Pharmacy Education (2021) 21(2) 225 - 229
https://doi.org/10.46542/pe.2021.212.225229

IAI CONFERENCE

RESEARCH ARTICLE

Comparing the quality of life of neuropathic patients treated with gabapentin and pregabalin at the neuropathic poly of the NTB provincial hospital in 2019

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Keywords
EQ-5D-3L
EQ-VAS
Gabapentin
Neuropathic pain
Pregabalin
Quality of life

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Abstract

Introduction: Neuropathic pain is caused by the malfunctioning of the central nervous system or the peripheral nervous system. This pain is chronic and so it disrupts a patient's quality of life which can lead to them becoming frustrated. **Aim:** The purpose of this study was to compare the quality of life of neuropathic patients using either gabapentin or pregabalin at the neuropathic clinic of the Regional General Hospital of West Nusa Tenggara Province in 2019. **Methods:** This study used a cross-sectional study design. The sampling technique that was used was purposive sampling which was carried out by filling out the EQ-5D-3L and EQ-VAS questionnaires. **Results:** The results showed no significant difference between the quality of life of the patients using gabapentin and the patients using pregabalin as the EQ-5D-3L questionnaire had a value of $p = 0.683$. There was no significant difference between the quality of life between the gabapentin and pregabalin groups using the EQ-VAS questionnaire which had a value of $p = 1.000$.

Introduction

Pain is an inseparable part of human life. Apart from causing suffering, pain is a defence response of the body. According to the International Association for the Study of Pain (IASP), pain is an unpleasant sensory and emotional experience that is related to tissue damage. Neuropathic pain originates from the malfunctioning of the central nervous system or peripheral nerves, which can be caused by degenerative spinal diseases, diabetes, herpes zoster, AIDS, surgery, and strokes (Harden, 2005). The classification of neuropathic pain includes trigeminal neuralgia, neuropathic DM, post-stroke, and post herpes. Trigeminal neuralgia or nerve pain occurs in the trigeminal nerve area, and paroxysmal pain occurs in some parts of the face. Such pain is caused by eating, light touches such as washing your face, brushing your teeth, talking, starting and stopping suddenly, and activities that can be associated with anxiety (Reynolds, 2005). The European Federation of Neurological Societies (EFNS) recommends venlafaxine, duloxetine, amitriptyline, gabapentin, valproate, opioids (morphine sulfate, tramadol, oxycodone CR) and topicals as treatments for the disease (Argoff *et al.*, 2006). Neuropathic pain usually responds poorly to the analgesics standardly used by the World Health Organization (WHO), such as nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids (Centre for Clinical Practice at NICE (UK), 2013).

Antidepressants and antiepileptic drugs are the first-line drugs used to treat neuropathic pain (Utami *et al*., 2013). Gabapentin has been shown to have analgesic effects when used as an antiepileptic drug. Gabapentin has been approved by the Food and Drug Administration (FDA) as an adjunct therapy for partial epilepsy and for the management of postherpetic neuralgia (Horizant Monograp*h*, 2012). Pregabalin (PGB) is a substance that is structurally analogous to gamma-aminobutyric acid (GABA), which is lipophilic and functionally unrelated to the neurotransmitter GABA. Based on clinical evidence, PGB is useful for treating epilepsy, psychiatric disorders, fibromyalgia and neuropathic pain (G *et al*., 2016). Gabapentin and pregabalin have antihyperalgesic and antinociceptive effects that reduce postoperative pain (Annisa, n.d.). The dose of pregabalin is 2-4 times smaller than that of gabapentin and is effectively used for neuropathic pain, usually at a dose of 150 mg (Annisa, n.d.). Neuropathic pain lasts a long time and makes patients frustrated, which decreases their quality of life. This condition highlights the need for drugs that help improve the quality of life of patients. This study aims to compare the quality of life of neuropathic patients that are treated with gabapentin and those that are treated with pregabalin at the Neuropathic Clinic of the NTB Provincial Hospital in 2019.

In the West Nusa Tenggara Province Hospital, pregabalin and gabapentin are included in the hospital drug formulary. A systematic review and meta-analysis of the use of pregabalin and gabapentin to manage neuropathic pain after a spinal cord injury resulted in proving that there was no significant difference in the effectiveness of either drug (Davari *et al*., 2020). However, no studies have been found that compare the quality of life of patients suffering from neuropathic pain that receive pregabalin or gabapentin therapy. Several previous studies that compared the quality of life of patients dealing with neuropathic pain due to strokes who were receiving gabapentin therapy with those receiving amitriptyline therapy also did not show a significant difference between both therapies. (Utami *et al*., 2013). This study aims to determine the quality of life of neuropathic patients using gabapentin compared to those using pregabalin. This study did not only deal with neuropathic stroke patients but patients suffering from neuropathic pain due to other causes such as diabetic neuropathy, post herpes, degenerative spinal disease, herpes zoster, and surgery at the Neuropathic Clinic of the West Nusa Tenggara Province Hospital in 2019.

