Section: Anaesthesia

Original Research Article

A COMPARATIVE STUDY BETWEEN TAPENTADOL AND TRAMADOL TO ALLEVIATE POSTOPERATIVE PAIN IN SINGLE-LEVEL LUMBAR LAMINECTOMY CASES DONE UNDER GENERAL ANAESTHESIA

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Abstract

Background: we want to compare the effects of Tapentadol and Tramadol for single-level lumbar laminectomy cases done under general anaesthesia to treat postoperative pain. **Materials and Methods:** was a prospective, randomized, comparative study conducted at ACSR Medical College, from March 2019 to April 2020 after obtaining Institutional Ethics Committee approval. **Results:** Analysis between the two groups demonstrated that VAS scores were comparable in both groups. However, the quality of analgesia was better in the Tapentadol group compared with the Tramadol group till our follow-up period of 4 hours postoperatively. Rescue analgesia requirement was higher in the Tramadol group compared to the Tapentadol group and this result was statistically significant. ($p = 0.02$). The duration of analgesia was longer in the Tapentadol group compared with tramadol and this was statistically significant. ($p = 0.03$). The Incidence of post-operative nausea and vomiting was comparable in both tramadol and tapentadol groups. Both oral tramadol and tapentadol may be used effectively in the prevention of post-anesthesia shivering. **Conclusion:** Tapentadol was better than Tramadol in quality of analgesia, duration of analgesia & and need of rescue analgesic time was longer for Tapentadol compared to Tramadol.

INTRODUCTION

Postoperative pain management is considered one of the challenging issues in anaesthesiology and an important part of a health professional's commitment. Proper management of it results in early mobilisation, increased patient satisfaction, and reduced hospitalisation period and costs.[1,2,3] After surgery, severe pain is experienced by 50% - 70% of patients postoperatively, while a further 20%-40% of patients experience moderate pain.[4] Postoperative pain not only causes considerable distress to the patient, it also contributes to prolonged recovery time and may adversely affect patient outcomes. Despite well-known disadvantages including respiratory depression and hypotension, opioid analgesics are the traditional first-line treatment in postoperative pain. Although opioids are effective analgesic drugs with no ceiling in their analgesic effect, their efficacy is often limited by their tolerability profile, therefore inadequate postoperative analgesia has been a problem for several decades. Opioids are a group of agents widely used for mentioned purposes but some side effects of them have limited their use. Synthetic opioids such as tramadol and newer agents like tapentadol have fewer side effects, especially respiratory depression, tolerance and dependence. Tramadol is a mixed centrally-acting opioid analgesic used to relieve moderate to severe pain. Tramadol exerts its analgesic effect through at least two complementary and synergistic mechanisms: by activating the μ-opioid receptor and inhibiting the neurotransmitter reuptake. Tapentadol is a centrally-acting drug with a combined mechanism of action. Tapentadol is a μ-opioid receptor (MOR) agonist (its affinity for the MOR is 50 times less than that of morphine) and inhibits neuronal reuptake of norepinephrine.[5,6] Both mechanisms act synergistically to produce analgesia.[7] Animal studies indicate that the opioidergic component is more important in the treatment of acute pain, whereas the noradrenergic component is largely involved in the treatment of chronic neuropathic pain.[8] The drug has better gastrointestinal tolerance and also can be safely used in patients with renal impairment. Recent evidence suggests that the administration of oral analgesics is more favourable for postoperative pain relief.[9,10,11] This mode of

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administration not only provides appropriate pain relief but also has other advantages such as ease of administration and low cost. We hypothesised that oral tapentadol is equally effective as oral tramadol in the treatment of acute post-operative pain in patients undergoing single-level lumbar laminectomy under general anaesthesia.

Aims & Objectives

Primary objective: The primary objective of our study was to compare postoperative pain severity using visual analogue scale grading with oral tapentadol versus oral tramadol in patients undergoing single-level lumbar laminectomy under general anaesthesia.

Secondary objective: Was to compare

a. Duration of analgesia, i.e., time for rescue analgesia requirement.
b. Rescue analgesic requirement.
c. Haemodynamic parameters.
d. Post-operative nausea and vomiting/shivering and other side effects with oral tapentadol versus oral tramadol in patients undergoing single-level lumbar laminectomy under general anaesthesia.

MATERIALS AND METHODS

Study Design: A prospective, randomised, comparative study was conducted after Institutional Ethics Committee approval.

