

## A comparative study of tapentadol versus tramadol in the treatment of low back pain

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### ABSTRACT

**Background:** Nontraumatic musculoskeletal disorders are the main reason for presentation to the emergency department with Rachialgia being the most common reason to request medical assessment among them.

**Methods:** This was a prospective, randomized, parallel group open labelled study conducted in a district level tertiary care hospital attached to a medical teaching institute. Patients were randomized into two groups. Group I (63 patients) received tablet tramadol 50 mg twice daily orally and group II (63 patients) received tablet tapentadol 50 mg twice daily orally.

**Results:** The mean age of the patients of group I was 40.6±9.6 years and in the group II was 42.7±10.6 years. A total of 61 males participated in the study of which 31 males were enrolled in group I and 30 in group II while 65 females participated in the study of which 32 females were enrolled in group I and 33 in group II. The mean reduction of pain intensity VAS score at the end of 4 weeks from baseline in group I and group II were 34.57 and 37.55 respectively. The difference in the mean reduction of pain intensity VAS between the two groups was not statistically significant.

**Conclusions:** We conclude that both the drugs show significant reduction in the pain intensity in moderate to severe CLBP patients. Tapentadol is as efficacious as tramadol in moderate to severe CLBP. However, tapentadol is better tolerated than tramadol.

**Keywords:** Tramadol, Tapentadol, Pain, VAS, Analgesic

### INTRODUCTION

Pain is one of the most common compelling reason for seeking medical attention. People takes health care for pain not only for diagnostic evaluation and symptom relief, but also because pain interferes with daily activities, causes worry and emotional distress, and undermines confidence in people's health.<sup>1</sup> The international association for the study of pain introduced the term neuropathic pain and defined it as pain initiated or caused by a primary lesion or dysfunction in the nervous system. Neuropathic pain is usually caused by

disease that affects any part of the nervous system. (somatosensory system).<sup>2</sup>

Low back pain (LBP) refers to pain and discomfort localized in the lumbosacral region, with or without radiating leg pain and is prevalent in the general population.<sup>3</sup> LBP can be acute, sub-acute and chronic. In acute pain the duration of low back pain can persists for less than 6 weeks, in sub-acute pain, LBP can persist for 6 to 12 weeks, while in chronic pain LBP can persists for 12 weeks or more.<sup>4</sup> LBP affects both genders and almost all age groups person. Most episodes of LBP are self-

limiting.<sup>5</sup> The lifetime prevalence of LBP is estimated to be at least 60 to 84%.<sup>6</sup>

People with chronic LBP experience social, mental, physical and occupational distress. The economic burden of LBP on the society is also enormous and tends to increase. About 40% of sick absences from work is just because of LBP - making it the second most common cause of workplace absenteeism.<sup>7</sup> Non-specific LBP is defined as low back pain that is not attributable to a recognizable, known specific pathology like infection, tumour, osteoporosis, fracture, structural deformity, inflammatory disorder, radicular syndrome, or cauda equina syndrome.<sup>8</sup>

The first line of treatment for CLBP is acetaminophen and NSAIDs while Short-term treatment of persistent unremitting CLBP require opioids, skeletal muscle relaxants, benzodiazepines, gabapentin and tricyclic antidepressants.<sup>2</sup> Guidelines produced over the last 4 years have shifted their emphasis from NSAIDs and COX-2 inhibitors to opioids.<sup>9</sup> The most commonly used opioids for the management of CLBP are analgesic like morphine, levorphanol, phenylpiperidines, fentanyl and methadone. These drugs are usually associated with serious side effects, along with addiction liability that limits their clinical usefulness. Therefore, there has been an intensive effort to find new analgesics that retain the effectiveness of morphine without or less potential side effects.<sup>2</sup>

Tramadol is centrally acting analgesic that is used for pain relief for more than a decade now. It acts by multiple mechanism like NA reuptake inhibition and serotonin reuptake inhibition, weak  $\mu$ -opioid receptor agonism. Tramadol appears similar to tapentadol, since both are  $\mu$ -opioid receptor agonist which also affects the monoaminergic system. However, there are important differences.

Studies have been carried out in the past which compared the efficacy and safety of tapentadol and tramadol in the treatment of low back pain, but most of have been carried out in the western countries.

