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ARTICLE

Effectiveness and Safety of Gabapentin versus Pregabalin in the Treatment of Postherpetic Neuralgia: A Retrospective Cohort Study

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Abstract

Aims/Background Postherpetic neuralgia (PHN) is a common chronic pain disease that persists after the rash (clusters of clear blisters on the surface of the skin) has healed, adversely affecting the quality of life of affected patients. Gabapentin (GPT) and pregabalin (PGB) are two commonly used drugs for the treatment of PHN, but there have been broad concerns regarding their efficacy and safety. Thus, this retrospective cohort study was conducted to investigate the effectiveness and safety of GPT versus PGB in the treatment of PHN.

Methods A total of 150 patients with PHN receiving routine antiviral and neurotrophic therapies, admitted between January 2022 and November 2023, were selected. 71 patients who were treated with GPT were included in the control group, while the remaining 79 patients who were given PGB were categorized in the observation group. Information on clinical effectiveness, safety (xerostomia, drowsiness, blurred vision, ataxia, and dizziness), analgesic effect (Visual Analogue Scale [VAS] and time to pain relief), sleep quality (Sleep Quality Scale [SQS] and Pittsburgh Sleep Quality Index [PSQI]), and adverse emotions (Self-rating Anxiety/Depression Scale [SAS/SDS]) was collected for analysis.

Results Compared to the control group, the observation group exhibited significantly higher clinical effectiveness of PGB in the treatment of PHN ($p < 0.05$). In other aspects, the overall incidence of adverse events such as xerostomia, drowsiness, blurred vision, ataxia, and dizziness ($p > 0.05$) was equivalent in these two groups. In addition, significantly lower VAS, SQS, PSQI, SAS, and SDS scores were observed in the observation group after treatment, compared with the control group ($p < 0.05$). The observation group showed evidently shorter time to pain relief than the other group ($p < 0.05$).

Conclusion PGB is an effective and safe medication for the treatment of PHN, by improving the analgesic effect and sleep quality, and alleviating negative emotions.

Key words: gabapentin; pregabalin; herpes zoster; neuralgia; effectiveness and safety

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Introduction

Herpes zoster (HZ) is a painful, itchy, and stinging rash caused by reactivation of the varicella-zoster virus (VZV), a DNA virus belonging to the neurotropic alpha human herpesvirus subfamily (HHV), characterized by a gradual progression into blisters and pustules, and then crusts, prior to resolution (Yeh et al, 2022). The risk for HZ development increases with age, with immunocompromised older adults in particular being more vulnerable to the infection (Han et al, 2023). A prior study

revealed that 12.6% of HZ patients are at risk of developing postherpetic neuralgia (PHN) (Zhang et al, 2023). PHN refers to the persistent rash and pain induced by HZ, negatively impacting the sleep quality and psychological state of the affected patients (Li et al, 2022; Sun et al, 2023). Its etiology has been linked to immunological responses triggered by virus reactivation, as well as damage to central and peripheral neurons. Factors such as advanced age, acute pain, prodromal pain, and severe rash are potential predictors for the occurrence of PHN (Bian et al, 2022; Gónima Valero et al, 2023). The treatments of PHN mainly include anticonvulsants, antidepressants, selective norepinephrine reuptake inhibitors, local anesthetics and minimally invasive interventional technique therapy (Isagulyan et al, 2023). However, these therapies are not only partially effective and having minimal improvement effects on sleep quality and negative emotions, but also putting the patients at increased risk of side effects (Anosike et al, 2022; Tang et al, 2023); these shortcomings warrant the exploration of more ideal anti-PHN therapies.

Gabapentin (GPT) is a γ-aminobutyric acid analogue that can be used to manage chronic, acute, and post-operative pain, including PHN (Marchand et al, 2021; Russo et al, 2023). GPT can easily pass through the blood-brain barrier and subsequently inhibit voltage-gated calcium channels to exert analgesic effects (Bongiovanni et al, 2022). GPT may have adverse effects like drowsiness, nausea, and dizziness, but it also has a certain preventative benefit on post-stroke nausea in HZ patients, according to a systematic analysis of randomized controlled trials (Menaldi et al, 2022). As a first-line therapy for peripheral and central chronic neuropathic pain, pregabalin (PGB), being both efficacious and safe, improves negative psychological states such as anxiety and depression in patients, thereby elevating their quality of life (Prnjavorac et al, 2023). A previous study has shown that the mechanism of the drug in relieving or treating neuropathic pain is associated with the inhibition of protein kinase Cε (PKCε)/transient receptor potential vanilloid receptor 1 (TRPV1) signaling pathway and spinal cord inflammation (Zhang et al, 2021).

