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ORIGINAL RESEARCH

Analgesic Efficacy of Tramadol and Butorphanol in Mandibular Third Molar Surgery: A Comparative Study

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ABSTRACT

Background: Butorphanol tartrate, a mixed synthetic agonist-antagonist opioid analgesic has been used for management of postoperative pain in minor and major surgical procedures.[14,20] Tramadol hydrochloride is a centrally acting opioid which is effectively used in postoperative pain in various minor and major surgeries.

Materials and methods: Twenty subjects selected randomly received butorphanol tartrate 1 mg intramuscular and 20 subjects received tramadol hydrochloride 50 mg intramuscular after the removal of mandibular third molars. Time of injection, amount of anesthetic injected, duration of surgery, adverse effects were recorded.[21]

Results: The mean amount of LA administered in butorphanol group was 2.6450 ml and in tramadol group was 2.640 ml respectively, the mean duration for surgery was 56.75 and 53.5 minutes for butorphanol and tramadol groups respectively which was statistically not significant. Pain assessment was done with VAS which showed mean of 19.2 and 15.5 mm ($p = 0.001$) which was significant for butorphanol and tramadol respectively after 12 hours. The mean time for rescue medication requirement was 5.9 hours (for tramadol) and 8.4 hours (for butorphanol). Effective analgesic activity was seen by butorphanol 1 mg intramuscular then tramadol 50 mg.

Conclusion: Butorphanol 1 mg was more effective than tramadol 50 mg in respect to postoperative analgesia.

Keywords: Butorphanol, Tramadol, Third molar surgery, VAS, Pain, Analgasia.

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INTRODUCTION

Tramadol, a centrally acting opioid analgesic, is agonist of the μ opioid receptor.[5] The analgesic efficacy of tramadol has been demonstrated in different acute and chronic pain, being comparable with that of various other opioid and non-opioid analgesics several recent studies have confirmed that repeated intramuscular administration of tramadol can provide effective and well tolerated postoperative analgesia comparable to that with morphine, pentazocine, etc.[7,48]

Butorphanol is a mixed agonist-antagonist opioid. Exact mechanism of action is unknown. Opioid induced analgesia is thought to involve several neurotransmitters at many sites in central nervous system. Butorphanol has been marketed for parenteral use since 1978.[8] It has been used effectively in the management of moderate to severe postoperative pain.[6,50,51]

Third molar surgeries are the most common oral surgical procedures done routinely under local anesthesia.[45,46] Various opioids (morphine, tramadol, butorphanol, etc.) or non-opioid (diclofenac, ketorolac, ibuprofen, etc.) medications have been used effectively for the management of post-surgical pain.[13,44,49]

The purpose of this study is to evaluate the efficacy of postoperative analgesia by butorphanol tartrate 1 mg intramuscular in comparison with tramadol hydrochloride 50 mg intramuscular after removal of impacted mandibular third molars.

MATERIALS AND METHODS

This study was done on 40 patients with impacted asymptomatic mandibular third molars who had been treated at Department of Oral and Maxillofacial Surgery, KVG Dental College and Hospital, Sullia, Karnataka, India.

Criteria for Selection of Patients

1. Subjects between age group of 20 and 30 years.
2. Impacted mandibular third molars not associated with acute infection.
3. No concomitant medical problems.

Exclusion Criteria

1. Known or suspected allergies or sensitivities to sulfites, amide type local anesthetics or any ingredients in the anesthetic solution.
2. Concomitant cardiac or neurological disease.
3. Pregnancy/lactation.
4. Concomitant use of monoamine oxidase inhibitors, tricyclic antidepressants, phenothiazine, vasodepressor drugs or ergot type oxytocic drugs.
5. Subjects who are on sedatives.
6. History of chronic alcoholism or drug abuse.
7. Patients with local and systemic acute infections.
8. Subjects who had taken aspirin, acetaminophen, NSAIDS 24 hours prior to administration of local anesthetic.

All impactions were removed under, 2% lignocaine with 1:100000 adrenaline in an outpatient department. Post-operatively, amoxicillin 500 mg, thrice daily for 5 days for all the patients was standardized after 24 hours. Patients after the procedure asked to wait in the outpatient department for 1 hour after which the study medications given. Patients were divided randomly into two groups for recieving study medications.

