Comparative Effectiveness of Gabapentin and Pregabalin Combination Therapy in Postherpetic Neuralgia: A Single-Masked Randomised Controlled Trial

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ABSTRACT

Objective: To compare the efficacy of gabapentin combined with pregabalin in postherpetic neuralgia (PHN) attenuation, focusing on patient-reported outcomes and inflammatory cytokine reduction.

Study Design: Single-blinded randomised controlled trial.

Place and Duration of the Study: Department of Dermatology, Zhongnan Hospital of Wuhan University, Wuhan, China, from June to December 2022.

Methodology: A total of 134 consecutive patients diagnosed with PHN were randomly allocated into two groups: gabapentin alone (GB group, n = 67) or a combination of gabapentin and pregabalin (GBP group, n = 67) administered orally for 8 weeks. The outcome measures, including the visual analogue scale (VAS) score, clinical efficacy rate, and serum inflammatory factors, were analysed using the t-test, paired t-test, or χ^2 test.

Results: At 8 weeks post-treatment, the VAS score of the GBP group was statistically lower than that of the GB group (t = 22.441, p <0.001). The clinical efficacy rate of the GBP group was statistically higher than that of the GB group (74.6% *vs*. 56.7%, p = 0.029). The GBP group had significantly lower serum levels of interleukin (IL)-6, IL-1β, and tumour necrosis factor-α (TNF-α) compared to the GB group (p <0.05). No significant differences were observed in adverse effects between the two groups (46.3% *vs*. 54.8%, χ^2 = 0.478, p = 0.489).

Conclusion: The combination therapy with gabapentin and low-dose pregabalin could help reduce pain and inflammatory factors.

Key Words: *Postherpetic neuralgia, Gabapentin, Pregabalin, Anti-inflammatory, Single-masked, Randomised controlled trial*.

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INTRODUCTION

Postherpetic neuralgia (PHN) is a neuropathic pain syndrome that persists for months to years following a rash of herpes zoster (HZ, shingles) rash.[1,2] Patients with PHN often find the condition unbearable, accompanied by emotional instability and sleep disorders, which seriously affect their quality of life.[3] The International Association for the Study of Pain (NeuPSIG) recommends antiseizure medications such as pregabalin, gabapentin, tricyclic antidepressants (TCAs), and topical lidocaine as a first-line therapy for PNH.[4] However, optimal pain control is difficult to achieve using currently available medicines, and no single medicine is completely effective for all patients.[5] The combination of analgesic medicines are usually used in clinical practice; however, they only partially relieve pain.[6]

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Additionally, the complexity and heterogeneity of the mechanisms underlying PHN suggest that symptoms are unlikely to be adequately relieved by a single agent.[7]

Combination therapy can provide more effective pain relief by activating multiple pain-inhibitory pathways. Gabapentin and pregabalin are commonly used as first-line treatments in combination with TCAs, serotonin and norepinephrine reuptake inhibitors (SNRIs), lidocaine, tramadol, and other drugs with different mechanisms of action for the treatment of PHN.[1] However, owing to their side effects and the regulation of psychotropic medicines in China, the aforementioned combination therapy has not been widely used. Gabapentin and pregabalin have the same mechanism of action, and the use of this combination has not been included in the current guidelines.[4] The gabapentin and pregabalin combination therapy is a feasible option for patients with PHN and an insufficient response to monotherapy.[8] In two case studies, oral gabapentin and pregabalin had a synergistic effect on treatment-resistant neuropathic pain.[8,9] However, these previous reports were either case reports or retrospective studies, and high-quality, prospective, controlled trials to inform clinical decisions are lacking.

This study aimed to investigate the efficacy of gabapentin and pregabalin combination therapy in patients with PHN and to

evaluate its ability to regulate inflammation factors. It was hypothesised that the combination therapy of gabapentin and pregabalin would have a synergistic effect in reducing inflammatory factors in patients with PHN.

