Nefopam: Another Pragmatic Analgesic in Managing Chronic Neuropathic Pain

Sir,

Nefopam hydrochloride is a benzoxazocine derivative and belongs to the category of a nonopioid, nonsteroidal, and centrally-acting analgesic drug.[1] It was developed in 1960s and was known as fenazocine at that time. Initially classified as an antidepressant, fenazocine was later renamed as nefopam in 1970. Nefopam bears structural resemblance to antihistaminic orphenadrine and diphenhydramine [Figure 1]. The exact mechanisms of analgesic action of nefopam are not fully understood and complex.

Nefopam has been used successfully as an analgesic for postoperative pain as a part of multimodal analgesic regimen along with acetaminophen, NSAIDS, and opioids. Several studies have shown that a preoperative dose of 30 mg of injectable nefopam leads to less opioid consumption perioperatively with lesser frequency of rescue analgesics.[2] Nefopam does not confer any sedation or lead to respiratory depression has no antiplatelet action and can be safely used in elderly patients. Although not contraindicated, a dose reduction is required in patients with renal and hepatic insufficiency. Adverse effects such as nausea, vomiting, pruritus, tachycardia, and sweating have been reported after parenteral nefopam. Oral preparation is usually well-tolerated. After an initial intravenous (IV) dose of 30 mg, nefopam can be prescribed with a dose of 90–180 mg/day in divided doses, 3–6 times a day per orally.

There is a recent interest among researchers about nefopam and its potential role in managing chronic neuropathic pain.[3] This is due to the multimodal mechanism of action of nefopam. Nefopam causes descending pain modulation by reuptake inhibition of monoamine, serotonin, dopamine, and norepinephrine similar to antidepressants used in the practice of chronic pain. It also leads to inhibition of long-term potentiation mediated by N-methyl-D-aspartate receptors by inhibiting calcium influx and by blocking voltage-sensitive sodium channels. These actions resemble the mechanism of action of drugs such as gabapentinoids, tricyclic antidepressants, and carbamazepine which is a sodium channel blocker. The centrally mediated analgesia is possibly due to the activation of inhibitory serotoninergic descending pathways. It has also been demonstrated that ATP-sensitive potassium channel is involved in mediating antiallodynic effects of nefopam in an experimental neuropathic pain model.[4]

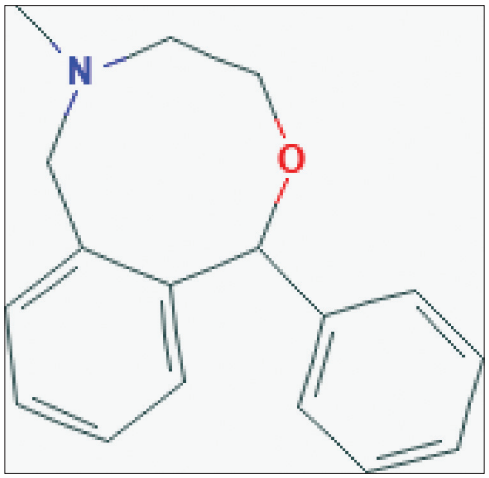

Figure 1: Chemical structure of nefopam (Image source: National Center for Biotechnology Information. PubChem Compound Database; CID = 4450, https://pubchem.ncbi.nlm.nih.gov/compound/4450, [accessed Dec 31, 2018]).

Using an agent like nefopam could really reduce the incidence of chronic postsurgical pain which is a distressing condition faced by patients due to poorly managed postoperative pain. This was demonstrated by Na *et al*. who administered 20 mg IV nefopam to 41 patients who underwent mastectomy and compared it with 42 patients in the other group who received placebo (normal saline).[5] The anesthesia management and peri-operative analgesia prescription were the same in both groups. The patients who received nefopam had a significantly less chronic pain at the end of 3 months compared to patients who received placebo.

The short-term safety of nefopam has been already established based on studies in acute peri-operative pain. Per orally, nefopam can be prescribed with a dose of 90–180 mg/day in divided doses, 3–6 times a day. For treating chronic neuropathic pain, the duration of therapy is for a longer duration. Further studies need to be conducted to establish safety and efficacy of nefopam in managing neuropathic pain followed by randomized controlled trials to prove that is in better or at least noninferior compared to already established medications.

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Conflicts of interest

There are no conflicts of interest.

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