Gabapentin in Pain Management

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Gabapentin [1-(aminomethyl)cyclohexane acetic acid] is a structural analog of \( \gamma \)-aminobutyric acid (GABA), which was initially introduced in 1994 as an antiepileptic drug (AED), particularly for partial seizures. For a long time, AEDs such as carbamazepine have been recognized as adjunctive drugs for treating certain symptoms of chronic pain syndromes. It is then not surprising that gabapentin was soon found to be promising in treating neuropathic pain associated with postherpetic neuralgia (PHN) (1,2), postpoliomyelitis neuropathy (3), and reflex sympathetic dystrophy (4). Placebo-controlled clinical trials also have indicated a role of gabapentin in treating pain related to diabetic neuropathy (DNP) (5) and PHN (6).

A number of animal studies have investigated the effect of gabapentin on signs of neuropathic pain, such as hyperalgesia and allodynia. Data derived from these studies are generally in agreement with clinical observations. More recently, studies on animal models of acute pain have indicated a role of gabapentin in ameliorating pain from incisional injury and arthritis (7,8), implicating even broader use of gabapentin in treating a variety of pain states. Indeed, it is a common experience that gabapentin has been increasingly prescribed by pain specialists, neurologists, primary care physicians, and other physicians for cases in which pain of nonnociceptive origin is suspected. The clinical impression that there are fewer side effects of gabapentin often becomes part of the rationale for initiating gabapentin therapy. However, both the efficacy and indications of gabapentin for pain treatment are yet to be established, and there is a lack of consensus with regard to the dosage, indications for use of gabapentin, and clinical outcome data.

In this article, three lines of evidence will be examined regarding the role of gabapentin in pain treatment: 1) clinical evidence (case reports and trials) for a role of gabapentin in pain treatment will be discussed with an attempt to identify pain symptoms that are likely to be responsive to gabapentin; 2) animal studies of gabapentin on neuropathic pain and other pain behaviors will be evaluated; and 3) possible mechanisms of gabapentin actions will be considered in relation to mechanisms of neuropathic pain in particular. Finally, clinical issues of gabapentin treatment will be discussed in the context of its role in neuropathic pain relief.

Clinical Data

Thus far, information pertaining to the effectiveness of gabapentin in pain relief is mainly derived from anecdotal case reports. Several open-label, nonplacebo-controlled clinical studies have been conducted. Two randomized, placebo-controlled clinical trials investigated the effect of gabapentin on pain from DNP and PHN.

Postherpetic Neuralgia

Gabapentin (900 mg/daily) was first reported to be beneficial in a 77-year-old female patient with burning pain in the right T4 dermatome three months after acute herpes zoster infection (1). Similar results of decreased PHN pain with gabapentin were shown in several case reports (2,9), including a retrospective case review (10). In 1998, a randomized, controlled clinical trial investigated the effect of gabapentin on PHN pain (6). In this clinical trial, patients with PHN pain were randomized into gabapentin (\( n = 113 \)) and placebo (\( n = 116 \)) groups. During the eight-week trial period, patients in the gabapentin group (a maximum daily dose of 3600 mg) reported a reduction of the daily pain score (0–10 scale) from 6.3 to 4.2 as compared with a half point reduction (from 6.5 to 6.0) in the placebo group. In addition, patients treated with gabapentin also showed some improvement in sleep, affective measures of pain, and quality-of-life outcome measures (6). However, it is not clear whether the improvement in sleep and quality of life is related to the direct effects of medication or secondary to the reduction of pain.

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One caveat concerning this clinical trial is that tricyclic antidepressants (TCAs) and/or opioids were not discontinued in those patients who were receiving a stable dose range of these co-medications before beginning gabapentin treatment (6). Because both opioids and TCAs are effective in reducing PHN pain (11,12), this design makes it difficult to determine the effect of gabapentin alone on PHN pain. Particularly, the study did not provide information about how many patients in the trial received both gabapentin and co-medications. Thus, the data do not necessarily establish a causal relationship between gabapentin and PHN pain reduction, although the trial indicates a favorable outcome in PHN patients treated with gabapentin. Gabapentin could have its effect on PHN pain via interacting with the effect of TCAs and/or opioids, because gabapentin enhances the antinoceceptive effects of spinal morphine in the rat tail-flick test (13). Nonetheless, this study suggests that gabapentin is likely to be helpful in reducing PHN pain symptoms.