To address the knowledge gaps in the current literature, we conducted a retrospective cohort study to comparatively analyze the clinical efficacy and safety of GPT and PGB in PHN patients, with the aim to provide new insights for better pain management in PHN cases.

Methods

General Data

A total of 150 PHN patients treated in Huai'an Hospital (Jiangsu, China) between January 2022 and November 2023 were selected for this retrospective cohort study. Out of the selected sample, 71 patients who received GPT were included in the control group, whereas the remaining 79 cases who were treated with PGB were categorized in the observation group. The study was conducted in accordance with the Declaration of Helsinki. This research project was conducted with the approval of the Ethics Committee of Huai'an Hospital (No. KY-2023-146-02) and informed consent was obtained from all the subjects prior to their participation.

Patient Selection Criteria

The patients included in the present study had met the relevant diagnostic criteria for PHN based on the evaluation by an experienced physician (Fan et al, 2023): (i) exhibited a Visual Analogue Scale (VAS) score of greater than 4; (ii) had healed herpes zoster skin lesion; and (iii) experienced severe and persistent intractable pain. In addition, only individuals with complete clinical data, clear consciousness, and the ability to cooperate during treatment were included.

Patients who were allergic to medication used in this study, pregnant and lactating women, and those enduring pain caused by neurological disorders and other factors were excluded. Besides, patients with nausea, vomiting, dizziness, constipation, urinary retention, coagulation disorders, autoimmune system deficiencies, and dysfunction of heart, lung or kidney were excluded.

Treatment Methods

Patients in both groups were given routine acyclovir and neurotrophic treatments, supplemented with 25 μg of vitamin B12 per day. Each patient in the control group was given one dose of oral GPT capsules (0.3 g) on the first day, two doses on the second day (0.6 g), and three doses on the third day (0.9 g). Subsequently, the GPT dosage was adjusted according to the pain level experienced by the patients, as long as the maximum dosage of 1.8 g/day was not exceeded. In the observation group, each patient was given oral PGB capsules, starting at a dose of 75 mg/time, twice a day. After one week, the dosage could be adjusted to 150 mg/time, twice a day, depending on the curative effect and patient's tolerance to the medication. If no significant relief of pain was achieved 2–4 weeks after the first medication intake, the dosage could be increased to 300 mg/time, twice a day. The whole treatment course took 4 weeks to complete, and the indicators were measured at the beginning and end of the treatment.

Measurement of Indicators

(1) *Clinical effectiveness.* The clinical symptoms and recovery of the two groups before and after treatment were compared and analyzed. The clinical effectiveness of the treatments self-reported by the study participants were categorized into three classes based on the clearly defined range of efficacy index: (i) markedly effective category (the efficacy index was $\geq$70%, indicating obvious alleviation of pain); (ii) effective category (the efficacy index was within the range of 30%–69%, indicating moderate relief of pain); and (iii) ineffective category (the efficacy index was $\leq$29%, indicating very minimal relief of pain reduced or exacerbation). The total effective rate of treatment was calculated by determining the percentage of the cases in the markedly effective and effective categories in the total sample.

(2) *Safety.* Patients were observed for adverse events such as xerostomia (XS), drowsiness, blurred vision, ataxia, and dizziness after treatment intervention, and the incidence of each adverse event was calculated.

(3) *Analgesic effect*. Pain severity assessment was conducted before and after treatment using the Visual Analogue Scale (VAS) (Kim et al, 2018). The score, ranging from 0 to 10, directly reflects the degree of pain, with '0' indicates ex-

tremely low level of pain while '10' extremely high level of pain. The time taken to achieving apparent pain relief, *i.e.*, the duration between taking drug and starting to experience milder pain, as indicated by bearable pain that would not substantially influence patients' lives and allowed for sound sleep, was also recorded.

