ORIGINAL ARTICLE

E f cacy of Multimodal Analgesia vs Unimodal Analgesia for Acute Postoperative Pain Relief after Abdominal Surgeries

Sharan Vasan[1], KS Navyashree[2], MJ Sowmya[3], Sahajananda Hiremathada[4]

Abstract

Background: Pain has a multifactorial origin; therefore, it may be difficult to achieve pain management with a single drug. Hence, multimodal analgesia was introduced. Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms and at different sites in the nervous system, resulting in additive or synergistic analgesics with lowered adverse effects of sole administration of individual analgesics. This is advantageous as it acts by both peripheral and central pain pathways; this minimizes pain with better tolerability and reduces recovery time. The multimodal strategy allows early mobilization, early enteral nutrition, and attenuation of the perioperative stress response which leads to reduced morbidity and accelerated convalescence.

Materials and methods: After institutional ethical committee approval, 60 patients undergoing abdominal surgeries and laparotomies belonging to the American Society of Anesthesiologists (ASA) I and II of either sex, aged between 20 years and 70 years were enrolled for this study. Thirty were provided unimodal analgesia with inj. tramadol and the other 30 received multimodal analgesia with quadratus lumborum block (QLB), inj. tramadol, and inj. diclofenac for postoperative analgesia. Our main aim was to assess the efficacy of multimodal analgesia *vs* unimodal analgesia for postoperative pain management.

Results: We observed the visual analog scale (VAS) pain scores in patients of both groups at 0, 2, 4, 8, and 12 hours. When the scores were above 7, rescue analgesia with inj. fentanyl was provided. The duration of the first analgesic request and the total number of rescue analgesics given were recorded along with any complications.

Conclusion: Multimodal analgesia was superior compared with the unimodal approach as it provided better analgesia with low VAS score values. Duration of analgesia was longer based on time of request of first rescue analgesia, with reduced adverse effects. It reduced the number of rescue analgesics required and the opioid side effects were overcome by non-steroidal anti-inflammatory drug (NSAID) use.

Keywords: Multimodal analgesia, Non-steroidal anti-inflammatory drugs, Postoperative pain.

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Introduction

The experience of pain is complex, multifaceted, and "an unpleasant sensory and emotional experience," as defined in part by the International Association for the Study of Pain.[1] All surgical procedures are followed by pain, which may amplify endocrine metabolic responses, autonomic reflexes, nausea, muscle spasm, and thereby delay in restoration of function. Pain after surgery is often treated inadequately and maximum utilization of the available resources is essential for improving pain management.[2]

Many options are available for the treatment of postoperative pain, including systemic (opioid and non-opioid) analgesics and regional (neuraxial and peripheral) analgesic techniques.[1] Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the synthesis of prostaglandins both in the spinal cord and at the periphery, thus diminishing the hyperalgesia state after surgical trauma. Opioids have a dual mode of action on opioid and monoaminergic receptors. These are efficacious against both nociceptive and neuropathic pain. Tramadol is now considered the first-line among the analgesics.[3] The quadratus lumborum block (QLB) is an abdominal truncal block for analgesia[4] and is known to alleviate somatic and visceral pain covering all the dermatomal segments from T4 cranially to L2 segments caudally.[5]

Pain has a multifactorial origin; therefore, it may be difficult to achieve pain management with a single drug. Hence, multimodal analgesia was introduced. Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms and at different sites in the nervous system, resulting in additive or synergistic analgesics with lowered adverse effects of sole administration of individual analgesics.[1] This is advantageous as it acts by both peripheral and central pain pathways; this minimizes pain with better tolerability and reduces recovery time.[3] A multimodal strategy allows early mobilization, early enteral nutrition, and attenuation of the perioperative stress response which leads to reduced morbidity and accelerated convalescence.

Abdominal surgeries cause pain due to cutting of the skin which stimulates nerve fibers and induce pain.[6] As the body begins to heal, pain should decrease and eventually stop. The amount of time pain lasts after surgery can depend on several factors. On rare occasions, pain may remain, though the cause of the pain cannot be identified. This condition can become long-term pain.[6] Adequate

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postoperative pain management helps in preventing the incidence of postoperative morbidity and delayed recovery.