Study Site: The study was conducted at ACSR Medical College, from March 2019 TO April 2020

Study Population: The study recruited adult patients, between the ages of 18 to 60 years, who were ASA I and ASA II, of both sexes, presenting for elective single-level lumbar laminectomy under general anaesthesia.

Sample Size Estimation: The sample size for the study was estimated by taking into consideration the results of a previous study by Pradeep et al,[128] In this study, the pain score 1 hour after extubation was 2 ± 1.08 in Group Tramadol and 2.92 ± 1.23 in Group Pregabalin. The effect size was calculated and it was 0.79.

The overall effect size was used to estimate sample size by the software G*Power 3.1.7 (Olshausenstr Kiel, Germany). The calculation is as follows: t-tests - Means: Wilcoxon-Mann-Whitney test (two groups)

Options: **A.R.E. method**

Analysis: A priori: Compute required sample size

Input: Tail(s) = Two
Parent distribution = Normal
Effect size d = 0.7948628
α err prob = 0.05
Power (1-β err prob) = 0.80
Allocation ratio N2/N1 = 1

Output: Noncentrality parameter δ = 2.9063096
Critical t = 2.0071331
Df = 51.4760609
Sample size group 1 = 28
Sample size group 2 = 28
Total sample size = 56
Actual power = 0.8137318.

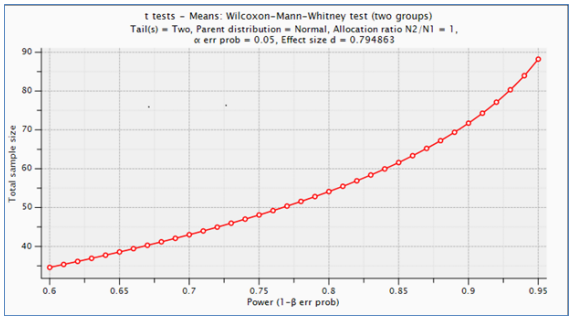

Figure 1: Graph depicting the Power analysis and Sample size

As dropout of cases would be expected, a sample size of 30 was selected for the study even though in the power analysis the sample size estimated was 28 with α = 0.05, power of (1- β) = 0 .80 and effect size = 0.8.

Sampling Procedure

The patients were assigned to one of the following two groups using simple randomisation, according to the computer-generated table of random numbers [MS – excel, and (0,1)].

GROUP TRA: Consists of 30 patients who received 100mg oral Tramadol IR 1 hour before surgery.

GROUP TAP: Consists of 30 patients who received 100 mg oral Tapentadol IR 1 hour before surgery.

Selection of Study Participants:

Inclusion Criteria

a. ASA I /II patients.
b. Patients undergoing elective single-level lumbar laminectomy procedure under general anaesthesia.
c. Age group 18- 60 years.
d. Duration of surgery < 2 hrs.

Exclusion Criteria

a. ASA – III and IV.
b. Creatinine > 2 mg/dl.
c. Bronchial asthma.
d. All contraindications to general anaesthesia like upper respiratory infection, full stomach etc.
e. The use of centrally acting substances during the study (i.e., hypnotics, sedatives, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and sympathomimetic amines)
f. Any history of upper gastrointestinal disorder within 6 months.
g. Hepatic disease
h. Raised Intra cranial tension
i. History of seizures

Procedure: Pre-operatively, the patient was explained about the study, visual analogue pain score and method of calculation in the pre-anaesthetic checkup. An informed written consent

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was obtained and demographic profiles such as height, weight, age and gender were noted. No pre-medication was administered to the recruited patients. On the day of surgery, all sixty patients were randomly allocated to receive 100 mg of either oral Tramadol IR or tapentadol IR one hour before the scheduled surgery time. The anaesthetic management of the patients was performed according to the standard protocol similarly in the two study groups. The anaesthesia was induced with IV fentanyl 2 μg/kg, atracurium 0.5 mg/kg and sodium thiopental 5 mg/kg. After orotracheal intubation, anaesthesia was maintained with air 50% in oxygen and isoflurane 1-1.5%.