METHODOLOGY

This prospective, randomised and single-blind study was conducted on patients attending the medical outpatient service of the Department of Dermatology, Zhongnan Hospital of Wuhan University, Wuhan, China, from June to December 2022. The study was approved by the Ethics Committee of the Zhongnan Hospital of Wuhan University, Wuhan, China (No. 2022046). Before inclusion in the trial, each patient provided written informed consent.

Inclusion criteria included age ≥18 years; a history of HZ with healed skin lesions and symptoms of persistent severe neuralgia; visual analogue scale (VAS) score ≥4 points; and no history of allergy to pregabalin or gabapentin. Patients with severe organ dysfunction of the heart, liver, or kidneys; creatinine clearance ≤60 mL/min determined using the Cockcroft–Gault formula; history of malignant tumours; breastfeeding or pregnancy; symptoms such as drowsiness, dizziness, nausea, and ataxia, which may influence the adverse drug reactions (ADRs) observed; and ongoing use of other analgesic medicines, including but not limited to nonsteroidal anti-inflammatory medicines, opioids, lidocaine patches, carbamazepine, TCAs, or SNRIs, were excluded from the study. Discontinuation criteria included the occurrence of serious ADRs that made the continuation of treatment impossible; need for emergency measures due to disease progression or serious complications; poor treatment compliance; and withdrawal request before completion of the trial. Elimination criteria included incorrect recruitment of patients who did not meet the inclusion criteria; failure to complete the prescribed treatment or data collection; and acceptance of additional treatments beyond the interventions in the present study.

Randomisation was performed using the sealed-envelope method with a table of random numbers in Microsoft Excel. Each randomisation number was placed into a sequentially numbered, sealed, opaque envelope. After being diagnosed with PHN, each patient was assigned to either the GB or GBP group based on the number inside the envelope. The randomisation process followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The generation, concealment, and allocation of random numbers were performed by three different researchers. Owing to the unique regulatory requirements for prescribing psychotropic medicines, blinding researchers was impractical, as prescriptions required signatures and supervision. However, patients were blinded to group allocation.

After randomisation, the participants underwent an 8-week therapy. Both groups were also prescribed conventional neurotrophic drugs, including oral vitamins B_1 and B_{12}. The gabapentin group (GB) was prescribed gabapentin. Gabapentin dosages were increased to 900 mg/d within 1 week according to the approved protocol [Day 1: 300 mg, *quaque die* (*qd*); Day 3: 300 mg, *bis in die* (*bid*); Day 7: 300 mg, *ter in die* (*tid*)] due to its analgesic properties. Patients continued on a stable dosage of 900 mg/d for an additional 7 weeks. In addition to gabapentin, the gabapentin and pregabalin (GBP) group was also prescribed pregabalin 25 mg, 50 mg, and 75 mg on days 1, 4, and 7, respectively.[9] Thereafter, the 75 mg dose of pregabalin was prescribed until the completion of the 8-week study period. Patient pain tolerance and drug-related side effects were evaluated weekly, and dosages were adjusted accordingly.

To evaluate VAS, participants were asked to rate their average pain intensity over the 8-week study period using a 0 to 10 scale, with 0 representing no pain and 10 representing the worst pain. The Cronbach's alpha value was 0.80, ensuring internal consistency.

The pain relief rate represented the clinical efficacy rate. The formula for calculating the clinical efficacy rate was: [(baseline pain VAS score–8-week pain VAS score)/baseline pain VAS score] ×100%. The evaluation criteria were: ≥50% was a significant effect; ≥30% and <50% was improvement; and <30% was inefficacy. Effective rate = [(significant effect + improvement)/ total number of cases] ×100%. The baseline pain VAS score was the pain VAS score before therapy.

Serum interleukin (IL)-6, IL-1β, and TNF-α levels were determined using an indirect enzyme-linked immunosorbent assay kit (Immunotech, a Genzyme Corporation, USA) in patients pre- and post-therapy.

