https://doi.org/10.48047/AFJBS.6.16.2024.2259-2270

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

"A PROSPECTIVE ANALYSIS OF TAPENTADOL NASAL SPRAY VERSUS INJECTION TRAMADOL IN POSTOPERATIVE PAIN MANAGEMENT IN A TERTIARY CARE CENTRE"

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Volume 6, Issue 16, Dec 2024

Received: 15 Oct 2024

Accepted: 25 Nov 2024

Published: 09 Dec 2024

doi:10.48047/AFJBS.6.16.2024.2259-2270

INTRODUCTION

Pain is a distressing feeling often caused by intense or damaging stimuli. The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."

Postoperative pain is an unpleasant sensory, emotional and mental experience, that is precipitated by surgical trauma and is linked with various autonomic, endocrine–metabolic, physiological and behavioral responses

Though postoperative pain is self-limiting and decreases with time, its relief is justified on humanitarian grounds, which helps to improve physiological function after surgery.

Commonly, nonsteroidal anti-inflammatory drugs (NSAIDs) were given to provide an effective postoperative analgesia but these drugs have many drawbacks .

The μ-opioid receptor and its corresponding agonists have been utilized in the treatment of mild to extreme pain for a really long time. A combined mechanism of action was accomplished by utilizing μ-opioid receptor agonist and norepinephrine reuptake inhibition for the therapeutic development of opioid analgesics . Tapentadol hydrochloride is one such intermediary analgesic considered to be manifested for effective pain management.

Tapentadol is a novel oral analgesic with a dual mode of action as an agonist of the μ-opioid receptor and as a norepinephrine reuptake inhibitor (NRI) all in a single molecule. Tapentadol shows its analgesic effect quickly, at around 30 minutes. Its MOR agonistic action produces acute nociceptive pain relief; its role as an NRI brings about chronic neuropathic pain relief. Tramadol is a weak opioid agonist which acts by interacting with opioid receptors named mu, alpha and delta. Tapentadol is available as nasal spray, whereas tramadol is available as iv formulation.

In view of less literature on comparison of Tapentadol with Tramadol as postoperative analgesics, especially in Indian settings, the current study was undertaken

REVIEW OF LITERATURE

Tapentadol, is a centrally acting opioid analgesic of the benzenoid class with a dual mode of action as an agonist of the μ-opioid receptor and as a norepinephrine reuptake inhibitor (NRI) .

Tapentadol is not a pro-drug and therefore does not rely on metabolism to produce its therapeutic effects; this makes it a useful moderate-potency analgesic option for patients who do not respond adequately to more commonly used opioids due to genetic disposition (poor metabolizers of CYP3A4 and CYP2D6), as well as providing a more consistent dosage response range among the patient population. Tapentadol was invented at the German pharmaceutical company Grünenthal in the late 1980s led by Helmut Buschmann; the team started by analyzing the chemistry and activity of tramadol, which had been invented at the same company in 1962.

Comparison of tapentadol and tramadol

Feature	Tapentadol	Tramadol	Advantage
Opioid activity	Potent opioid	Weak opioid	Better analgesia with tapentadol
Additional action	Inhibition of NA reuptake and weak inhibition of serotonin reuptake	Inhibition of reuptake of serotonin and NA	Improved side-effect profile of tapentadol
Active metabolite	Active drug	Prodrug; active metabolite is O-desmethyl-tramadol	Early onset of action with tapentadol
Onset of action	32 min	Within 60 min	Early onset of action with Tapentadol
Drug interactions	Lack of CYP 450 interaction	Metabolised by CYP 450 enzymes	Minimal risk of adverse drug interactions with tapentadol
Interindividual variation	Lack of CYP interaction	Primarily metabolised by CYP450 isoenzyme 2D6; poor metabolisers may not get satisfactory analgesia with usual doses of tramadol	No inter-individual variation with tapentadol

RESEARCH QUESTION

- Is TAPENTADOL NASAL SPRAY more efficacious and safer than INJECTION TRAMADOL in post op pain management!

