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Original Research Article

Comparative study of efficacy and safety of pregabalin and gabapentin for treatment of neuropathic pain in oral cavity cancer patients: a comparative, randomized and prospective study

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ABSTRACT

Background: Pain in patients with oral cancers can limit the normal functioning and quality of life. Neuropathic pain raises the anxiety and depression levels, increases the morbidity and decreases the efficiency to work. Neuropathic pain is frequently diagnosed as a complication of cancer pain due to direct invasion of nerves, plexus or compression, and side effect of chemotherapy, radiation injury or surgery.
Methods: A total of 60 patients were divided randomly into two groups based on treatment: group P (pregabalin) and group G (gabapentin). The intensity of pain was measured using visual analog scale (VAS) and DN4 questionnaire (Douleur Neuropathique 4) was used to evaluate neuropathic component. Changes in pain score and neuropathic component was assessed at 2nd and 4th week of follow up. Data was collected and analysed using SPSS 20.0 software at level of significance being $p<0.05$.
Results: At baseline, the mean±SD of VAS score in group P was 7.20±0.79; in group G was 7.13±0.66. At 2nd week, the mean±SD of VAS score in group P was 4.5±0.91; in group G was 4.46±0.88. At 4th week, the mean±SD of VAS score in group P was 3.66±0.69; in group G was 3.83±0.85. At baseline, the mean±SD of DN4 score in group P was 7.13±0.80; in group G was 6.93±0.85. At 2nd week, the mean±SD of DN4 score in group P was 4.73±0.92; in group G was 4.46±0.82. At 4th week, the mean±SD of DN4 score in group P was 3.73±0.42; in group G was 3.93±0.62.
Conclusions: Pregabalin was found to be more effective with lesser side effects than gabapentin.

Keywords: Gabapentin, Oral cancer, Pain, Palliative care, Pregabalin

INTRODUCTION

Worldwide, oral squamous cell carcinoma (OSCC) is known to be the sixth most prevalent cancer.[1] Although in past 20 years, there is gross improvement in diagnosis and treatment modalities of oral cancers, but still outcomes of treatment and prognosis is compromised.[2] Malignancy is associated with a severity of pain causing extreme suffering to the patient. Neuropathic pain is frequently diagnosed as a complication of cancer pain due to direct invasion of nerves, plexus or compression, and side effect of chemotherapy, radiation injury or surgery. Radiation and chemotherapy in patients with oral cancers can cause prolonged pain. These adverse effects limit the normal functioning and quality of life. Pain also causes impairment in speech, eating, swallowing and other motor activities of the oral cavity.[3] Pain in patients with oral cancer is complex in nature and it generally exists along with the neuropathic cancer pain (NCP) or nociceptive pain or mixed pain. NCP can be primary or secondary in nature, being linked with effect on somatosensory system. Primary neuropathic pain occurs due to direct infiltration or compression of nerve, whereas secondary NCP occurs because of inflammation of tumor affecting secretion of cytokine and chemokine, leading to changes in pH.[4]

The awareness of severity, frequency of neuropathic pain, its role and utilization of management techniques is still limited in cancer patients, causing difficulty in managing the symptoms. Neuropathic pain not only effect quality of life of patients, but also raises the anxiety and depression levels, increase the morbidity and decrease the efficiency to work.[5] Management of NCP is observed to be a complex mechanism. It shows a limited response to treatment done with opioids alone. Treatment of NCP usually require combination of various drugs like anticonvulsants, antiarrhythmic and antidepressants.[6]

Now-a-days, pregabalin and gabapentin are being used as the preliminary drugs for management of NCP in cancers. Pregabalin and gabapentin are anticonvulsants, which decreases the secretion of excitatory neurotransmitters which are linked to perception of pain. It acts by binding to the presynaptic neuronal calcium channels.[7]

Till now, only few comparative studies have been conducted assessing the role of pregabalin and gabapentin in neuropathic pain. In Indian population, no study has been conducted till date, comparing pregabalin and gabapentin for treating neuropathic pain in patients with oral cancer. The present study was conducted with the aim to assess and compare the efficacy of gabapentin and pregabalin in managing the neuropathic pain of oral cancer patients.

METHODS

A prospective, randomised study was conducted in the Department of Palliative Medicine, SMS Medical College, Jaipur from May 2023 to December 2023, on patients suffering from neuropathic pain due to oral cancer.

Inclusion and exclusion criteria

Patients who were registered in palliative care centre, age between 18-70 years of both sexes, suffering from a histologically diagnosed advanced oral cavity cancer and having neuropathic pain were included in the study. Pregnant and lactating females, patients with known history of hypersensitivity to study drugs, having severe renal or liver impairment, taking drugs (antipsychotic, sedative- psychotropic, atropine and its substitute), those who were non-cooperative and not giving consent were excluded from the study.

