COMPARING THE EFFICACY OF PREGABALIN AND GABAPENTIN IN TREATING NEUROPATHIC PAIN

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ABSTRACT: Neuropathic pain affects an estimated 10% of the United States population. Burning and shooting sensations of pain often elicited by non-harmful stimuli are characteristic symptoms of this condition, affecting central and peripheral regions of the body. While opioids have been observed to provide pain relief, studies have shown this class of drugs to pose high risks of dependency with potentially fatal results. In the clinical setting, the focus has shifted to using low-dependency risk drugs like anti-epileptics such as pregabalin and gabapentin. This paper compares the efficacy of pregabalin and gabapentin in treating neuropathic pain on the basis of the 11-point Likert scale by using four existing empirical research publications on this topic. Backonja (1999) and Serpell (2002) specifically investigated the treatment of neuropathic pain with gabapentin and found this drug to reduce pain by 1.5-2.5 units, a result that was significantly different from the placebo group ($p<0.05$, $p<0.001$, respectively). Moon et al. (2010) and van Seventer et al. (2010) focused on pregabalin, and found that pain was reduced by 1.4-1.67 units from baseline, which was significantly different from the placebo-treated group ($p<0.05$ for both studies). Pregabalin appears to have similar analgesic effects at lower doses compared to gabapentin, which may indicate greater efficacy, although this inference is not fully established and needs more rigorous research. These findings can provide clinicians with more information on whether pregabalin or gabapentin may provide more of an analgesic effect for neuropathic pain on the basis of a common pain metric.

Keywords: pregabalin, gabapentin, neuropathic pain, drug efficacy, Likert scale

Introduction

An estimated 10% of the United States population is affected by neuropathic pain (DiBonaventura et al., 2017), a condition characterized by burning and shooting sensations of pain in peripheral and central regions of the body, often in response to non-harmful stimuli like the light touch of skin (Colloca et al., 2017). Neuropathic pain has been observed to stem from damage of peripheral and central nerves that make up the somatosensory system, which in many cases is the result of pre-existing medical conditions like spinal cord injury, multiple sclerosis, and chemotherapy treatments associated with cancer (Colloca et al., 2017). Diabetes mellitus has also been linked to the onset of this pain syndrome, where nearly 50% of patients diagnosed with diabetes are reported to experience neuropathic pain (Xiao-Die et al., 2020). Additionally, the rising rates of obesity in the United States linked to increasing prevalence of diabetes mellitus have indicated that the proportion of individuals experiencing neuropathic pain is likely to increase (DiBonaventura et al., 2017; Gökmen et al., 2018). Coupled with a poor prognosis for recovery in adults (Kaguelidou et al., 2019), these data highlight the importance of investigating clinical interventions for neuropathic pain and their efficacy in clinical outcomes.

In addition to the classic symptoms of neuropathic pain, other conditions like anxiety, depression, loss of sensory function, and

interrupted sleep patterns may present themselves in conjunction with this condition, leading to a decrease in overall quality of life (Colloca et al., 2017). Despite extensive research, the pathophysiological mechanisms underlying neuropathic pain are complex and not fully understood, posing challenges to the development of new treatments for this condition (Colloca et al., 2017; Kaguelidou et al., 2019). Non-pharmacological clinical intervention for neuropathic pain includes the use of spinal cord stimulation, a biotechnology that involves the placement of electrodes in close proximity to central nerves, emitting electrical impulses that amplify pain inhibitory pathways and dull pain (Guttman et al., 2009). Pharmacological treatments include the use of a variety of drugs selected based on the severity of pain experienced, including tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), serotonin noradrenaline reuptake inhibitors (SNRIs), and strong opioids in the many cases when pain is debilitating (Colloca et al., 2017).