RESEARCH HYPOTHESIS

TAPENTADOL NASAL SPRAY is more efficacious and safer than INJECTION TRAMADOL in post op pain management

NULL HYPOTHESIS

TAPENTADOL NASAL SPRAY is not more efficacious and safer than INJECTION TRAMADOL in post op pain management

AIM

To study and compare the efficacy of TAPENTADOL NASAL SPRAY with INJECTION TRAMADOL in Post op pain management

OBJECTIVE

To study and compare the efficacy of TAPENTADOL NASAL SPRAY with INJECTION TRAMADOL in Post op pain management with respect to

1.Effectivenes of pain relief based on VAS pain scoring

2.Side effects

3.Rescue analgesic requirement

4.Duration of hospital stay

5.Mode of administration

METHODOLOGY

Study Design: Prospective comparative study

Study Location:A.C.S. MEDICAL COLLEGE AND HOSPITAL,CHENNAI

Study Duration: 4 months

Sample size: 80 subjects GROUP A -40 TAPENTADOL NS

GROUP B-40 TRAMADOL INJECTION

Subjects & selection method: The study population was drawn from patients who were admitted at our tertiary care center scheduled for various lower abdominal surgeries. The study is randomized, as patients were divided into two groups .

Group A: 40 adults- TAPENTADOL Nasal spray

Group B: 40 adults- received Injection tramadol-100 mg given IM route twice daily

Inclusion criteria:

1. Patients aged 20 to 60 years, scheduled for various lower abdominal surgeries
2. Either sex
3. Patients of ASA physical status I and II
4. Patients who provided informed consent.

Exclusion criteria:

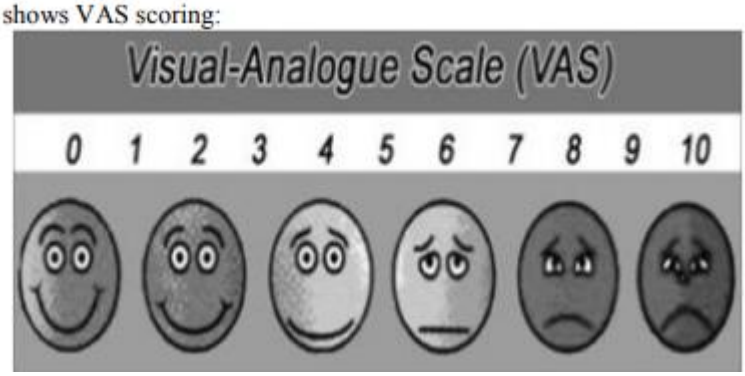
1. Patients with a history of allergy to study medications.
2. Pregnant and lactating women
3. Patients with a history of opioid abuse

Methodology: After getting informed consent from the patients, from 10 p.m. of day before surgery, all patients were kept nil by mouth. They were given Alprazolam 0.25mg along with cap. Omeprazole as pre medications. Before giving anaesthesia, multiparameter monitor were connected to record blood pressure, pulse rate, respiratory rate, oxygen saturation and ECG continuously.Surgery was performed under spinal anaesthesia. During surgery, no analgesics were given, and the patient was taken to the post-operative ward once

the surgery was completed. Patients were given either tapentadol NS or tramadol in the postoperative ward. Patients' pain was monitored every sixth hourly till 2 days postop. Pain was assessed using 11-point VAS.

Wong Baker Faces Rating Scale

The following image shows VAS scoring:



Patients were also monitored PulseRate,BP,RR As an objective way of assessing pain relief.