The incidence of treatment-related adverse events in each group was evaluated and recorded promptly during the treatment and follow-up periods. The treatment-related adverse events included drowsiness, dizziness, fatigue, visual impairment, and ataxia. If any serious adverse events were reported, participation was immediately stopped, and rescue measures were taken in a timely manner. An independent Data Monitoring Committee (DMC) reviewed the safety findings, evaluated all available accumulated safety data, investigated compliance with the trial, and monitored adverse events. Nurses contacted the patients by phone every week, requesting them to visit the hospital to evaluate the efficacy and treatment-related adverse events.

To improve participant adherence and reduce dropout rates, all treatment costs, including pharmacotherapy and examination fees, were provided free of charge during the trial period. Before inclusion in the study, all patients were provided a detailed explanation of the trial process.

The sample size was calculated using the PASS software (version 16.0; NCSS LLC, Kaysville, UT, USA). The clinical efficacy rate was selected as the main evaluative indicator for observation. Based on previous clinical trial experience with PHN at the medical centre, the estimated effective rates of the GBP and GB groups were 0.75 and 0.5, respectively. The

sample size required to detect differences was 110 patients, with a two-sided significance set at 0.05 and 90% power. Considering a dropout rate of approximately 10%, the study aimed to enrol at least 123 participants.

Statistical analyses were performed using the SPSS software, version 26.0 (SPSS, Chicago, IL, USA). The normality test was performed using the Shapiro-Wilk test. Quantitative data were reported as mean ± SD. Two-sample t-test was used for inter-group comparisons, and paired t-test was used for analyses before and after the treatment. Categorical data presented as counts with percentages were compared using χ^2 or Fisher's exact tests. Statistical significance was set at 5%.

RESULTS

A total of 139 patients were diagnosed with PHN during the study period, of which 134 patients were eligible for inclusion in the study. Five patients were excluded because of refusal or failure to meet the inclusion criteria. Table I shows the demographic variables of the 134 patients recruited (67 in each group). Both groups had similar baseline demographics (Table I).

Before treatment, the VAS pain scores of the GB and GBP groups averaged 6.32 ± 1.15 and 6.47 ± 1.36, respectively, with no statistically significant differences observed (t = -0.689, p = 0.492). After treatment, the VAS pain score of the GBP group averaged 2.22 ± 0.55, which was significantly lower than that of GB group (3.42 ± 0.63, t = 22.441, p <0.001; Table II).

The pain relief rate was significantly lower in the GB group (56.7%) compared to that in the GBP group (74.6%; χ^2 = 4.767, p = 0.029; Table III).

As shown in Figure 1, the levels of pro-inflammatory cytokines IL-1β, IL-6, and TNF-α in the two groups significantly decreased (p <0.05). In addition, IL-1β, IL-6, and TNF-α levels were more significantly reduced in the GBP group compared to those in the GB group (p <0.05).

No significant increase in treatment-related adverse events were observed in the GB and GBP groups (46.3% *vs*. 53.7%, respectively, χ^2 = 0.478, p = 0.489; Table IV). No severe ADRs were observed.

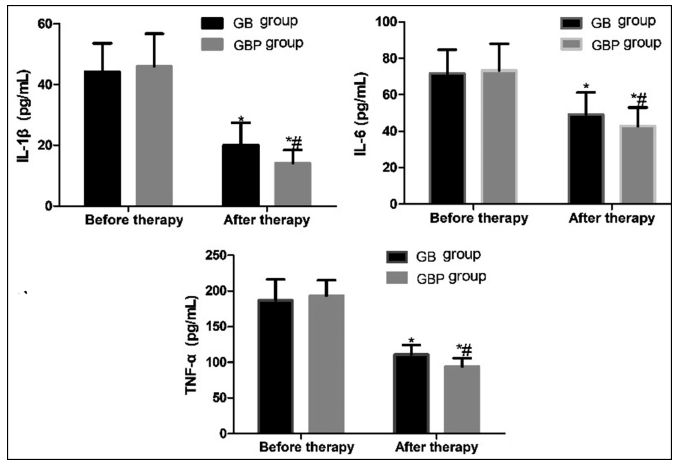

Figure 1: Comparison of the inflammatory factors.

Table I: Baseline characteristics.