The use of opioids has shown to be potentially problematic when used to treat neuropathic pain, with studies providing evidence that increasing doses of opioids are needed to exert the same analgesic effects with prolonged use, significantly increasing the risk of dependance and overdose (Colloca et al., 2017; Salas et al., 2017). Additionally, studies have indicated that while opioids like oxycodone and morphine may temporarily alleviate the symptoms of neuropathic pain (Colloca et al., 2017), they have a significant potential to elicit and exacerbate associated conditions like depression (Scherrer et al., 2016; Salas et al., 2017). These data have motivated clinicians to seek alternative methods of treatment. Recently, the focus of clinical intervention for neuropathic pain has shifted to using commonly prescribed anti-epileptics like pregabalin and gabapentin, which are relatively low-safety-risk drugs compared to stronger treatments like opioids (Colloca et al., 2017; de Leeuw et al., 2019). This class of drugs exert their effect by reducing the activity of the α2δ (alpha-2-delta) subunit of voltage-gated calcium channels in the nervous system that are important to the transmission of electrical signals that mediate nociception (Colloca et al., 2017; de Leeuw et al., 2019). What remains to be better understood is how using multiple forms of therapy may interact in a way that provides the greatest analgesic benefit to the patients. More studies are needed to better understand how staggering the use of antiepileptic drugs (Markman et al., 2016) or combining them with other classes of drugs like opioids may potentially provide more pain relief to the patient (Colloca et al., 2017).

Studies examining the efficacy of pregabalin and gabapentin in treating neuropathic pain have found that pregabalin at doses of 150-600 mg/day significantly reduced levels of pain (Markman et al., 2016), while gabapentin at doses of 100-300 mg/day produce significant analgesic effects while minimizing adverse effects (Kamble et al., 2017). A previous study indicated that pregabalin had a greater efficacy than gabapentin based on pain intensity reported after treatment (Tong et al., 2021). Pregabalin has been noted to exhibit greater bioavailability and absorption rates after oral administration than gabapentin, which may explain potential differences in efficacy (Bockbrader et al., 2010; Markman et al. 2016).

The efficacy of anti-epileptic drugs in alleviating symptoms of neuropathic pain can be assessed using different metrics, including the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale which is out of 24 points and consists of a sensory evaluation component and questionnaire (Hardy et al., 2013). Alternatively, the McGill Pain Questionnaire assesses responses to treatment by asking patients to select descriptors of pain (Hardy et al., 2013), while the Visual Analog Scale (VAS) asks patients to rate their pain along a 10-centimeter horizontal line where one endpoint corresponds to no pain and the other corresponds to the worst pain experienced

(Hawker et al., 2011). While these metrics are useful ways to assess pain in response to treatments, not all studies use the same metrics in their evaluation. This discrepancy may confound the translation of the results of these studies to the clinical setting, where it may be more straightforward to use a commonly used metric by which efficacy is measured. A more widely used pain metric that may be a simpler way to assess pain is the 11-point Likert scale, where the lowest score of 0 indicates no pain and the highest score of 10 indicates the worst pain experienced by a patient (Plan et al., 2012).

This paper focuses on comparing the clinical efficacy of using two anti-epileptic drugs, pregabalin and gabapentin, in treating symptoms of neuropathic pain solely in terms of reported pain ratings on the Likert scale made by patients before and after treatment conditions. To address this research question, I conducted a comparative study of four existing empirical research publications that analyzed the clinical efficacy of using pregabalin and gabapentin to treat diagnosed neuropathic pain by measuring the effectiveness of these drugs in terms of reported pain levels during the treatment period.

Methods

Finding and Evaluating Studies

For this comparative study, I used PubMed and Web of Science databases to search for relevant data by entering the keywords "neuropathic pain and gabapentin and efficacy" and "neuropathic and gabapentin and efficacy" into the search engines. To search for pregabalin-specific empirical studies, I used the keywords "neuropathic pain and pregabalin and efficacy".

While these searches yielded several potentially useful publications, I filtered the results to only display empirical research publications made in the last 25 years, between 1996-2021. I also filtered the database search by preliminarily selecting studies that only compared the efficacy of gabapentin and pregabalin in terms of pain ratings measured on the Likert scale. Additionally, I filtered the publication search to display placebo-controlled empirical studies that lasted anywhere between 8-12 weeks.