Tramadol as an opioid is one of the most commonly used intravenous analgesic agents for postoperative pain relief. Based on its potency, tramadol has comparatively few disadvantages associated with other opiates, such as cardiovascular reactions and physical dependency.[7] More recent work suggests that non-opioid receptor mechanisms of action may contribute to the analgesic profile of tramadol in humans and result from the inhibition of noradrenaline uptake and stimulation of serotonin release.[7] Previous studies indicate that the 50-mg treatment dose of tramadol fulfills the requirements of an analgesic for the treatment of moderate postoperative pain, whereas for severe pain a higher dose is recommended.[1]

Non-steroidal anti-inflammatory drugs inhibit the synthesis of prostaglandins both in the spinal cord and at the periphery, thus diminishing the hyperalgesic state after surgical trauma. Non-steroidal anti-inflammatory drugs are useful as the sole analgesic after minor surgical procedures and may have a significant opioid-sparing effect after major surgery.[1] Non-steroidal anti-inflammatory drugs have many adverse effects like nausea and present a significant GI bleeding risk, along with a risk of a variety of renal complications, and myocardial infarction, and other serious cardiovascular complications. The recent guidelines issued by numerous professional medical societies recommend NSAIDs at the lowest effective dose and shortest possible period, in view of the associated gastrointestinal, renal, and cardiovascular toxicity.

Ultrasonography-guided QLB was reported in 2007 by Blanco et al. Using contrast dye, the spread of the local anesthetic after QLB showed extension into the thoracic paravertebral space. The extension of the local anesthetic agent into the thoracic paravertebral space after QLB may be responsible for the extent of analgesia and prolonged duration of pain relief. Also, there is somatic as well as visceral analgesia without any significant motor blockade. Several studies have shown that QLB has an important contributory role in the treatment of postoperative pain after abdominal surgeries.[5]

Combination therapy of analgesics from different groups is advantageous in targeting both peripheral and central pain pathways and hence, helps in the production of analgesia at lower and more tolerable doses of the constituent drugs.[1] Combination therapies can have a positive influence on the ability of individual components to minimize pain, with better tolerability and reduced recovery time. These combination therapies, now termed multimodal analgesia is the call of the day with ever-increasing numbers of ambulatory or daycare surgeries.[7,8]

So, in this study, we compare the adequacy of postoperative analgesia provided by the unimodal approach by administering intravenous tramadol with that of the multimodal approach by administering intravenous tramadol, diclofenac, and performing QLB block.

Aims and Objectives

This study was undertaken

- To compare the effectiveness of the single parenteral agent (tramadol) with a combination of agents (parenteral diclofenac, parenteral tramadol, and preoperative QLB) in the immediate 12 hours postoperative period.
- To look for any possible side effects.

Materials and Methods

After institutional ethical committee approval, 60 patients undergoing abdominal surgeries and laparotomies belonging to the American Society of Anesthesiologists (ASA) I and II of either sex, aged between 20 years and 70 years were enrolled in this study. Among them, patients with known hypersensitivity to local anesthetic drugs, who are mentally unstable or are unable to comprehend/use the visual analog scale (VAS) score, those with a history of preexisting opioid dependence or epilepsy, raised intracranial pressure, peptic ulcer disease, cardiac, renal, hepatic or coagulation disorders were excluded.

In this perspective two-arm comparative study, 60 subjects were allocated into 2 groups, using computer-generated random numbers into tramadol (100 mg) only (T group), and inj. diclofenac (75 mg) + inj. tramadol (100 mg) + QLB (QTD group). All the patients were explained about the study and written informed consent was obtained. Surgery was performed under standard general anesthesia, using inj. fentanyl 2 µg/kg, propofol 1–2 mg/kg, and vecuronium 0.1 mg/kg. Patients were intubated with cuffed endotracheal tubes and anesthesia was maintained with sevoflurane, oxygen, and nitrous oxide. Top-up doses of vecuronium were given as required. The neuromuscular bock was reversed with inj. neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg).

