# Comparison of tapentadol with tramadol for analgesia after cardiac surgery

# Srinivas Kalyanaraman Iyer, Gokulakrishnan Mohan, Sivakumar Ramakrishnan, Sanjay Theodore

Department of Cardiac Anaesthesia, Chettinad Hospital and Research Institute, Kelambakkam, Chennai, Tamil Nadu, India

#### ABSTRACT

Background: Tapentadol is a relatively new analgesic. We decided to compare it with tramadol for their various effects after cardiac surgery. Setting: A study in a tertiary care hospital. Materials and Methods: Sixty adults undergoing cardiac surgery were divided into 2 groups of 30 each by computerized random allotment (Group X = tapentadol 50 mg oral and Group Y = tramadol 100 mg oral). Informed Consent and Institutional Ethics Committee approval were obtained. The patients were given either drug X or drug Y after extubation in this single blinded study, wherein the data collectors and analyzers were blinded to the study. All patients received oral paracetamol qds and either drug X or drug Y tds. The pain score was noted on a Visual Analog Scale before each drug dose, 3 h later and on coughing. Heart rate, respiratory rate, and blood pressure were recorded before the drug dose and 3 h later. Postoperative nausea or vomiting (PONV), temperature, and modified Glasgow Coma Scale readings were recorded. The above readings were obtained for 6 doses (up to 48 h after extubation). Statistics: t-test, Pearson Chi-square test, Fisher exact test, and Mantel-Haenszel test were used for statistics. Results: Tapentadol group patients had significantly better analgesia 3 h after the drug and "on coughing" than tramadol group. The difference in their effects on blood creatinine levels, temperature, hemodynamics, oxygen saturation, and respiratory rate were not clinically significant. Tapentadol produced lesser drowsiness and lesser vomiting than tramadol. Conclusions: Tapentadol, due to its norepinephrine reuptake inhibition properties, in addition to mu agonist, is a better analgesic than tramadol and has lesser PONV.

Received: 04-03-15 Accepted: 20-06-15

Key words: Analgesia; Tapentadol; Tramadol

#### INTRODUCTION

Tramadol, a mu agonist, has been used for acute pain relief in the immediate postoperative period. Pain after cardiac surgery could be due to sternotomy, intercostal drain sites, or saphenous vein harvesting sites incisions.

Access this article online Website: www.annals.in DOI: 10.4103/0971-9784.159805 Quick Response Code:

Pain management is an essential element of patient care. Active physiotherapy and cardiorespiratory rehabilitation help to reduce patient morbidity, anxiety, discomfort, and associated costs. Pain relief is an important aspect of rehabilitation. Multimodal approach to postoperative pain management have included the use of paracetamol, morphine through intravenous (IV) or patient-controlled analgesia (PCA) routes, nonsteroidal anti-inflammatory drugs (NSAIDs), local anesthetics, opioid analogs such as tramadol and regional anesthetic techniques.

Tapentadol is a relatively new analgesic. It is a mu agonist and has additional norepinephrine reuptake inhibition properties. Tapentadol is

Address for correspondence: Dr. Srinivas Kalyanaraman Iyer, Chettinad Hospital and Research Institute, Rajiv Gandhi Salai, Kelambakkam District, Chennai - 603 103, Tamil Nadu, India. E-mail: drks23814@yahoo.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

**Cite this article as:** Iyer SK, Mohan G, Ramakrishnan S, Theodore S. Comparison of tapentadol with tramadol for analgesia after cardiac surgery. Ann Card Anaesth 2015;18:352-60.

reported to be an important addition in the management of moderate and severe pain.<sup>[1]</sup> We decided to compare the effects of tapentadol with that of tramadol for analgesia in adult patients undergoing cardiac surgery. We also compared the effects of the two drugs on various systems.

# MATERIALS AND METHODS

A total of 60 patients undergoing cardiac surgery were divided into 2 groups of 30 each by computerized random allotment (Group X = tapentadol 50 mg oral 3 times daily [tds] or Group Y = tramadol 100 mg oral tds, total 6 doses of each, since the doses were equipotent). The study protocol was approved by our Institutional Ethics Committee. The study was conducted according to standards of good clinical practice. After explaining the details of the study, written consent was obtained from all patients.