**Diabetic Neuropathy**

Pain associated with DNP was responsive to gabapentin in both case reports (2,14,15) and controlled clinical trials (5,16). In a multi-center randomized (gabapentin 84 subjects; placebo 81 subjects), placebo-controlled trial, monotherapy with gabapentin (a maximum dose of 3600 mg/day), except for the addition of acetaminophen, aspirin, or serotonin reuptake inhibitors as indicated, was shown to reduce DNP pain from 6.4 to 3.9 (0–10 scale), as compared with 6.5 to 5.1 in the placebo control group (5). The data also showed a favorable outcome of gabapentin in improving sleep disturbance and quality of life in patients with DNP pain. It should be noted that global pain scores were used in both DNP and PHN trials (5,6), and no information was generated regarding the effect of gabapentin on individual pain symptoms such as allodynia (nociceptive responses to innocuous stimulation) and hyperalgesia (exaggerated nociceptive response to noxious stimulation).

**Multiple Sclerosis (MS)**

Several case reports have shown a reduction of pain associated with MS (17–20). In two open-label, nonplacebo-controlled clinical studies (18,20), gabapentin (up to 1200 mg/day) was found to be helpful in reducing several types of pain in MS patients. Such pain conditions include painful tonic spasms and dysesthetic or paresthetic symptoms. In general, gabapentin treatment appears to be more effective in reducing paroxysmal pain with throbbing, prickling, and cramping quality than dull aching pain in MS patients. These findings suggest that a large-scale, controlled clinical trial may be warranted to determine the effectiveness of gabapentin in improving pain in MS patients.

**Neuropathic Cancer Pain**

In an uncontrolled clinical study (21), gabapentin was added to the opioid treatment regimen in 22 cancer patients whose pain was only partially responsive to opioid treatment. It was found that pain decreased from 6.4 to 3.2 (0–10 scale) at one to two weeks after the addition of gabapentin. In particular, burning pain was decreased from 5.1 to 2.0 and daily episodes of shooting pain from 7.2 to 2.2. Allodynia also disappeared in seven of nine patients after the addition of gabapentin into the treatment regimen. Although a number of variables including opioid doses and other co-medications were not controlled in this clinical observation, the data seem encouraging for those cancer patients suffering from intractable neuropathic pain.

**Miscellaneous Case Reports**

Sporadic case reports suggest that gabapentin may be effective in reducing pain associated with reflex sympathetic dystrophy (4), erythromelalgia (22), idiopathic trigeminal neuralgia (23), peripheral neuropathy (24,25), postthoracotomy neuropathy (26), central pain syndromes (27,28), Guillain-Barre syndrome (29), and taxane-induced myalgias (30). Information from these case reports suggests that neuropathic pain with lancinating and steady-burning quality is more likely to respond to gabapentin as compared with pain of other qualities.

An important issue unaddressed in the aforementioned clinical trials and case reports is the effectiveness of gabapentin in attenuating individual symptoms of neuropathic pain. In an open-label, nonplacebo-controlled clinical study (31), effects of gabapentin on both spontaneous and stimulation-evoked pain were investigated in 18 patients with either peripheral or central neuropathic pain. Responses to stimulation-evoked pain were detected by using the quantitative sensory tests, which included the use of mechanical (von Frey filaments) and thermal (a contact thermode) stimulation. It was found that, at a maximum dose of 2400 mg/day, gabapentin moderately reduced spontaneous pain, particularly spontaneous paroxysmal pain. Both tactile and cold allodynia were reduced by gabapentin treatment. However, gabapentin did not change pain thresholds to either mechanical or thermal (hot) stimulation, and it did not reduce mechanical and thermal hyperalgesia.

Several points may be mentioned from the currently available clinical data. First, except for a few randomized, controlled clinical trials, most information regarding the efficacy of gabapentin on pain relief has been derived from anecdotal clinical observations. Second, gabapentin appears to be helpful in reducing spontaneous, paroxysmal pain with burning and lancinating quality as well as allodynia to cold and tactile stimuli. Dull, aching pain and hyperalgesia are less likely to be responsive to gabapentin treatment. It is,
Preclinical Data

A major advantage of preclinical trials is that the effect of gabapentin can be differentially examined on individual signs of neuropathic pain such as allodynia, hyperalgesia, and spontaneous pain. A number of animal studies have been performed in the last several years. The data from these studies are summarized below based on the effect of gabapentin on nociceptive thresholds, allodynia, and hyperalgesia.

