



Original Research Article

Tramadol-paracetamol combination for postoperative pain relief in elective single level lumbar microdiscectomy surgery: A comparison of two different doses of tramadol

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ABSTRACT

Background & Aims: Pain is a suffering and every individual has the right to be pain free. Moreover, pain in the post-operative period may lead to sense of being unwell as well as many complications like nausea, vomiting, hypertension, tachycardia, restricted mobility, breathlessness etc. Thus, it is essential to obtain sufficient pain relief in the perioperative period. The objective of our study was to compare the postoperative pain scores in patients receiving two different doses of tramadol, 1mg/kg and 1.5mg/kg in combination with paracetamol 1gm for elective single-level microdiscectomy.

Materials and Methods: Patients were randomly divided into two groups of thirty each. Group A received injection tramadol 1mg/kg intravenously and group B received injection tramadol 1.5mg/kg intravenously. In addition, both groups received injection paracetamol 1gm intravenous infusion. Pain intensity (VAS score) recorded at 1 minute, 30 minutes, 1 hour, 2, 3 and 4 hours in both the groups. Side effects like nausea, vomiting, sedation was also noted. Injection fentanyl 1 mcg/kg intravenously was used as rescue analgesic. Total dose of fentanyl used was also noted. Data was analyzed using appropriate statistical tests.

Results: On the basis of the present study, paracetamol(1g) and tramadol (1mg/kg or 1.5mg/kg) intravenously were found to be safe and effective in post-operative pain relief in elective single-level microdiscectomy surgery.

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1. Introduction

According to the American Society of Anesthesiologist practice guidelines, acute pain in the perioperative setting is defined as pain after a surgical procedure.¹ The World Health Organization and International Association for the Study of Pain have recognized pain relief as a human right.² Poorly managed postoperative pain can lead to complications and prolonged rehabilitation and may be associated with the development of chronic pain with the reduction in quality of life.^{3,4}

Recent trends in minimally invasive surgery and enhanced recovery protocols have addressed that effective postoperative pain control decreases postoperative

pain-related complications and improves patient outcome.⁵ The goal of postoperative pain management is to relieve pain while keeping side effects to a minimum. This is often best accomplished with a multimodal approach. Systemic opioids are regarded as the gold standard for the relief of postoperative pain; however, their use is limited by dose-related side effects.⁶ To overcome this problem, the adjunctive administration of analgesics that act via different mechanisms is recommended for effective postoperative pain control.

Tramadol has recently been recommended as the first-line drug for postsurgical pain because it does not cause significant respiratory depression, sedation, constipation and dizziness as compared to morphine.⁷

The objective of our study was to compare the postoperative pain score in patients receiving two

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different doses of tramadol 1mg/kg and 1.5mg/kg in combination with paracetamol 1gm for elective single-level microdiscectomy.

2. Materials and Methods

Following institutional ethics board approval and signed written informed consent, 60 American Society of Anesthesiologists (ASA) grade I and II patients scheduled for elective single-level microdiscectomy, aged 18-50 years were included in the study.

The exclusion criteria were age less than 18 years or more than 50 years, ASA $\geq$ III, patients with a history of drug abuse, allergic to analgesics, hepatic dysfunction; and those on steroids, opioids or any other drug therapy.

The study was planned as a double blind, randomized comparative study. Patients were allocated randomly into one of the study groups using a computer-generated table. Group A (n=30) received intravenous injection tramadol 1 mg/kg, group B(n=30) received injection tramadol 1.5mg/kg intravenously. In addition, all the patients received injection paracetamol 1 gram intravenously after endotracheal intubation. The study drugs were supplied as clear transparent solutions in pre filled syringes diluted in normal saline to a total volume of 10 ml and were administered approximately 20 minutes before extubating. Neither the patient nor the anesthetist conducting the study were aware of the drug administered.

