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An Update on the Management of Diabetic Neuropathic Pain: A Few Comments

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LETTERS TO EDITORS

I read with great interest the article by Nam et al. [1] entitled "Effects of nefopam on streptozotocin-induced diabetic neuropathic pain in rats", published in the Korean Journal of Pain. The authors aimed to investigate the preventive role of nefopam in the control of diabetic neuropathic pain. The authors concluded that nefopam pretreatment presented strong antiallodynic effects in diabetic rats. Although the study was well-managed — and I commend the authors for the valuable and detailed information they provided — some additional comments regarding the reduction of the hyperalgesic and allodynic actions of a potent selective μ opioid receptor agonist (remifentanil) in diabetic conditions may be beneficial.

A range of pharmacological agents, including opioids, anesthetics, analgesics, antiepileptic, and antidepressants drugs, are used in diabetic neuropathy. Despite the use of these agents, the successful therapy of diabetic neuropathy remains limited. Moreover, hyperglycemia may be attributed to the pathogenesis of diabetic neuropathy due to its association with the attenuated functional expression of opioid receptors. Thus, opioid receptors are an eminent target for the management of diabetic neuropathic pain. Nevertheless, opioid treatment can also lead to a state of nociceptive sensitization, referred to as opioid-induced allodynia and hyperalgesia [2]. On the other hand, the blockade of N-methyl-d-aspartate (NMDA) receptors inhibits opioid-induced hyperalgesia and sensitization. In addition, an in-vitro study showed that the application of remifentanil could potentiate the NMDA-induced current [3].

Furthermore, opioid receptors have been identified to contribute to the effects of opioids on their terminals and on the peripheral afferent axons of sensory neurons. Remifentanil is a high potent agonist of opioid receptors with cardioprotective effects against ischemia-reperfused injury, and it has been revealed that diabetes can decrease remifentanil-induced cardioprotection [4]. In light of this, the hypo/hyperalgesic effects of remifentanil in patients with diabetic conditions may be affected. A recent animal study showed that the excessive release of nitric oxide, the overproduction of reactive oxygen species, and the excessive activation of the NMDA receptors, may modify the sensitivity to the opioid receptor agonist (remifentanil) in diabetes-induced neuropathic pain states [5].

As is obvious from the above discussion, the allodynic and hyperalgesic effects of a potent selective μ opioid receptor agonist (remifentanil) can be reduced in patients with diabetes. Interestingly, human studies are required for the confirmation of this theory.

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REFERENCES

1. Nam JS, Cheong YS, Karm MH, Ahn HS, Sim JH, Kim JS, et al. Effects of nefopam on streptozotocin-induced diabetic neuropathic pain in rats. Korean J Pain 2014; 27: 326-33.
2. Mert T, Gunes Y, Ozcengiz D. Modification of local anesthetic-induced antinociception by fentanyl in rats. Pharmacol Rep 2011; 63: 1427-34.
3. Guntz E, Dumont H, Roussel C, Gall D, Dufrasne F, Cuvelier L, et al. Effects of remifentanil on N-methyl-D-aspartate receptor: an electrophysiologic study in rat spinal cord. Anesthesiology 2005; 102: 1235-41.
4. Kim HS, Cho JE, Hwang KC, Shim YH, Lee JH, Kwak YL. Diabetes mellitus mitigates cardioprotective effects of remifentanil preconditioning in ischemia-reperfused rat heart in association with anti-apoptotic pathways of survival. Eur J Pharmacol 2010; 628: 132-9.
5. Mert T, Oksuz H, Tugtag B, Kilinc M, Senoglu N, Bilgin R. Modulating actions of NMDA receptors on pronociceptive effects of locally injected remifentanil in diabetic rats. Pharmacol Rep 2014; 66: 1065-72.