Nefopam analgesia and its role in multimodal analgesia: A review of preclinical and clinical studies.

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Abstract
Nefopam is a non-opioid, non-steroidal, centrally acting analgesic drug used to prevent postoperative pain, primarily in the context of multimodal analgesia. This paper reviews preclinical and clinical studies in which nefopam has been combined with opioids, non-steroidal anti-inflammatory compounds, and paracetamol. This report focuses on the literature during the last decade and discusses the translational efforts between animal and clinical studies in the context of multimodal or balanced analgesia. In preclinical rodent models of acute and inflammatory pain, nefopam combinations including opioids revealed a synergistic interaction or enhanced morphine analgesia in six out of seven studies. Nefopam combinations including non-steroidal anti-inflammatory drugs (NSAIDs) (aspirin, ketoprofen or nimesulide) or paracetamol likewise showed enhanced analgesic effects for the associated compound in all instances. Clinical studies have been performed in various types of surgeries involving different pain intensities. Nefopam combinations including opioids resulted in a reduction in morphine consumption in 8 out of 10 studies of severe or moderate pain. Nefopam combinations including NSAIDs (ketoprofen or tenoxicam) or paracetamol also demonstrated a synergic interaction or an enhancement of the analgesic effect of the associated compound. In conclusion, this review of nefopam combinations including various analgesic drugs (opioids, NSAIDs and paracetamol) reveals that enhanced analgesia was demonstrated in most preclinical and clinical studies, suggesting a role for nefopam in multimodal analgesia based on its distinct characteristics as an analgesic. Further clinical studies are needed to evaluate the analgesic effects of nefopam combinations including NSAIDs or paracetamol.

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