Original Article

A Comparative Study to Analyze the Effect of Gabapentin with Amitriptyline Versus Pregabalin with Amitriptyline in Neuropathic Pain in Cancer Patients Undergoing Palliative Care

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Abstract

Introduction: Antiepileptics and antidepressant medications are known for managing neuropathic pain. We aim to compare the effects of pregabalin with low-dose amitriptyline and gabapentin with low-dose amitriptyline in managing neuropathic pain in cancer patients undergoing palliative care. **Materials and Methods:** We conducted our study on 160 cancer patients who were having neuropathic pain and were undergoing palliative care treatment in our institute. It was a hospital-based, randomized, tertiary cancer center-based observational study. After taking approval from the institutional ethics committee and taking written informed consent from patients, the patients were divided into two groups and the effect of medicines on incidence of neuropathic pain was observed; the incidence of burning sensation and the incidence of adverse effects of medications were also analyzed. Statistical analysis was done using paired t-test and SPSS version 20 software. **Results:** The onset of relief in pain was earlier in the pregabalin group as compared to the gabapentin group. There was more reduction in a burning sensation in the pregabalin group as compared to the gabapentin group. The incidence of headaches was the same in both groups. Nausea and vomiting were more in the pregabalin group but the overall difference in adverse effects was not statistically significant ($P > 0.05$) **Conclusions:** 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.

Keywords: Amitriptyline, gabapentin, pain medicine, palliative care, pregabalin

Introduction

Gabapentin and pregabalin are adjuvant antiepileptic medications which are used for the relief of neuropathic pain. Amitriptyline is a tricyclic antidepressant medication which apart from its mood-elevating properties also has an effect on neuropathic pain.

Cancer-related mortality has been on decreasing trend and survival is increased.[1] Neural dysfunction due to cancer is the cause of neuropathic pain and this dysfunction may be spontaneous or may be due to a painful stimulus.[2]

In cancer patients who are undergoing palliative care, the role of neuropathic medicines in providing relief is well known. Inadequate pain relief is the most common cause of treatment discontinuation and distress to the patient. Multimodal analgesia using the WHO step ladder is the most common mode of standardized treatment. Relief from pain is a basic human right. We, in our study, have tried to compare the effects of the medications and tried to provide better pain management guidelines for patients.

Materials and Methods

We conducted our study in a tertiary care cancer center in the pain and palliative medicine department. It was a prospective, observational, randomized, comparative study. SRCC was

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the place of study. This study was conducted in 160 patients undergoing supportive care. We conducted our study after taking due permission from the institutional ethics committee and taking written informed consent from our participants. IEC No./MGMC&H/IEC/JPR/2021/1154. One hundred and sixty patients were enrolled in the study, and for study purposes, we have divided participants into two groups. Patients in Group A received pregabalin 75 mg and 25 mg amitriptyline at bedtime, and patients in Group B received gabapentin 300 mg and 25 mg amitriptyline. We have used the Visual Analog Scale (VAS) for analyzing pain scores. Follow-up was done for 30 days. For statistical analysis, we have used paired *t*-test and IBM SPSS Statistics for Windows, version 20.0. Armonk, NY, USA: IBM Corp software.

- Group A: Eighty cases were given pregabalin 75 mg and amitriptyline 25 mg
- Group B: Eighty cases were given gabapentin 300 mg and amitriptyline 25 mg.

Inclusion criteria

- Patients undergoing cancer treatment having neuropathic pain were included in the study.

Exclusion criteria

- Patient refusal
- Patients having organ dysfunction
- Patients with clouded sensorium.

Results

The mean age in Group A was 39.24 ± 7.12 and Group B was 40.22 ± 7.32, having $P > 0.05$. These groups were comparable. Mean weight in Group A was 73.24 ± 6.18 and Group B was 72.21 ± 7.23 $P > 0.05$ [Table 1].

Incidence of burning sensation in Group A was 93.75%, 80%, 72.50%, and 65% at respective 1, 2, 3, and 4 weeks and in Group B was 96.25%, 90%, 94%, and 75% at respective weeks [Table 2].

In Group A incidence of spontaneous pain was in 76.25% patients, this reduced to 65.00% in 1st week, 57.5% in 2nd week, 37.50% in 3rd week and 27.50% in 4th week and in Group B baseline incidence of spontaneous pain was in 78.75% patient's and it reduced to 71.25% in 1st week, 52.50% in 2nd week, and 47.50% in 3rd week and 33.75% in 4th week. There was more reduction in the incidence of spontaneous pain in patients of Group A as compared to Group B [Table 3].

There was more reduction in pain in Group A from 8.23 ± 2.42 to 3.24 ± 4.41 as compared to Group B from 8.54 ± 2.27 to 3.92 ± 4.79 at 4 weeks. The mean improvement in pain on VAS was more in Group A as compared to Group B was 4.63 ± 4.24–4.24 ± 4.16 [Table 4].