The patients were given either drug X or drug Y 1-h after extubation in this single blinded study, wherein the data collectors and data analyzers were blinded to the study. The nurse who administered the drug to the patient was different from the nurse who collected the data. The patients could not be blinded to the study for two reasons: (1) Oral tapentadol 50 mg was available as a white colored tablet, while two green colored capsules of tramadol, 50 mg each were needed to be administered for every dose. Thus, the color difference was recognizable. (2) If a study involves treatment in which active participation of the patient is necessary (e.g., physical therapy), then the participants cannot be easily blinded to the intervention. All 60 patients received oral paracetamol 650 mg 4 times daily. IV fentanyl 25–50 mcg/kg was used intraoperatively.

# Patient selection criteria

- Both males and females aged 18–65 years, weighing 40 kg or above, who were posted for cardiac surgery such as mitral valve replacement, coronary artery bypass graft surgery, atrial septal defect repair, and aortic valve replacement. Some of the patients undergoing coronary artery bypass graft surgery were done off-pump
- Those patients who gave written informed consent were studied.

# Patient exclusion criteria

Those who gave a history of the following:

• Persistent nausea or vomiting at the time of randomization

- Epilepsy
- Treated with mono amino oxidase inhibitors, tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors
- Traumatic brain injury, stroke, transient ischemic attack, or brain tumor
- Drug abuse
- Opioid tolerance or opioid dependence
- Renal disease (creatinine >1.4 mg/dL)
- Liver disease (total bilirubin >1.5 mg/dL)
- Allergies to any drug
- Major psychiatric disorder
- Pregnancy
- Preoperative intraaortic balloon pump (IABP)
- Preoperative vasoactive drugs
- Emergency surgery and
- Patients who were on high inotropic support and/or IABP at the time of extubation.

All the incisions were midline sternotomy. The pain score was noted on a Visual Analog Scale (VAS) before each drug dose, 3 h after the drug and "on coughing," for 6 doses. Similarly heart rate, respiratory rate, systolic blood pressure (BP), diastolic BP, and oxygen saturation were recorded before the drug dose and 3 h later, for 6 doses. Postoperative nausea or vomiting (PONV) were recorded (if they occurred or not) after each dose. Patient's temperature was recorded 3 h and 5 h after administration of the drug. Modified Glasgow Coma Scale (GCS) was recorded 5 h after each drug dose. The blood creatinine levels were noted before the first dose, after dose 3, and after the sixth dose. Thus, the above readings were obtained for 48 h after extubation. The effects of the two drugs on any other body systems were noted and managed.

A modified Wong-Baker Faces Scale (VAS) combined with a numeric pain rating scale (1–10) was used 1–4 was rated as mild pain, 5 and 6 were rated as moderate pain while 7–10 was rated as severe pain. The Pasero Sedation Scale was not used since it was not considered to be enough for our study purpose. The Pasero Scale has been used to titrate opioid dose (particularly IV dose) and naloxone dosage if there is a severe central nervous system (CNS) and/or respiratory depression. We wanted to grade "eye opening" as per our modified GCS. Hence, a modified GCS was used, wherein the best eye response and the best verbal response were recorded. It was decided that the best motor response will not be recorded since that may need a painful stimulus to elicit limb localization movement or withdrawal or flexion or extension. Richmond Agitation Sedation Score (RASS) has been used in other studies to monitor essentially patients on ventilator, those who are delirious and to scale their levels of restlessness and agitation. RASS was not applicable to our study.

## **Statistical analysis**

IBM-SPSS (IBM Corporation, New York, United States) version 21 software was used. A *t*-test was used to compare the two mean values drawn from the same population. The null hypothesis was that the means of the two groups were the same. If the significance P value was  $\leq 0.05$ , the null hypothesis was rejected.

The incidence of PONV among the two groups were compared using the Pearson Chi-square test. The significance value of the Chi-square test was 0.02, and the null hypothesis was rejected [Table 1].