Searches done on Web of Science database yielded three of the studies—Serpell, 2002; Moon et al., 2010; van Seventer et al., 2010—and the fourth study—Backonja, 1999 —was found in PubMed. The studies by Backonja (1999) and Serpell (2002) focused on the efficacy of gabapentin, while the studies by Moon et al. (2010) and van Seventer et al. (2010) focused on the efficacy of pregabalin.

Analysis of Data

For each of the studies selected for this comparative study, I first looked for the reported data sets and found that all data were expressed as exact numerical values, therefore no estimation of data was done. In these data sets, I looked for baseline pain ratings measured prior to the treatment period for both the placebo and drug-treated groups, all expressed on the Likert scale. Then, I looked for the post-treatment pain ratings reported for the placebo, gabapentin, and pregabalin-treated groups in each study. I then plotted all these numerical values by creating a bar graph. Additionally, I calculated the numerical difference between the post-treatment and baseline pain rating values in the placebo and drug-treated groups, and created a bar graph that depicted these values as well. Lastly, I looked for the number of participants in each study, duration of each study, and the range of drug doses administered to patients, and added these data to a table.

Results

Participant data indicates a difference between the number of participants in each group tested across all studies analyzed (Table 1). There are differences in the range of dosage administered in the gabapentin-treated groups, with the largest range being 900-3600 mg/day in the group by

Backonja (1999), while both of the pregabalin-treated groups Moon et al., (2010) and van Seventer et al., (2010) were administered 150-600 mg/day (Table 1).

Drug Studied	Study	Duration of Study	Number of Participants (n) in Placebo Group	Number of Participants (n) in Drug Group	Range of Drug Dosages Administered during Treatment Period
Gabapentin	Serpell 2002	8 weeks	152	153	900-2400 mg/day
Gabapentin	Backonja 1999	8 weeks	81	84	900-3600 mg/day
Pregabalin	Moon et al. 2010	10 weeks	78	162	150-600 mg/day
Pregabalin	van Seventer et al. 2010	8 weeks	127	127	150-600 mg/day

Table 1:
Overview of Relevant Data Collected in Comparative Study: Data regarding duration of study, number of participants in each group examined and range of drug dosages administered during the treatment period for each drug-treated group are included in this table.

All of the studies used in this comparative study showed a decrease in pain ratings on the Likert scale in the drug-treated groups, as shown in Figure 1. The placebo-treated groups across all studies analyzed reported a decrease in pain levels from baseline of approximately 1 point on the Likert scale (Figure 1).

Gabapentin

Serpell (2002) found that after the treatment period of 8 weeks, participants that were administered doses of gabapentin ranging from 900-2400 mg/day reported a decrease in pain from a baseline pain score of 7.10 to 5.60, a statistically significant decrease in pain ($p<0.05$) compared to the placebo group (Figure 1). Post-treatment data for Serpell (2002) showed a difference of 0.50 units between the placebo and gabapentin-treated group (Figure 2).

Backonja (1999) found that after administering gabapentin in doses between 900-3600 mg/day for 8 weeks resulted in a decrease from an average baseline pain level of 6.40 to 3.60, a result that was significantly different ($p<0.001$) compared to the placebo-treated group (Figure 1). There was an observed difference of 1.10 units between the placebo and gabapentin-treated groups for Backonja (1999) after the treatment period (Figure 2).

Pregabalin

Moon et al. (2010) showed that participants who were administered pregabalin in doses ranging from 150-600 mg/day over a period of 10 weeks reported a decrease in pain from 6.28 to 4.61, which was significantly greater

pain relief ($p<0.05$) compared to the placebo group (Figure 1). Post-treatment data for Moon et al. (2010) showed a difference of 0.53 units between the placebo and pregabalin-treated groups (Figure 2).

van Seventer et al. (2010) found that participants who received doses of pregabalin ranging from 150-600 mg/day for 8 weeks reported that their pain decreased from an average baseline of 6.00 to 4.60, which was significantly greater pain relief ($p<0.05$) than the placebo group (Figure 1). van Seventer et al. (2010) found a difference of 0.60 units between the placebo and pregabalin-treated group after the treatment period (Figure 2).