Demographic variables	GB groups (n = 67)	GBP groups (n = 67)	t/χ^2	p-values[b]
Age (n/%)				
18-60 years	10 (14.9)	9 (13.4)	0.135	0.935
61-69 years	26 (38.8)	25 (37.3)		
≥71 years	31 (46.3)	33 (49.3)		
Gender (n/%)				
Male	30 (44.8)	31 (46.3)	0.030	0.862
Female	37 (55.2)	36 (53.7)		
BMI (kg/m^2)	22.5 ± 1.9	22.8 ± 2.1	-0.867	0.387
PHN duration (days)	43.2 ± 10.0	41.1 ± 9.9	1.222	0.224
At least one comorbidity (n/%)				
No	27 (40.3)	22 (32.8)	0.804	0.370
Yes	40 (59.7)	45 (67.2)		
Ganglion segments involved (n/%)				
Lumbosacral segment	21 (31.4)	23 (34.3)	0.285	0.963
Trigeminal/facial ganglion segment	8 (11.9)	7 (10.4)		
Neck segment	8 (11.9)	9 (13.4)		
Thoracic segment	30 (44.8)	28 (41.8)		

b: t-test and χ^2 test.

Table II: Comparison of the VAS scores.

Groups	GB groups (n = 67)	GBP groups (n = 67)	Mean difference-values (95% CI)	t-test	p-values[b]
Before therapy	6.32 ± 1.15	6.47 ± 1.36	0.15 (-0.28, 0.58)	-0.689	0.492
After therapy	3.42 ± 0.63	2.22 ± 0.55	1.20 (0.99, 1.40)	11.745	<0.001
Mean difference-value (95% CI)	2.80 (2.56, 3.24)	4.25 (3.87, 4.63)			
t-test	16.922	22.441			
p[a]	<0.001	<0.001			

a: Paired t-test; b: Two-sample t-test.

Table III: Comparison of the clinical efficacy rate.

Groups	GB groups (n = 67)	GBP groups (n = 67)	χ^2	p-values[b]
Significant effect (%)	25 (35.5)	31 (46.8)		
Improvement (%)	13 (21.0)	19 (29.0)		
Inefficacy (%)	29 (43.5)	17 (24.2)		
Effective rate (%)	38 (56.7)	50 (74.6)	4.767	0.029

b: χ^2 test.

Table IV: Comparison of the treatment-related adverse events.

Groups	GB groups (n = 67)	GBP groups (n = 67)	χ^2	p-values[b]
Dizziness (%)	11 (16.4)	13 (19.4)		
Drowsiness (%)	7 (10.4)	9 (13.4)		
Visual impairment (%)	5 (7.5)	4 (6.0)		
Ataxia (%)	5 (7.5)	6 (9.0)		
Fatigue (%)	3 (4.5)	4 (6.0)		
Total (%)	31 (46.3)	36 (53.7)	0.478	0.489

b: χ^2 test.

DISCUSSION

HZ is a discomfort and pain-causing disease caused by a recurrent latent *varicella-zoster* virus (VZV).[2] Up to one-third of patients with HZ in China experience PHN.[10] This refractory pain causes a series of unpleasant symptoms, including poor quality of life, sleep disorders, depression, unemployment, and even suicidal tendencies.[3,11] Multiple national and regional guidelines recommend gabapentin and pregabalin as first-line treatments for PHN.[4,12] Previous systematic reviews have shown that gabapentin and pregabalin significantly improve pain in patients with PHN compared to a placebo.[1] However, achieving satisfactory pain relief with existing monotherapy regimens, even at the maximum tolerated dose, where <50% of patients achieve adequate pain relief, is difficult.[13] Therefore, a combination regimen should be considered as the next treatment option.