The present study aims to compare the efficacy of tapentadol and tramadol for relief of low back pain and to compare the safety of tapentadol and tramadol for relief of low back pain as well as to analyze side effects, if any while the objective of the present study was to compare changes in pain intensity visual analogues scales (VAS) score caused by tapentadol versus tramadol that caused by tramadol in low back pain.

Hence to fill this gap this study was conducted which evaluated the efficacy and safety of tapentadol and tramadol on a comparative basis for relief of low back pain in the Indian population.

## METHODS

This was a prospective, randomized, parallel group open labelled study conducted in a district level tertiary care hospital attached to Dr. V.M. GMC medical teaching institute, Solapur, Maharashtra. This study was conducted at the orthopaedic outpatient department of a tertiary care hospital attached to medical college. The study was commenced following approval from an Institutional Ethics Committee from the period of January 2014 to May 2015. Patients who were diagnosed to have chronic nonspecific LBP satisfying the following inclusion and exclusion criteria, were enrolled in the study.

### *Inclusion criteria*

Inclusion criteria were patients aged >18 years and  $\leq$ 60 years, of either sex with moderate to severe chronic low back pain (non-specific low back pain).

### *Exclusion criteria*

Exclusion criteria were patients diagnosed with serious underlying spinal conditions (neoplasia, inflammation, infection). Subjects with back pain symptoms related to abdominal, pelvic, thoracic or renal pathology. Patients with history of hepatic or renal dysfunction. Patients with uncontrolled diabetes or hypertension, pregnant and lactating women, patients with h/o hypersensitivity to the study drugs or any other opioid.

The present study was conducted on 126 patients after obtaining the written informed consent and baseline values were recorded on the day of enrolment. Patients were then randomly allocated to two groups by chit method. Group I (63 patients) received tablet tramadol 50 mg twice daily orally. Group II (63 patients) received tablet tapentadol 50 mg twice daily orally.

Demographic data like age, sex was assessed at the time of enrolment of patients. Investigations like X-ray of lumbar region to rule out spine pathology and complete blood count (CBC), erythrocyte sedimentation rate (ESR) to rule out infections, were done only at baseline. Treatment was then started on the day of randomization and continued for 4 weeks. Follow up visits were scheduled at 7<sup>th</sup> day, 14<sup>th</sup> day and on 28<sup>th</sup> day.

### *Efficacy measures*

Efficacy assessment was done by calculating pain intensity on visual analogue scale (VAS).<sup>10</sup>

VAS was measured on day 1 (baseline), before starting the treatment and then at 7th day, 14th day and 28th day after starting the treatment. 0-4 mm- No pain, 5-44 mm- mild pain, 45-74 mm- moderate pain, 75-100 mm- severe pain. The distance between that mark and the origin is measured to obtain the patient's score.

### Statistical analysis

Categorical data in demographic parameters at baseline was analyzed by using 'Z' test for difference between two proportions. Continuous variables between the two treatment groups were analysed by unpaired t-test. Safety parameters were analysed using 'Z' test for difference between two proportions. A 'p' value <0.05 was considered statistically significant.

### RESULTS

Table 1 shows baseline characteristics of age in both the study groups. The mean age of the patients of group I was 40.6±9.6 years and in the group II was 42.7±10.6 years. Both the groups were comparable as regards to age distribution as there was no statistically significant difference between the two groups (p>0.05).

**Table 1: Age distribution of study groups (n=63).**

Age in years	Group I tramadol	Group II tapentadol
	N (%)	N (%)
18-20	1 (1.6)	2 (3.2)
21-30	9 (14.2)	7 (11.1)
31-40	18 (28.6)	17 (27.0)
41-50	22 (35.0)	19 (30.1)
51-60	13 (20.6)	18 (28.6)
Mean ±SD	40.6±9.6	42.7±10.6

Unpaired t test, p>0.05.

Table 2 shows that a total of 61 males participated in the study of which 31 males were enrolled in group I and 30 in group II. A total of 65 females participated in the study, 32 females were enrolled in group I and 33 in group II. Both the groups were comparable as regards to

sex distribution as there was no statistically significant difference between the two groups (p>0.05).