Nociceptive Thresholds

Consistent with human studies that indicate no changes in nociceptive thresholds by gabapentin (31), gabapentin did not alter nociceptive thresholds in animal models of neuropathic pain (32), acute arthritic pain (8), formalin-induced nociception (33,34), or thermal injury (35). Interestingly, gabapentin has been reported to facilitate responses of spinal cord dorsal horn neurons to noxious C fiber and Aδ fiber, but not Aβ fiber, stimulation in normal rats (36). In sharp contrast, gabapentin dose-dependently reduced dorsal horn neuronal responses to C fiber, but not Aβ fiber, stimulation in inflammatory rats three days after the carrageenan injection (36). A similar effect of gabapentin was shown in an animal model of selective nerve root (L5 and L6) ligation (37). These findings suggest 1) a differential effect of gabapentin in normal and inflammatory pain states, 2) a selective effect of gabapentin on spinal cord neuronal responses to noxious (Aδ and C fiber) versus innocuous (Aβ fiber) peripheral stimulation, and 3) an adverse (facilitatory) effect of gabapentin on nociceptive responses of spinal cord dorsal horn neurons in the absence of pathological pain states.

Allodynia

Allodynia to tactile or thermal stimuli could be elicited in animals with nerve injury (32,38,39), incisal injury (7), diabetes (40), and abnormal immunoresponses to anti-GD2 ganglioside (41). Gabapentin given systemically reduced mechanical and/or cold-induced allodynia in each of these animal models. The gabapentin-related compound pregabalin also reduced mechanical allodynia in diabetic rats (40). Three observations from these studies are worth mentioning: 1) the antiallodynic dose of gabapentin did not affect nociceptive thresholds (32); 2) although lamotrigine (an AED) and gabapentin both decreased cold allodynia in rats with nerve injury, only gabapentin also decreased mechanical allodynia in these same rats (32); and 3) although systemic morphine or amitriptyline blocked static mechanical allodynia (von Frey filament stimulation) in diabetic rats, gabapentin or pregabalin dose-dependently blocked both static and dynamic (lightly stroking the skin with a cotton bud) mechanical allodynia in the same rat model (40). These observations are consistent with a clinical study that indicates a selective reduction of alldynia by gabapentin (31).

Hyperalgesia

Both thermal and mechanical hyperalgesia have been shown to be reduced by systemic or intrathecal gabapentin in animal models of incisal injury (7), peripheral nerve injury (42), thermal injury (35,43), substance P-induced hyperalgesia (44), and acute arthritis (8). Pretreatment with gabapentin also blocked the development of hyperalgesia, suggesting a preventive effect of gabapentin (7,8,43). The antihyperalgesic effect of gabapentin is likely to be mediated at a central site, because intrathecal gabapentin injection produced an effect similar to that of systemic gabapentin administration (8,35). It should be noted that, unlike the results shown in the animal studies, both mechanical and thermal hyperalgesia were unchanged by gabapentin in patients with neuropathic pain, as assessed by quantitative sensory tests (31).

Subcutaneous injection of formalin into a rat’s hind paw elicits a two-phase response (45). This two-phase response is unique in that the first phase (Phase 1) is related to a normal (physiological) nociceptive process, whereas the second phase (Phase 2) may reflect a hyperalgesic condition involving a state of central sensitization. Except for one study that reported a moderate reduction of Phase 1 nociceptive behaviors by systemic gabapentin (46), gabapentin given either systemically or intrathecally reduced hyperalgesic behaviors only in Phase 2 of the formalin test (33,34,46,47). Co-administration of gabapentin and formalin into the rat’s hind paw itself also reduced Phase 2 hyperalgesic behaviors (48).

In summary, the present laboratory studies indicate that 1) gabapentin does not affect nociceptive thresholds, 2) gabapentin is effective in reducing both allodynia and hyperalgesia in animal models, and 3)
gabapentin may have a selective effect on the nociceptive process involving central sensitization. Among these findings, evidence suggesting an antiallodynic effect of gabapentin and the lack of effect on nociceptive thresholds is consistent with that seen in clinical studies. No data are available with regard to the effect of gabapentin on spontaneous pain in animal models.