- *Group A:* Butorphanol tartrate 1mg intramuscular was injected in the gluteus maximus muscle over the lateral aspect of buttocks.
- *Group B:* Tramadol hydrochloride 50 mg intramuscular was injected in the gluteus maximus muscle over the lateral aspect of buttocks.

Acquisition of Data

All patients were explained about the study medications which were used. Time of injection, amount of anesthetic injected, duration of surgery, efficacy, adverse events and the need of rescue medication were recorded. The performa was filled by the patient based on their pain experiences postoperatively. They were told to report to the doctor about time of experiencing pain as soon as noticed. All patients were reviewed next day.

Assessment of Pain

Visual analog scale was used for the assessment of post-operative pain. The assessment was done postoperatively 6th hour, 12th hour after injection of study medications. If the patient needed rescue medication, the time of taking medication along with the VAS rating at the time was recorded.

PARAMETERS

Drug Volume

Amount of local anesthetic used (volume in ml) in each case was recorded.

Duration of Surgery

Time taken for the surgical procedure was recorded.

Pain Assessments

Patients were asked to record on 100 mm visual analog scale (VAS), the pain intensity at 6th hour, 12th hour after study medications given postoperatively or when the rescue medication becomes necessary for the patient. If the patient takes rescue medication, the time of this event was recorded and also the VAS rating at the time was recorded. With 0—no pain and 100—worst pain possible.

Safety Assessments

Safety and drug tolerability was assessed by vital sign measurements and reports of adverse drug reactions.[52]

Overall Evaluation

The overall evaluation of the study medications was recorded by the patient on a five point categorical scale at the end of the trial. The categories of scale were 0—poor, 1—fair, 2—good, 3—very good, 4—excellent. Excellent—minimum pain and adverse events and poor—severe pain and adverse events.

RESULTS

Demographic Profile

We randomized 40 patients into:

- *Group A:* Consisting of 20 subjects with mean age of 23.15 years, including 10 females and 10 males, with mean weight 56.85 kg, who received butorphanol 1mg intramuscular postoperatively after surgical removal of impacted mandibular third molars.
- *Group B:* Consisting of 20 subjects with mean age 20.75 years, including 12 males and 8 females, with mean weight of 56.85 kg, who received tramadol 50 mg intramuscular postoperatively after surgical removal of impacted mandibular third molars.

Even though, there were differences in the mean age, sex distribution, weight of the study subjects, statistically there was no significance. Student's t-test was done for weight and age profile, Chi-square test was done for sex distribution. Results summarized in Tables 1A to C.

Amount of Local Anesthesia

The surgical removal of mandibular third molars was done under 2% lignocaine with 1:100000 epinephrine. The amount of LA administered was noted. The mean amount of LA administered in butorphanol group was 2.6450 ml

Table 1A: Weight

Groups	N	Mean	Std. deviation	t
Tramadol	20	57.2500	8.85482	0.14500
Butorphanol	20	56.8500	8.61012	p = 0.886 NS

NS: Not significant

Table 1B: Sex* group

			Groups		Total
			Tramadol	Butorphanol	
Sex	M	Count	12	10	22
		%	60.0%	50.0%	55.0%
	F	Count	8	10	18
		%	40.0%	50.0%	45.0%
Total		Count	20	20	40
		%	100.0%	100.0%	100.0%

χ^2: 0.404; p: 0.525 NS

Table 1C: Age

Groups	N	Mean	Std. deviation	t
Tramadol	20	20.7500	6.71115	1.35700
Butorphanol	20	23.1500	4.18361	p = 0.186 NS