In existing treatment schemes with gabapentin or pregabalin, many patients are concerned about the addictive nature of second-line opioid medicines. Gabapentin and pregabalin are analogues of the neurotransmitter γ-aminobutyric acid (GABA). Both may share a similar mechanism of action, competitively binding to the α2δ subunit. Notably, the use of these two therapies in combination is not recommended. However, recent literature provides evidence that gabapentin combined with low-dose of pregabalin administered increases analgesic effects, leading researchers to hypothesise that combination therapy may have potential significant clinical utility.[8,9,14] Tan and Chow reported that this off-label approach could significantly alleviate pain in most patients compared to monotherapy.[8,9] A preclinical study in rats revealed that gabapentin and pregabalin administered at 1:1 or 10:1 ratios produced synergistic rather than additive effects.[15] The gabapentin-to-pregabalin ratio used in the present study was approximately 10:1, consistent with the dosage reported by Brummel and Singh . Further research is warranted to establish the appropriate synergistic dose ratio of gabapentin and pregabalin. It was also unclear whether adding gabapentin to concurrent pregabalin would reduce pain.

The results of the present study showed that after 8 weeks of treatment, the VAS scores of the GBP group were significantly lower than those of the GB group [2.22 *vs*. 3.42, D-value 1.20 (0.99, 1.40)]. However, further exploration is needed to determine whether there would be clinical differences in VAS score. When VAS <4 and 4-7, the minimum clinically important difference (MCID) values were 0.6 (0.4-0.8), 1.3 (1.1-1.4), respectively. Most research on the MCID of VAS has focused on comparing patients before and after treatment.[16] There is a lack of data on the differences between groups, which require further investigation.

Playing a crucial role in neuropathic pain,[17] pro-inflammatory cytokines, including TNF-α, IL-6, and IL-1β, can directly or indirectly enhance neuronal excitability and reduce pain threshold by stimulating signalling pathways within neurons, glial cells, and immune cells, subsequently leading to pain.[17] After eight weeks of treatment, the serum levels of IL-1β, IL-6, and TNF-α in the GBP group were significantly lower than those in the GB group, suggesting that pregabalin may have exerted analgesic activity by reducing inflammation levels. Lin *et al*. found that IL-6 levels are elevated in patients with PHN, causing damage to the nervous system.[18] Pregabalin has antinociceptive effects in neuropathic and inflammatory pain.[19] In animal models of neuropathic pain, gabapentin or pregabalin attenuate the production of pro-inflammatory cytokines induced by injury, such as TNFα, IL-1β, and IL-6.[1,11-12,20] How such immunomodulatory effects are mediated remains controversial, and few studies have focused on their underlying mechanisms. Yamaguchi *et al*. reported that U373 MG cells, the concentrations of SP-induced IL-6 and IL-8 were reduced in *via* inhibition of the p38/MAPK/NF-κB signalling pathways, thus exerting anti-neuroinflammatory effects.[21] Mercan *et al*. investigated the role of immune mechanisms of neuropathic pain in patients with PHN as well as the effective-

ness of pregabalin.[22] The authors found significant differences in immune markers, particularly $CD4^+$, Th17 T-cell numbers, and T-cell metastasis, after the treatment with pregabalin. Therefore, combination therapy with pregabalin may improve immune function by inhibiting pro-inflammatory mediators. However, more evidence is required to support this hypothesis.

No significant differences were observed in ADR between the two groups, and no patient discontinued medication owing to adverse effects. When two medicines produce the same mechanism, their combination may produce more serious adverse effects than the sum of those caused by each medicine individually. A single report described a patient who experienced ADRs such as drowsiness, dizziness, fatigue, and ataxia after the simultaneous use of pregabalin and gabapentin.[23] These symptoms typically disappear after the discontinuation of pregabalin. In 15 trials of combination therapy with gabapentin and pregabalin, only one patient reported experiencing tolerable dizziness.[8] Both drugs have different pharmacokinetic profiles, potency, and off-target effects. Additionally, gabapentin has an apparent non-linear and unpredictable bioavailability, while pregabalin has a linear and predictable bioavailability.[9] Hence, pharmacokinetics and potential drug interactions must be carefully considered before indicating combination therapy, particularly in refractory pain conditions and in patients with low tolerance to individual agents.