**Potential Mechanisms of Gabapentin Actions**

Neuropathic pain is characterized by distinctive clinical symptoms and signs such as spontaneous pain, allodynia, hyperalgesia, and pain summation. Neuropathic pain is often considered to be poorly responsive to conventional analgesic medications, including non-steroid antiinflammatory drugs and opioid analgesics. Both peripheral and central mechanisms of neuropathic pain have been proposed (49,50). Peripherally, abnormal activation of sodium channels leading to the generation of ectopic discharges is likely to be attributable to symptoms of neuropathic pain, particularly spontaneous, paroxysmal pain. Centrally, sensitization of spinal cord dorsal horn neurons in response to abnormal, repetitive peripheral nociceptive input after nerve/tissue injury plays a significant role in both development and maintenance of neuropathic pain symptoms. A key process of this central sensitization is the activation of N-methyl-d-aspartate (NMDA) receptors by glutamate/aspartate within the central nervous system. In addition, an imbalance between the spinal cord inhibitory and excitatory circuitry, presumably the result of a decreased spinal cord inhibitory (GABA) influence, may also contribute to a central hypersensitization state. Perplexingly, actions of gabapentin on pain relief do not seem to interact with any of these known mechanisms.

Gabapentin is ineffective in blocking sodium channel-mediated repetitive action potentials in cultured neurons (51). Consistent with this in vitro observation, both conduction velocity and responses of Aδ- and C-afferent fibers to noxious mechanical stimulation were not changed by gabapentin in normal rats (39). However, IV gabapentin (30–90 mg/kg) dose-dependently suppressed ectopic discharges in rats with partial sciatic nerve ligation (39). The gabapentin dose range effective for suppressing ectopic discharges is equivalent to that for reducing mechanical allodynia in the same rat model (39). These findings would suggest a selective blockade of nerve injury-induced ectopic discharges by gabapentin, an effect similar to that after systemic lidocaine (52). In complete contrast, gabapentin (50 mg/kg) given systemically failed to reduce ectopic discharges in a rat model of selective nerve root ligation, although the same dose of gabapentin was effective in attenuating mechanical allodynia (38). The results from this study strongly argue against a peripheral effect of gabapentin on allodynia.

Gabapentin is a structural analog of GABA, which readily crosses the blood-brain barrier when given systemically (53). Gabapentin, however, does not bind to GABA receptors (54,55). Although gabapentin may influence the synthesis and release of GABA (55), it does not affect the uptake and metabolism of endogenous GABA (56,57). Importantly, the antiallodynic effect of gabapentin is not affected by antagonists of GABA receptors (58). It is thus unlikely that the antiallodynic effect of gabapentin, as shown in animal studies, is caused by an enhancement of the inhibitory (GABA) influence via its direct interaction with GABA receptors or its indirect effect via increasing endogenous GABA.

The NMDA receptor is a molecular complex consisting of a glutamate-binding site and several regulatory sites including a strychnine-insensitive glycine binding site. D-serine is an agonist for the NMDA-glycine site. The antihyperalgesic effect of gabapentin has been shown to be reversed by D-serine in animal models of formalin-induced nociception (34,48), substance P- and NMDA-induced hyperalgesia (44), and thermal injury (35). These data would suggest that gabapentin acts as an antagonist at the NMDA-glycine site, and D-serine competently replaces gabapentin thereby reversing the gabapentin effect. However, receptor binding studies fail to detect any specific interactions between gabapentin and the NMDA receptor.

**Table 1. Summary of Clinical Trial Data**

<table>
<thead>
<tr>
<th>Pain Type</th>
<th>Study Type</th>
<th>Subjects</th>
<th>Daily Dosage</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHN</td>
<td>Controlled</td>
<td>229</td>
<td>3600 mg</td>
<td>Improved VAS</td>
<td>6</td>
</tr>
<tr>
<td>DNP</td>
<td>Controlled</td>
<td>165</td>
<td>3600 mg</td>
<td>Improved VAS</td>
<td>5</td>
</tr>
<tr>
<td>MS</td>
<td>Open-label</td>
<td>21</td>
<td>1200 mg</td>
<td>Pain reduction</td>
<td>20</td>
</tr>
<tr>
<td>MS</td>
<td>Open-label</td>
<td>25</td>
<td>Various</td>
<td>Pain reduction</td>
<td>18</td>
</tr>
<tr>
<td>CNP</td>
<td>Open-label</td>
<td>22</td>
<td>Various</td>
<td>Improved VAS</td>
<td>21</td>
</tr>
<tr>
<td>Complex</td>
<td>Open-label</td>
<td>18</td>
<td>2400 mg</td>
<td>Various (QST)</td>
<td>31</td>
</tr>
<tr>
<td>DNP</td>
<td>Randomized</td>
<td>21</td>
<td>1565 mg</td>
<td>52% responders</td>
<td>67</td>
</tr>
</tbody>
</table>