Patients belonging to the T group received 100 mg of tramadol intravenously half an hour after the end of the surgery, in the postoperative care unit. In patients belonging to the QTD group, anterior QLB was performed at the beginning of the surgery, before induction. The block was performed under ultrasound guidance using a linear probe and 20 mL of 0.5% inj. ropivacaine was instilled bilaterally. Half an hour after the end of the surgery, inj. tramadol 100 mg and inj. diclofenac 75 mg were given intravenously. Each patient serves as his/her own standard with respect to the request for analgesia, which is predetermined at not <4-h intervals. All patients were blinded to the analgesic agents.

The primary outcome measure is control of postoperative pain, while secondary outcome measures are the duration of action of analgesia (determined from the interval between drug administration and the patient's request for repeat analgesia), patient satisfaction (determined by assessing patients' desire for the same treatment for the next surgery), and adverse outcomes.

Pain control was assessed using a VAS. Each patient received teaching on the VAS at enrolment into the study (before the surgery). This VAS technique uses a 10 cm-long scale marked from 0 to 10, where 0 represents "no pain" and 10 represents "worst possible pain." Scores of 1 to 4 were classified as mild pain, >4 to 8 as moderate pain, and above 8 as severe pain. If the VAS score pain assessment was severe, inj. fentanyl 0.5 µg/kg was administered intravenously as rescue analgesia. To assess the sedative effect of the agents, a sedation score was applied. The sedation was evaluated on a scale of 0 to 4; where 0 = asleep and not arousable, 1 = asleep but arousable, 2 = drowsy, 3 = awake and not alert, and 4 = awake and alert. Increased sedation score indicated a less

sedative effect of the drug. Trained research assistants, who were also blinded to the agents of study, undertook assessments 1 hour after administration of the analgesic agents.

Statistics

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean ± SD (Min–Max) and results on categorical measurements are presented in number (%). Significance is assessed at a 5% level of significance.

Student's *t*-test (two-tailed, independent) has been used to find the significance of study parameters on a continuous scale between two groups (intergroup analysis) on metric parameters.

Chi-square/Fisher's exact test has been used to find the significance of study parameters on a categorical scale between two or more groups, non-parametric setting for qualitative data analysis. Fisher's exact test is used when cell samples are very small.

Observations and Results

The two groups were comparable in the demographic variables, types of surgeries, and average duration of surgery (Figs 1 and 2).

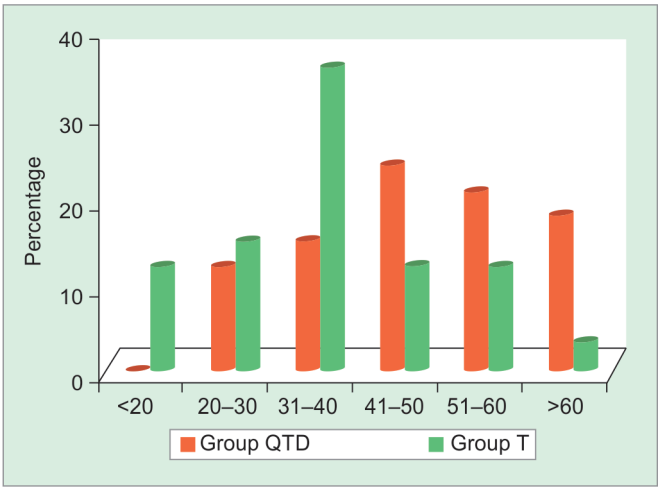


Fig. 1: Age distribution of patients in both the groups

In the Table 1, we observe that VAS scores of patients in the QTD group lie in mild (1–3) to moderate (4–6) range when recorded serially at regular intervals of time. Whereas the VAS scores of the patients in the T group lie in the severe (7–10) range requiring administration of the rescue analgesic.