Vital signs, oxygen saturation, electrocardiography (ECG), non-invasive blood pressure (NIBP), pulse oximetry (SpO2), and end-tidal carbon dioxide (EtCO2) were recorded before and during surgery. EtCO2 during surgery was maintained at 30-35 mmHg and depth of anaesthesia at 1-1.2 MAC isoflurane. Systolic and diastolic blood pressure and pulse rate were measured before the start of surgery (baseline), intraoperatively at post induction, 5, 10, 30, 60, 90 and 120 mins. Residual neuromuscular blockade was antagonised using neostigmine 0.04 mg/kg and glycopyrrolate 10 mcg/ kg at the end of surgery. After completion of surgery, no local infiltration was given at the operative site. When the patient had adequate respiratory efforts and responded to verbal commands properly, the trachea was extubated. After surgery, all patients were evaluated for postoperative pain. Severity of pain was assessed using Visual Analogue Scale (VAS) at immediate post extubation, 1, 2 and 4 hrs after surgery. VAS upto 3 was taken as mild grade; 4 to 7 was taken as moderate grade; 7 to 10 was taken as severe grade. Rescue analgesia (IV paracetamol 1 gm) was given to patients whenever the VAS score was greater than 3. Any episode of nausea, retching and vomiting was recorded, assessed and evaluated on a four-point PONV ordinal scale: 0 = none, 1 = nausea and no vomiting, 2 = one episode of vomiting, 3 = more than one episode of vomiting. In case of any event of nausea and vomiting, this was noted and intravenous ondansetron 4mg was administered as the rescue drug. Other side effects of the study drug including constipation, lightheadedness, dizziness, drowsiness, headache, seizure, fever, diarrhoea, rash and itching were recorded.

Data recording and Statistical analysis

All the data was collected, tabulated and checked for correctness and consistency. There were no dropouts during the study. Statistical analysis was carried out using NCSS 9 version 9.0.8 statistical software. Continuous data were represented as mean (SD), both categorical data and ordinal data as frequency and percentages. The normality distribution of data was assessed graphically and by Shapiro Wilk W test. Equality of variance was also assessed, by the modified-Levene Equal-Variance test, for all the parameters. The imbalance of baseline parameters was assessed by the Chi-square test and observing the mean values in the two groups.

Table 1: Normality test for AGE and MAP in both Groups

Group Variable	Shapiro Wilk W test statistic	P Value	Decision (5%)
GROUP TRA (AGE)	0.98	0.80	Can't reject normality
GROUP TAP (AGE)	0.96	0.40	Can't reject normality
GROUP TRA (MAP bl)	0.96	0.26	Can't reject normality
GROUP TAP (MAP bl)	0.99	0.99	Can't reject normality

Table 2: Equality of variance test for AGE and MAP in both Groups

Group Variable Name	Modified-Levene Equal-Variance Test	p-Value	Decision (5%)
Group TRA and Group TAP (AGE)	0.176	0.675	Can't reject normality
Group TRA and Group TAP (MAP bl)	1.57	0.27	Can't reject normality

RESULTS

The data was collected for all 60 recruited patients of either gender who underwent single-level lumbar laminectomy for PIVD under general anaesthesia. This was tabulated and analysed and the following observations were made.

Demographic data

The two groups were comparable in terms of demographic data as there were no significant differences in terms of age, weight, height, sex, body mass index (BMI) and ASA grading.

VAS SCORE AT POST EXTUBATION

VAS score at post-extubation was comparable between both groups. The p-value calculated by the Pearsons' Chi-square test was P = 0.12. So, the VAS score at post-extubation was not statistically significant between both groups.

VAS score at 1 hour

VAS score at 1 hour was comparable between both the groups. The p-value calculated by the Pearsons' Chi-square test was P = 0.137. So, the VAS score at 1 hour was not statistically significant between both groups. (Table 7) (Fig 12) Patients with VAS scores of moderate & severe grades were higher in the tramadol group compared to the tapentadol group at 1 hour after surgery. One (3.3%) & seven (23%) patients in the tramadol group compared to three (10%) & two (6.6%) patients in the tapentadol group had moderate and severe VAS scores respectively.

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VAS SCORE AT 2 Hours

VAS score at 2 hours was comparable between both the groups. The p value calculated by the Pearsons' Chi-square test was P = 0.167. So, the VAS score at 2 hours was not statistically significant between both groups. Patients with VAS scores of moderate & severe grades were higher in the tramadol group compared to the tapentadol group at 2 hrs after surgery. Fourteen (46%) & three (10%) patients in the tramadol group compared to nine (30%) & one (3.3%) patients in the tapentadol group had moderate and severe VAS scores respectively.