NS: Not significant

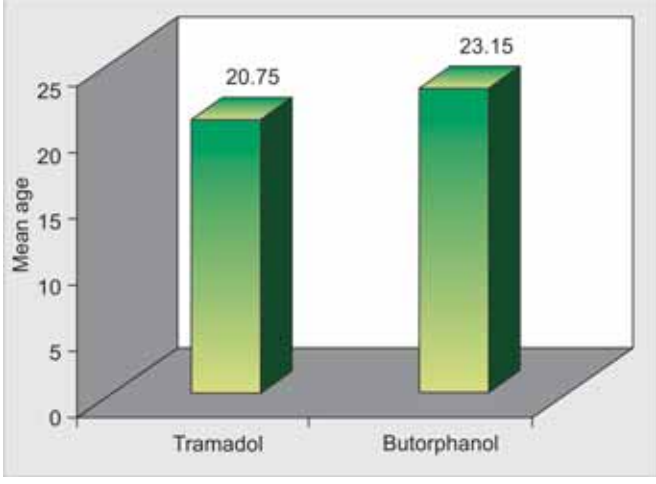

Fig. 1A: Age distribution

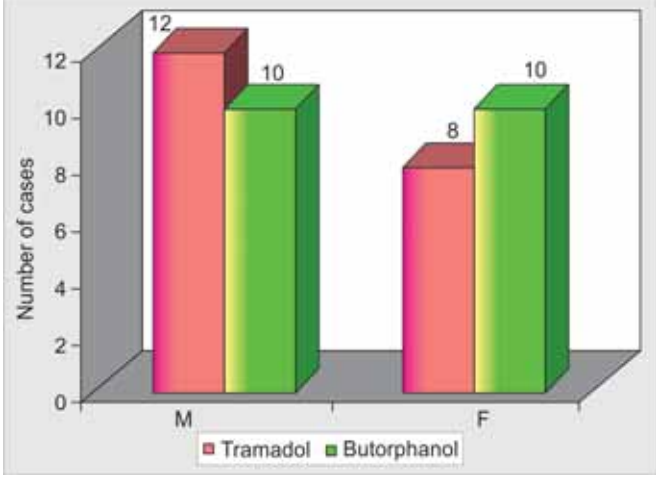

Fig. 1B: Sex distribution

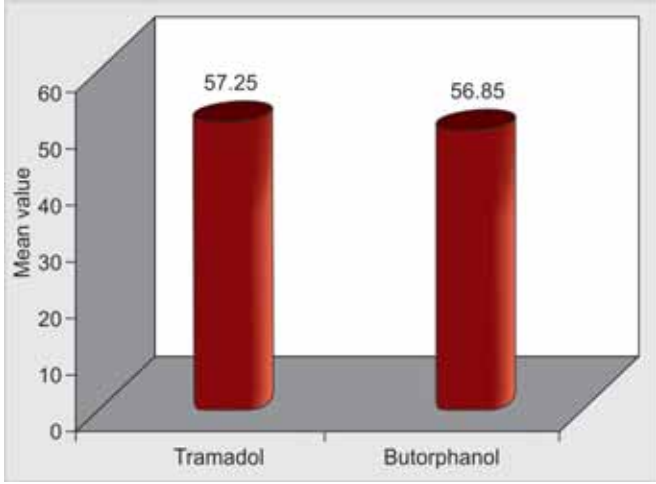

Fig. 1C: Weight

and in tramadol group was 2.640 ml respectively without any statistical significance. The statistical analysis used to analyze this data was done by Mann-Whitney U test. Results summarized in Table 2.

Table 2: Amount of LA

Groups	N	Mean	Std. deviation	Z
Tramadol	20	2.6400	0.57619	0.02900
Butorphanol	20	2.6450	0.50729	p = 0.977 NS

Z: Mann-Whitney U test; NS: Not significant

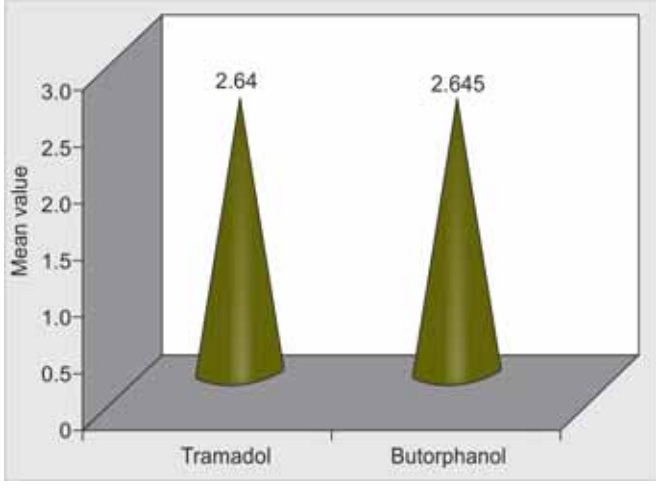

Fig. 2: Amount of LA

Duration of Surgery

Duration of surgery was defined as the total time taken from the injection of LA to the closure of the mucoperiosteal flap. The mean duration taken for the butorphanol group was 56.75 minutes and tramadol group was 53.50 minutes. Although there was a difference in the duration of surgery, statistically was not significant. The statistical analysis that was used was Mann-Whitney U test. Results tabulated in Table 3.