On receiving the patient in the operation theatre, routine monitoring was applied i.e. noninvasive blood pressure, pulse oximeter, electrocardiogram, end tidal CO₂ and these parameters were continuously monitored. After pre oxygenation for 3 minutes, injection midazolam was administered in the dose of 1mg intravenously; patients were anaesthetized using injection propofol 2mg/kg intravenously and intubated using succinyl choline 100mg intravenously. Anesthesia was maintained using inhalation of mixture of air: oxygen 50%, isoflurane 0.8%-1.2%; and injection vecuronium bromide intravenously as muscle relaxant. All the precautions were taken during prone positioning. When approximately 20 minutes were remaining for extubating, the study drugs were administered. Also all patients were administered injection ondansetron 4 mg intravenously. The reversal was done with injection neostigmine 0.05mg/kg and injection glycopyrrolate 0.01mg/kg in the usual manner in supine position.

After extubating, pain intensity was evaluated with a 10point visual analogue scale at 0minute, 30 minutes, 1 hour, 2 hours, 3 hours and 4 hours. (0=no pain, 10= severe pain)⁸. At VAS score >3 the rescue analgesia was administered in the form of injection fentanyl 1mcg/kg intravenously. Adverse events like sedation, nausea, vomiting, respiratory depression, pruritus was also assessed at these time points.

The primary outcome was pain scores at 3 hours post operatively. The secondary outcomes were vomiting and respiratory depression. Patients were considered to have completed the study if they had received at least one treatment dose and assessments of pain intensity with a 10-cm visual analog scale (VAS), pain relief ratings, and sustained adverse event 3 hours after taking study medication. There was no drop out in this study.

The statistical analyses were performed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). Patient demographic characteristics were presented as mean $\pm$ standard deviation for continuous variables and proportions for categorical variables. The comparison between the two groups was tested by Wilcoxon rank-sum test for continuous variables and by χ^2 test for categorical variables. The primary set of analysis data was an intent-to-treat population, that is, having completed a post-randomization efficacy assessment and taken the study medication.

The efficacy variables were the VAS changes from baseline after administration of a drug and the changes in VAS for each time point were presented by each group and analyzed by the signed-rank test. The incidence of adverse events was analyzed by the χ^2 test and Fisher's exact test. All statistical tests of the efficacy parameters were conducted at the two-sided, 5% significance level.

3. Results

Pain intensity (VAS score) recorded at 1 minute, 30 minutes, 1, 2, 3 and 4 hours in both the groups are illustrated in Table 2. At 1-minute assessment, group B i.e. patient on 1.5 gm tramadol helped decrease the mean pain intensity. Otherwise both the doses of tramadol were comparable in terms of beneficial and adverse effects.

4. Discussion

The goal for postoperative pain management is to reduce or eliminate pain and discomfort with a minimum of side effects. Although traditionally the mainstay of postoperative analgesia is opioid-based, increasingly more evidence exists to support a multimodal approach with the intent to reduce opioid side effects like nausea, vomiting, pruritus, sedation, respiratory depression, ileus etc. Moreover, enhanced recovery protocols to reduce the length of stay in surgery are becoming more prevalent and include multimodal opioid-sparing regimens as a critical component. Hence, postoperative pain can be managed by opioids like morphine, fentanyl, nalbuphine, butorphanol; or non-opioids like paracetamol, NSAIDs.

Microdiscectomy is one of the standard procedures for symptomatic disc herniation and involves removal of the portion of the intervertebral disc compressing the nerve root or spinal cord. The procedure causes moderate to severe

Table 1: Demographic variables and fentanyl dose

S. No.	Variable	Group A	Group B	P value
1	Age (years) (Mean $\pm$ SD)	46.13 $\pm$ 11.87	51.40 $\pm$ 16.51	0.123
2	Male: Female	16:14	15:15	
3	ASA I/II	23/7	22/8	
4	Weight(kg) (Mean $\pm$ SD)	71.93 $\pm$ 9.36	65.80 $\pm$ 11.83	0.181
5	Height(cm) (Mean $\pm$ SD)	169.57 $\pm$ 7.9	169.10 $\pm$ 7.9	0.753
6	Duration of surgery(hours)	2.837 $\pm$ 0.312	2.88 $\pm$ 0.215	0.366
7	Total Fentanyl dose (mcg)	210.30 $\pm$ 26.845	198.93 $\pm$ 36.585	0.175

Table 2: Comparison of post operative pain score

Time Interval	Group A		Group B		P-value
	MEAN	SD	MEAN	SD	
One min	0.30	0.83	0.13	0.43	0.043*
Thirty min	0.13	0.51	0.23	0.66	0.226
One hour	0.07	0.25	0.10	0.40	0.418
Two hours	0.17	0.64	0.20	0.66	0.736
Three hours	1.43	1.01	0.93	1.01	0.122
Four hours	3.50	0.57	3.33	0.60	1.0