VAS SCORE AT 4 HOURS

VAS score at 4 hours was comparable between both the groups. The p-value calculated by the Pearsons' Chi-square test was P = 0.06. So, the VAS score at 4 hours after surgery was not statistically significant between both groups. (Table 9, Fig 14) Patients with VAS scores of moderate & severe grades were higher in the tramadol group compared to the tapentadol group at 4 hrs after surgery. Thirteen (43%) & five (16%) patients in the tramadol group compared to seventeen (56%) & 0(0%) patients in the tapentadol group had moderate and severe VAS scores respectively.

COMPARISON OF DURATION OF ANALGESIA IN TWO GROUPS

The time for rescue analgesia requirement was statistically significant between both groups. (p-value = 0.04) The mean time for rescue medication requirement was 274 min (for Tramadol) and 336 min (for Tapentadol)

COMPARISON OF RESCUE ANALGESIA (IV PARACETAMOL 1g) REQUIREMENT IN TWO GROUPS

P value calculated by Pearsons' Chi-square test was P = 0.028. So, the rescue analgesia requirement was statistically significant between both groups. It was higher in group Tramadol.

HAEMODYNAMIC PARAMETERS: Within Group Analysis using Repeated Measures ANOVA.

All parameters such as HR, SBP, DBP and MAP at various time intervals were compared within the two groups TRA & TAP using repeated measures of ANOVA. It was found to be statistically significant ($p < 0.05$). Later, the Tukey Kramer multiple comparison test was done within the groups.

Heart Rate

The heart rates in comparison with the Tukey Kramer test within the tramadol group were found to be statistically not significant ($p > 0.05$) from the baseline values after induction.

The heart rates on comparison with the Tukey Kramer test within the tapentadol group was found to be statistically not significant ($p > 0.05$) from the baseline values except during 120 min.

Systolic Blood Pressure (SBP)

The SBP in comparison with the Tukey Kramer test within the tramadol group was found to be statistically significant ($p < 0.05$) from the baseline values except during 120 min.

The SBP in comparison with the Tukey Kramer test within the tapentadol group was found to be statistically significant ($p < 0.05$) from the baseline values except during 120 min.

Diastolic Blood Pressure (DBP)

The DBP on comparison with Tukey Kramer test within the group tramadol was found to be statistically significant ($p < 0.05$) from the baseline values up to 30min after induction, and not significant ($P > 0.05$) from 60 min to 120 min.

The DBP in comparison with the Tukey Kramer test within the tapentadol group was found to be statistically significant ($p < 0.05$) from the baseline values up to 60 min after induction and not significant ($P > 0.05$) from 90 min to 120 min post-induction.

Mean Arterial Blood Pressure (MAP)

The MAP on comparison with the Tukey Kramer test within the Tramadol group was found to be statistically significant ($p < 0.05$) from the baseline values after induction, except during 90 min and 120 min of surgery.

The MAP on comparison with the Tukey Kramer test within the tapentadol group was found to be statistically significant ($p < 0.05$) from the baseline values after induction, except during 90 min of surgery.

HR, SBP, DBP and MAP were compared between groups 0 and 1 at various time intervals using repeated measures of ANOVA. HR changes were found to be statistically ($P > 0.05$) between the two groups but SBP, DBP and MAP changes were found to be statistically significant($P < 0.05$) between the two groups. Later, Tukey Kramer multiple comparison tests were also done between the two groups.

Heart Rate

The heart rates on comparison with Tukey Kramer multiple comparison test between the groups were found to be statistically insignificant ($p > 0.05$) from the baseline values up to 120 mins after induction.

Systolic Blood Pressure (SBP)

The SBP on comparison with the Tukey Kramer test between the groups was found to be statistically insignificant ($p > 0.05$) from the baseline values up to 120 min after induction. (Table 23, Fig 21)

Diastolic Blood Pressure (DBP)

The DBP on comparison with the Tukey Kramer test between the groups was found to be statistically insignificant ($p > 0.05$) from the baseline values up to 120 min of surgery.

Mean Arterial Blood Pressure (MAP)

The MAP on comparison with the Tukey Kramer test between the groups was found to be statistically insignificant ($p > 0.05$) from the baseline values.

Comparison of Post-Operative Nausea and Vomiting Score in Two Groups: Post-operative nausea and vomiting score was not statistically significant between both the groups.

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Post Op Shivering: None of the patients in both groups had any incidence of post anaesthesia shivering.

Other side effects: None of the patients had urinary retention, increased creatinine, seizures, itching or jaundice.