It is worthy to note that participants in both of the pregabalin-treated groups were administered the same dosage range, 150-600 mg/day, and reported a decrease in pain levels from baseline that were similar to those seen in the gabapentin-treated groups (Figure 2).

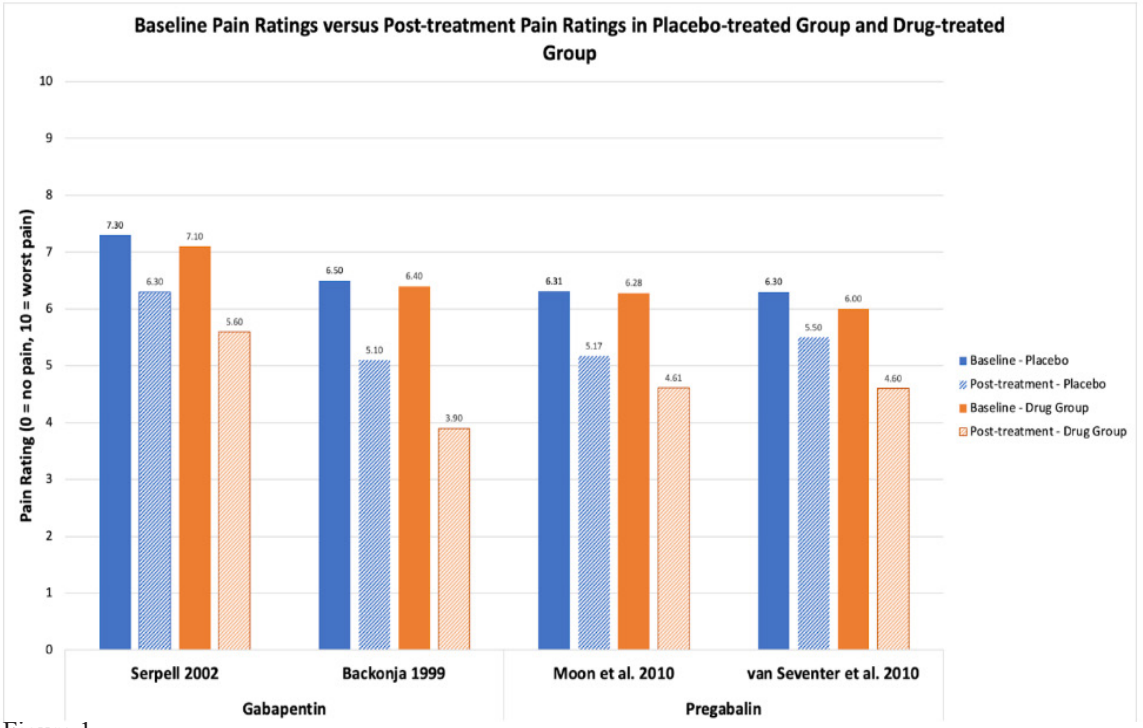

Figure 1.

Comparison of average baseline pain ratings versus average post-treatment pain ratings in the placebo-treated groups and drug-treated groups across all studies analyzed.

