## Original Article

# A Comparative Study on the Efficacy of Pregabalin Over Gabapentin in Controlling Neuropathic Pain due to Spinal Cord Disc Diseases in Bankura Sammilani Medical College and Hospital

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**Background :** Neuropathic Pain (NP) due to Spinal Cord Disc Diseases (SDD) have been treated extensively with medical therapy before surgery. Gabapentin (GBP) and Pregabalin (PGB) are anti-convulsants which have proved effective in controlling NP due to SDD.

**Aims and Objectives :** (1) To determine the efficacy of GBP and PGB individually in controlling NP due to SDD. (2) To compare their efficacy in doing so.

**Materials and Method :** This study was conducted among the patients with SDD in the Neurosurgery OPD of Bankura Sammilani Medical College & Hospital between April, 2023 to September, 2023 with 50 patients receiving GBP (600mg/day) tablets and another 50 patients receiving PGB (150mg/day) tablets, along with Amitriptyline (25mg/day) tablets and Multivitamin tablets (given to all).The pain scores were recorded according to the visual analog scale before the drug usage followed by at the end of 1st, 2nd and 3rd month after consumption of the drugs, along with their opinion on the action of the drug according to the Odom's criteria. The data were compared using paired 't' test in MS Excel and values <0.05 were considered significant.

**Results :** Among the patients receiving GBP, the mean pain score initially was 6.66±1.52 while after the administration of the drug, it decreased to 4.84±1.80, 4.14±1.64 and 3.52±1.42 at the end of 1st, 2nd and 3rd month respectively. Among the patients receiving PGB, the mean pain score initially was 6.78±1.33 while after drug usage, it decreased to 4.64±1.71, 3.74±1.58 and 3.16±1.58 at the end of 1st, 2nd and 3rd month respectively.

**Conclusion :** Both GBP and PGB are equally effective in controlling NP. PGB is more effective than GBP possibly owing to it's better pharmacokinetic profile.

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***Key words*** **: Gabapentin, Pregabalin, Neuropathic Pain.**

Spinal Cord Disc Diseases (SDD) include degeneration of intervertebral discs which leads to pain in the back and the neck with radiating pain to the legs and arms respectively[1]. These SDD leads to central canal stenosis and/or foraminal stenosis, which causes entrapment of the nerve roots, leading to pain, numbess and tingling sensations to their respective areas as well as neurological deficits[2]. SDD is estimated to affect about 5 percent of the population in developed countries each year[1]. The annual incidence of an episode of Lumbosacral Disc Disease (sciatica) ranges from 1 to 5%[3]. These diseases incur a huge financial and social cost for the country as well as causes emotional sufferings.

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***Editor's Comment :***

- Both GBP and PGB are effective in producing significant relief of neuropathic pain. However, due to certain pharmacological advances, PGB is more effective than GBP.

Initially all SDD are managed by medical and physical therapy. Medical therapy includes the usage of NSAIDS, analgesics like tramadol, morphine, epidural inoculation of corticosteroids and transforaminal periradicular injections of corticosteroids[4], use of stimulated form of methylcobalamine (Vitamin $B_{12}$)[5] along with physical therapy, behavioral therapy and multidisciplinary treatment have shown promising results. However, for patients for whom medical therapy has failed and have presented with neurofocal deficits, surgery in the form of discectomy and laminectomy is attempted.

Gabapentin (GBP), an analog of the c amino butyric acid (neurotransmitter) and Pregabalin (PGB) a lipophilic GABA analog are anticonvulsants which binds with the $\alpha 2\delta$ subunit of the voltage gated calcium channels have proved to be efficacious in the management of the Neuropathic Pain (NP). They

decrease the release of neurotransmitter associated with central sensitization[6].

Despite being similar in action, they have some differences in their pharmacokinetics and pharmacodynamics. There have been many individual studies exploring the effects of only GBP or only PGB on their efficacy in controlling NP. However, there are only a few studies comparing the effectiveness of GBP and PGB on NP. Also, PGB is newer drug in this field of pain relief, through this study we shall explore the effectiveness of the drug.

## Aims and Objectives

(1) To assess the efficacy of PGB and GBP individually in contolling NP due to Spinal Cord Diseases.

(2) To compare the efficacy of PGB with GBP in contolling NP due to Spinal Cord Diseases.

## Materials and Method

This is an institution based prospective study carried out among patients in the Out Patients Department (OPD) of Neurosurgery of Bankura Sammilani Medical College and Hospital between April, 2023 to September, 2023 with final sample size of 100 patients, 50 each in 2 groups.

**Inclusion Criteria :** All patients between the ages 18 and 70 suffering from SDD with the complaint of NP.

**Exclusion Criteria for Patient Selection :** (1) Having already received either PGB or GBP for treatment of SDD in the past.