Table 1: Normality test for AGE and MAP in both Groups

Group Variable	Shapiro Wilk W test statistic	P Value	Decision (5%)
GROUP TRA (AGE)	0.98	0.80	Can't reject normality
GROUP TAP (AGE)	0.96	0.40	Can't reject normality
GROUP TRA (MAP bl)	0.96	0.26	Can't reject normality
GROUP TAP (MAP bl)	0.99	0.99	Can't reject normality

Table 2: Equality of variance test for AGE and MAP in both Groups

Group Variable Name	Modified-Levene Equal-Variance Test	p-Value	Decision (5%)
Group TRA and Group TAP (AGE)	0.176	0.675	Can't reject normality
Group TRA and Group TAP (MAP bl)	1.57	0.27	Can't reject normality

Table 3: Demographic parameters in both Groups

Demographic parameters	Group TRA	Group TAP	P value
Age(Years) Mean (SD)	41.23 (11.24)	40.6 (12.70)	0.84
Weight (Kgs) Mean (SD)	60.53 (8.27)	63(8.28)	0.25
Height (cms) Mean (SD)	162.86 (7.62)	163.23(6.33)	0.84
Sex (M:F) (N) (%)	21:9(30:70)	21:9(30: 70)	1.00
BMI (kg/m^2) Mean (SD)	22.9 (2.87)	23.6(2.5)	0.38
ASA grading (I: II) (N) (%)	24:6 (80:20)	25:5(81.3: 16.7)	0.73

Table 4: Level of PIVD lesions in two groups

	GROUP TRA	GROUP TAP	TOTAL
L1-L2	1 (3.33 %)	0 (0.0 %)	1 (1.67 %)
L2-L3	1 (3.33 %)	1 (3.33 %)	2 (3.33 %)
L3-L4	3 (10%)	2 (6.67 %)	5 (8.3 %)
L4-L5	19 (63.3%)	18 (60.0%)	37 (61.67%)
L5-S1	6 (20%)	9 (30%)	15 (30%)

Table 5: VAS score (%) at post extubation

	Mild	Moderate	Severe	Total
Group TRA	26 (86.6%)	3 (10%)	1 (3.3%)	30 (100%)
Group TAP	30 (100 %)	0 (0.00%)	0 (0.00%)	30 (100%)

Table 6: VAS Score (%) at 1 hour

	Mild	Moderate	Severe	Total
Group TRA	22 (73.3%)	1 (3.3%)	7(23.3%)	30 (100%)
Group TAP	25 (83.3%)	3 (10%)	2 (6.6%)	30(100%)

Table 7: VAS Score (%) at 2 hours

	Mild	Moderate	Severe	Total
Group TRA	13(43.3 %)	14(46.6%)	3(10%)	30 (100%)
Group TAP	20 (66.6%)	9(30%)	1(3.3%)	30 (100%)

Table 8: VAS Score (%) at 4 hours

	Mild	Moderate	Severe	Total
Group TRA	12(40%)	13 (43.3%)	5 (16.6%)	30 (100%)
Group TAP	13 (43.3%)	17(56.6%)	0 (0%)	30(100%)

Table 9: Comparison of Duration of Analgesia in Two Groups

	Mean (SD) (in min)	P value
Group TRA	274 (154.12)	**0.04**
Group TAP	336 (112.08)	

Table 10: Comparison of Rescue Analgesia (Iv Paracetamol 1g) Requirement in Two Groups

	NO	YES	TOTAL
GROUP TRA	20 (66.6%)	10 (33.3%)	30 (100%)
GROUP TAP	27 (90%)	3 (10%)	30 (100%)

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Table 11: Results of repeated measures of ANOVA within the groups (TRA& TAP)

Parameters	Degree of freedom	Sum of Squares	Mean Square	F value	P value
HR	7	5422.83	77.69	7.63	0.00
SBP	7	28869.63	4124.23	33.6	0.00
DBP	7	56800.53	8114.36	41.03	0.00
MAP	7	17944.41	2563.48	24.69	0.00

Table 12: Intra-group comparison of heart rates at different time intervals using Tukey-Kramer test in Group TRA - Baseline to different time intervals

Time Intervals	Group TRA Mean HR (bpm)	Mean difference (Tb - Various time intervals)	P value
Tb	83.2		
Tpi	83.5	-0.36	1.00
T5	85.06	-1.86	0.99
T10	82.3	0.9	1.00
T30	82.1	-1.03	1.00
T60	81.5	1.7	1.00
T90	84.7	-1.56	1.00
T120	91.6	-8.46	0.09

Table 13: Intra-group comparison of Heart Rates at different time intervals using Tukey-Kramer test in Group TAP - Baseline to different time intervals

