas only 33 patients (53.2%) in placebo group had complete sensory block (29 patients [46.8%] patients had pain or discomfort) which was significant when comparing placebo with fentanyl or tramadol group. This agrees with Techanivate *et al.*,^[2] that demonstrated complete sensory block in the patients that received either 20 μ g or 10 μ g of fentanyl as compared with the placebo group which had complete sensory block in only 65% of patients. This is also in agreement with Bogra *et al.*,^[19] who demonstrated that fentanyl was required to abolish visceral pain experienced by pregnant women during Caesarean section.

The need to add intrathecal opioid to bupivacaine whenever peritoneum and intestine are manipulated was supported by numerous researchers^[2,17,20] in different studies. Other studies have demonstrated the need to add opioids to local anaesthetic in order to improve intra-operative analgesia.^[5,22-25] Intrathecal tramadol is capable of mitigating visceral pain and discomfort as observed by Parthasarathy and Ravishkar,^[6] Alhashemi and Kaki^[8] and Chakraborty *et al.*,^[7] Their finding is supported by the finding in this study.

In this study, time to first analgesic request was significantly prolonged in fentanyl group compared with placebo group. This result corroborates the findings of Techanivate *et al.*,^[2] in which time to first request for post-operative analgesic was significantly prolonged when comparing fentanyl group with placebo group (11.0 h vs. 4.7 h respectively, $P < 0.05$). The time to first request for analgesic in the fentanyl group was much longer when comparing studies of Techanivate *et al.*, with this present study. This was probably due to a high volume of heavy bupivacaine administered. It has been reported that increasing doses of bupivacaine leads to increased duration of action.^[19,26] The trial conducted by Goel *et al.*,^[22] also supported the result of this study. The patients in the fentanyl group who received 25 μ g fentanyl had longer post-operative analgesia (305 min) compared with placebo group (197 min) and this was statistically significant amongst the obstetric population studied.

Roussel and Heindel^[21] achieved prolonged sensory and motor block when 25 μ g of fentanyl with 12 mg of bupivacaine was administered to a particular group of patients. They found that time to first analgesic requirement was 617 min in fentanyl group compared with 418 min in placebo group; this was in support of the study of Motiani

et al.,^[5] that reported a prolonged duration of sensory block with 25 µg fentanyl. This was also in agreement with results obtained by other researchers for varying types of procedures, including Caesarean section, lower limb surgery and labor analgesia.^[27-30] The average duration of analgesia produced by lipophilic opioid (fentanyl and sufentanil) is between 2 h and 5 h whereas that of hydrophilic opioid (morphine) is between 12 h and 24 h.^[31,32]

The findings in this study showed no significant difference in the episode of hypotension between fentanyl, tramadol and control groups which was supported by many researchers.^[2,6,8,9,21,27] This signified that the episodes of hypotension in these different studies was probably due to the effect of different doses of bupivacaine. Shivering occurrence in this study was not in accordance with Techanivate *et al.*,^[2] who observed shivering in all the groups. This might be due to the sympatholytic effect of high dose (4 ml) of 0.5% intrathecal bupivacaine used in their study. In this study, itching occurrence was 6.5% in the fentanyl group. The high incidence of itching reported by Frikha *et al.*,^[10] might be associated with high dose of opioids (50 mg of tramadol plus 10 µg of fentanyl) administered to each of the patients in one of the groups in the obstetric population studied.

Post-operative vomiting was significantly highest in the tramadol group in this study which was high compared with the work of Parthasarathy and Ravishkar,^[6] where low dose (10 mg) of intrathecal tramadol was administered to each of the patients in the tramadol group Frikha *et al.*,^[9] recorded more frequency in vomiting. This might be due to high dose (50 mg) of intrathecal tramadol administered.

Conclusion

This study shows that intrathecal tramadol 25 mg is equipotent with 25 µg of intrathecal fentanyl in mitigating intra-operative pain and discomfort following peritoneal and intestinal manipulation during bupivacaine subarachnoid block for appendicectomy. The intrathecal opioids both produce comparable haemodynamic changes and post-operative analgesia with minimal peri-operative side-effects.

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