There are certain limitations associated with this study. First, the results of single-centre studies may not be generalisable to other centres or the entire population. The number of patients included in this study was relatively small, and sampling errors may have occurred. Second, other combination therapy regimens were excluded, and subgroup analysis was not conducted, which limited their real-world applications. Third, lifestyle factors, concurrent treatments, or comorbidities could influence the outcomes. Finally, the treatment period of this study was eight weeks, and a lack of long-term follow-up evaluating treatment efficacy and recurrence existed, which highlights the need for future studies with expanding samples. Considering this possible bias, this present work is reported as a pilot study. Large, multi-centre, well-designed randomised controlled trials are needed to determine the optimal dose ratio for combination therapy and to explore its long-term effects and safety.

CONCLUSION

The present study demonstrated that the combination of gabapentin and low-dose pregabalin has a synergistic therapeutic effect in the treatment of PHN, which may be related to the inhibition of the inflammatory response. No ADRs were observed.

ETHICAL APPROVAL:
The study was approved by the Institutional Ethics Committee of the Zhongnan Hospital of Wuhan University, Wuhan, China (No. 2022046). This study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision).

PATIENTS' CONSENT:
Before inclusion in the trial, each patient signed an informed consent.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
LT, DY: Conceived and designed the study, analysed the data, prepared the first draft, revised the manuscript, and confirmed the authenticity of all the raw data.
JX: Conceived and designed the study and confirmed the authenticity of all the raw data.
All authors approved the final version of the manuscript to be published.

REFERENCES

1. Tang J, Zhang Y, Liu C, Zeng A, Song L. Therapeutic strategies for postherpetic neuralgia: Mechanisms, treatments, and perspectives. *Curr Pain Headache Rep* 2023, **27(9)**: 307-19. doi: 10.1007/s11916-023-01146-x.
2. Gross GE, Eisert L, Doerr HW, Fickenscher H, Knuf M, Maier P, *et al*. S2k guidelines for the diagnosis and treatment of herpes zoster and postherpetic neuralgia. *J Dtsch Dermatol Ges* 2020; **18(1)**:55-78. doi: 10.1111/ddg.14013.
3. Zhang X. Nursing intervention of postherpetic neuralgia. *MEDS Clin Med* 2024; **5(3)**:57-62. doi: 10.23977/medsc.2024.050309.
4. Haanpaa M, Attal N, Backonja M, Baron R, Bennett M, Bouhassira D, *et al*. NeuPSIG guidelines on neuropathic pain assessment. *Pain* 2011; **152(1)**:14-27. doi: 10.1016/j.pain.2010.07.031.
5. Snedecor SJ, Sudharshan L, Cappelleri JC, Sadosky A, Desai P, Jalundhwala Y, *et al*. Systematic review and meta-analysis of pharmacological therapies for pain associated with postherpetic neuralgia and less common neuropathic conditions. *Int J Clin Pract* 2014; **68(7)**:900-18. doi: 10.1111/ijcp.12411.
6. Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, *et al*. Pharmacotherapy for neuropathic pain in adults: Systematic review, meta-analysis and updated NeuPSig recommendations. *Lancet Neurol* 2015; **14(2)**: 162-73. doi: 10.1016/S1474-4422(14)70251-0.
7. Peng WW, Guo XL, Jin QQ, Wei H, Xia XL, Zhang Y, *et al*. Biological mechanism of post-herpetic neuralgia: Evidence from multiple patho-psychophysiological measures. *Eur J Pain* 2017; **21(5)**:827-42. doi: 10.1002/ejp.985.
8. Tan H, Li Y, Lv F, Zeng X, Wang S. Combination therapy of gabapentin and pregabalin for postherpetic neuralgia in 15 Patients. *RPS Pharma Pharmacol Rep* 2024; **3(2)**:rqae006. doi: 10.1093/rpsppr/rqae006.
9. Chow SP, Stevens S, Tran S, Donelenko S. Case series: Synergistic effect of gabapentin and adjuvant pregabalin in neuropathic pain. *J Pain Palliat Care Pharmacotherapy* 2023; **37(1)**:106-9. doi: 10.1080/15360288.2022.2149669.