Time Intervals	Group TAP Mean HR (bpm)	Mean difference (Tb-Various time intervals)	P value
Tb	82.7		
Tpi	83.6	0.93	1.000
T5	84.8	2.13	0.99
T10	84.3	1.6	1.000
T30	80.3	2.36	0.99
T60	81.1	1.6	1.000
T90	83.6	-0.86	1.000
T120	93.5	-10.7	0.003

Table 14: Intra-group comparison of SBP at different time intervals using Tukey-Kramer test in group TRA - Baseline to different time intervals

Time Intervals	Group TRA Mean SBP (mm of Hg)	Mean difference (Tb-Various time intervals)	P value
Tb	129.63		
Tpi	103.6	25.9	0.00
T5	105.3	24.3	0.00
T10	107.06	22.5	0.00
T30	107.8	21.7	0.00
T60	112.5	17.06	0.00
T90	115.06	14.5	0.006
T120	132.03	-2.4	1.00

Table 15: Intra-group comparison of SBP at different time intervals using the Tukey-Kramer test in Group TAP- Baseline to different time intervals

Time Intervals	Group TAP Mean SBP (mm of Hg)	Mean difference (Tb-Various time intervals)	P value
Tb	121.5		
Tpi	96.1	25.4	0.00
T5	98.2	23.3	0.00
T10	104	17.3	0.00
T30	103.03	18.5	0.00
T60	106.6	14.9	0.004
T90	109.5	12.06	0.07
T120	133.1	-11.5	0.112

Table 16: Intra-group comparison of DBP at different time intervals using Tukey-Kramer test in group TRA - Baseline to different time intervals

Time Intervals	Group TRA Mean DBP (mm of Hg)	Mean difference (Tb-Various time intervals)	P value
Tb	78.6		
Tpi	65.3	13.1	0.00
T5	67.9	10.66	0.005
T10	68.6	10	0.014
T30	69.06	9.56	0.02
T60	72.2	6.4	0.53
T90	74	4.63	0.93

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T120	84.3	5.66	0.73

Table 17: Intra-group comparison of DBP at different time intervals using Tukey-Kramer test in group TAP - Baseline to different time intervals

Time Intervals	Group TAP Mean DBP (mm of Hg)	Mean difference (Tb-Various time intervals)	P value
Tb	74.9		
Tpi	61.2	13.7	0.00
T5	63.9	11	0.002
T10	65.5	9.4	0.03
T30	65.5	9.4	0.03
T60	65.9	9	0.05
T90	70.2	4.63	0.93
T120	82.1	-7.2	0.31

Table 18: Intra-group comparison of MAP at different time intervals using Tukey-Kramer test in group TRA - Baseline to different time intervals

Time Intervals	Group TRA Mean MAP (mm of Hg)	Mean difference (Tb-Various time intervals)	P value
Tb	99.5		
Tpi	81.2	18.23	0.000
T5	83.7	15.8	0.000
T10	84.4	15.1	0.00
T30	85.2	14.3	0.00
T60	88.3	11.3	0.01
T90	90.9	8.6	0.17
T120	102.7	-3.2	0.99

Table 19: Intra-group comparison of MAP at different time intervals using Tukey-Kramer test in group TAP - Baseline to different time intervals

Time Intervals	Group TAP Mean MAP (mm of Hg)	Mean difference (Tb-Various time intervals)	P value
Tb	93		
Tpi	75.8	17.1	0.00
T5	78.06	14.93	0.00
T10	81.2	11.8	0.003
T30	81.4	11.5	0.005
T60	82.7	10.2	0.03
T90	86.5	6.43	0.66
T120	102.9	-9.96	0.04

Hemodynamic Data: Between Group Analysis using repeated measures of ANOVA

Table 20: Results of repeated measures of ANOVA in between the two groups

Parameters	Degree of freedom (df)	Sum of squares	Mean square	F-value	P value
HR	1	0.0020	0.0020	0.00	0.99
SBP	1	3105.91	3105.91	4.70	0.03
DBP	1	1813.5	1813.5	5.82	0.019
MAP	1	2197.35	2197.35	5.92	0.017

Table 21: Inter group comparison of heart rates at different time intervals using Tukey-Kramer test in group TRA & group TAP