Parameters assessed:

1. Age

2. Gender

3. ASA grade

4. VAS score at 6,24 hours and 48 hours of surgery

5. Rescue analgesia requirement

6. Side effects

All the above parameters were compared between two groups and efficacy and safety of tapentadol will be proved

RESULTS

A total of 80 participants were enrolled in our study and given the test drugs during the study time. This population has been selected from the total of 186 patients who had under gone the different surgeries in our generalsurgery department. Of the 80 participants 40 were given Tramadol 100 mg IM and for other 40 patients it was Tapentadol nasal spray.

As shown in Table 1, at 6 hours after surgery which was considered as baseline, 17 patients (42.5%) had shown moderate pain and 23 patients (57.5%) had suffered with severe postoperative pain in Tapentadol intervention group. 14 patients (35%) with moderate pain and 26 patients (65%) with severe pain in Tramadol intervention group. At 24 hours of surgery 40 patients (100%) in Tapentadol intervention group had shown mild pain, and it was 22 patients (56.4%) in Tramadol intervention group, remaining 17 patients (43.6%) in Tramadol intervention group had shown moderate pain.

Table 1: Distribution of pain on visual analogue scale (VAS).

Time interval	No. of patients in Tapentadol group	No. of patients in Tramadol group	P- value	Odds ratio
6 hours				
Moderate pain	17 (42.5%)	14 (35%)	0.25	1.37 (0.55-3.38)
Severe pain	23 (57.5%)	26 (65%)		
24 hours				
Mild pain	40 (100%)	22 (56.4%)	<0.001	Can't be calculated
Moderate pain	0 (0%)	17 (43.6%)		
48 hours				
No pain	30 (75%)	7 (20%)	<0.001	12.0 (4.01-35.9)
Mild pain	10 (25%)	28 (80%)		

Missing data: 1 subject didn't take the medicine at 24hours, 5 subjects didn't take the drug at 48hours in Tramadol group.

The pain reduction was higher in Tapentadol group on chi-square test where p value is <0.001, here the odds ratio couldn't have calculated (because there were no patients with moderate pain in Tapentadol group). At 48 hours of surgery 30 patients (75%) in Tapentadol intervention group had shown no pain, and it was 7 patients (20%) in Tramadol intervention group. 10 patients (25%) in Tapentadol intervention group had shown mild pain, and it was 28 patients (80%) in Tramadol intervention group. The pain reduction was higher in Tapentadol group on chi-square test where P- value is <0.001.
Here the odds ratio was 12 with 95% confidence interval of 4.01-35.9.

Table 2: Comparison of adverse effects between the two study groups.

Adverse effect	No. of patients in Tapentadol group	No. of patients in Tramadol group	P value	Odds ratio (95% C.I)
Nausea				
No	33 (82.5%)	25 (62.5%)	0.045	2.83 (1.01-7.98)
Yes	7 (17.5%)	15 (37.5%)		
Vomiting				
No	35 (87.5%)	31 (77.5%)	0.24	2.032 (0.62-6.72)
Yes	5 (12.5%)	9 (22.5%)		
Dizziness*				
Fully awake and oriented	31 (77.5%)	23 (57.5%0	0.15	
Drowsy	6 (15%	10 (25%)		
Eyes closes but arousable to command	3 (7.5%)	7 (17.5%)		

*Dizziness according to modified Wilson sedation scale.

