

Clinical Trial Assessing the Efficacy of Gabapentin plus B complex (B1/B12) versus Pregabalin for Treating Painful Diabetic Neuropathy

Painful diabetic neuropathy (PDN) is one of the most common causes of chronic pain that requires a multidisciplinary intervention and, sometimes, use of multimodal treatments. This situation has required using combination drugs as a treatment alternative, towards improving the patient prognosis. ^[1]

There is evidence suggesting that more than half of chronic pain patients receive two or more analgesics, although evidence supporting most of these combinations is limited. Treatment of painful diabetic neuropathy includes using of antidepressants, anticonvulsants (calcium channel blockers), and opioid drugs, among others. One of the main problems when using these drugs is adverse events (AE), occasionally limiting the possibility to use drugs recommended in clinical trials. ^[2]

Complex B vitamins, specifically thiamine (B1) and cyanocobalamin (B12), have been shown to be of clinical use in some painful diseases, derived from their effects on the central nervous system, synthesis, and secretion of serotonin in several brain area, blocking metabolic pathways related to oxidative stress, as well as their effects on the nitric oxide/guanosine monophosphate cyclic (NO/GMPc) pathway, among other mechanisms. Synergy of these vitamins with other drugs, for example, gabapentin, allows for reducing recommended doses of these vitamins as monotherapy, achieving greater reduction effects on pain intensity with less AE occurrence. ^[3, 4, 5]

A study published in 17 Jan 2016 was to determine the efficacy of gabapentin/vitamins B1 and B12 (GBP/B1/B12) versus pregabalin (PGB) in patients with moderate to severe intensity painful diabetic neuropathy during 12 weeks of treatment. In this Phase IV, multicenter, randomized, open-label, parallel group, 459 subjects were selected, 353 of which were randomized; 346 constituted the intention-to-treat population, 5 patients had type 1 diabetes (2 in the group of GBP and two in the group of PGB). They were divided in parallel groups: 173 patients treated with GBP/B1/B12 and 173 patients treated with PGB. With a 7/10 pain intensity on the Visual Analog Scale (VAS). Two patients were discontinued from the study due to missing information after their initial visit (one of each group), remaining 346 (intention-to-treat population, ITT). Seventy-two (72) patients were discontinued from the study due to several reasons, remaining **270** patients, as per protocol population (PPP). Five visits (12 weeks) were scheduled. The GBP/B1 (100 mg)/B12 (20 mg) group started with 300 mg at visit 1 to 3600 mg at visit 5. The PGB group started with 75 mg/d at visit 1 to 600 mg/d at visit 5. Different safety and efficacy scales were applied, as well as adverse event assessment. ^[6]

The results were; both drugs resulted in reduction of pain intensity, without significant statistical difference ($P = 0.900$). In the GBP/B1/B12 group, an improvement of at least 30% on VAS correlated to a 900 mg/d dose, compared with PGB 300 mg/d. Likewise, occurrence

of vertigo was lower in the GBP/B1-B12 group, with a significant statistical difference, ($P = 0.014$).^[6]

Several mechanisms of action have been proposed to explain the effect of (B1) and (B12) when treating pain. The synergy of GBP/B1-B12 as consequence of multiple effects of these vitamins at a metabolic level. These effects can be divided into two categories, those decreasing damage mechanisms on nervous fibers and those with antihyperalgesic and antinociceptive effects.^[2]

In conclusion, GBP/B1-B12 combination is as effective as PGB; also vitamins B1 and B12 have a synergistic effect in combination with gabapentin in PDN treatment, since pain intensity reduction was obtained with 50% of the GBP dose required as monotherapy. Likewise, regarding GBP dose reduction, there are less adverse events (vertigo). Nonetheless, it is necessary to confirm the role of vitamins, isolated and versus placebo, to prove the absolute and potential benefit of this combination.

References:

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