PHN = postherpetic neuralgia, DNP = diabetic neuropathic pain, MS = multiple sclerosis, CNP = cancer-related neuropathic pain, Complex = including both central pain and peripheral neuropathic pain, Various = including positive and negative responses to gabapentin (quantitative sensory tests), VAS = visual analog scale score.

a Moderate-to-excellent pain relief in 52% of the participants treated with gabapentin.
complex (51,55), including the strychnine-insensitive glycine site (59). In the absence of specific binding data, it is unlikely that gabapentin has its effect by means of interacting with the NMDA receptor.

A gabapentin-specific binding site was initially identified in the central nervous system (54). This site was later identified as the α2δ subunit of voltage-dependent calcium channels (60). Besides gabapentin, S(+)-3-isobutylgaba (pregabalin), but not R(−)-3-isobutylgaba, stereo-specifically binds to this calcium channel subunit (60). It has been proposed that gabapentin reduces hyperalgesia by binding to this common site, because S(+)-3-isobutylgaba, but not R(−)-3-isobutylgaba, produces similar antihyperalgesic effects (7,43,44,47,48,61). Although voltage-dependent calcium channels have been implicated in hyperalgesia (62), it is difficult to envision that binding to voltage-dependent calcium channels alone by gabapentin would account for its effects on allodynia and hyperalgesia in animal studies. In addition, the specificity of gabapentin in blocking calcium channels is not clear. In particular, the average dose of gabapentin used in the clinical setting is several hundred-fold larger than that of specific calcium channel blockers.

Taken together, mechanisms of gabapentin on pain relief remain largely elusive. Gabapentin does not directly interact with NMDA and GABA receptors. Although gabapentin modulates GABA synthesis, this action is unlikely to be attributable because the blockade of GABA receptors does not change the gabapentin’s effect on allodynia. A peripheral mechanism of gabapentin on abnormal sodium channel activation has been proposed, but the data remain controversial. A specific binding site (the α2δ subunit of voltage-dependent calcium channels) has been described for gabapentin and pregabalin. However, a causal relationship between this gabapentin/pregabalin binding site and pain relief is yet to be established. Animal studies show some similarities in the reduction of hyperalgesia between gabapentin and NMDA receptor antagonists (63). Such parallel results would suggest that the α2δ subunit of voltage-dependent calcium channels would be mechanistically critical, like the NMDA receptor, to the development and maintenance of hyperalgesia. Thus far, little information is available to support this hypothesis.

### Clinical Issues Concerning Gabapentin Treatment

Pain of nonnociceptive origin including neuropathic pain is a daily challenge both to patients and clinicians who devote their efforts to pain management. Any novel treatment that might provide beneficial outcomes in patients with such intractable pain will be a valuable addition to the current pain treatment armamentarium. Indeed, gabapentin has been regarded as a promising new drug in pain management, although it was initially approved by the Food and Drug Administration as an adjunctive drug for partial seizure controls. However, several clinical issues of gabapentin should be addressed to introduce a rational use of this drug in pain management. These issues include the efficacy and indications, side effect profiles, and comparisons between gabapentin and other currently available pain medications.

#### Is Gabapentin an All-Purpose Painkiller?

Data from both preclinical and clinical studies clearly demonstrate that gabapentin does not change nociceptive thresholds. Thus, gabapentin is unlikely to be a conventional analgesic like opioids that produce analgesia by means of elevating nociceptive thresholds. No evidence shows gabapentin to be effective in reducing nociceptive pain. With regard to neuropathic pain, the two controlled clinical trials (5,6) show a small but statistically significant reduction of global pain scores in patients with DNP and PHN. These two trials, however, used global pain scores and did not examine the effect of gabapentin on individual pain symptoms such as spontaneous pain versus stimulation-evoked pain (allodynia, hyperalgesia) in DNP and PHN patients. In addition, these two trials did not assess the effects of gabapentin on various indices of mental and physical functions.