A total of 60 cases were selected on the basis of inclusion and exclusion criteria, and were divided randomly into two groups based on treatment: group P (pregabalin): pregabalin 75 mg orally twice daily for 4 weeks (n=30); and group G (gabapentin): gabapentin 300 mg orally twice daily for 4 weeks (n=30). Randomisation was done on the basis of closed envelope system. The intensity of pain was measured and recorded using visual analog scale (VAS) in quantitative manner using scoring criteria from 0 (no pain) and 10 (very severe pain). DN4 questionnaire (Douleur Neuropathique 4) was used to evaluate the neuropathic component. Changes in pain score and neuropathic component was also assessed and recorded at 2nd and 4th week of follow up. Data was collected and analysed using SPSS 20.0 software at level of significance being $p<0.05$.

RESULTS

The study comprised of 60 patients, with 30 patients in each group. Demographic variables were assessed. Maximum number of patients was aged between 41-60 years of age, with male gender predominance. Most of the patients resided in rural areas, belonging to Hindu religion and were illiterate. In both the groups, insignificant population of patients had habits of tobacco chewing and smoking (Table 1).

Table 1: Comparison of demographic variable in the study groups.

Parameters		Group P		Group G	
		N	%	N	%
Age groups (years)	<20	0	0	0	0
	20-40	4	13.33	5	16.67
	41-60	18	60	19	63.33
	>60	8	26.67	6	20
Age mean/SD		52.3±10.2		51.96±9.45	
Gender	Female	5	16.67	4	13.33
	Male	25	83.33	26	86.67
Education	Illiterate	17	56.67	16	53.33
	Literate	13	43.33	14	46.67
Area	Rural	16	53.33	17	56.67
	Urban	14	46.67	13	43.33
Religion	Hindu	23	76.67	26	86.67
	Muslim	7	23.33	4	13.33
Addiction	No	11	36.67	9	30
	Alcohol	2	6.67	4	13.33
	Smoking	7	23.33	8	26.67
	Tobacco	10	33.33	9	30
Mean weight/SD		49.83	7.01	52	9.07
Total		30	100	30	100

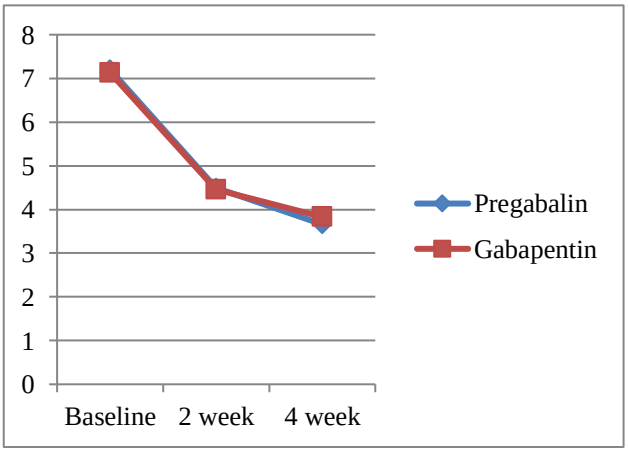

Figure 1: Comparison of mean VAS scores in both groups.

We evaluated the improvement in pain score after treatment with oral pregabalin and gabapentin with VAS scoring criteria. At baseline, the mean±SD of VAS score in group P was 7.20±0.79; in group G was 7.13±0.66. At 2nd week, the mean±SD of VAS score in group P was 4.5±0.91; in group G was 4.46±0.88. At 4th week, the mean±SD of VAS score in group P was 3.66±0.69; in group G was 3.83±0.85. It was observed that although pain score significantly decreased from baseline to 4th week in both the groups, the mean improvement in pain was found to be significantly more in patients subjected to pregabalin than gabapentin (Table 2).

Neurological improvement was assessed using DN4 questionnaire. At baseline, the mean±SD of DN4 score in group P was 7.13±0.80; in group G was 6.93±0.85. At 2nd week, the mean±SD of DN4 score in group P was 4.73±0.92; in group G was 4.46±0.82. At 4th week, the mean±SD of DN4 score in group P was 3.73±0.42; in group G was 3.93±0.62. It was observed that although the mean score significantly decreased from baseline to 4th week in both the groups, the mean improvement in neurological component was found to be significantly more in patients subjected to pregabalin than gabapentin (Table 3).

Table 2: Comparison of VAS scores in the study groups.