Mantel-Haenszel test was used to assess the odds ratio (OR) of the two groups compared. An OR of >1 indicates that the drug used increases the odds of recovery. The 95% confidence interval of the OR obtained were such that the lower bound limit was 1.20 while the upper bound limit was 15.60 [Table 2]. Thus, both the values were >1.

# RESULTS

The two groups were similar in their body weight (in a kilogram) and age (in years) [Tables 3 and 4]. Mean weight (58.4 vs. 59.6) and mean age (41.1 vs. 40.4) between the two groups were statistically insignificant. There was a slight increase in the proportion of males in Group Y (tramadol) as compared with Group X (tapentadol) (73% vs. 60%) [Table 5].

The mean VAS for pain at 3 h after the drug dose was significantly lesser in tapentadol group as compared with tramadol group (2.68 vs. 3.91). Similarly, the VAS on coughing was also lesser for the tapentadol group versus tramadol group (3.86 vs. 4.93). The *P* value as per the *t*-test was 0.001 [Table 6, Figures 1 and 2]. VAS before the drugs is as per Figure 3.

The oxygen saturation (in percentage divided by 100), heart rate, respiratory rate, BP, and temperature were not significantly different between the two groups [Table 6].

The mean creatinine levels (mg/dL) ranged from 1 to 1.2 for tapentadol group versus 1.05 to 1.15 for tramadol group and were thus similar between the two groups [Figure 4].

PONV occurred in 4 out of 30 tapentadol group patients as compared with 12 out of 30 tramadol group patients [Table 7]. Postoperative nausea was noted after 22 out of 180 tramadol doses as compared with 5 out of 180 tapentadol doses.[Tables 8 and 9]. Similarly, postoperative vomiting was noted after 17 out of 180 tramadol doses as compared with 2 out of 180 tapentadol doses [Tables 8 and 9].

As per the Pearson Chi-square and Fisher's exact tests, for the analysis of (PONV), the P < 0.05 [Table 1]. The Mantel–Haenszel 95% confidence interval of the OR was between 1.20 and 15.60 for PONV [Table 2].

As per our modified GCS, all patients in tapentadol group had spontaneous eye opening while after 8 out of 180 tramadol doses, there was "eye opening" to speech stimulus [Table 10].



**Figure 1:** Mean Visual Analog Scale at 3 h after the drug Y is compared with that of drug X for the 6 doses

# Table 1: PONV Chi-square test

			Chi-square tests		
	Value	df	Asymptotic significant (two-sided)	Exact significant (two-sided)	Exact significant (one-sided)
Pearson Chi-square	5.455	1	0.020		
Fisher's exact test				0.039	0.020

The significance value was 0.02. PONV: Postoperative nausea or vomiting

Rescue analgesia was provided the moment pain score reached 6 (moderate pain). Rescue analgesia was administered to 6 out of 30 patients in tramadol group versus 3 out of 30 patients in tapentadol group [Table 11 and Figure 5].

Bilevel positive airway pressure (BIPAP) ventilation was used in three patients in tramadol group versus two patients in tapentadol group temporarily [Figure 6] in the form of noninvasive ventilation with the face mask.

In both groups, epicardial ventricular pacing was used for a few hours in 2 out of 30 patients each [Figure 7].

One patient in tramadol group had Intensive Care Unit (ICU) related psychosis after the administration of the final (6<sup>th</sup>) dose. None of the patients in tapentadol group had any form of psychosis. Otherwise, all patients in both groups were well oriented as far as a verbal response (as per our modified GCS) is concerned [Figure 8].

