

# 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.<sup>1</sup> 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.<sup>2</sup> Similarly, 7-nitroindazole blocks the neurotoxicity secondary to ketamine in animal models.<sup>3</sup> 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.<sup>4</sup> Tian et al have shown that 7-nitroindazole decreases physical dependence on opioid agonist/antagonist agents such as butorphanol.<sup>5</sup> Medvedev et al have recently shown that administration of 7-nitroindazole also decreases symptoms of opioid withdrawal, such as tremors and diarrhea.<sup>6</sup> 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.<sup>7</sup>

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.<sup>8</sup> 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.

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