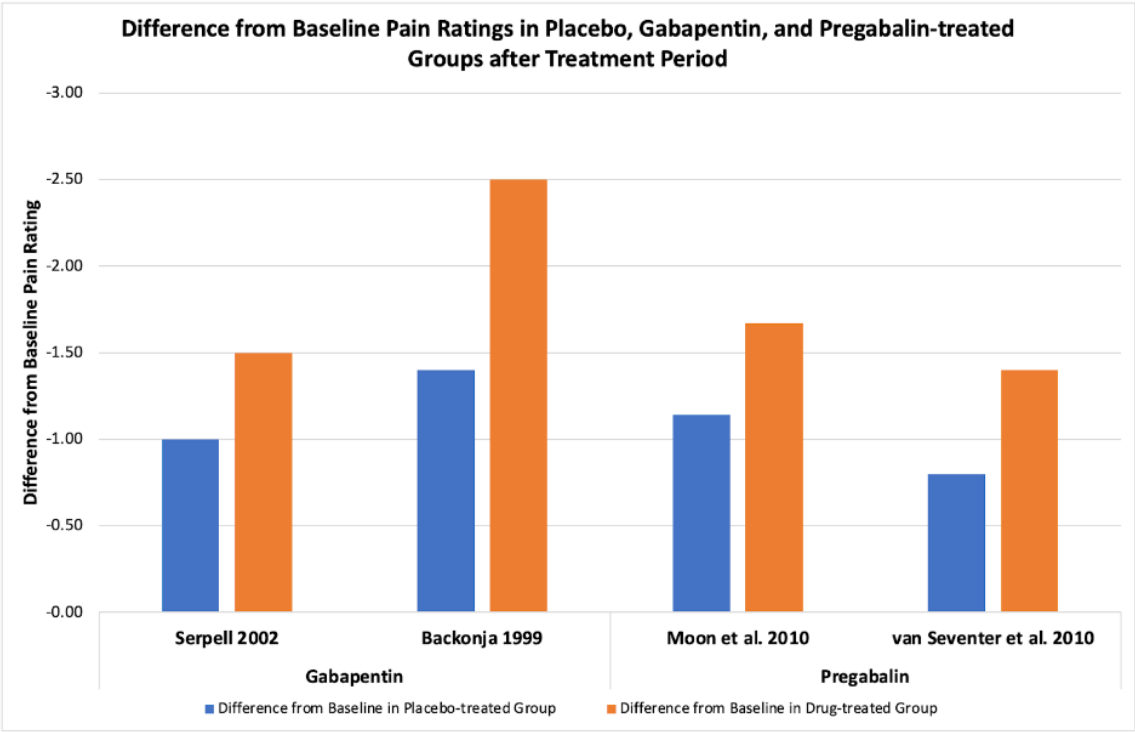

Figure 2:
Difference from average baseline pain ratings in placebo, gabapentin, and pregabalin-treated groups after the treatment period in each study analyzed.

Discussion

Researchers investigating the effect of drugs in treating pain use a variety of metrics to assess efficacy, ranging from more simple metrics that use an 11-point system like the Likert scale, to more complex metrics that involve various components like the LANSS scale (Plan et al., 2012; Hardy et al., 2013). However, not all studies that investigate gabapentin and pregabalin use the same metrics to assess efficacy. Therefore, the value of this comparative study is that assessing the efficacy of drugs with a single, more widely used metric can provide for a concise way to interpret data such that it may facilitate translation of results to clinical practices in treating neuropathic pain.

Efficacy of Gabapentin

Serpell (2002) found that administering (n=153) 900-2400 mg/day of gabapentin over the course of 8 weeks resulted in a statistically significant reduction of pain compared to the placebo group, where a difference of 0.50 units was observed between the placebo and gabapentin-treated group. Similarly, Backonja (1999) found that administering (n=84) 900-3600 mg/day of gabapentin resulted in a significant reduction of pain compared to the placebo group, where the difference between the placebo and gabapentin-treated group was 1.10 units. What is interesting is that both of these studies yielded similar statistically significant results but had different sample sizes for the drug-treated group. Overall, these values indicate that gabapentin does significantly reduce neuropathic pain.

Efficacy of Pregabalin

Moon et al. (2010) found that patients (n=162) who received doses of 150-600 mg/day of pregabalin over the course of 10 weeks reported a statistically significant decrease in pain compared to the placebo group, where the observed difference was 0.53 units between the

placebo group and the pregabalin-treatment group. This was very similar to the results found by van Seventer et al. (2010) where patients (n=127) received the same dose range of pregabalin and reported a post-treatment difference of 0.60 units between the placebo and pregabalin-treated group after an 8-week treatment period, which was also found to be a statistically significant difference. These data indicate that pregabalin is also effective at significantly reducing neuropathic pain.