Time intervals	Group TRA Mean HR(bpm)	Group TAP Mean HR(bpm)	Mean difference	P value
Tb	83.2	82.7	0.46	1.00
Tpi	83.5	83.6	-0.1	1.00
T5	85.06	84.8	0.2	1.00
T10	82.3	84.3	-2.03	0.99
T30	82.1	80.3	1.8	1.00
T60	81.5	81.1	0.36	1.00
T90	84.7	83.6	1.16	1.00
T120	91.6	93.5	-1.83	1.00

Table 22: Intergroup comparison of SBP at different time intervals using Tukey Kramer test in group TRA & group TAP

Time intervals	Group TRA Mean SBP(mm of Hg)	Group TAP Mean SBP(mm of Hg)	Mean difference	P value
Tb	129.63	121.5	8.06	0.69
Tpi	103.6	96.1	7.56	0.78
T5	105.3	98.2	7.03	0.86

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T10	107.06	104.2	2.8	0.99
T30	107.8	103.03	4.83	0.99
T60	112.5	106.6	5.9	0.96
T90	115.06	109.5	5.56	0.97
T120	132.03	133.1	-1.06	1.00

Table 23: Intergroup comparison of DBP at different time intervals using Tukey-Kramer test in group TRA & group TAP

Time intervals	Group TRA Mean DBP(mm of Hg)	Group TAP Mean DBP (mm of Hg)	Mean difference	P value
Tb	78.6	74.9	3.73	0.99
Tpi	65.3	61.2	4.33	0.96
T5	67.9	63.9	4.06	0.97
T10	68.6	65.5	3.13	0.99
T30	69.06	65.5	3.56	0.99
T60	72.2	65.9	6.33	0.55
T90	74	70.2	3.73	0.99
T120	84.3	82.1	2.2	0.99

Table 24: Intergroup comparison of MAP at different time intervals using Tukey-Kramer test in group TRA & group TAP

Time intervals	Group TRA Mean MAP(mm of Hg)	Group TAP Mean MAP(mm of Hg)	Mean difference	P value
Tb	99.5	93	6.5	0.65
Tpi	81.2	75.8	5.43	0.88
T5	83.7	78.06	5.63	0.84
T10	84.4	81.2	3.2	0.99
T30	85.2	81.4	3.73	0.99
T60	88.3	82.7	5.6	0.85
T90	90.9	86.5	4.33	0.98
T120	102.7	102.9	-0.2	1.00

Table 25: Comparison of Post-Operative Nausea and Vomiting Scores in Two Groups

PONV SCORE	GROUP TRA	GROUP TAP
0	26(86.6%)	26(86.6%)
1	0 (0.00%)	1 (3.3%)
2	1 (3.3%)	1(3.3%)
3	3 (10%)	2(6.6%)
Total	30 (100%)	30 (100%)

DISCUSSION

The results of our study suggest that the VAS score following surgery was almost comparable in both groups. The rescue analgesia requirement was higher with tramadol than the tapentadol group. The duration of analgesia was significantly longer in the tapentadol group compared to the tramadol group. Patients who received tramadol or tapentadol did not show any significant changes in heart rate or mean arterial pressure at induction and extubation, sympathetic responses were equally decreased with the use of either of the drugs.

Tramadol has been used commonly for postoperative analgesia following various surgeries.[14] It has an oral bioavailability of 95% after multiple doses.[15] It is a prodrug whose active metabolite is desmethyltramadol,[16] and its onset of action is within 60 min. It is mainly metabolised by CYP450. Poor metabolisers do not get good analgesia. It has mu agonist and very less norepinephrine reuptake inhibition properties. It is 85% metabolised by the liver, 85% excreted by the kidneys, and has an elimination half-life of about 8 h.

In contrast, tapentadol is an active drug, which is metabolised by glucuronidation. It has a quicker onset of 32 min as compared with that of tramadol. It has no CYP450 interaction and has much greater norepinephrine reuptake inhibition besides mu agonist.[17] It is metabolised 70% by the liver, 95% excreted by the kidneys, and has an elimination half-life of 4 h.

A thorough understanding of the neurophysiology of pain is essential for its proper management.[18] Different groups of analgesics such as NSAIDs and local anesthetics have been used for pain relief. Tramadol has been stated to be as effective and safe as compared with ibuprofen. In their study, Banerjee et al. have stated that the need for "rescue medication" was lesser with tramadol.[19] We did not use paracetamol and NSAIDs regularly to avoid any bias for the analgesic efficacy of the study drugs. In addition, NSAIDs have been implicated in causing other side effects such as gastritis and renal dysfunction. Tapentadol has norepinephrine reuptake inhibition properties. Due to its synergistic effects with mu agonist, it leads to "opioid-sparing" and decreases the gastrointestinal side effects besides providing good analgesia.[20] The above mechanisms could explain why we obtained better

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quality analgesia with tapentadol as compared with tramadol.