Method

This research is an analytic observational study that used a cross-sectional study method. An observational analysis is used to determine the causal relationship between two observational variables. The forms of these relationships can be differences, relationships, or effects (Kukkar *et al*., 2013). This research aims to measure the quality of life of patients using the EQ-5D-3L and EQ-VAS questionnaires. The sample used in this study was composed of patients experiencing neuropathic pain at the Neurology Clinic of the Regional General Hospital of NTB Province from July to August 2019. The sample population was selected according to what researchers needed, based on inclusion and exclusion criteria.

The samples in this study were selected through a purposive sampling technique in order to sort out the subjects that met the inclusion and exclusion criteria. The subjects used between July and August were the total research sample. The independent variable in this study was which drug was used; this was either gabapentin or pregabalin. The dependent variable in this study was the patient's quality of life. The instruments used in this study were the EQ-5D-3L and EQ-VAS questionnaires that measured the quality of life of the patients. The Indonesian versions of these questionnaires were validated by the 2013 Indonesian EuroQol Group. The EQ-5D TM is a trademark of the EuroQol Group. This study has received approval from the Regional General Hospital of West Nusa Tenggara Province's ethics committee, and all research subjects have signed informed consent.

Results and discussion

A total of 20 patients met both the inclusion and exclusion criteria. Ten of these patients were treated with gabapentin therapy, and the other ten patients were treated with pregabalin therapy; both groups used the EQ-5D-3L and EQ-VAS questionnaires. The results were presented based on the characteristics of research subjects: sex, age and level of education. This can be seen in Table I.

Table I: Patient characteristics based on gender

Gender	N	%
Male	8	40
Female	12	60
Total	**20**	**100**

Table I indicates that there were 12 female subjects (60%) and eight male subjects (40%) dealing with neuropathic pain. Several studies have shown varying results depending on the sex distribution. Men and women have the same chance of suffering from neuropathic pain. The research data regarding the

patient's age was categorised into two levels: those over the age of 50 and those 50 or under. In this study, there were 16 people over the age of 50 and four people aged 50 or under. This distribution can be seen in Table II.

Table II: Patient characteristics based on age

Age	N	%
>50 years	16	80
≤50 years	4	20
Total	**20**	**100**

Based on Table II, 80% of the respondents were over the age of 50, and 20% of the respondents were 50 or under. The subjects were also classified into two groups based on their education level, with one group having been educated beyond senior high school and another group that had not. This distribution can be seen in Table III.

Table III: Patient characteristics based on education

Education	N	%
> Senior High School	4	20
≤ Senior High School	16	80

Table III shows that 20% of the respondents with diabetic neuropathic pain had been educated beyond senior high school, and 80% had not. This sample is therefore mainly predominated by patients with a level of education below high school. It is assumed that the level of education influences the way an individual responds to external forces. Someone who has received a higher level of education will respond more rationally than those with a middling or lower level of education (Asri, 2006). This fact is in accordance with the results of the study, which showed that when viewed from the latest education level, the number of respondents that had not been educated beyond a senior high school level was higher than the number of respondents who had been educated beyond a senior high school level.

This study used the EQ-5D questionnaire to determine the quality of life of the respondents. The EQ-5D questionnaire consisted of 2 types of questionnaires, one of which was the EQ-5D-3L questionnaire. The EQ-5D-3L had questions relating to five topics: the ability to walk/move, practice self-care, and participate in regular activities, as well as the level of pain/discomfort and anxiety/depression felt by the patient. It also classified the patients into three groups: those with no problems, those with several problems, and those with extreme problems.

Results from the EQ-5D-3L questionnaire showed that, on average, respondents who received gabapentin therapy perceived they had some problems, in which the most common problems were related to the ability to practice self-care and carry out regular activities, both with a score of 10%. For those who perceived having moderate problems, the highest level was in pain/discomfort with a result of 90%, the ability to walk/move as much as 50% and anxiety/depression as much as 50%, self-care 30% and 30% of the regular activities. For those who perceived no problems, the highest level was attained by the ability to walk/move, and regular activities with 60%, followed by the ability to walk/move and anxiety/depression, namely with 50%, and lastly was pain/discomfort with 10%. This shows that even though the patients feel pain, they can still take care of themselves.

On the other hand, respondents who received pregabalin had no correlation with the quality of life, which was indicated by their ability to walk/move, practice self-care, participate in regular activities, feel pain/discomfort, and anxiety/depression. For those who perceived having moderate problems, the most common problem was in pain/discomfort with 30%, followed by the ability to walk/move, do regular activities, feel anxiety/depression by 10%, and do self-care as much as 0%. Finally, the results showed that those without any problems had 100% ability to carry out self-care, followed by a score of 90% regarding the ability to walk/move and do regular activities, and the last level was those feeling 30% of pain/discomfort.