Efficacy of Gabapentin versus Pregabalin

It is important to note that even at relatively low doses compared to the studies that examined gabapentin, pregabalin reduced pain levels by similar amounts as gabapentin. This evidence indicates that pregabalin may be a better option for treating neuropathic pain, as relatively lower doses of pregabalin are needed to exert a significant analgesic effect similar to gabapentin. While this inference is solely based on the studies examined in this paper, it does seem to be supported by other studies. It has been found that the doses of gabapentin that exert a significant analgesic effect range from 300-1800 mg/day and 900-3600 mg/day, while 150-600 mg/day of pregabalin are used (Davari et al., 2020). Similarly, it has been found that doses of pregabalin between 50-75 mg/day are effective at significantly reducing neuropathic pain while simultaneously minimizing common side effects like drowsiness and dizziness (Kamble et al., 2017). However, a previous study that specifically compared the efficacy of both gabapentin and pregabalin found that there was no statistically significant difference between either drug in reducing neuropathic pain (Davari et al., 2020). These conflicting results call for a more extensive and rigorous comparative study of these two drugs and their efficacy in treating neuropathic pain.

Interestingly, Moon et al. (2010) reported that 88.3% of patients in the test group were treated with other drugs prior to the experimental treatment of pregabalin, with 55.6% of those patients reporting the use of gabapentin prior to the start of the study. Moon et al. (2010) found that despite the prior and continued use of other drugs, pregabalin was found to significantly reduce pain. It is possible that there is a relationship between patient response to pregabalin after treatment with gabapentin, or vice versa; however, more research is needed to better establish this relationship. Recently, a study specifically investigated how patients with neuropathic pain who previously received gabapentin responded to starting the use of pregabalin and compared these results to a group of patients who only received pregabalin (Markman et al., 2016). It was found that while pregabalin significantly reduced pain in both test groups compared to placebo, there was no significant difference in reported pain reduction between the two treatment groups (Markman et al., 2016).

Another aspect worth noting is that Serpell (2002) allowed their patients to continue using additional drug treatments during the experimental period, which included the use of antidepressants, aspirin, and mild opioids like codeine, sometimes in combination with the analgesic paracetamol. This indicates that while gabapentin was the focus of the study, it was not an exclusive treatment for neuropathic pain. The interaction of gabapentin with other drug classes is an important point to consider because treatment of neuropathic pain can involve a combination of drugs, including gabapentin and oxycodone (Hanna et al., 2008). A study found that administering gabapentin alongside oxycodone significantly reduced neuropathic pain by 33% compared to the group that was only administered gabapentin (Hanna et al., 2008).

The interactions of other drugs with gabapentin and pregabalin may have impacted the reported efficacy of these drugs in treating neuropathic pain. As noted in the case of Serpell (2002), future studies could investigate how the efficacy of gabapentin is different when

it is used as the only treatment compared to when other drugs are used in conjunction with gabapentin. As observed in the case of Moon et al. (2010), future studies could also focus on how previously using pregabalin or gabapentin may affect treatment results with a new drug. Another potential limitation of this comparative study was the use of different sample sizes for the gabapentin-centered studies, Serpell (2002) and Backonja (1999). While results were statistically significant in both studies, the differences in sample size may account for the slight difference noted between the placebo and drug-treated groups after the treatment period. In the future, it would be ideal to specifically examine whether gabapentin is also seen to significantly reduce pain across a wide range of sample sizes larger than the ones used in the studies examined, but still at an appropriate size for examining drug efficacy without compromising the validity of results.

Conclusion

While the results of this comparative study appear to indicate that pregabalin may have a greater efficacy in treating neuropathic pain compared to gabapentin, more research is needed to better establish this relationship as other studies in the field seem to contradict this inference. It is also important to consider that the studies chosen only evaluated either gabapentin or pregabalin as part of their analysis. Therefore, definitive conclusions comparing both of these drugs cannot be precisely made from just the results presented. Overall, this analysis indicates that pregabalin and gabapentin are promising pharmacological treatments for neuropathic pain, as both are able to significantly reduce pain, a finding that is consistent with results from prior studies in the field. Neuropathic pain continues to be a condition that calls for clinical intervention, and this study may provide clinicians with more insight into whether pregabalin or gabapentin may provide for a stronger analgesic effect on the basis of a common evaluation metric.

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