



## Suggested, Less-Explored Agents for Opioid Free Anesthesia

**Abhijit S Nair, MD\***

*Department of Anaesthesiology, Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana, India*

The review article titled 'The Benefits of Opioid Free Anesthesia and the Precautions Necessary When Employing It' by Bohringer, et al. was a pleasure to read [1]. Authors lucidly covered the topic by reviewing relevant literature. The timing of the article is perfect as clinicians are facing the problems with opioid epidemic in many countries. Through this communication, I want to add a few agents which could also be considered in the armamentarium of opioid free anesthesia (OFA) in regular practice.

Flupirtine is a centrally-acting, non-opioid analgesic, non-sedative medication with N-methyl-D-aspartate (NMDA) receptor antagonist property. It belongs to a group of drugs called SNEPCO (selective neuronal potassium channel opener). Due to its skeletal muscle relaxation properties, flupirtine has been found useful in orthopedic cases and in managing musculoskeletal pain [2]. It does not have anti-pyretic properties and does not interfere with coagulation cascade. Although used in European and Asian countries, flupirtine is yet not approved by US-FDA for use in managing acute pain [3]. Dose used ranges from 100-400 mg 12<sup>th</sup> hourly orally as no intravenous preparation is available yet. Warfarin toxicity could be precipitated with flupirtine although the exact mechanism is not known. Therefore, it is best avoided in such a situation [4].

Another drug is nefopam which is a non-opioid, non-steroidal, centrally acting agent having NMDA receptor antagonistic properties with serotonin and noradrenaline reuptake inhibition properties. Nefopam has no effect on platelet function, does not cause constipation or respiratory depression. It is available in oral (30-90 mg 8<sup>th</sup> hourly) as well as injectable form (20 mg 4-6 hourly). Clinical studies have shown encouraging results of nefopam when used with other agents like non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol [5].

Nefopam should be avoided in patients having seizure disorder or a propensity have a seizure (a head injury patient) as it can lower the threshold for seizure.

Other undesirable effects of nefopam are tachycardia and sweating which can be addressed by infusing it slowly.

HTX-011 is a fixed-dose, dual-acting local anesthetic which comprises of bupivacaine and low-dose meloxicam. Meloxicam decreases reduce local inflammatory response to tissue injury from surgery to maintain physiologic pH at the surgical site and thus reduce cytokine-induced peripheral sensitization [6]. The combination drugs are mixed using polymer technology and thus when injected at surgical site, a slow diffusion occurs providing analgesia for up to 72 hours. Although phase 2 and 3 clinical studies appears promising, randomised controlled studies are awaited to establish its efficacy in major surgeries as an opioid sparing analgesic.

To conclude, flupirtine and nefopam could be reasonable inclusion to the armamentarium of OFA with HTX-011 having a good potential if shown superior or non-inferior in randomized trials.

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**Corresponding Author:** *Abhijit S. Nair, MD, Department of Anaesthesiology, Basavatarakam Indo American cancer Hospital and Research Institute, Hyderabad-500034, Telangana, India, Tel: +91-9963180495, E-mail: abhijit-nair95@outlook.com*

**Editor:** *Renyu Liu, MD, PhD, Associate Professor, Department of Anesthesiology and Critical Care, Perelman School of Medicine at the University of Pennsylvania, Center of Penn Global Health Scholar, Director of Stroke 120 Special Task Force, Chinese Stroke Association, 336 John Morgan Building, 3620 Hamilton Walk, Philadelphia, PA 19104, USA, Phone: 2157461485, Fax: 2153495078, E-mail: RenYu.Liu@penmedicine.upenn.edu*

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