(4) *Sleep quality.* We employed the Sleep Quality Scale (SQS) (Snyder et al, 2018) and Pittsburgh Sleep Quality Index (PSQI) (Chehri et al, 2020) to evaluate patients' sleep quality. The former scale features 4 items, each rated in 0–3 points denoting good, fair, poor, and very poor, respectively; the total SQS score was obtained by adding up all the component scores (maximum score = 12 points). The latter scale measures 7 items, each rated in 0–3 points; the total PSQI score was obtained by adding up all the component scores (maximum score = 21 points), a score of >7 is considered a sleep disorder. Higher scores on both scales are indicative of worse sleep quality.

(5) *Negative emotions.* Patients were assessed by the Self-rating Anxiety/Depression Scale (SAS/SDS) (Guo and Huang, 2021) before and after treatment to evaluate the anxiety and depression they experienced. Each of these scales has 20 items, with a total score of 80 points. Higher scores on both scales are symptomatic of greater levels of anxiety and depression.

Statistical Analysis

Data of continuous variables are expressed as mean ± standard deviation, and were analyzed using either independent sample *t*-test (for between-group comparisons) or paired *t*-test (for within-group comparisons). Data that do not conform to the normal distribution are presented as median (upper and lower quartiles), and were analyzed using Mann-Whitney *U* test. Data of categorical variables are expressed as counts and percentages, and were analyzed between groups using the chi-squared test. All data of the present study were analyzed using SPSS version 22.0 (IBM, Chicago, IL, USA). $p < 0.05$ was considered statistically significant.

Results

Analysis of Patients' General Information

The observation and control groups were equivalent in terms of sex ratio, age, duration of disease, body mass index (BMI), and lesion site ($p > 0.05$), as shown in Table 1.

Table 1. Analysis of patients' general information.

Indicators	Control group ($n = 71$)	Observation group ($n = 79$)	$Z/\chi^2/t$	p
Sex (male/female)	45/26	42/37	1.602	0.206
Age (years)	48.23 ± 8.43	48.84 ± 9.28	0.420	0.675
Course of disease (months)	26.00 (15.82, 32.06)	21.80 (15.59, 29.54)	–1.460	0.144
Body mass index (kg/m^2)	24.32 ± 5.68	23.90 ± 5.63	0.454	0.650
Lesion site (head and face/neck and chest/waist and legs)	20/38/13	18/42/19	1.006	0.605

Analysis of Clinical Effectiveness

The total effective rate of the treatment received by the observation group was 96.20%, which was significantly higher than the rate of 84.51% in the control group ($p < 0.05$), as shown in Table 2.

Analysis of Treatment-Induced Adverse Events

In the aspect of adverse events, we found an overall incidence of 11.39% in the observation group, which was not statistically different from 14.08% in the control group ($p > 0.05$). Table 3 presents the summarized incidence data of the treatment-induced adverse events.

Analysis of Analgesic Effects

No notable inter-group difference was found in VAS scores before treatment ($p > 0.05$); both groups experienced markedly reduction in VAS scores after treatment, particularly in the observation group ($p < 0.05$). Besides, shorter time to pain relief was determined in the observation group versus the control group ($p < 0.05$). Table 4 presents the summarized data of the analysis of analgesic effects.

Analysis of Sleep Quality

An evaluation of the patients' sleep quality using the SQS and PSQI scales revealed that there was no significant inter-group difference for both scales before treatment ($p > 0.05$). A significant reduction in the scores of SQS and PSQI was detected in both the groups after treatment, with even lower scores in the observation group ($p < 0.05$). Table 5 presents the summarized data of the SQS and PSQI scores before and after treatments for both control and observation groups.

Table 2. Analysis of clinical effectiveness.

Clinical effectiveness category	Control group ($n = 71$)	Observation group ($n = 79$)	χ^2	p
Markedly effective	35 (49.30)	45 (56.96)		
Effective	25 (35.21)	31 (39.24)		
Ineffective	11 (15.49)	3 (3.80)		
Total effectiveness	60 (84.51)	76 (96.20)	6.044	0.014

Table 3. Incidence of treatment-induced adverse events.