Table 3: Duration of surgery

Groups	*N*	*Mean*	*Std. deviation*	*Z*
Tramadol	20	53.5000	26.95513	0.36700
Butorphanol	20	56.7500	29.07680	p = 0.716 NS

NS: Not significant

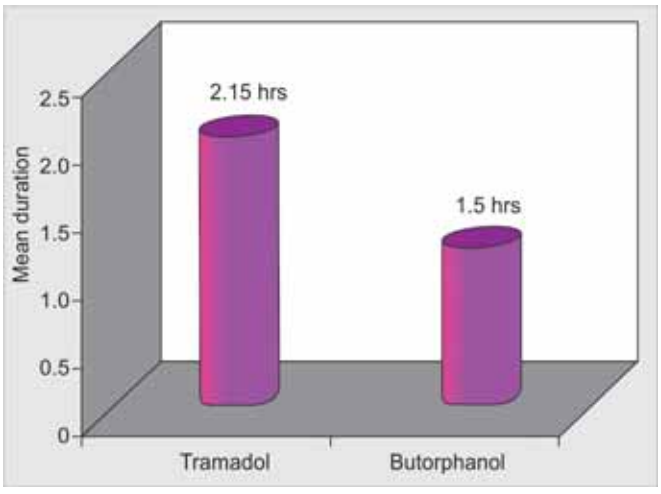

Fig. 3: Duration of surgery

Pain Assessment

Pain assessment was done by recording the intensity of pain twice in 12 hours with 100 mm VAS or when there was a necessity for the rescue medication (diclofenac, ibuprofen, etc). The statistical analysis used was Mann-Whitney U test. The mean VAS for butorphanol group was 15.50 mm and for tramadol group was 19.20 mm which was statistically significant (p = 0.001), the mean time of rescue medication was 8.400 hours for butorphanol group and 6.34 hours for tramadol group which was statistical significant (p = 0.001). The study showed butorphanol 1mg IM is much effective in controlling postoperative pain than Tramadol 50 mg IM. Results summarized in Tables 4A and B.

Table 4A: Pain assessment—VAS

Groups	*N*	*Mean*	*Std. deviation*	*Z*
Tramadol	20	19.2000	3.17225	3.87700
Butorphanol	20	15.5000	2.83772	p = 0.001 VHS

VHS: Very highly significant

Table 4B: Time for rescue medications

Groups	*N*	*Mean*	*Std. deviation*	*Z*
Tramadol	19	5.9368	0.90567	5.92500
Butorphanol	15	8.4000	1.50238	p = 0.001 VHS