# DISCUSSION

Tramadol has been used commonly for postoperative analgesia following various surgeries.<sup>[2]</sup> It has an oral bioavailability of 95% after multiple doses.<sup>[2]</sup> It is a

# Table 2: PONV - Mantel-Haenszel OR estimate

Mantel-Haenszel common OR estimate					
Estimate	4.333				
Asymptotic significant (two-sided)	0.025				
Asymptotic 95% CI					
Common OR					
Lower bound	1.203				
Upper bound	15.605				

The 95% CI of the OR was from 1.20 to 15.60. OR: Odds ratio, CI: Confidence interval, PONV: Postoperative nausea or vomiting

58.43

#### Table 3

30

prodrug whose active metabolite is desmethyltramadol,<sup>[3]</sup> and its onset of action is within 60 min. It is mainly metabolized by cyp450. Poor metabolizers do not get good analgesia. It has mu agonist and very less norepinephrine reuptake inhibition properties. It is 85% metabolized 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 metabolized 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.[3] It is metabolized 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.<sup>[4]</sup> 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.<sup>[5]</sup> In their study, Banerjee et al. have stated that the need for "rescue medication" was lesser with tramadol. In another study, tramadol was found to be equally effective as ketorolac in the first 6 h postoperatively.<sup>[6]</sup> We used paracetamol regularly in our study while we did not use NSAIDs on a regular basis. NSAIDs have been implicated to cause other side effects such as gastritis and renal dysfunction. Tapentadol and NSAIDs belong to a different group of drugs. They have different side effects and so are difficult to compare with each other.

Pregabalin too has been used for postoperative analgesia.<sup>[7-9]</sup> We did not use pregabalin in our study.

Tapentadol has norepinephrine reuptake inhibition properties. Due to its synergistic effects with mu

: Weight distribu	tion				
W	leight - group stat	istics		Independer	t samples <i>t</i> -test
п	Mean	SD	SEM	Value	Significant
30	59.63	10.858	0.809	1.039	0.299

0.823

Mean weight was 59.6 kg in Group Y as compared with 58.4 kg in Group X. SD: Standard deviation, SEM: Standard error of mean

11.045

#### Table 4: Age distribution

Drug Y Х

Age - group statistics					Independen	t samples <i>t</i> -test
Drug	п	Mean age	SD	SEM	Value	Significant
Y	30	40.40	14.521	2.651	-0.241	0.811
Х	30	41.13	8.203	1.498		

Mean age was 40.4 years in Group Y as compared with 41.1 years in Group X. SD: Standard deviation, SEM: Standard error of mean



**Figure 2:** Mean Visual Analog Scale on coughing after the drug Y is compared with that of drug X for the 6 doses



Figure 4: Mean blood creatinine levels for the two groups are compared



Figure 6: Bilevel positive airway pressure was needed for 2 out of 30 patients in Group X versus 3 out of 30 patients in Group Y

agonist, it leads to "opioid sparing" and decreases the gastrointestinal side effects besides providing good



Figure 3: Mean Visual Analog Scale before the drug dose for both the groups are compared for the 6 doses



Figure 5: Rescue analgesia was needed for 3 out of 30 patients in Group X versus 6 out of 30 patients in Group Y



Figure 7: Two out of 30 patients in both the groups needed epicardial pacing

analgesia.<sup>[10]</sup> The above mechanisms could explain as to why we obtained better analgesia "at 3 h after

the drug dose" with tapentadol as compared with tramadol (mean VAS 2.68 vs. 3.91) [Table 6].

"Rescue analgesia" was needed for 6 out of 30 patients in tramadol group versus 3 out of 30 patients in



Figure 8: One out of 30 patients in Group Y had psychosis while none had it in Group X

# Table 5: Gender distribution

Sex	Drug	(n (%))
	Y	Х
Male	22 (73.33)	18 (60.00)
Female	8 (26.67)	12 (40.00)

About 60% of the patients in Group X and 73% of the patients in Group Y were males

tapentadol group. Rescue analgesia was provided by using IV ketorolac 30 mg. Thus, 51 out of 60 patients studied (85%) did not need rescue analgesia since the pain was managed effectively by using the study drugs.

In our study, tramadol caused a little more drowsiness than tapentadol [Table 10]. Tapentadol has been reported to cause lesser confusion than tramadol.<sup>[11]</sup> None of the patients who received tapentadol had ICU psychosis. One patient in tramadol group had ICU psychosis after the 6<sup>th</sup> dose, which responded to antipsychotic drugs.

