Short communication

Effect of licofelone against mechanical hyperalgesia and cold allodynia in the rat model of incisional pain

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Abstract:
Hyperalgesia from an incisional pain is evoked by noxious stimuli (mechanical and cold). The present study was aimed to examine the effect of licofelone, a dual inhibitor of cyclooxygenases (COX-1/COX-2) and 5-lipoxygenase (5-LOX) against mechanical hyperalgesia and cold allodynia in the rat model of incisional pain. Mechanical hyperalgesia and cold allodynia was assessed employing Randall and Sellitto analgesymeter and cold water maintained at 10°C, respectively. Zileuton (25–100 mg/kg, po), a 5-LOX inhibitor, indomethacin (1–30 mg/kg, po), a non-selective COX inhibitor, and licofelone (10–100 mg/kg, po) a dual inhibitor, significantly reversed the mechanical hyperalgesia and also caused an increase in cold allodynia threshold with different pharmacologic profile. The rank order of potency based on ED₉₅ values in both the paradigms was found to be licofelone > indomethacin > zileuton.

The results of the present study are indicative of the role of leukotrienes along with prostaglandins in the rat model of incisional pain (a paradigm of postoperative pain). The results suggested that dual inhibition approach of simultaneous inhibition of COX and LOX pathways might prove beneficial in combating hyperalgesia of postoperative pain.

Key words: incisional pain, mechanical hyperalgesia, cold allodynia, lipoxygenase, cyclooxygenase, dual inhibitor, licofelone

Introduction

Postoperative pain is a hyperalgesic condition that affects one of every two patients undergoing surgery. Hyperalgesia after tissue injury is modulated by locally released mediators. The essential role of arachidonic acid (AA) metabolites, prostaglandins (PGs) derived from cyclooxygenase (COX) action and leukotrienes (LTs) derived by lipoxygenase (LOX) pathway during hyperalgesia is evidenced [1, 8]. Peripherally acting PGs sensitize the nociceptors leading to lower threshold of polymodal C- and A-δ fibers. At central level, activation of spinal PG receptor sensitizes primary afferent fibers and increases the excitability of the dorsal horn neurons. Thus, the use of non-steroidal anti-inflammatory drugs (NSAIDs) that inhibit PG synthesis have been shown to be effective in postoperative pain [15]. However, other studies demonstrate that PGs cannot account for all of the hyperalgesia associated with tissue injury. Studies in animals and humans have demonstrated that LTs, the products of NSAIDs resistant 5-LOX-catalyzed metabolism of AA, also produce hyperalgesia. Peripher-