**Table 2: Gender distribution of study groups.**

Gender	Group I tramadol	Group II tapentadol
	N (%)	N (%)
Male	31 (49.2)	30 (47.6)
Female	32 (50.8)	33 (52.4)

Table 3 shows categorization of patients using VAS in group I as no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm) and severe pain (75-100 mm) in VAS scores at baseline, 1<sup>st</sup> week, 2<sup>nd</sup> week and 4<sup>th</sup> week in the group I. Table 4 show categorization of patients using VAS in group II as no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm) and severe pain (75-100 mm) in VAS scores at baseline, 1<sup>st</sup> week, 2<sup>nd</sup> weeks and 4<sup>th</sup> weeks in the group I.

Table 5 shows the mean values VAS scores in the study groups at baseline, at 1<sup>st</sup> week, 2<sup>nd</sup> weeks and at 4<sup>th</sup> weeks. VAS scores progressively decreased from baseline value of 73.87±10.6 to 39.30±19.0 at the end of 4<sup>th</sup> weeks in group I. Similarly, VAS scores decreased from baseline value of 75.08±11.8 to 37.52±19.8 at the end of 4<sup>th</sup> weeks in group II.

When the VAS scores of the two groups were compared with each other at baseline, 1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup> weeks, the difference was not statistically significant (p>0.05). Table 6 shows that the difference in the mean values VAS scores between study groups from baseline to 4 weeks were 34.57 and 37.55 respectively. The difference between the two groups was not statistically significant (p>0.05).

**Table 3: Categorization of patients using VAS in group I (tramadol).**

VAS	Baseline	1st week	2nd week	4th week
	N (%)	N (%)	N (%)	N (%)
0-4 mm (no pain)	0 (0)	1 (1.6)	3 (4.8)	5 (7.9)
5-44 mm (mild pain)	0 (0)	7 (11.1)	16 (25.4)	19 (30.2)
45-74 mm (moderate pain)	47 (74.6)	48 (76.2)	39 (61.9)	36 (57.1)
75-100 mm (severe pain)	16 (25.4)	7 (11.1)	5 (7.9)	3 (4.8)

**Table 4: Categorization of patients using VAS in group II (tapentadol).**

VAS	Baseline	1st week	2nd weeks	4th weeks
	N (%)	N (%)	N (%)	N (%)
0-4 mm (no pain)	0 (0)	0 (0)	3 (4.8)	6 (9.5)
5-44 mm (mild pain)	0 (0)	6 (9.5)	14 (22.2)	17 (27)
45-74 mm (moderate pain)	44 (69.8)	49 (77.8)	41 (65.1)	37 (58.7)
75-100 mm (severe pain)	19 (30.2)	8 (12.7)	5 (7.9)	3 (4.8)

**Table 5: VAS pain scores in the study groups.**

VAS scores	Group I* (tramadol)	Group II* (tapentadol)
<b>Baseline</b>	73.87±10.6	75.08±11.8
<b>1<sup>st</sup> week</b>	59.14±13.5	58.25±12.3
<b>2<sup>nd</sup> weeks</b>	49.44±16.3	49.73±15.6
<b>4<sup>th</sup> weeks</b>	39.30±19.0	37.52±19.8

**Table 6: VAS scores between study groups over the 4 weeks period.**

Variable	Group I* (tramadol)	Group II* (tapentadol)
<b>Difference in VAS scores</b>	34.57±19.1	37.55±18.5

\*Figures are (mean ±SD).

Table 7 show the incidence of adverse effects in the study groups over 4 weeks period, who reported a particular adverse effect like nausea, vomiting, dizziness, somnolence and constipation. These side effects were mild and none of the patients from either group discontinued the study drugs because of it. The incidence of nausea/vomiting, dizziness/somnolence was significantly less in group II with a p value=0.05, which is statistically significant when compared to that of group I.

**Table 7: Incidence of adverse effects in the study groups over 4 weeks period.**

Side effects	Group I* tramadol	Group II* tapentadol
<b>*Nausea/vomiting</b>	15 (23.8)	6 (9.5)
<b>*Dizziness/somnolence</b>	23(36.5)	12 (19.0)
<b>#Constipation</b>	2 (3.2)	1 (1.6)

\*Figures are numbers of patients. Z test, \*p=0.05, #p>0.05.