It has been advised not to use tapentadol when the patient has CNS and/or respiratory depression.<sup>[12]</sup> Tapentadol has no active metabolites. The respiratory rate and oxygen saturation were similar between the two groups. BIPAP was used prophylactically in two patients temporarily who received tapentadol as compared with three patients who received tramadol when mild lung basal atelectatic changes were seen on the chest roentgenogram. None of the patients needed reintubation since we could obtain oxygen saturation of 95% or above. PCO2 levels were not compared for the six doses between the two drugs. The arterial blood gas (ABG) samples taken in the ICU were randomly based on multiple system factors like

# Table 6: VAS, heart rate, respiratory rate, BP, and oxygen saturation findings after the 3rd dose

Dose	Parameters		Dr	ug		Independent samples	
		Y	1	>	(	i	t-test
		Mean	SD	Mean	SD	<i>t</i> -test	Significant
3	VAS-before drug	5.42	1.11	4.91	1.40	1.564	0.123
	VAS-3 h	3.91	1.01	2.68	1.27	4.163	0.000
	VAS-on coughing	4.93	1.04	3.86	1.31	3.482	0.001
	Heart rate	91.37	16.42	92.87	13.32	-0.389	0.699
	Respiratory rate	21.40	2.36	21.87	2.57	-0.733	0.467
	Systolic BP	115.00	11.90	116.90	12.64	-0.600	0.551
	Diastolic BP	61.23	7.50	62.33	9.43	-0.500	0.619
	SpO <sub>2</sub> (%)	1.00	0.01	1.00	0.01	1.022	0.311
	After 3 h						
	Heart rate	90.97	15.83	92.00	13.02	-0.276	0.783
	Respiratory rate	21.27	2.00	26.10	17.45	-01.508	0.142
	Systolic BP	114.40	14.15	116.97	12.63	-0.741	0.461
	Diastolic BP	60.87	7.74	62.60	9.64	-0.768	0.446
	SpO <sub>2</sub>	1.00	0.00	0.99	0.05	1.419	0.166
	Temperature	99.41	1.05	98.98	0.71	0.708	0.506
	Temperature after 3 h	97.62	6.30	99.11	2.17	-1.226	0.225
	Temperature after 5 h	98.05	4.38	98.67	0.42	-0.762	0.449

The above findings were noted before the drug, on coughing and 3 h after the 3<sup>rd</sup> dose of the drug. Similarly, readings were obtained for the two groups after the doses 1, 2, 4, 5, and 6. The oxygen saturation values obtained were divided by 100 for statistical purpose. VAS: Visual Analog Scale, BP: Blood pressure, SD: Standard deviation

"during hypotension" or oliguria. ABG sampling was not consistent with the timing of the drug dose. E.g., one ABG sample was taken just after the drug was administered while another sample was taken during the peak effect of the drug.

IV opioids have a greater risk of CNS and/or respiratory depression and aspiration as compared with oral opioids

# Table 7: PONV findings

Drug * nausea and/or vomiting cross tabulation						
Drug	Nausea von	a and/or niting	Total			
	Yes	No				
Y						
Count	12ª	18 <sup>b</sup>	30			
Row %	40.00	60.00	100.00			
Column %	75.00	40.91	50.00			
Х						
Count	4 <sup>a</sup>	26 <sup>b</sup>	30			
Row %	13.33	86.67	100.00			
Column %	25.00	59.09	50.00			
Total						
Count	16	44	60			
Row %	26.67	73.33	100.00			
Column %	100.00	100.00	100.00			

4 out of 30 patients in Group X versus 12 out of 30 patients in Group Y had PONV. PONV: Postoperative nausea or vomiting

# Table 8: PONV findings after each dose of drug Y

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. We gave titrated IV 3 or 4 mg morphine boluses if needed, as analgesics before extubation, that is, before the commencement of our study.