The resulting data was analysed using SPSS 16.0. The data generated a normal distribution in the normality test. Afterwards, it was analysed using an independent t-test in order to determine whether there was a difference or not in the mean (average) of the two independent data groups as a result of the use of gabapentin or pregabalin on neuropathic patients. The results of the research conducted using the EQ-5D-3L questionnaire can be seen in Table IV.

Table IV: Analysis of EQ-5D-3L questionnaire data

Group	n±mean rank	Normality	P
Gabapentin	15±16.20	0.046	0.683
Pregabalin	15±14.80		

Table IV shows that the answers from the EQ-5D-3L questionnaire after being analysed using the Mann-Whitney U test data were not normally distributed. There was no significant difference in the quality of life

of patients with neuropathic pain that were given gabapentin compare to those that were given pregabalin. This result was also reinforced by previous researches that indicated that gabapentin and pregabalin have antihyperalgesic and antinociceptive effects of reducing postoperative pain (Annisa, n.d.).

Neuropathic pain therapy generally aims to improve the quality of life of the patients by taking a holistic approach in the form of treatment of the pain triad. This therapy is carried out by a multidisciplinary team, and it involves the treatment of pain, sleep disorders and mood disorders. Common pharmacological therapies for neuropathic pain are analgesics, adjuvant analgesics, and pharmacological interventions (Snedecor *et al*., 2014). Several different therapies for neuropathic pain have been studied. Based on these clinical studies, the drugs that are recommended as first-line therapy for neuropathic pain include antidepressants (tricyclic antidepressant (TCA), serotonin-norepinephrine reuptake inhibitors (SSRI)), calcium channel α2-δ ligands (gabapentin and pregabalin), and topical lidocaine (Boyle *et al*., 2012).

Second-generation anticonvulsant drugs, such as gabapentin and pregabalin, are considered to have fairly good efficacy in dealing with neuropathic pain (Myr *et al*., 2015). Both of these drugs can be used as first-line therapy in patients with diabetic neuropathic pain who are contraindicated with the use of TCAs or who do not respond to the TCAs treatment (Backonja *et al*., 1998).

Gabapentin and pregabalin act by several mechanisms that can have pain-reducing effects in people with neuropathic pain. These two drugs are synthetic analogues of gamma-aminobutyric acid (GABA), which bind or act selectively on the α2δ subunit of the calcium channel (Myr *et al*., 2015). The effect that this has is the inhibition of the release of excitatory neurotransmitters, such as glutamate and noradrenaline. It also modulates the release of substance P (Imdad *et al*., 2013). Another mechanism that both of these drugs use is that they are antagonistic to the receptors N-methyl-D-aspartate (NMDA) and alpha-amino-3-hydroxy-5methyl-4-isoxazolepropionic acid (AMPA) (Myr *et al*., 2015). EQ-VAS is a 20cm vertical visual analogue scale used to assess the personal health of respondents, with the highest score being 100, which is labelled as 'the best health you can imagine' and with the lowest score being 0, which is labelled as 'the worst health you can imagine' (Hutapea *et al*., 2016). The resulting data is then inputted using SPSS 16.0. The resulting data were normally tested with the normality test and analysed after by the independent t-test in order to determine whether there was a difference in the mean (average) of the quality of life of the two groups of neuropathic patients that were independent or unrelated in terms of those treated with gabapentin and those with pregabalin. The results of the research conducted using the EQ-VAS questionnaire can be seen in Table V below:

Table V: Analysis of EQ-VAS questionnaire data

Group	Mean±SD	*p*
Gabapentin	60.00±13.33	1,000
Pregabalin	68.00±13.16	

Table V demonstrates that the average value of the quality of life of patients taking the drug gabapentin was found to be 60.00 ± 13.33 while the value of those who received pregabalin therapy was 68.00 ± 13.16. Systematically, there was no significant difference between the two groups, which was then strengthened by the result of a *p*-value of 1.000 ($p > 0.05$). This result proves that there was no significant difference in the quality of life between neuropathic patients treated with gabapentin and those treated with pregabalin based on imagined health.

The limitations of this study were the relatively minimal number of samples as well as a relatively short sampling duration, and the study subjects were patients with non-specific neuropathy pain. This study is the only one that has compared the quality of life of neuropathic pain patients that received gabapentin with those that have received pregabalin.

Conclusion

Based on the research conducted at the NTB Provincial Hospital, it is possible to conclude the following points:

There was no significant difference in the quality of life between the gabapentin group and the pregabalin group based on the EQ-5D-3L questionnaire (p =0.683, > 0.05).

There was no significant difference in the quality of life between the gabapentin group and the pregabalin group based on the EQ-VAS questionnaire (p = 1,000, > 0.05).

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