(2) Receiving GBP or PGB as part of treatment of other diseases like epilepsy, anxiety.

(3) Motor deficits like drop foot, claw hands etc.

(4) Have underwent surgery for Spinal Cord Diseases or are planning to undergo surgery for the same.

**Data Collection :** The patient on being diagnosed (through clinical and radiolological methods) with NP due to SDD, had their pain assessed after informed consent. The patients were put into two groups by simple random sampling. One group was started on GBP, at a dose of 300 mg twice a day; while the other group was put on PGB, at a dose of 75 mg twice a day. Both groups were given Amitriptyline 25 mg/day and multivitamin.

**Assessment of Pain :** The pain was assessed on the very first visit of the patient, followed by after consumption of PGB or GBP at the end of each for 3 months by using Visual Analogue Scale (Table 1)[7] and Odom's Criteria (Table 2)[8].

Data analysis was done using means, median and standard deviation. The pre-treatment and post-treatment scores were compared by paired 't' test. Any p value <0.05 was considered significant. The data was represented via tables and charts. For determining which drug is more effective, head to head comparison method was used. All the calculations have been done in MS Excel version 2007.

## Results

The age distribution of the patients receiving GBP and PGB is represented in the Table 3 (below). The mean age of the patients receiving GBP is 45.56 ± 13.44 years while the mean age of the patients receiving PGB is 44.24±11.18 years.

The number of male and female patients receiving GBP were 25 each.

The number of male patients receiving PGB were 27 while the number of female patients receiving PGB were 23.

Among the patients receiving GBP, the mean score for pain before its administration was 6.66±1.52 while after the administration of the drug , the mean scores for pain were 4.84±1.80, 4.14±1.64 and 3.52±1.42 at the end of 1st, 2nd and 3rd month respectively. When compared with paired t test , all the reduction in pain was found to be significant as shown in Table 4. There were 5 patients who had no reduction in pain despite using the drug for 3 months, while 2 patients had nearly complete (pain score <2) remission of pain at the end of 3 month. The number of patients who considered the drug to be good or excellent (Odom's criteria 1 and 2) at the end of 1st month was 21 which increased to 28 and 36 at the end of 2nd and 3rd month respectively. Table 5 shows the trend of working of the drug according to Odom's Criteria.

Among the patients receiving PGB, the mean score for pain before the administration was 6.78±1.33 while after the administration of the drug , the mean scores for pain were 4.64±1.71, 3.74±1.58 and 3.16±1.58 at the end of 1st, 2nd and 3rd month respectively. When compared with paired 't' test, all the reduction in pain was found to be significant as shown in Table 2. There were 1 patients who had no reduction in pain despite

Table 1 — *The Visual Analog Scale for Assessment of Pain*

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| No pain | | Mild Pain (Annoying) | | Moderate Pain (Uncomfortable) | | Severe Pain (Dreadful) | | Very Severe Pain (Horrible) | | Worst Pain (Agonizing) |

Table 2 — *The Odom's Criteria*

| Rating | Description | Criteria |
|---|---|---|
| 1 | Excellent | Completely relieved of symptoms and daily lives and occupation not impaired |
| 2 | Good | Intermittent discomfort but no interference in occupational activities |
| 3 | Fair | Subjective improvement but physical activities still significantly limited |
| 4 | Poor | No improvement or symptoms had deteriorated |

Table 3 — *The Distribution of Patients in the Different Age Groups*

| Age Groups (in years) | Number of Patients Receiving GBP | Number of Patients Receiving PGB |
|---|---|---|
| 18 - 30 | 8 | 5 |
| 31 - 40 | 10 | 13 |
| 41 - 50 | 13 | 12 |
| 51 - 60 | 12 | 17 |
| >60 | 7 | 3 |

using the drug, while 6 patients had nearly complete (pain score <2) remission of pain at the end of 3 month. The number of patients who considered the drug to be good or excellent (Odom's criteria 1 and 2) at the end of 1st month was 31 which increased to 42 and 43 at the end of 2nd and 3rd month respectively.

## Discussion

Antiepileptic drugs like GBP and PGB were reported to produce significant pain relief as compared to placebo and achieved significant improvements in Quality of Life in patients with postherpetic neuralgia, painful diabetic neuropathy and postsurgical pain.[9] Analgesic action of GBP is owed to its indirect interaction with the glycine binding sites of the NMDA receptors while PGB decreases the release of excitatory neurotransmitter Glutamate by decreasing the calcium influx after binding to the voltage gated calcium channels leading to decreased AMPA receptor activation[9]. Randomized Clinical Trials (RCTs) that administered GBP for chronic pain reported that with a daily dosages of up to 3600 mg, there was significant pain reduction compared with a placebo in patients with mixed NP syndromes while those trials where

Table 5 — *The Ratings of the Patients According to Odom's Criteria Regarding the Working of the Drugs*

| Drugs | Median Rating at the end of 1st Month | Median Rating at the end of 2nd Month | Median Rating at the end of 3rd Month |
|---|---|---|---|
| GBP | 3 (fair) | 2 (good) | 2 (good) |
| PGB | 2 (good) | 2 (good) | 1.5 (good to excellent) |

PGB was administered showed effective pain control at a daily dose ranging from 50 to 300 mg[10].