	Baseline Mean±SD	2nd week Mean±SD	4th week Mean±SD	P value	Mean improvement
Pregabalin	7.2±0.79	4.5±0.91	3.66±0.69	P<0.0001	3.54
Gabapentin	7.13±0.66	4.46±0.88	3.83±0.85	P<0.0001	3.3

Table 3: Comparison of DN4 questionnaire scores in the study groups.

	Baseline Mean±SD	2nd week Mean±SD	4th week Mean±SD	P value	Mean improvement
Pregabalin	7.13±0.80	4.73±0.92	3.73±0.42	P<0.0001	3.4
Gabapentin	6.93±0.85	4.46±0.82	3.93±0.62	P<0.0001	3.0

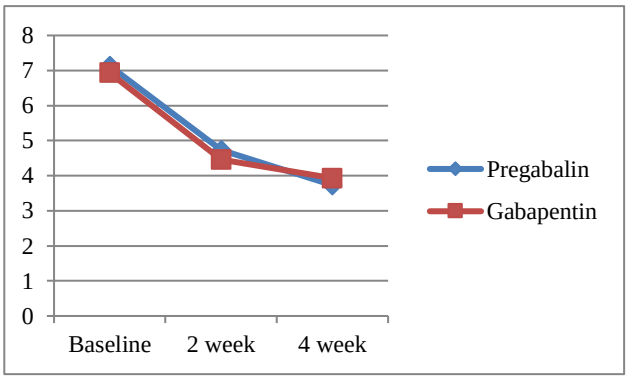

Figure 2: Comparison of mean DN4 questionnaire scores in both groups.

Table 4: Side effects among the study groups.

Adverse effects	Pregabalin	Gabapentin
Sedation	2	1
Drowsiness	1	3
Blurring of vision	0	1
Nausea	2	1
Headache	1	2
Total	6	8

Besides assessing efficacy of both the drugs, we also studied their side effects. It was found that patients suffered from more episodes of drowsiness, headache, blurring of vision with the use of gabapentin as compared to pregabalin (Table 4).

DISCUSSION

The present study was conducted to assess and compare the efficacy of oral 75 mg pregabalin and 300 mg gabapentin in managing the neuropathic pain in oral cancer patients. Demographic variables like age, gender, habit, education, area, weight were evaluated and found to be comparable in both the groups. We evaluated the improvement in pain score after using pregabalin and gabapentin with the help of VAS scoring criteria. Pregabalin and gabapentin are anticonvulsants that act by inhibiting the pain sensors and calcium ion channels in the pain fibres of the postsynaptic dorsal root. They increase the threshold of pain in patients. We found that both the drugs significantly reduce the pain score from baseline to 4th week, but the mean improvement in pain was found to be significantly more in patients subjected to treatment with pregabalin than with gabapentin. Similar to our study Mishra et al found that there was a significant difference in pain score in pregabalin group as compared to other groups [group amityrptiline (p=0.003), group gabapentin (p=0.042), group placebo (p=0.024].[8] We compared pregabalin with gabapentin in our study, but it is known that both act by modulation of alpha-2 delta subunit of voltage-gated calcium channels. Thus, results of above studies can be applied and are comparable with our study. Richter et al reported that pregabalin 300 mg/day provides

>50% reduction in pain from baseline in about 40% of total patients.[9] In a study by Ghosh et al found that by end of study pregabalin has significant efficacy in reducing the quality of pain than gabapentin (p=0.0146) but there was no significant difference in final VAS scores between both the groups.[10] However, there was no significant difference in reduction of pain intensity.

In our study, improvement in neuropathic pain was assessed using DN4 (Douleur Neuropathique 4 questions) questionnaire.[11] This questionnaire comprises of 10 items that depicts both the signs related to bedside sensory assessment and sensory descriptors. It is a tool which is being used for diagnosing the neuropathic pain. Its seven items are linked to symptoms like tingling, prickling and cold sensation, burning, electric shocks, itching and numbness). Rest three items are related to clinical assessment (hypoesthesia while injecting or touching, and pain while rubbing). We found that although mean score of DN4 significantly decrease from baseline to 4th week in both the groups, but the mean improvement in neurological component was found to be significantly more in patients subjected to pregabalin than gabapentin. Rosenstock et al described a 67% reduction in neuropathic pain in patients treated with pregabalin.[12] Similar to our study Lamba et al found that the pregabalin is a better medication for the management of neuropathic pain as compared to gabapentin.[13] Similar to our study Lamba et al found that in the management of neuropathic pain in cancer patients who are undergoing palliative care, a combination of pregabalin with amitriptyline was found to be more effective in pain relief than gabapentin with amitriptyline.[14]

In present study we found that gabapentin had more side effects than pregabalin in terms of more episodes of drowsiness, headache, blurring of vision with the use of gabapentin, whereas with pregabalin few patients suffered from sedation and nausea. Similar to our study, Madhanagopal et al stated that pain relief was better in the pregabalin group than in gabapentin and placebo with an equal incidence of adverse effects except for nausea which was more in the pregabalin group.[15]

The present study reveals that both pregabalin and gabapentin are well tolerated by patients with oral cancers. Pregabalin revealed better efficacy in relieving neuropathic pain and had less side effects than gabapentin.