Table 3: Comparison of side effects

		Group A	Group B	P-value
Sedation	Absent	4	5	0.478
	Present	26	25	
Nausea/ Vomiting	Absent	4	5	1.0
	Present	26	25	
Respiratory depression	Absent	30	30	-
	Present	0	0	
Pruritus	Absent	30	30	-
	Present	0	0	

pain which is most intense during the initial two weeks requiring combination of opioids and NSAIDs. Thereafter opioids may be discontinued and pain can be managed with NSAIDs or other non- opioid agents.

The goal of our study was to compare the postoperative pain score and adverse events in patients receiving two different doses of tramadol i.e.1mg/kg and 1.5mg/kg in combination with paracetamol 1gm intravenously as part of multimodal technique in elective single-level microdiscectomy. We chose single level so as to minimize the effect of procedure related factors such as duration of surgery, degree of pain caused etc. Various studies have been conducted so as to study various drugs alone and as combinations for multimodal analgesia technique.

A study compared the effect of fentanyl alone versus in combination with intravenous paracetamol after laparoscopic cholecystectomy and reported that mean VAS score in first and second hour after surgery and the fentanyl consumption over first 24 h was less in the group receiving injection paracetamol intravenously.⁸ We however administered paracetamol in both groups. This may be the reason that we did not obtain statistically different VAS scores in the study groups.

The combination of low-dose tramadol (1 mg/kg) and paracetamol was found to provide comparable analgesia and a decreased incidence of nausea and vomiting compared with the higher dose of tramadol (1.5 mg/kg) and paracetamol combination.⁹ We also used similar doses of tramadol and found them to be equally effective in terms of pain scores. However, we did not observe any difference in side effects like vomiting etc.in the two groups. This may be because we administered injection ondansetron 4 mg intravenously before completion of the surgery in all patients. They administered paracetamol at the end of surgery along with study drugs but we administered in the beginning of surgery.

Some observers compared the use of injection tramadol (1 mg/kg) alone and in combination with injection paracetamol (1 g) 30 minutes before the end of surgery. They concluded that administration of tramadol with paracetamol was more effective than tramadol alone for early acute postoperative pain therapy following lumbar discectomy.¹⁰ We also used a combination of these drugs but we compared two different doses of tramadol. Also, we administered paracetamol before the start of surgery. It was observed by some researchers observed that pre- emptive

paracetamol administration was found to be as effective as post-operative administration in providing post-operative analgesia.¹¹

In a study, immediately after dissection of the gallbladder, intravenous administration of injection tramadol 0.75 mg/kg (in normal saline; total volume, 5 mL), followed by injection paracetamol 1 g (100 mL) intravenously had significantly reduced postoperative pain scores, decreased postoperative analgesic requirements, and prolonged the time to first postoperative analgesia.¹² We used higher doses of tramadol assuming that microdissection causes greater pain.

Mohammed Jawad et al. conducted a comparative study of intravenous paracetamol versus tramadol for postoperative pain management in patients undergoing laparoscopic cholecystectomy. Paracetamol appeared as effective as tramadol in the management of mild to moderate pain in female patients, while tramadol seemed to be more effective than Paracetamol in male groups.¹³ This may be a coincidental finding; we did not find any such difference.

Findings in the present study will pave the way for further work on the issue. More studies on use of drugs with fewer side effects and optimum analgesic efficacy are recommended.

Limitations of our study were small sample size, lack of placebo arm, and these were reasons we could not draw further conclusions.

5. Conclusions

On the basis of the present study, combination of paracetamol with tramadol is safe and effective. Both doses of tramadol were comparable in terms of efficacy and safety. Although tramadol 1.5mg/kg showed better results in terms of significantly lower mean VAS pain scores for most of the postoperative follow-up intervals, it could not attain statistical significance. Thus, intravenous administration of paracetamol and tramadol can be safely and effectively recommended for postoperative pain relief in elective single-level microdissection surgery.

6. Source of Support

Nil.

7. Conflict of Interest

None.

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