Mirogabalin, a selective gabapentinoid for managing neuropathic pain—A curtain raiser

Dear Editor,

Gabapentinoid anticonvulsants namely gabapentin and pregabalin have been used successfully and extensively for managing chronic neuropathic pain due to various etiologies including cancer pain. Gabapentinoids bind to the α2δ-1 and α2δ-2 subunits of voltage-gated calcium channels (VGCCs) nonselectively and thus relieve neuropathic pain because it is speculated that the maladaptation and dysregulation of the α2δ-1 subunits of VGCCs is one of the causes of neuropathic pain.[1] Central nervous system (CNS) adverse events like dizziness, drowsiness, somnolence, and cerebellar ataxia are known problems with gabapentinoids, especially in high doses. The nonselective binding of these drugs to the α2δ-1 and α2δ-2 subunits of VGCCs is considered a major reason for CNS adverse effects along with other sedatives, age, and renal and hepatic impairment.

Mirogabalin besylate is an orally administered gabapentinoid developed by Daiichi Sankyo, Japan and approved for the treatment of peripheral neuropathic pain like diabetic peripheral neuropathic pain and postherpetic neuralgia [Figure 1]. Researchers have also used it successfully for conditions like lumbar spine disease and cancer, although the data is anecdotal. Mirogabalin binds selectively and with greater affinity to the α2δ-1 and α2δ-2 subunits of human VGCCs *in vitro* (Kd 13.5 and 22.7 nmol/L). However, mirogabalin takes a considerably longer time to dissociate from α2δ-1 (dissociation half-life 11.1 h) than α2δ-2 *in vitro* (dissociation half-life 2.4 h) when compared to

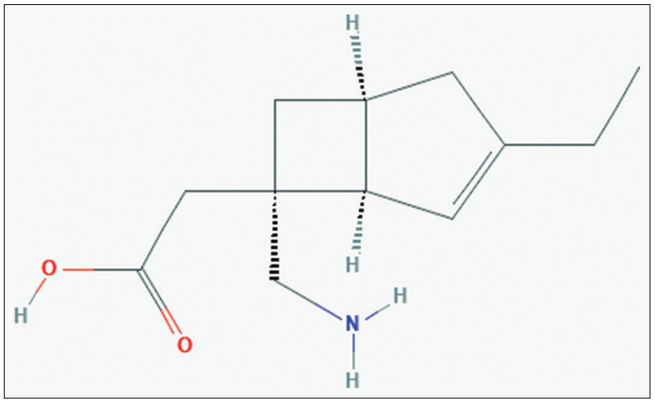

Figure 1: Chemical structure of mirogabalin. (Figure source: PubChem [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2004-. PubChem Compound Summary for CID 59509752, Mirogabalin; [cited 2021 Jan. 11]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Mirogabalin)

pregabalin and gabapentin. Mirogabalin has high affinity and dissociates slowly from the α2δ-1 subunits, thereby leading to longer duration of action. At the same time, it has a low affinity to and dissociates fastly from the α2δ-2 subunits in the cerebellum leading to lesser incidence of ataxia and other CNS adverse events.[2]

Mirogabalin is rapidly absorbed when taken orally (Tmax: 0.5–1.5 h) as a single dose or divided doses. With daily dosing, a steady-state plasma concentration is achieved at the end of the third day. With doses of 10 mg/day to 30 mg/day (as a single dose or divided dose), clinicians have found mirogabalin to be better tolerated in patients with mild to moderate renal and hepatic impairment with negligible CNS adverse events (dizziness: 8–16%, somnolence: 6–24%; and headache: 6–14%). Researchers have cautioned regarding the concomitant administration of sedatives like high-dose opioids, benzodiazepines, and ethanol.[3] The feasibility of mirogabalin has not been adequately explored in cancer neuropathic pain in the form of a multicentric and randomized study.[4] To date, there is no data regarding the suitability of mirogabalin as an addition to multimodal postoperative pain management. A large trial was conducted to explore the efficacy of mirogabalin for managing pain in cases of fibromyalgia but the results were not convincing.[5]

Further well-designed studies need to be conducted to explore its efficacy in treating cancer pain, postoperative pain, and other chronic pain conditions. This is possible only after the drug is approved in other parts of the world.

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Conflicts of interest
There are no conflicts of interest.

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