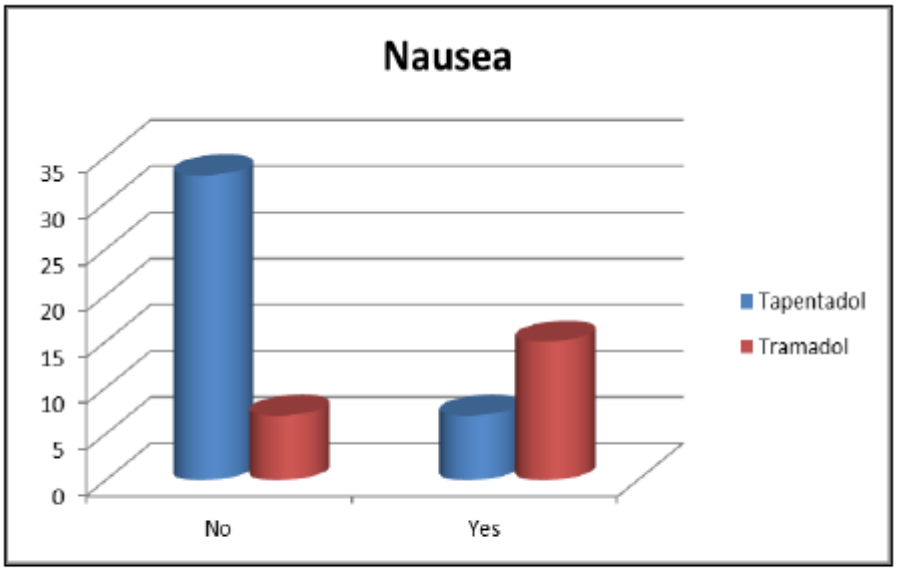


Figure 1: Comparison of adverse effects nausea between the two study drugs.

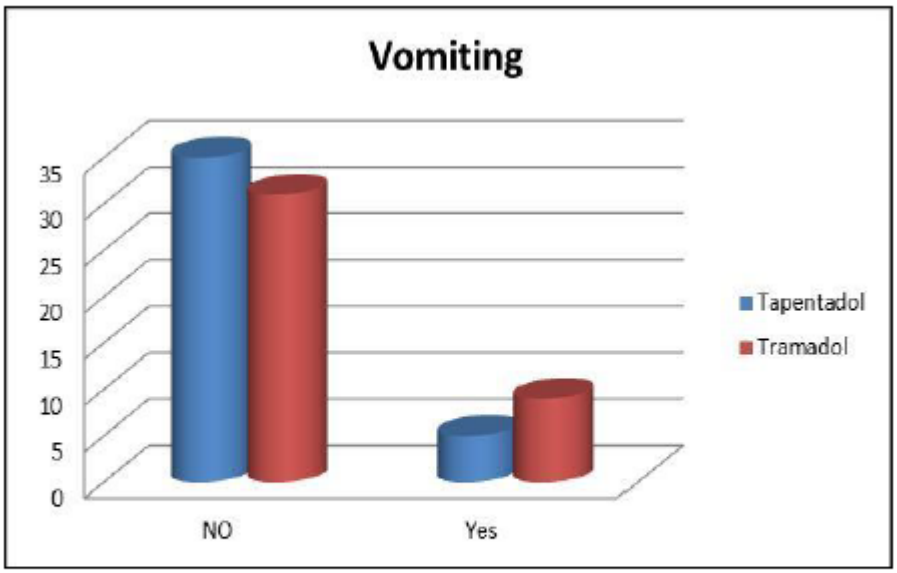


Figure 2: Comparison of adverse effect vomiting between two groups.

