Editorial

Efficacy of pregabalin in patients with sciatica: a randomized, double-blind, placebo controlled trial

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Lumbar spinal disorders such as lumbar disc herniation or lumbar spinal stenosis are a cause of sciatica with or without low back pain (LBP). The natural course, typical age, and efficacy of non-surgical treatments for each disorder are different, and the evidence of pharmacological treatment for spinal disorders remains insufficient. Pregabalin is one of the first-line drugs for pharmacotherapy of neuropathic pain (1). Various diseases can cause neuropathic pain, including immune disorders, entrapment, and neurodegenerative disorders. Pregabalin inhibits the release of neurotransmitters via binding to alpha 2-delta subunits of voltage-dependent calcium channels. Several articles have reviewed trials comparing the efficacy of pregabalin and placebo for neuropathic pain (2-5). However, given the methodological limitations including variable subject populations and study designs, strong evidence has yet to be shown for the efficacy of pharmacological treatment (6).

This editorial examined the results of a randomized, double-blind, placebo-controlled trial of pregabalin in patients with sciatica (7). A total of 208 patients were examined and randomly divided into pregabalin and placebo groups. Patients received either pregabalin or placebo for 8 weeks. The primary outcome of leg pain intensity score at weeks 8 and 52 did not differ significantly between groups. Likewise, the secondary outcomes of disability due to sciatica, LBP intensity, quality of life, or workplace absenteeism did not differ significantly between groups. This paper concludes that pregabalin did not offer any benefit for improving sciatica, whereas the prevalence of adverse events was higher in the pregabalin group than in the placebo group.

This study showed some strengths. The number of subjects was adequate and the selection bias seemed minimal, since subjects were enrolled from multiple sites. The follow-up rate for the 52 weeks was high. The methodology for double-blinding was adequate.

Some limitations of this study need to be considered. Sciatica is a term used to describe leg pain of lumbar-sacral radicular origin due to the lumbar spinal disorders. Radicular pain often shows intricate overlap of nociceptive and neuropathic pain, and pain control is not easy to achieve. Differences in intensity and duration of pain have been compared between neuropathic and non-neuropathic pain. Patients with neuropathic pain show higher intensity of leg pain and percentage of longer pain duration than patients with non-neuropathic pain (8). In addition, health-related quality of life is significantly lower in patients with neuropathic pain than in the general population (1). This trial did not compare neuropathic and non-neuropathic components. The prevalence of neuropathic component was 34% in the pregabalin group and 22% in the placebo group. There are two negative points. First, the prevalence of neuropathic component was higher in the pregabalin group than in the placebo group, even though patients were allocated randomly. Second, effects of pregabalin were not compared between neuropathic and non-neuropathic components. The possibility must be considered that pregabalin has efficacy for sciatica with a neuropathic component compared with the placebo group. In addition, mean duration of leg pain intensity was less than 12 weeks in this trial, and duration of leg pain was adjusted. However, the characteristics of patients differed between acute and

chronic phases, including the natural course and effect of pharmacological treatments. This would lead to differences in the efficacy of pregabalin and placebo between acute and chronic phases. Moreover, mean dose in the pregabalin group was decreased at week 8 compared with week 7. According to the protocol in this trial, patients were allowed to decrease doses before week 8 due to leg pain score. This indicated that patients in whom leg pain had been alleviated were included. Furthermore, whether outcomes at week 52 really reflected the treatment for 8 weeks is unclear, for the following reasons: (I) the data did not include whether patients were allowed to continue any treatments from week 8 to 52; (II) the natural course for improvement of sciatica according to the cause of spinal disorder differs; (III) disability and QOL differed by age and influence of treatment effect. Treatment effects for secondary outcomes were not evaluated according to age groups; (IV) prevalence of leg pain and LBP were not compared with those at baseline; (V) new onset of sciatica and LBP were not evaluated during the 52 weeks; (VI) some patients had sciatica combined with or without LBP, and some cases had sciatica with non-specific LBP. Therefore, LBP was not always linked with the sciatica.

Additional analysis using the data from this trial could show potential benefit of pregabalin for sciatica with a neuropathic component and chronic-phase pain lasting more than 12 weeks.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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