We can see that the average VAS scores of all the patients in the QTD group are <3 whereas, in the T group, it is >3 on serial observation. The *p* value at 0, 2, 4, and 8 hours are statistically significant (<0.001) when analyzed using the Student's *t*-test (Fig. 3).

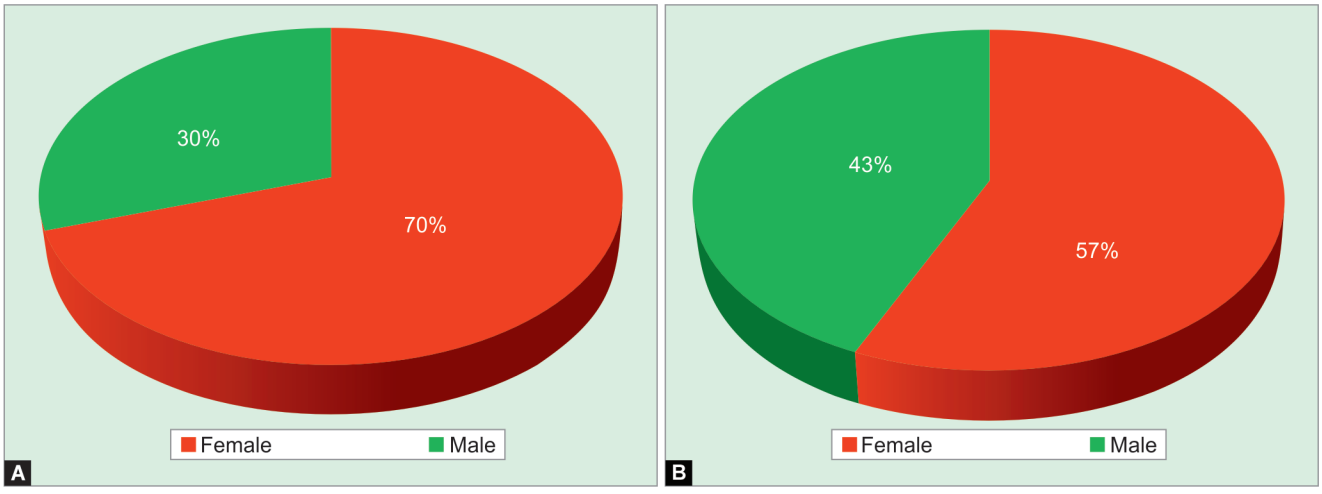
From Figure 4, we can see that majority of the patients, >20 out of 30 of the QTD group did not require inj. fentanyl rescue analgesia at 0, 2, 4, 8, and 12 hours. In the T group, 19 out of 30 patients, 19/30, 17/30, 13/30, and 5/30 patients required rescue analgesia at 0, 2, 4, 8, and 12 hours, respectively. The *p* value was <0.05 at 0, 2, 4, and 8 hours proving its statistical significance. Also, from Figure 4, we can conclude that majority of patients required rescue analgesia at the first 2 and 4 hours after surgery in the T group, suggesting that the duration of action of inj. tramadol given postoperatively lasted for only about 2–4 hours in these patients.

In the Table 2, we see that 15/30 patients of the QTD group did not ask for any rescue analgesia, and 11/30 of them required one dose of rescue analgesia. And only 4/30 required more than one dose. In the T group, 10/30 did not require rescue analgesia, 1/30 required one dose, and the rest 19/30 required multiple doses of the rescue analgesic.[9-13]

When the complications/adverse effects like sedation, nausea, vomiting, gastric irritation, headache, pain due to a full bladder and respiratory depression were compared between the two groups, it was seen that the patients of the T group experienced more sedation when compared with the QAD groups on serial observation. The *p* value for sedation score is consistently <0.001 showings that it is statistically significant. There was not much difference seen between the two groups with respect to other complications (Fig. 5).

