J Pharmacol Exp Ther. 2000 Nov;295(2):546-51.

Analgesic synergy between topical lidocaine and topical opioids

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PMID: 11046087

Abstract

Topical drugs avoid many of the problematic side effects of systemic agents. Immersion of the tail of a mouse into a solution of dimethyl sulfoxide (DMSO)-containing morphine produces a dose-dependent, naloxone-sensitive, analgesia (ED(50) 6.1 mM; CL 4.3, 8.4) limited to the portion of the tail exposed to the drug. DMSO alone in this paradigm had no analgesic activity. Like morphine, the opioids levorphanol (ED(50) 5.0 mM; CL 3.8, 7.8) and buprenorphine (ED(50) 1. 1 mM; CL 0.7, 1.5) were effective topical analgesics. Lidocaine also was active in the tail-flick assay (ED(50) 2.5 mM; CL 2.0, 3.4), with a potency greater than morphine. As expected, the free base of lidocaine was more potent than its salt. Combinations of a low dose of lidocaine with a low dose of an opioid yielded significantly greater than additive effects for all opioids tested. Isobolographic analysis confirmed the presence of synergy between lidocaine and morphine, levorphanol and buprenorphine. These studies demonstrate a potent interaction peripherally between opioids and a local anesthetic and offer potential advantages in the clinical management of pain.