Tapentadol has better gastrointestinal tolerability than other opioids.<sup>[13]</sup> The incidence of PONV ranges from 12% to 38%.<sup>[14]</sup> Risk factors for PONV include a history of PONV, female sex, nonsmokers, postoperative opioids, use of neostigmine, inhalational agents, and a certain type of surgeries. The use of continuous positive airway pressure mask may have produced gastric distension and PONV. Tapentadol patients had lesser PONV than tramadol group in our study. PONV was managed by using IV ondansetron, metoclopramide, and dexamethasone as 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> line of treatment, respectively. One patient in tramadol group had constipation, which was treated with 10 mg bisacodyl oral tablet while no patient in tapentadol group had any constipation.

The temperature reading difference was not statistically significant between the two groups. The Postoperative fever could be due to infection, inflammation, drug fever, etc.

Drug	Dose ( <i>n</i> (%))					
	1	2	3	4	5	6
Y						
Nausea						
Yes	6 (20.00)	2 (6.67)	2 (6.67)	6 (20.00)	4 (13.33)	2 (6.67)
No	24 (80.00)	28 (93.33)	28 (93.33)	24 (80.00)	26 (86.67)	28 (93.33)
Vomiting						
Yes	3 (10.00)	3 (10.00)	3 (10.00)	3 (10.00)	3 (10.00)	2 (6.67)
No	27 (90.00)	27 (90.00)	27 (90.00)	27 (90.00)	27 (90.00)	28 (93.33)

Nausea was noted after 22 out of 180 drug Y doses while vomiting was noted after 17 out of 180 drug Y doses. PONV: Postoperative nausea or vomiting

# Table 9: PONV findings after each dose of drug X

Drug						
	1	2	3	4	5	6
Х						
Nausea						
Yes	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	3 (10.00)	2 (6.67)
No	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	27 (90.00)	28 (93.33)
Vomiting						
Yes	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (6.67)	0 (0.00
No	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	28 (93.33)	30 (100.00)

Nausea was noted after 5 out of 180 drug X doses while vomiting was noted after 2 out of 180 drug X doses. PONV: Postoperative nausea or vomiting

Drug			Dose	e (n (%))		
	1	2	3	4	5	6
Y						
Eye opening						
To speech	1 (3.33)	2 (6.67)	3 (10.00)	0 (0.00)	1 (3.33)	1 (3.33)
Spontaneous	29 (96.67)	28 (93.33)	27 (90.00)	30 (100.00)	29 (96.67)	29 (96.67)
Verbal response						
Obeys command	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)
Х						
Eye opening						
Spontaneous	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)
Verbal response						
Obeys command	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)	30 (100.00)

# Table 10: Modified GCS findings

Eye opening and verbal response between Group X and Group Y are compared after each of the 6 doses which the patients received. GCS: Glasgow Coma Scale

### Table 11: Rescue analgesia

Rescue	Drug (	n (%))	Binomial test
analgesia	Y	Х	Significant
Yes	6 (20.00)	3 (10.00)	0.508
No	24 (80.00)	27 (90.00)	

3 out of 30 patients in Group X versus 6 out of 30 patients in Group Y needed rescue analgesia

Four out of thirty patients in each group had atrial fibrillation (AF) at some point of time, which was treated with titrated IV metoprolol and/or IV amiodarone followed by oral antiarrhythmics. Opioids have traditionally not been implicated to cause AF.

Two patients in each group needed temporary epicardial pacing for better hemodynamics. As stated earlier, most cardiac patients were receiving beta-blockers in the postoperative period for prevention of "AF with the uncontrolled high ventricular rate." Although opioids have been known to cause bradycardia, it is not clear from our study whether tapentadol or tramadol causes significant bradycardia on their own. These patients were not symptomatic; otherwise, they responded to temporary ventricular epicardial pacing.

Tapentadol extended-release tablets allow for twice daily dosing and better patient compliance.<sup>[15]</sup> We used both the drugs thrice daily and the creatinine levels of both groups were similar. One patient in tramadol group had a rise in creatinine level from 1.35 to 1.71 mg/dL after the 5<sup>th</sup> dose. The patient needed dopamine at 3–5 mcg/kg/min and frusemide infusion, which were weaned off later. However, that patient tolerated tramadol and was awake and alert.