Discussion

Postoperative pain, especially when poorly controlled, may produce a range of detrimental acute (i.e., adverse physiological responses) and chronic effects (i.e., delayed long-term recovery and chronic pain).[1] Good pain control after surgery is important to prevent negative outcomes such as tachycardia, hypertension, myocardial



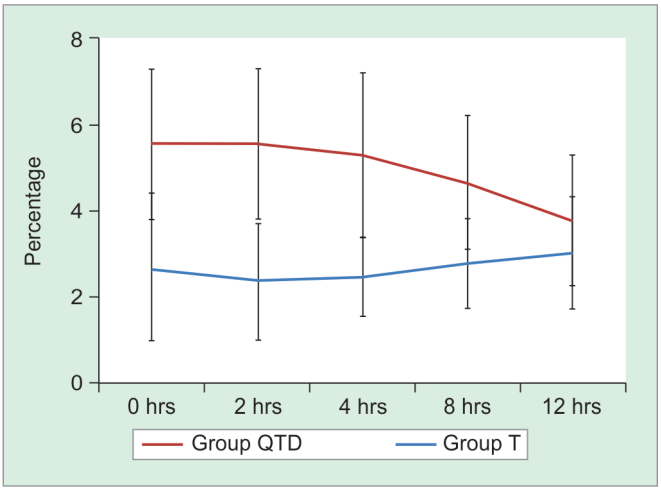
Figs 2A and B: Gender distribution pie charts for both the groups

Table 1: VAS score-distribution in two groups of patients studied at different study points

VAS score	*0 hour*	*2 hours*	*4 hours*	*8 hours*	*12 hours*	*% Difference*
Group QTD ($n = 30$)						
0	3 (10)	3 (10)	1 (3.3)	0 (0)	0 (0)	−10.0
1–3	19 (63.3)	23 (76.7)	24 (80)	24 (80)	20 (66.7)	3.4
4–6	8 (26.7)	4 (13.3)	5 (16.7)	6 (20)	10 (33.3)	6.6
7–10	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.0
Group T ($n = 30$)						
0	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.0
1–3	6 (20)	6 (20)	8 (26.7)	9 (30)	16 (53.3)	33.3
4–6	15 (50)	15 (50)	14 (46.7)	19 (63.3)	13 (43.3)	−6.7
7–10	9 (30)	9 (30)	8 (26.7)	2 (6.7)	1 (3.3)	−26.7

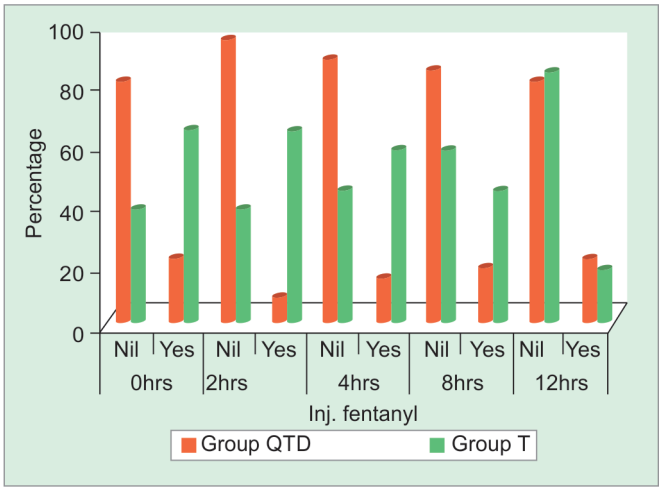
VAS, visual analog scale

VAS score	*Group QTD*	*Group T*	*p value*
0 hours	2.73 ± 1.74	5.63 ± 1.75	<0.001**
2 hours	2.43 ± 1.33	5.63 ± 1.75	<0.001**
4 hours	2.50 ± 0.90	5.37 ± 1.90	<0.001**
8 hours	2.83 ± 1.05	4.73 ± 1.55	<0.001**
12 hours	3.10 ± 1.32	3.83 ± 1.53	0.052+



VAS, visual analog scale
Student't *t*-test (two-tailed, independent)
Fig. 3: VAS score comparison in two groups of patients studied at different study points