VHS: Very highly significant

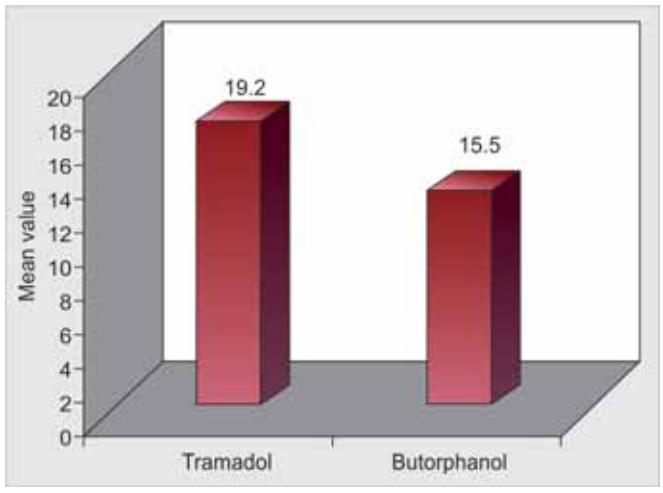

Fig. 4A: Pain assessment—VAS

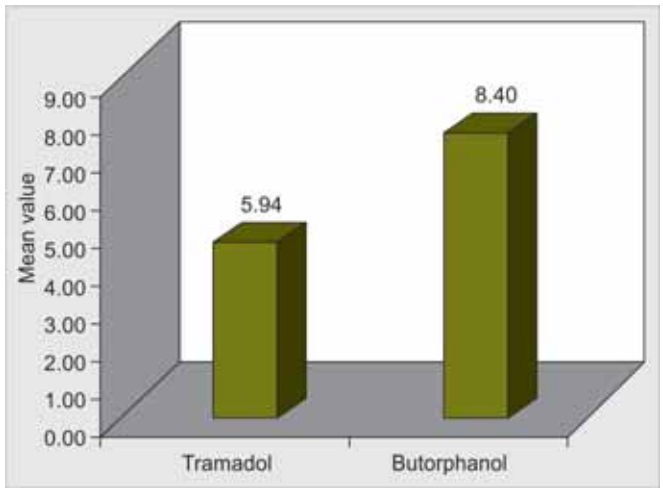

Fig. 4B: Time for rescue medications

Overall Evaluation

Patients were asked to provide an overall evaluation of the efficacy of study medication with regard to pain and adverse events on a five point categorical scale, at the end of the trial. The categories of scale were 0—poor, 1—fair, 2—good, 3—very good, 4—excellent. Excellent—minimum pain, no or mild adverse events, Poor—lots of pain, moderate to severe adverse events. In the butorphanol group, six patients complained of nausea, dizziness, where as in tramadol group only four patients experienced mild nausea. The overall evaluation noted by butorphanol group was 0 = 1; 1 = 9; 2 = 9; 3 = 1; 4 = 0, where as that given by tramadol group was 0 = 0; 1 = 5; 2 = 9; 3 = 4; 4 = 2. The statistical test used was Chi-square test. Even though there was slight higher adverse events noted by butorphanol group compared to tramadol group it was not statistically significant (χ^2 = 5.943 p = 0.203), results summarized in Tables 5A and B.

Table 5A: Overall evaluation* group

			Groups		Total
			Tramadol	Butorphanol	
Overall evaluation	0.00	Count	0	1	1
		%	0.0%	5.0%	2.5%
	1.00	Count	5	9	14
		%	25.0%	45.0%	35.0%
	2.00	Count	9	9	18
		%	45.0%	45.0%	45.0%
	3.00	Count	4	1	5
		%	20.0%	5.0%	12.5%
	4.00	Count	2	0	2
		%	10.0%	0%	5.0%
Total		Count	20	20	40
		%	100.0%	100.0%	100.0%

$\chi^2 = 5.943$; p = 0.203 NS

Table 5B: Overall evaluation

Groups	N	Mean	Std. deviation	Z
Tramadol	20	2.1500	0.93330	2.21100
Butorphanol	20	1.5000	0.68825	p = 0.027 Sig

Sig: Significant

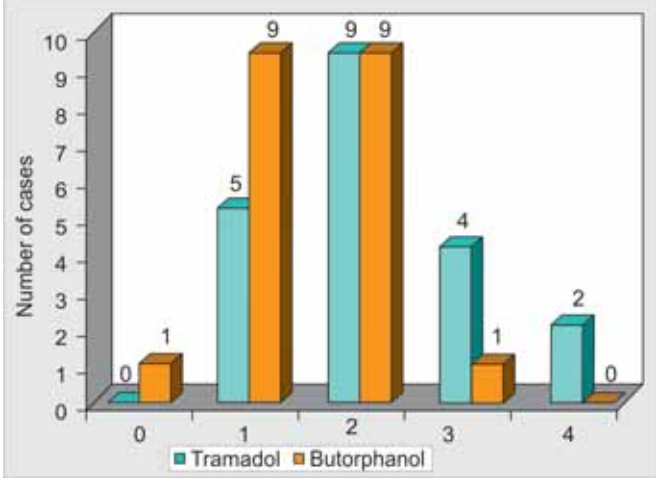

Fig. 5: Overall evaluation

Butorphanol 1 mg IM was comparable with tramadol 50 mg IM with respect to adverse events and overall evaluation.

DISCUSSION

Butorphanol is used to treat moderate to severe acute pain. Butorphanol injection was approved in 1978; the nasal spray was approved in 1991,[4] it is agonist at kappa-receptor, but is a weak antagonist at μ-receptor.[16] Several clinical studies with the injectable form of butorphanol have shown its effectiveness in relieving moderate-to-severe postoperative pain.[31] Tramadol a weak opioid which acts on μ receptor has been most commonly used for management of post-operative pain. Tramadol has been chosen as a reference substance, as its effects are well documented. Since the study used identical protocols, the result obtained were comparable, combine analysis of the trial was valid.