Noncontrolled, open-label clinical studies support a role of gabapentin in reducing spontaneous pain and allodynia to both thermal and mechanical stimuli regardless of the etiology. Gabapentin appears particularly helpful in reducing paroxysmal pain with lancinating and burning quality in these studies. It remains controversial whether gabapentin is effective in attenuating hyperalgesia. Much of the information regarding gabapentin in treating neuropathic pain comes from case reports with a limited number of patients. Yet, gabapentin is extensively used for numerous chronic pain conditions mainly based on these anecdotal reports. One obvious shortcoming of case reports is that favorable clinical outcomes are selectively reported without showing negative clinical experiences. Thus, the validity of these case reports should be confirmed by controlled clinical trials.

#### Does Gabapentin Have Fewer Side Effects than Other Adjunctive Pain Medications?

G gabapentin is considered to be better tolerated with fewer side effects and minimal interactions with other drugs. In an open-label study, the safety and tolerability of gabapentin in seizure treatment were investigated in two groups of patients receiving a daily dose of either <1800 mg or >1800 mg (64). This study shows that the tolerability was statistically better in
patients receiving more than 1800 mg/day of gabapentin than those receiving <1800 mg/day, a result awaiting a plausible explanation. With regard to the safety issue, 48.3% (2216 subjects) of the participants reported at least one of the following adverse events: somnolence (15.2%), dizziness (10.9%), asthenia (6%), headache (4.8%), nausea (3.2%), ataxia (2.6%), weight gain (2.6%), and amblyopia (2.1%). A total of 10.6% (234 of 2216) subjects discontinued the gabapentin therapy secondary to adverse events. The study did not compare the safety and tolerability of gabapentin with other commonly used AEDs, and it did not provide the outcome analysis of seizure reduction in relation to the occurrence of adverse events.

Similar side effects have been observed in pain patients treated with gabapentin. The major side effects related to gabapentin treatment include dizziness (24%), somnolence (23%–27%), confusion (8%), and ataxia (7%) (56). There are sporadic case reports of gabapentin-induced polyneuropathy (65) and psychomotor agitation (66). Thus far, only one study directly compared the side effect profiles of gabapentin and amitriptyline, a commonly used adjunctive pain medication (67). This study failed to prove a better side effect profile of gabapentin over amitriptyline. A higher rate of sedation and dizziness was observed in the gabapentin group, whereas a higher rate of dry mouth was seen in the amitriptyline group. Patients in both groups tolerated the side effects and had comparable outcomes in pain relief.

Is Gabapentin Better than Other Adjunctive Pain Medications?

Although it is difficult to compare directly the efficacy of different medications, the decision of choosing one particular medication over the other should include the consideration of outcome measures, side effect profiles, and cost/efficiency ratios. To date, there is only one randomized, double-blinded, cross-over study that compared the efficacy of gabapentin and amitriptyline on DNP pain (67). Moderate-to-great pain relief was reported in 52% (11 of 21) patients treated with gabapentin (a mean daily dose of 1565 mg) and 67% (14 of 21) with amitriptyline (a mean daily dose of 59 mg). This relatively small-scale clinical trial failed to prove an advantageous effect of gabapentin over amitriptyline. One caveat concerning this clinical trial is that no comparisons on individual symptoms of DNP pain were made between gabapentin and amitriptyline treatments. Thus, it is not clear whether gabapentin would be more effective than amitriptyline in ameliorating neuropathic pain with a certain quality, such as burning pain and spontaneous, paroxysmal pain. The side effect profiles do not significantly differ between these two medications as discussed earlier (67). There is, however, a remarkable cost difference between a month supply of gabapentin ($200–$300 with the dose range of 1800–2700 mg/day) and the generic amitriptyline ($3) and nortriptyline ($12).

In summary, gabapentin has been shown to be effective in reducing neuropathic pain associated with DNP, PHN, MS, and cancer-related neuropathic pain. Gabapentin appears to be helpful in reducing spontaneous, paroxysmal pain with burning and lancinating quality as well as allodynia to cold and tactile stimuli. Dull, aching pain and hyperalgesia are less likely to be responsive to gabapentin treatment. The results from preclinical studies are generally consistent with clinical findings. In particular, both clinical and preclinical trials have clearly shown an antiallodynic effect of gabapentin and a lack of effect on nociceptive thresholds. Although gabapentin was effective in relieving certain neuropathic pain symptoms, thoughtfully designed, large-scale clinical trials should be performed to confirm the efficacy of gabapentin. For example, the effect of gabapentin on distinct symptoms and signs of neuropathic pain should be assessed in patients with neuropathic pain. At present, more data are needed to support the notion that gabapentin is the first-line treatment for neuropathic pain with a better efficacy, fewer side effects, and a favorable cost/efficiency ratio.