Inj. fentanyl	*Group QTD (n = 30)*	*Group T (n = 30)*	*Total (n = 60)*	*p value*
0 hours				
Nil	24 (80%)	11 (36.7%)	35 (58.3%)	0.001**
Yes	6 (20.0%)	19 (63.3%)	25	
2 hours				
No	28 (93.3%)	11 (36.7%)	39 (65%)	<0.001**
Yes	2 (6.7%)	19 (63.3%)	21 (35%)	
4 hours				
No	26 (86.7%)	13 (43.3%)	39 (65%)	<0.001**
Yes	4 (13.3%)	17 (56.7%)	21 (35%)	
8 hours				
No	25 (83.3%)	17 (56.7%)	42 (70%)	0.024*
Yes	5 (16.7%)	13 (43.3%)	18 (30%)	
12 hours				
No	24 (80%)	25 (83.3%)	49 (81.7%)	0.739
Yes	6 (20%)	5 (16.7%)	11 (18.3%)	



Chi-square/Fisher's exact test
Fig. 4: Inj. fentanyl distribution in two groups of patients studied

ischemia, decrease in alveolar ventilation, immobility, deep venous thrombosis, and poor wound healing.[1]

The analgesic benefits of controlling postoperative pain are generally maximized when a multimodal strategy to facilitate the patient's convalescence is implemented.[1] The concept of multimodal analgesia was introduced more than a decade ago as a technique to improve analgesia and reduce the incidence of opioid-related adverse events. Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms at different sites in the nervous system, reducing the incidence of side effects owing to the lower doses of the individual drugs.

In the study conducted by Buvanendran and Kroin in 2009, a lower incidence of adverse effects and improved analgesia has been demonstrated with multimodal analgesia techniques, which may

Table 2: Total number of rescue analgesics used distribution in two groups of patients studied

Total number of rescue analgesics used	*Group QTD (%)*	*Group T (%)*	*Total (%)*
0 numbers	15 (50)	10 (33.3)	25 (41.7)
1 numbers	11 (36.7)	1 (3.3)	12 (20)
2 numbers	2 (6.7)	3 (10)	5 (8.3)
3 numbers	2 (6.7)	3 (10)	5 (8.3)
4 numbers	0 (0)	8 (26.7)	8 (13.3)
5 numbers	0 (0)	5 (16.7)	5 (8.3)
Total	30 (100)	30 (100)	60 (100)

Complications	*Group QTD (n = 30)*	*Group T (n = 30)*
Gastric irritation	0	0
Nausea	1 (3.3)	1 (3.3)
Headache	0 (0)	1 (3.3)
Pain due to full bladder	1 (3.3)	0 (0)
Respiratory depression	0	0
Vomiting	0	0

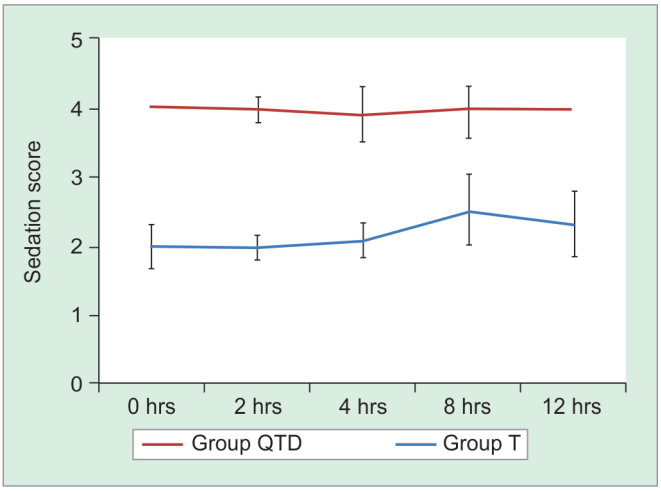


Fig. 5: Complications that occurred in the postoperative care unit among patients of the two groups

provide for shorter hospitalization times, improved recovery and function, and possibly decreased healthcare costs. In our study, we compared the efficacy of analgesia provided by the unimodal approach (tramadol only) and the multimodal approach (QLB + tramadol + diclofenac). In Tables 1 and 2, we can see that the VAS scores of the patients belonging to the multimodal group were significantly less (average VAS score of 2.3 ± 0.5) than the unimodal group (average VAS score was 5.5 ± 1), thereby proving the efficacy (*p* value <0.001) of multimodal analgesia.