## DISCUSSION

Pain is one of the most common and among the most personally compelling reason for seeking medical attention. The present study was carried out to evaluate the efficacy and safety of tramadol and tapentadol in chronic nonspecific moderate to severe low back pain for the study period of 4 weeks.

A total 126 patients were included in the study, of which 63 patients were allocated to group I (tramadol 50 mg BD) and 63 patients to group II (tapentadol 50 mg BD) were considered for the analysis of data. The present study was aimed to evaluate the reduction in values of the VAS pain score and to assess improvement in quality of life after administration of the study drugs. Both the groups were comparable as regards to age and sex distribution.

In the present study, the mean±SD values of VAS scores at baseline, 1<sup>st</sup> week, 2<sup>nd</sup> week and 4<sup>th</sup> week, were

73.87±10.6, 59.14±13.5, 49.44±16.3 and 39.30±19.0 respectively in the group I whereas the mean ±SD values of VAS scores in group II at similar follow up were 75.08±11.8, 58.25±12.3, 49.73±15.6 and 37.52±19.8 respectively. The improvement in VAS scores was observed in both the study groups. However, the difference in the VAS scores between the groups I and II was not statistically significant at baseline, 1<sup>st</sup>, 2<sup>nd</sup>, and 4<sup>th</sup> weeks (p value >0.05).

The mean reduction of pain intensity VAS score in the present study, at the end of 4<sup>th</sup> weeks from baseline in group I and group II were 34.57 and 37.55 respectively. The difference was not statistically significant (p>0.05).

In a study conducted by Schnitzer et al, a mean reduction in pain intensity VAS score at the end of 4 weeks was 35 with a dose of 200-400 mg of tramadol.<sup>11</sup> This reduction in mean pain intensity VAS score achieved by tramadol was higher compare to that of our study which can be attributed to higher doses of tramadol (200-400 mg) used in the study conducted by Schnitzer et al.<sup>11</sup>

Vasani et al conducted a study in which tramadol 50 mg BD was compared with tapentadol 50 mg BD for a duration of 4 weeks.<sup>12</sup> They found that the mean reductions in pain intensity VAS score at the end of 4 weeks were 34.86 and 39.71 in tramadol and tapentadol group respectively. This reduction in mean pain intensity VAS score achieved by tramadol and tapentadol in Vasani et al study was comparable to that of our study.<sup>12</sup>

The side effects observed in the two groups in our study were nausea/vomiting, dizziness/somnolence and constipation. These side effects were mild and none of the patients from either group discontinued the study drugs because of it. The incidence of nausea/vomiting, dizziness/somnolence and constipation was significantly less in group II (tapentadol) compared to group I (tramadol) with a p value=0.05. Similar findings were observed in studies conducted by Zaman et al and Vasani et al where the safety and tolerability of tapentadol was superior than tramadol with a smaller number of patients experiencing adverse drug reactions.<sup>13,12</sup>

Several studies have been conducted using tramadol and tapentadol and comparing them with either placebo or oxycodone or NSAIDS, in chronic pain. Few studies have been conducted in the past, wherein head on comparison between tramadol and tapentadol was done in the treatment of low back pain. However, limited study evaluated the drugs with VAS score as it has been done in the present study.

## CONCLUSION

LBP is the most frequently self-reported form of musculoskeletal pain.<sup>14</sup> There are a variety of effective treatments for CLBP. Medication-based management and alternative treatment modalities, such as exercise, are

effective in the management of CLBP.<sup>15</sup> Opioids are very effective in moderate to severe pain while the other drugs like NSAIDS are more effective in mild to moderate pain.

Few studies have been carried out in the past which compared the efficacy and safety of tramadol and tapentadol i.e. centrally acting analgesic agents; for low back pain. But most of the studies involving these opioids have been carried out in the western countries and not in the Indian population. Therefore, it was worthwhile to conduct a study to evaluate the efficacy and safety of tramadol and tapentadol on comparative basis for relief of moderate to severe CLBP.

Therefore, based on the results of the present study, we conclude that both the drugs show significant reduction in the pain intensity in moderate to severe CLBP patients. Tapentadol is as efficacious as tramadol in moderate to severe CLBP. However, tapentadol is better tolerated than tramadol. Furthermore, as the present study was of only 4 weeks duration, more studies are required to be conducted to compare the long-term effect of tramadol and tapentadol.

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