Indicators	Control group ($n = 71$)	Observation group ($n = 79$)	χ^2	p
Xerostomia	2 (2.82)	1 (1.27)		
Drowsiness	2 (2.82)	3 (3.80)		
Blurred vision	2 (2.82)	1 (1.27)		
Ataxia	1 (1.41)	1 (1.27)		
Dizziness	3 (4.23)	3 (3.80)		
Total	10 (14.08)	9 (11.39)	0.245	0.621

Table 4. Analysis of analgesic effects.

VAS scores	Control group (n = 71)	Observation group (n = 79)	Z	p
Before treatment	7.00 (5.00, 8.00)	7.00 (6.00, 8.00)	–0.364	0.716
After treatment	4.00 (3.00, 5.00) [a]	3.00 (2.00, 4.00) [a]	–6.614	<0.001
Time to pain relief (min)	6.00 (5.00, 7.00)	4.00 (3.00, 5.00)	–7.099	<0.001

Notes: [a] $p < 0.05$ vs. before treatment. VAS, Visual Analogue Scale.

Table 5. Analysis of sleep quality.

Sleep quality scales	Control group (n = 71)	Observation group (n = 79)	Z	p
SQS				
Before treatment	9.00 (8.00, 11.00)	10.00 (7.00, 12.00)	–0.176	0.860
After treatment	6.00 (5.00, 8.00) [a]	5.00 (3.00, 7.00) [a]	–2.662	0.008
PSQI				
Before treatment	15.00 (13.00, 18.00)	16.00 (13.00, 18.00)	–0.911	0.362
After treatment	7.00 (6.00, 9.00) [a]	5.00 (4.00, 6.00) [a]	–5.363	<0.001

Notes: [a] $p < 0.05$ vs. before treatment. SQS, Sleep Quality Scale; PSQI, Pittsburgh Sleep Quality Index.

Analysis of Negative Emotions

Anxiety and depression were assessed using the SAS and SDS scales, respectively. The two groups differed in neither scale scores before treatment ($p > 0.05$); however, evidently reduced SAS and SDS scores were observed in both the groups after treatment ($p < 0.05$), with more significant decreases in the observation group compared with the other ($p < 0.05$). The analysis data of the SAS and SDS scores before and after treatments for both control and observation groups are summarized in Table 6.

Discussion

As the most common form of neuropathic pain after HZ, PHN not only elicits persistent pain to patients, but also induces uncomfortable symptoms such as paresthesia, sleep interruption, and emotional distress among the affected individuals (Chen et al, 2022a). The course of PHN could span a few months, and in some cases appear as a life-long complication of HZ, implying the challenges in treatment (Jiao et al, 2023). The present study explores two commonly used drugs for PHN—GPT and PGB—providing a new line of data to establish the therapeutic efficacy and safety of these medications in the treatment of PHN.

First, PGB used in the observation group manifested higher efficacy in the clinical treatment of PHN (96.20%), when compared to GPT used in the control group (84.51%), indicating the superior advantage of utilizing PGB over GPT in improving treatment for and alleviating pain endured by the PHN patients. The PGB imparts its analgesic effects predominantly through the inhibition of dorsal horn neuron hyperexcitation associated with tissue injury, rather than the inhibition

Table 6. Analysis of negative emotions.

Negative emotion scales	Control group (n = 71)	Observation group (n = 79)	t	p
SAS				
Before treatment	45.11 ± 5.58	45.68 ± 6.01	–0.601	0.549
After treatment	40.79 ± 4.93 [a]	33.39 ± 3.91 [a]	10.234	<0.001
t	4.889	15.235		
p	<0.001	<0.001		
SDS				
Before treatment	58.37 ± 4.76	57.86 ± 5.42	0.609	0.543
After treatment	49.17 ± 6.93 [a]	45.41 ± 4.59 [a]	3.954	<0.001
t	9.221	15.58		
p	<0.001	<0.001		

Notes: [a] $p < 0.05$ vs. before treatment. SAS, Self-rating Anxiety Scale; SDS, Self-rating Depression Scale.