The aim of this study was to know the efficacy of butorphanol in comparison with tramadol with regard to postoperative pain. The patient's age, gender, weight, amount of local anesthesia, duration of surgery was statistically not significant in two groups. Therefore, the effect of age, gender, weight, amount of local anesthesia and duration of surgery would be minimized.

The study shows that postoperative intramuscular butorphanol is better than tramadol in preventing postoperative pain after removal of impacted mandibular third molars. Seymour et al[16] have studied that the pain after complex dentoalveolar procedures is most severe between 6 and 8 hours. In our study, the mean analgesic duration is 8.40 hours for butorphanol group is clinically significant as pain for this type of procedure is usually most severe between 6 and 8 hours after the surgery according to various studies.[1,26,27,29,32,33,35] This analgesic technique provides adequate analgesic coverage during the 8-hour peak pain period and is an advantage.[37] When tramadol was administered postoperatively in this study, it has a mean analgesic duration of 6.34 hours. The analgesic effect of the drug would be reducing at the time when the postoperative pain would be at its peak.

Analgesia after impacted third molar surgery is necessarily a balance between achieving adequate pain relief, whilst causing minimum side effects.[15,17,19,30] The five-point categorical overall evaluation (0—poor *vs* 4—excellent) of the study medication in relation to pain control and adverse events, showed 0 = 1; 1 = 9; 2 = 9; 3 = 1; 4 = 0; for butorphanol group and 0 = 0; 1 = 5; 2 = 9; 3 = 4; 4 = 2 for tramadol group which was statistically not significant (p = 0.203). In the study, six patients in the butorphanol group had experienced nausea and dizziness which was seen mostly within 2 hours of administration and did not require any antiemetics or H_2 blocker, while only four patients in the tramadol group experienced mild nausea within half an hour of administration.

Many studies have shown that adjunctive preemptive or postoperative analgesic administration will reduce overall postoperative discomfort with relation to pain. The concept of using analgesics postoperatively before the onset of significant pain ('preventive analgesia') has been used.[8,9,11,12,15] Each of these modalities has lead to decreased total pain after surgery and decreased pain intensity at fixed postoperative time intervals when measured by visual analog scale.[22,33] In our study, the administration of the study medications was followed after 1 hour postoperative period. The intensity of pain was evaluated with VAS twice in 12 hours or when there was necessity of rescue medication.

Arend et al[10] have shown that tramadol has an analgesic effect equivalent to pentazocine but with fewer side effects. The butorphanol group experienced slightly higher adverse events then tramadol group in our study although it was not significant statistically. The common side effect encountered with butorphanol group in our study was nausea and dizziness which was experienced by six (25%) patients. Only four (20%) patients in tramadol group experienced mild nausea. No patient required any symptomatic medications for the side effects and lasted till few minutes.

We found VAS scores between 0 and 100 and significant difference in pain experience with butorphanol and tramadol. Four patients reported no pain and also had not taken any rescue medications for 24 hours in butorphanol group when compared to tramadol group; mild-to-moderate pain was experienced by both the groups with a mean analgesic time of 8.40 hours for butorphanol and 6.34 hours for tramadol group. Pain measurement is difficult to establish, because its perception and intensity are multifactorial, encompassing sensorial and affective factors.[42,43,47] Although VAS may show deficiencies regarding understanding and perception, it provides a validated and meaningful measure of anesthetic efficiency, being used for this purpose by many authors.[3,23,30,31,34,36]

Multiple variable factors exist, like technique variability, anatomic variations, complexity of procedure and reporting error. Pain itself is multifactorial; perception and pain reaction varies greatly among individuals.[24,25,33]

CONCLUSION

In this randomized parallel group study, the following conclusions were drawn; butorphanol 1 mg IM is adequate for postoperative analgesia after surgical removal of mandibular third molar impactions. It is more efficacious than tramadol 50 mg IM in controlling postoperative pain following removal of impacted mandibular third molars and also has longer duration of action. There were no significant differences in postoperative complications.

Hence, butorphanol can be used as an alternative to tramadol for postoperative analgesia after impacted third molar surgeries.

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