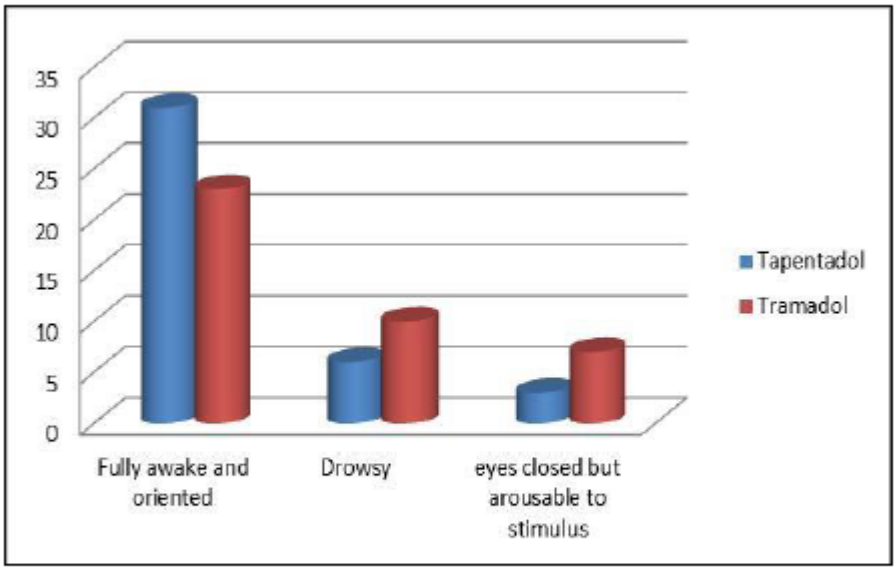


Figure 3: Adverse effect dizziness between two groups.

Table 2 and Figure 1, 2, 3 compares the adverse effects between two groups. Seven patients (17.5%) had shown Nausea with Tapentadol intervention group, and it was 15 patients (37.5%) in Tramadol intervention group. On chi square test it was found that the tramadol drug is associated with more nausea compared to Tapentadol, where the P- value is 0.045

(OR= 2.83, 95% C.I. 1.01-7.98). It was found that other adverse effects i.e. vomiting and dizziness were similar in both groups.

And there were no significance association found on chi square test. It was about 5 patients(12.5%) had shown vomiting with Tapentadol intervention group, and it was 9 patients (22.5%) in Tramadol intervention group. The P- value is 0.24. The odds ratio was 2.032 (95% C.I. 0.62-6.72). Nine patients (22.5%) had shown Dizziness with Tapentadol intervention group, and it was with 17 patients (42.5%) in Tramadol intervention group. The P- value is 0.06 (OR-2.55, 95% C.I. 0.96-6.73).

Table 3: Age distribution of study groups.

Age (years)	No. of patients in Tapentadol group	No. of patients in Tramadol group	Total
18-25	14	5	19
26-35	10	9	19
36-45	12	11	23
46-55	4	15	19
Total	40	40	80
Mean	32.62 (SD-9.7)	39.27 (SD-10.2)	35.95 (SD-10.47)

Table 4: Gender distribution of study subjects.

Gender	Tapentadol	Tramadol	Total
Female	13 (32.5%)	19 (47.5%)	32 (40.0%)
Male	27 (67.5%)	21 (52.5%)	48 (60.0%)
Total percentage	40 (100%)	40 (100%)	80 (100.0%)

DISCUSSION

In this study, a potential treatment effect was evaluated on changes in pain intensity determined by spontaneous patient self-report using a standard validated unimodal rating scale (VAS). Based on the above study and other studies we have categorised our VAS scale into no pain, mild, moderate and severe pain as explained in methodology.. Both treatments were well tolerated with only six patients in the Tramadol group (15%) withdrawing from the study because of intolerance to the drug The study demonstrated that Tapentadol had more effectiveness in reducing post-operative pain on Visual Analogue Scale compared to Tramadol. This is in contrast to previous studies where they have compared tramadaol and other opiods to NSAIDs like diclofenac in reducing the pain.

The most common adverse events in both groups (nausea and dizziness) were considered to be treatment-related, probably since investigator was aware of the safety profile of both drugs. On chi square test it was found that the Tramadol drug is associated with more nausea compared to Tapentadol. It was found that other adverse effects i.e. vomiting and dizziness were similar in both groups. And there were no significance association. It was observed that the study subjects did not experience any prolonged side effects during their recovery period.

CONCLUSION

From the results of the present study it can be concluded that both Tapentadol and Tramadol are effective in the treatment of Postoperative pain. The pain reduction was higher in Tapentadol group on chi-square test where p value is <0.001. So, we can conclude from our study findings that Tapentadol is efficacious compared to Tramadol in reducing Post-operative pain. Both the study drugs were well tolerated.

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