The present study was a single-center study conducted on less sample size with a limited follow up of 4 weeks. Thus, further multi-centre studies should be conducted on large sample size, and with longer follow up. In future clinical trials should be conducted to study and compare various other drugs to manage neuropathic pain in oral cancer cases. In our study, we used fixed dose of drugs instead of comparing different dose ranges by dose titration. Thus, future studies should be conducted assessing efficacy of drugs at various dose ranges.

CONCLUSION

Both pregabalin and gabapentin are effective in treating the neuropathic pain in patients with oral cancers. But pregabalin was found to be more effective with lesser side effects than gabapentin. We assessed patients using readily available evaluation scales. In future there is a need to conduct multicentric studies, having a large sample size with long follow up period using even better scales, on different drug combinations to get more authentic, conclusive and accurate results.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Givony S. Oral squamous cell carcinoma (OSCC) an overview. J Med Sci. 2020;8:67-74.
2. Yang Y, Zhang P, Li W. Comparison of orofacial pain of patients with different stages of precancer and oral cancer. Sci Rep. 2017;7:203.
3. Epstein JB, Miaskowski C. Oral pain in the cancer patient. JNCI Monographs. 2019;2019(53):lgz003.
4. Salwey L, L'Huillier V, Zaid M, Vené Y, Tavernier L, Mauvais O. Neuropathic pain at diagnosis of head and neck squamous cell carcinoma. Euro Ann Otorhinolaryngol Head Neck Dis. 2020;137(5):377-80.
5. Epstein JB, Wilkie DJ, Fischer DJ, Kim YO, Villines D. Neuropathic and nociceptive pain in head and neck cancer patients receiving radiation therapy. Head Neck Oncol. 2009;1:26.
6. Gül ŞK, Tepetam H, Gül HL. Duloxetine and pregabalin in neuropathic pain of lung cancer patients. Brain Behav. 2020;10(3):e01527.
7. Shahid W, Kumar R, Shaikh A, Kumar S, Jameel R, Fareed S. Comparison of the efficacy of duloxetine and pregabalin in pain relief associated with diabetic neuropathy. Cureus. 2019;11(7):e5293.
8. Mishra S, Bhatnagar S, Goyal GN, Rana SP, Upadhya SP. A comparative efficacy of amitriptyline, gabapentin, and pregabalin in neuropathic cancer pain: a prospective randomized double blind placebo controlled study. Am J Hosp Care. 2012;29(3):177-82.
9. Richter RW, Portenoy R, Sharma U, Lamoreaux L, Bockbrader H, Knapp LE. Relief of painful diabetic peripheral neuropathy with pregabalin: a randomized, placebo-controlled trial. J Pain. 2005;6(4):253-60.
10. Ghosh AK, Kundu A, Das AP, Bhattacharya KB. Comparative study of the efficacy and safety of pregabalin and gabapentin in neuropathic pain. Asian J Pharm Life Sci. 2012;2(1):64-71.
11. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain. 2005;114(1-2):29-36.

12. Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. Pain. 2004;110(3):628-38.
13. Lamba N, Makkar R, Gupta N, Sarna S, Khandelwal S. Effect of oral gabapentin and pregabalin in the management of neuropathic pain in palliative care patients: an institution-based comparative study. J Mahatma Gandhi Univ Med Sci Tech. 2021;6(2):46-7.
14. Lamba N, Pareek A, Dhal S, Goyal S, Makkar R, Sarna S. A comparative study to analyze the effect of gabapentin with amitriptyline versus pregabalin with amitriptyline in neuropathic pain in cancer patients undergoing palliative care. Acta Med Int. 2022;9:124-6.
15. Madhanagopal R, Balasubramanian AK, Gowda PS, Rathnasabapathy B, Shankar R. Comparison of post operative analgesic effect between pregabalin and gabapentin given as premedication drugs for patients undergoing laparoscopic cholecystectomy. Indian J Clin Anaesth. 2021;8:179-84.

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