"Rescue analgesia" was needed for 10 out of 30 patients in the tramadol group versus 3 out of 30 patients in the tapentadol group. Rescue analgesia was provided by using IV Paracetamol 1g. Thus, 47 out of 60 patients studied (78.2%) did not need rescue analgesia since the pain was managed effectively by using the study drugs. Our study is supported by another similar study. Iyer SK et al conducted a study to compare tapentadol with tramadol for analgesia after cardiac surgery. Sixty adults undergoing cardiac surgery were divided into 2 groups of 30 each by computerised random allotment (Group X = tapentadol 50 mg oral and Group Y = tramadol 100 mg oral). They concluded that tapentadol was a better analgesic than tramadol given less rescue analgesic requirement.[136] However, the duration of analgesia was not compared in this study. In our study, both the duration of analgesia was longer and the rescue analgesic requirement was less in the tapentadol group. This may be attributed to the use of 100 mg of tapentadol rather than the usual dose of 50 mg of tapentadol.

Opioids have a risk of CNS and/or respiratory depression and aspiration. But this side effect was more with the IV opioids as compared with oral opioids, due to their sudden increased blood and cerebrospinal fluid levels. Besides, there can be mechanical or technical problems with infusion (syringe) pumps or PCA pumps. Since we have used oral opioids, none of our patients had these problems.

In many of previous studies, it was shown that tapentadol has less incidence of postoperative nausea and vomiting compared to other opioids. Biondi et al conducted a randomised, double-blinded study and studied the tolerability and efficacy of tapentadol IR and oxycodone IR for acute low back pain. They concluded that tapentadol IR 50mg and 75mg were non-inferior to oxycodone IR 10 mg for the treatment of acute pain. The incidence of nausea and vomiting was statistically significantly lower for tapentadol IR 50mg and numerically lower for tapentadol IR 75 mg than oxycodone IR 10 mg.[12]

Afilalo M et al conducted a randomised, double-blinded study of the tolerability of tapentadol IR in patients with osteoarthritis of hip or knee over 90 days. It was proven that tapentadol was associated with improved gastrointestinal tolerance compared to oxycodone IR.[13] In contrast to other studies, our results showed that the incidence of postoperative nausea and vomiting was comparable in both groups.

None of our patient's experienced post-operative shivering. This may be clinically useful especially in the management of post anaesthesia shivering. Studies have shown the effective use of IV tramadol in the prevention of PAS.[21] However, there are very few studies with oral use of the same and with oral tapentadol.[21] Further studies with oral tramadol and tapentadol may provide beneficiary evidence to confirm the same. None of the patients had jaundice though bilirubin levels were not regularly recorded for the study. The dose of paracetamol, which we used, was not known to be a hepatotoxic dose.

None of the patients had any incidence of itching. Opioids, particularly after the intrathecal route of administration, have been known to cause itching.

Clinically, we observed that tapentadol patients had lower haemodynamics at all-time intervals intraoperatively than patients who received the tramadol group. Overall, there was haemodynamic stability in both groups and no major haemodynamic alterations were observed during the intraoperative period. Similar results were found in one of the studies by Sayyed Morteza et. al in which pre-emptive analgesia with oral tramadol was compared with oral codeine.[22]

CONCLUSION

1. Analysis between the two groups demonstrated that VAS scores were comparable in both groups. However, the quality of analgesia was better in the tapentadol group compared with the tramadol group till our follow-up period of 4 hours postoperatively.
2. The rescue analgesia requirement was higher in the tramadol group compared to the tapentadol group and this result was statistically significant. ($p = 0.02$)
3. The duration of analgesia was longer in the tapentadol group compared with tramadol and this was statistically significant. ($p = 0.03$)
4. The incidence of post-operative nausea and vomiting was comparable in both tramadol and tapentadol groups.
5. Both oral tramadol and tapentadol may be used effectively in the prevention of post-anaesthesia shivering.

Through our study, we conclude that tapentadol provides better quality of analgesia compared to tramadol in terms of pain scores, rescue analgesia requirement, duration of analgesia and side effects profile similar to that of tramadol.

Limitations of Our Study: Patients in whom the duration of surgery has prolonged more than 2 hours were excluded from our study.

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