

7-Nitroindazole and its rapidly emerging role in opioid pain management and withdrawal

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To the editor

I read with great interest the paper by Jin et al in a recent issue of your journal.¹ The article is highly thought-provoking. Interestingly, the past few years have also seen the emergence of nitric oxide synthetase inhibitors, especially 7-nitroindazole, as novel new agents with significant benefits in opioid pain management and withdrawal.

For instance, 7-nitroindazole attenuates the development of tolerance to the anti-nociceptive activity of kappa and mu opioid receptors.² Similarly, 7-nitroindazole blocks the neurotoxicity secondary to ketamine in animal models.³ This may very well play a significant role in protecting the human brain from the toxicity of ketamine, especially in the pediatric population.

7-Nitroindazole also has a negative impact on morphine dependency.⁴ Tian et al have shown that 7-nitroindazole decreases physical dependence on opioid agonist/antagonist agents such as butorphanol.⁵ Medvedev et al have recently shown that administration of 7-nitroindazole also decreases symptoms of opioid withdrawal, such as tremors and diarrhea.⁶ The clinical benefit of 7-nitroindazole in individuals with opioid withdrawal is that it does not cause hypertension, unlike other nitric oxide synthase inhibitors, such as L-NG-nitroarginine methyl esters.⁷

7-Nitroindazole may also have other benefits. For instance, 7-nitroindazole injection into the bronchial vasculature decreases pulmonary changes such as edema secondary to hypoxic trauma.⁸ The examples cited here clearly illustrate the beneficial effects of 7-nitroindazole and the need for further large-scale studies to elaborate fully its beneficial effects in pain management.

Disclosure

The author reports no conflicts of interest in this work.

References

1. Jin RC, Loscalzo J. Vascular nitric oxide: formation and function. *J Blood Med*. 2010;2010:147–162.
2. Bhargava HN, Cao YJ, Zhao GM. Effect of 7-nitroindazole on tolerance to morphine, U-50,488H and [D-Pen2, D-Pen5] enkephalin in mice. *Peptides*. 1997;18:797–800.
3. Wang C, Sadvova N, Patterson TA, et al. Protective effects of 7-nitroindazole on ketamine-induced neurotoxicity in rat forebrain culture. *Neurotoxicology*. 2008;29:613–620.

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4. Teppema L, Sarton E, Dahan A, Olivier CN. The neuronal nitric oxide synthase inhibitor 7-nitroindazole (7-NI) and morphine act independently on the control of breathing. *Br J Anaesth*. 2000;84:190–196.
5. Tian YH, Lee KW, You JJ, Lee SY, Jang CG. 7-Nitroindazole, nitric oxide synthase inhibitor, attenuates physical dependence on butorphanol in rat. *Synapse*. 2008;62:582–589.
6. Medvedev IO, Dravolina OA, Beshpalov AY. Differential effects of nitric oxide synthase inhibitor, 7-nitroindazole, on discriminative stimulus and somatic effects of naloxone in morphine-dependent rats. *Eur J Pharmacol*. 1999;377:183–186.
7. Vaupel DB, Kimes AS, London ED. Comparison of 7-nitroindazole with other nitric oxide synthase inhibitors as attenuators of opioid withdrawal. *Psychopharmacology (Berl)*. 1995;118:361–368.
8. Hamahata A, Enkhbaatar P, Lange M, et al. Direct delivery of low-dose 7-nitroindazole into the bronchial artery attenuates pulmonary pathophysiology after smoke inhalation and burn injury in an ovine model. *Shock*. 2011;36:575–579.

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