

Gabapentin for the Treatment of Neuropathic Pain

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Neuropathic pain, a persistent chronic pain resulting from damage to the central or peripheral pain signaling pathway, has become an area of intense research activity—largely because it represents a disorder with high unmet medical need. It is not a single entity but rather includes a range of heterogeneous conditions that differ in aetiology, location and initiating cause. Despite this diversity, the clinical presentation is frequently surprisingly similar which suggests a common biological basis. Until recently, little was known of the mechanisms underlying the various neuropathic pain conditions. However, the steady increase in understanding of anatomical, cellular and molecular basis of neuropathic pain, coupled with the availability of a number of experimental models of neuropathy has permitted relatively rapid progress and the prospects for the emergence of new, and effective therapy. Gabapentin is one of the additions in such therapy.

Gabapentin was primarily approved by the Food and Drug Administration (FDA) in 1993 for treating partial seizures with or without generalization. It is a lipophilic structural analogue of the neurotransmitter i.e. Gamma-aminobutyric acid (GABA). Despite its design as a GABA agonist, it does not bind to GABA_A or GABA_B receptors. It is neither converted to GABA, nor it is a GABA agonist and even it is not an inhibitor of GABA re-uptake or degradation. Gabapentin may promote non-vesicular release of GABA (1). Gabapentin has antihyperalgesic and antiallodynic properties but does not have significant actions as an anti-nociceptive agent (2). The mechanism by which gabapentin exerts its analgesic actions in human has not been clearly established.

However, its mechanisms of action appear to be a complex synergy between increased GABA synthesis, non-NMDA receptor antagonism and binding to the alpha2delta subunit of voltage dependent L-type of calcium channels (VDCC). The latter action inhibits the release of excitatory neurotransmitters (2, 3). The binding of gabapentin to VDCC may also modulate GABAergic, Glutamergic and monoamine function. The site of action of gabapentin is unclear, although effects at peripheral primary afferent neurons, spinal neurons and supraspinal sites have been reported (4). Gabapentin reduces allodynia and/or hyperalgesia in several animal models of neuropathic pain including models of acute herpes zoster infection, thermal injury, nerve injury, postoperative pain and streptozocin-induced diabetic neuropathy (5). Gabapentin even in human beings have been well suggested recently for the treatment of neuropathic pain. One of the most common and disabling complications of herpes zoster is postherpetic neuralgia (PHN). Gabapentin appears to be effective and is well tolerated for the short-term treatment of PHN (6, 7). Pain syndromes of Guillain-Barre are neuropathic as well as nociceptive in origin. The therapeutic efficacy of gabapentin in relieving the bimodal nature of pain in Guillain-Barre syndrome (GBS) in a randomized, double-blinded, placebo-controlled, crossover study suggested that gabapentin has minimal side effects and is an alternative to opioids and nonsteroidal antiinflammatory drugs for management of the bimodal nature of pain of GBS patients (8). Neuropathic pain associated with spinal cord injury is quite refractory, and current treatments are not effective. Gabapentin can be added to the list of first-

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line medications for the treatment of chronic neuropathic pain in spinal cord injury patients (9, 10). The analgesic effect of the addition of gabapentin to opioids in the management of neuropathic cancer pain indicated that gabapentin is effective in improving analgesia in patients with neuropathic cancer pain already treated with opioids (11). Severe phantom limb pain after surgical amputation affects 50% to 67% of patients and is difficult to treat. After 6 weeks, gabapentin monotherapy was better than placebo in relieving postamputation phantom limb pain (12). Gabapentin produced improvement in pain and paresthesia associated with diabetic neuropathy (13). Gabapentine also has been suggested to benefit in migraine (14) and pain of trigeminal neurologia (2). Gabapentin is widely approved for the treatment of neuropathic pain of different origin. In adults 600-1800 mg per day in three divided doses is used through oral route. The adverse events reported are usually mild to moderate in intensity and are in the form of dizziness, somnolence, peripheral oedema, asthenia, diarrhoea. The adverse events that most frequently lead to discontinuation in gabapentin therapy are dizziness and somnolence (1, 2, 8).

To conclude gabapentin is a promising new agent which offers many advantages over currently available medication in the treatment of neuropathic pain. It is efficacious (6, 7), well tolerated with minimal side effects that may occur during titration phase (2) and are transient only, as well as it can potentiate the analgesic effects of other conventionally available drugs (9-11). In addition, it has been also shown to improve the quality of sleep in patients (1, 2). In view of all these advantages, gabapentine has emerged as one of the important drug in the treatment of neuropathic pain.

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