10. Liu X, Fan B, Li Y, Zhang J, Hu H, Jiang Y, *et al*. [Influence factors of occurrence of postherpetic neuralgia and establishment of clinical prediction model]. *Chin J Pain Med* 2022; **28(02)**:106-12. doi: 10.3969/j.issn.1006-9852.2022.02.005.
11. Wu Y, Gan M, Wu J. Effect and immune mechanism of BCG-PSN on postherpetic neuralgia: A single-masked, randomised controlled trial. *J Coll Physicians Surg Pak* 2025; **35(5)**:590-5. doi: 10.29271/jcpsp.2025.05.590.
12. Yu S, Wan Y, Wan Q. Chinese expert consensus on diagnosis and treatment of postherpetic neuralgia. *Chin J Pain Med* 2016; **22(3)**:161-7. doi: 10.3969/j.issn.1006-9852.2016.03.001.
13. Mathieson S, Lin CC, Underwood M, Eldabe S. Pregabalin and gabapentin for pain. *BMJ* 2020; **369**:m1315. doi: 10.1136/bmj.m1315.
14. Senderovich H, Jeyapragasan G. Is there a role for combined use of gabapentin and pregabalin in pain control? Too good to be true? *Curr Med Res Opin* 2018; **34(4)**:677-82. doi: 10.1080/03007995.2017.1391756.
15. Brummel RN, Singh L. A synergistic combination: Gabapentin and pregabalin. *Eur Patent specif* 2005; EP1196160B1. Available from: https://patents.google.com/patent/EP1196160B1/en.
16. Olsen MF, Bjerre E, Hansen MD, Hilden J, Landler NE, Tendal B, *et al*. Pain relief that matters to patients: Systematic review of empirical studies assessing the minimum clinically important difference in acute pain. *BMC Med* 2017; **15(1)**:35. doi: 10.1186/s12916-016-0775-3.
17. Gu J, Yuan Y, Wang J, Liu H, Zhang Z, Yan Y. Serum inflammatory cytokine levels in herpes zoster patients and their association with postherpetic neuralgia: A prospective study. *Med Sci Monit* 2023; **29**:e941878-1. doi: 10.12659/MSM.941878.
18. Lin D, Zhong C, Jiang Q, Huang A, Liu Y. Serum interleukin-6 levels are increased in post-herpetic neuralgia: A single-center retrospective study. *An Bras Dermatol* 2023; **98(2)**:202-7. doi: 10.1016/j.abd.2022.03.007.
19. Yang X, Zhang Y, Yu H, Sun J, He Y. Efficacy of pregabalin in neuropathic pain after spinal cord injury. *J Coll Physicians Surg Pak* 2020; **30(1)**:106-7. doi: 10.29271/jcpsp.2020.01.106.
20. Kilic FS, Kaygisiz B, Aydin S, Yildirim C, Karimkhani H, Oner S. Pregabalin attenuates carrageenan-induced acute inflammation in rats by inhibiting proinflammatory cytokine levels. *Eurasian J Med* 2018; **50(3)**:156-9. doi: 10.5152/eurasianjmed.2018.17261.
21. Yamaguchi K, Kumakura S, Someya A, Iseki M, Inada E, Nagaoka I. Anti-inflammatory actions of gabapentin and pregabalin on the substance P-induced mitogen-activated protein kinase activation in U373 MG human glioblastoma astrocytoma cells. *Mol Med Rep* 2017; **16(5)**:6109-15. doi: 10.3892/mmr.2017.7368.
22. Mercan A, Uzun ST, Keles S, Hacibeyoglu G, Yilmaz R, Reisli R. Immunological mechanism of postherpetic neuralgia and effect of pregabalin treatment on the mechanism: A prospective single-arm observational study. *Korean J Pain* 2021; **34(4)**:463-70. doi: 10.3344/kjp.2021.34.4.463.
23. Ghayur MN. Potential adverse consequences of combination therapy with gabapentin and pregabalin. *Case Rep Med* 2021; **2021**:5559981. doi: 10.1155/2021/5559981.