of pain transmission at the injured site (Quan et al, 2022), whereas the mechanism of GPT underlying the analgesic effect of PHN is correlated with the positive regulation of interleukin (IL)-10, CXC chemokine ligand 10 (CXCL10), prostaglandin E2 (PGE2), and cyclooxygenase 2 (COX-2) (Li et al, 2023). In terms of safety concerns regarding the treatments given, this study found dizziness and drowsiness as the most common adverse events in the observation group, while the most common adverse events in the control group were dizziness, followed by XS, drowsiness, and blurred vision, consistent with the studies of Chen et al (2022b) and Huerta et al (2023). It has been shown that both the PGB and GPT demonstrate effectiveness in the treatment of neuropathic pain associated with PHN and diabetic polyneuropathy, with PGB being more cost-effective (Rodríguez et al, 2007). In the present study, the total incidence of adverse events such as XS, drowsiness, blurred vision, ataxia, and dizziness was lower in the observation group than in the control group (11.39% vs. 14.08%), suggesting that PGB can to some extent abrogate the incidence of adverse events. As reported by Yu et al (2013), PGB and GPT are both well tolerated by patients experiencing pain post-lumbar surgery, when compared with placebo, presenting consistent findings with our research results.

Marked by the greater reduction of VAS scores and the shorter time to pain relief in the observation group than the control group, the utilization of PGB presented more favorable analgesic effects on PHN patients. This finding aligns with a report by Ifuku et al (2011) that PGB shows excellent analgesic effects in PHN patients, which is six times that of GPT (in terms of the effectiveness of dose conversion). Athanasakis et al (2013) also revealed that in the treatment of PHN and peripheral neuropathic pain associated with diabetic neuropathy, PGB helped shorten the number of days patients had to endure with moderate-to-severe pain. Regarding sleep quality, the utilization of PGB had a significant advantage over the use of GPT, as evidenced by a significantly lower SQS and PSQI scores after treatment in the observation group compared to the control group. This shows that PGB is more effective in improving sleep quality in PHN patients. Consistent to our results, Cao

et al (2023) demonstrated in their meta-analysis that PGB was superior to GPT in pain relief and sleep improvement in PHN patients. Furthermore, as reported by Sabatowski et al (2004), the administration of PGB improved the sleep quality of PHN patients, relative to the placebo, while enhancing the patients' quality of life. Regarding negative emotions, we found that compared to the control group, the observation group had significantly lower post-treatment SAS and SDS scores, indicating that PGB treatment has a significant relieving effect on anxiety and depression in PHN patients. This may be due to the more significant analgesic effect of PGB compared to GPT, reducing the psychological stimulation and distress caused by pain they experience. Mechanistically speaking, PGB can reduce the influx of calcium ions into hippocampal neurons, which is has implication for depression, advantageously improving the neuroplasticity of patients and thus helping to alleviate adverse emotions such as anxiety and depression (Taylor and Harris, 2020). The antidepressant and anxiolytic effects of PGB, which acted in dose-dependent, have also been validated in Wistar albino rats (Aydın et al, 2023).

This study has some limitations. Due to a lack of data available between the starting and ending time points, we were unable to portray a more complete picture regarding the changes of the investigated indicators or the measured scale scores over the duration of the study. In addition, due to the small sample size of this study, the results of the present study might present bias, which is a major pitfall for data generalizability. These limitations are anticipated to be addressed and optimized in future studies.

Conclusion

PGB can be effectively and safely used in the treatment of PHN. Compared to GPT, PGB has a more pronounced positive impact on analgesic effect, sleep quality, and negative emotions.

Key Points

- Both gabapentin and pregabalin are effective in relieving postherpetic neuralgia.
- Both gabapentin and pregabalin have a favorable safety profile.
- Compared with gabapentin, pregabalin is more effective in relieving postherpetic neuralgia.
- Compared with gabapentin, pregabalin can better improve the sleep quality of patients.
- Compared with gabapentin, pregabalin is more effective in relieving patients' anxiety.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

YS and CHS designed the research study and drafted the manuscript. YS and CHS performed the research. YS and CHS analyzed the data. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. This research project has received approval from the Ethics Committee of Huai'an Hospital (No. KY-2023-146-02) and informed consent signed by all the subjects.

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Conflict of Interest

The authors declare no conflict of interest.

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