Opioid analgesics continue to play an important role in the acute treatment of moderate-to-severe pain in the early postoperative period.[1] Their effects can be summarized as hyperpolarization of first- and second-order sensory neurons, with inhibition of synaptic transmission. They act by binding to μ receptors, which initially results in increased G protein activity.[1] Tramadol and fentanyl belonging to this class of drugs are commonly used for postoperative pain relief. However, the problem with these drugs is the variety of perioperative complications, e.g., drowsiness and sedation, postoperative nausea and vomiting (PONV), pruritus, urinary retention, constipation, and ventilatory depression.

In a study conducted by Padmaja et al., in 2014, they compared the efficacy of multimodal analgesia by epidural anesthesia, intravenous opioid intermittent doses, and intravenous opioid infusions. They concluded that in the opioid group (both intermittent bolus and infusion) the incidence of nausea and vomiting was significant with nausea scores >1. In our study though, there was no significant increase in PONV, sedation seen among the T only patients were high (with *p* value <0.001).

Non-steroidal anti-inflammatory drugs inhibit the synthesis of prostaglandins both in the spinal cord and at the periphery, thus diminishing the hyperalgesic state after surgical trauma.[1] Non-steroidal anti-inflammatory drug use is not appropriate in all patients because of their age or renal or hematological status or because of previous dyspeptic symptoms. Study[1] has shown that the addition of an NSAID to an opioid not only decreases the adverse effects but also has an opioid-sparing action. Diclofenac used in our study helped in providing better analgesia in the QTD group (average VAS score was 2.3 ± 0.5) and probably also played a role in decreasing the complications associated with tramadol (sedation) which was seen in the tramadol only group (*p* value for sedation score <0.001).

The main motto of our study was to reduce the use of opioid analgesics to as minimum as possible and provide analgesia devoid of all the above-mentioned complications. By using a combination of QLB, tramadol, and diclofenac, the total number of rescue analgesic fentanyl used was significantly reduced. Four out of 30 patients required more than one dose in the QTD group, but 19/30 required multiple doses of rescue analgesia in the T group, this also resulted in opioid-sparing.

A study was conducted by Blanco et al., in 2015, for postoperative analgesia after cesarean section using QLB vs patient-controlled intravenous morphine doses. In this study, they found that the patients who received QLB had significantly less morphine consumption than the control group 6 and 12 hours after the operation. They also had significantly fewer morphine demands at all time points after cesarean section. The VAS scores were significantly better at every observation time in the QLB group than in control patients. Similarly, in our study, we saw that patients belonging to the QTD group had better VAS scores (*p* value < 0.001), less fentanyl consumption, and decreased side effects.

Kadam described ultrasound-guided QL block with a single-shot injection of 0.5% ropivacaine in a patient undergoing laparotomy for excision of a duodenal tumor. The block resulted in appropriate pain control during the first day after surgery.[5] In our study, we saw that the spread of the drug and the level of sensory block achieved by using the anterior approach is adequate and when supplemented with intravenous tramadol and diclofenac, provided remarkable postoperative analgesia (as seen by % of VAS scores in both the groups).[14,15]

Conclusion

By monitoring the VAS scores at regular intervals in the postoperative period, we observed that the postoperative analgesia after abdominal surgeries was better in the multimodal group than the unimodal group. We were able to overcome the adverse outcomes

which are associated with repeated high doses of opioid analgesics. By opting for a multimodal approach, we not only achieved better analgesia but also the duration of analgesia obtained was prolonged requiring a fewer number of rescue analgesics.

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