None of the patients had urinary retention. None of the patients had jaundice though bilirubin levels were not regularly recorded for the study. The dose of paracetamol, which we used, is not known to be a hepatotoxic dose.

One patient in tramadol group had a re-exploration for pericardial effusion drainage following aortic valve replacement after the 4<sup>th</sup> dose of the drug. However, we continued the study after the extubation (postdrainage).

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

There were no deaths during the study. Those patients who were on high inotropic support and/or IABP at the time of extubation had been excluded from the study.

# Limitations of our study

- We could not exactly time Romson's respirometer with the drug doses in spite of good physiotherapy, which provided valuable deep breathing exercises, use of acapella, etc. Respiratory volumes (in milliliters) from Romson's respirometer needs to be recorded and analyzed in future studies
- We did not study geriatric patients (>65 years) since the safety of tapentadol in this age group is not established.

We conclude that in the patients who are receiving paracetamol, the drug tapentadol is a better analgesic than tramadol for adult patients undergoing cardiac surgery.

## Financial support and sponsorship

Funding was provided solely by Chettinad Hospital and Research Institute.

# **Conflict of interest**

There are no conflict of interest.

# REFERENCES

- 1. Fidman B, Nogid A. Role of tapentadol immediate release in the management of moderate to severe pain. J Pharm Ther 2010;35:330-3.
- 2. Duthie DJ. Remifentanil and tramadol. Br J Anaesth 1998;81:51-7.
- 3. Singh DR, Nag K, Sheti AN, Krishnaveni N. Tapentadol hydrochloride: A novel analgesic. Saudi J Anaesth 2013;7:322-6.
- 4. Cohen MJ, Schecter WP. Perioperative pain control: A strategy for management. Surg Clin North Am 2005;85:1243-57, xi.
- 5. Banerjee M, Bhaumik DJ, Ghosh AK. A comparative study of oral tramadol and ibuprofen in postoperative pain in operations of lower abdomen. J Indian Med Assoc 2011;109:619-22, 626.
- 6. Mishra H, Khan FA. A double-blind, placebo-controlled randomized comparison of pre and postoperative administration of ketorolac and tramadol for dental extraction pain. J Anaesthesiol Clin Pharmacol 2012;28:221-5.
- 7. Joshi S, Jagadeesh AM. Efficacy of perioperative pregabalin

in acute and chronic postoperative pain after off pump coronary artery bypass – A random double blind placebo controlled trial. Ann Card Anaesth 2013; 16:180-5.

- 8. Jain PN. Oral pregabalin holds promise to reduce pain after cardiac surgery. Ann Card Anaesth 2013;16:180.
- 9. Pradeep Kumar K, Kulkarni DK, Gurujala I, Gopinath R. Pregabalin versus tramadol for postoperative pain management in patients undergoing lumbar laminectomy: A random double blinded placebo controlled study. J Pain Res 2013;2013:471-8.
- Tzschentke TM, Christoph T, Kögel B, Schiene K, Hennies HH, Englberger W, et al. (-)-(1R,2R)-3-(3-dimethylamino-1-ethyl-2-methyl-propyl)- phenol hydrochloride (tapentadol HCl): A novel mu-opioid receptor agonist/norepinephrine reuptake inhibitor with broad-spectrum analgesic properties. J Pharmacol Exp Ther 2007;323:265-76.
- 11. Power I. An update on analgesics. Br J Anaesth 2011;107:19-24.
- 12. Mendis V. Role of tapentadol in pain management. Br J Hosp Med (Lond) 2012;73:143-7.
- 13. Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. Yale J Biol Med 2010;83:11-25.
- 14. Chandrakantan A, Glass PS. Multimodal therapies for postoperative nausea and vomiting, and pain. Br J Anaesth 2011;107 Suppl 1:i27-40.
- 15. Vadivelu N, Huang Y, Mirante B, Jacoby M, Braveman FR, Hines RL, *et al.* Patient considerations in the use of tapentadol for moderate to severe pain. Drug Healthc Patient Saf 2013;5:151-9.