GR Grice and MK Mertens, in 2008[11] reported of two cases where GBP had shown to reduce NP due to sciatica within a couple of days of starting the drug when hydrocodone-acetaminophene had failed. It also mentions an open labeled trial where the pain relieving efficacy of GBP was evaluated in controlling centrally mediated pain and peripherally mediated pain and tremors[12], where it proved to reduce the latter significantly.

According to an article review by Noor M Gajraj in 2007,[13] certain advances in the pharmacology of PGB may have led to the increased efficacy of PGB over GBP in this study. PGB binds to the $\alpha_2\delta$ subunit of voltage gated calcium channels just like GBP. However, it's binding affinity and potency for the above mentioned receptor is six times more than GBP. Unlike GBP, PGB has a linear pharmacokinetic profile as absorption of PGB is not saturable. It's peak concentration reaches within 1 hour with a bioavailability of 90%; while the peak concentration of GBP reaches between 2-3 hours and has a bioavailability of 27-60%. PGB does not bind to any plasma protein. Time to reach the effective dose is 1 day for PGB, while it is 9 days for GBP. According to L Gianesello[14], patients who have been treated with PGB in the pre-operative period require less opioids and have improved Quality of Life 3 months after spinal surgery.

K Robertson[15] and co in their article review explored the efficacy of PGB and GBP in controlling NP by considering various RCTs that had been conducted with these drugs. One specific review from their article was the NICE UK[16] guidelines which stated PGB better than GBP in controlling NP because of its lower NNT

Table 4 — *The Mean Scores for Pain Before and After the Usage of the Respective Drugs*

| Drugs | Mean Score for pain before usage of the drug | Mean Score for pain after usage of the drug at the end of 1st month | P value | Mean Score for pain after usage of the drug at the end of 2nd month | P value | Mean Score for pain after usage of the drug at the end of 3rd month | P value |
|---|---|---|---|---|---|---|---|
| GBP | 6.66±1.52 | 4.84±1.80(18.2%) | <0.05 | 4.14±1.64(25.2%) | <0.05 | 3.52±1.42(31.4%) | <0.05 |
| PGB | 6.78±1.33 | 4.64±1.71(21.4%) | <0.05 | 3.74±1.58(30.4%) | <0.05 | 3.16±1.58(36.2%) | <0.05 |

The mean scores at the end of each month were compared with the mean score before the usage of the drug using paired 't' test. All the p values which are in bold are significant.
The numbers in the simple brackets show the percentage of pain reduction at the end of each month with respect to before the beginning of the trial

values from meta-analysis, simpler dosing schedule and titration regimen and its cost effectiveness. Another trial which has been mention in this review, is by Pinto, *et al*[17] which showed positive results in reducing NP significantly by GBP but didn't comment on the efficacy of PGB.

According to Saxena, *et al*[18], the treatment approach to neuropathic pain in Indian set up has oral Gabapentinoids (GBP and PGB) as first line of therapy[19]. It was recommended that PGB to be initiated at 50 mg/day and titrated up to 75 mg/day to a maximum of 450 mg/day in two divided doses, while for GBP, the initiating dose was 100 mg/day thrice daily to a maximum of 1800 mg/day in divided doses. A double blinded placebo controlled RCT in New Delhi compared PGB, GBP, amitriptyline and placebo only to find PGB to stand out in controlling NP[20].

However, this study has limitations. The sample size is small and is only limited to patients attending the place of study presenting with chronic NP with no restrictions in motor functions. Secondly, the doses of GBP and PGB have been fixed to 600 mg/day and 150 mg/day – since both the drugs cause significant pain reduction, it can be speculated, that GBP may be better than PGB in higher doses; but such evaluations have not been done. Thirdly, the adverse effects of either of the drugs have not been recorded. Fourthly, this being a study in a government hospital all the drugs that were given to the patients were free of cost. For a drug to be considered better than the other drug, both the adverse effects of the drug and the cost effectiveness of the drug according to it's dosing schedule should also be considered.

## Conclusion

In our study, PGB appears to be marginally better than GBP, but further studies with larger subjects is needed to prove or disprove this. As of now, we can say both drugs reduces NP significantly.

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