There was an incidence of nausea, vomiting, dizziness, drowsiness, headache, and visual disturbances in both Group A and Group B. There was no incidence of urinary retention and respiratory depression [Table 5].

Discussion

Pregabalin and gabapentin both are adjuvant antiepileptic medications which are used in the management of neuropathic pain. The addition of an antidepressant as an adjuvant, in this case, amitriptyline was done. Their effects were evaluated

Table 1: Patients demographics

	Group A (*n*=80)	Group B (*n*=80)	*P*
Age (years)	39.24±7.12	40.22±7.32	>0.05
Sex male\female	42\38	41\39	>0.05
Weight (kg)	73.24±6.18	72.21±7.23	>0.05

Table 2: Incidence of burning sensation

Duration weeks	Study population with burning sensation, number of cases (%)	
	Group A (*n*=80)	Group B (*n*=80)
Baseline	80 (100.0)	80 (100.0)
1 week	75 (93.75)	77 (96.25)
2 weeks	64 (80.0)	72 (90.0)
3 weeks	58 (72.50)	68 (85.00)
4 weeks	52 (65.00)	60 (75.00)

Table 3: Incidence of spontaneous pain

Duration in weeks	Study population with spontaneous pain, number of cases (%)	
	Group A (*n*=80)	Group B (*n*=80)
Baseline	61 (76.25)	63 (78.75)
1 week	52 (65.00)	57 (71.25)
2 weeks	46 (57.5)	42 (52.50)
3 weeks	30 (37.50)	38 (47.50)
4 weeks	22 (27.50)	27 (33.75)

Table 4: Visual Analog Score

Visual Analog Score	Group A	Group B
Baseline	8.23±2.42	8.54±2.27
At 4 weeks	3.24±4.41	3.92±4.79
Mean improvement	4.63±4.24	4.24±4.16

Table 5: Adverse effects

	Group A (*n*=80), *n* (%)	Group B (*n*=80), *n* (%)	*P*
Nausea	20 (25)	12 (15)	>0.05
Vomiting	11 (13.75)	10 (12.5)	>0.05
Dizziness	8 (10)	7 (8.75)	>0.05
Drowsiness	4 (8)	4 (8)	>0.05
Headache	5 (6.25)	5 (6.25)	>0.05
Visual disturbances	1 (1.25)	2 (4)	>0.05
Urine retention	0	0	
Respiratory depression	0	0	

in the management of neuropathic pain and a comparative analysis was done. Their effects were evaluated for 1 month. It is well known that pain is a symptom of the underlying disease and it may be caused by nerve damage.[3] There are many causes of neuropathic pain. It may be central or peripheral neuropathic origin in nature.[4] Amitriptyline has a role in relieving neuropathic pain and also has antitumor properties.[5] Adjuvant medications are useful when neuropathic pain becomes opioid unresponsive.[6] Yilmaz *et al*. found no difference between gabapentin and pregabalin statistically in managing neuropathic pain.[7] Hong *et al*.'s results showed that gabapentinoids used in psychiatric states are not supported by evidence.[8] Richter *et al*. reported that pregabalin provides >50% decrease in pain intensity in about 40% of patients.[9] Rayani *et al*. reported that pregabalin is more effective in relieving pain and quality of life in chronic inflammatory demyelinating polyneuropathy, patients as compared to gabapentin.[10] In pain due to spinal cord injury, pain relief was better with pregabalin and gabapentin has a better safety profile.[11] Pregabalin has a better pain-relieving effect than gabapentin and amitriptyline but gabapentin was found to have less side effects.[12] Pregabalin and gabapentin were both effective in pain relief but gabapentin provided better pain relief with lesser side effects than pregabalin.[13]

Manjushree *et al*. state that for treatment of chemotherapy-induced peripheral neuropathy, gabapentin and pregabalin were equally effective but adverse effects were found to be more in the gabapentin group.[14] Madhanagopal *et al*. state 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] In our study, we concluded that there was a reduced incidence of spontaneous pain, and better improvement in VAS score in the pregabalin group than in the gabapentin group. There was an increased incidence of nausea and vomiting in the pregabalin group than gabapentin group. Dizziness was slightly more incident in the pregabalin group and headache and drowsiness were equal in both groups. The overall difference in the incidence of adverse effects was found to be insignificant while comparing both groups $P > 0.05$.

Conclusions

In the management of neuropathic pain in cancer patients who are undergoing palliative care, pregabalin with amitriptyline was found to be more effective in providing pain relief than gabapentin with amitriptyline.

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Conflicts of interest

There are no conflicts of interest.

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