

■ HIGHLIGHTS

Systemic Lidocaine Blocks Nerve Injury-induced Hyperalgesia and Nociceptor-driven Spinal Sensitization in the Rat

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THE article published in this issue of ANESTHESIOLOGY by Abram and Yaksh (page 383) sends a powerful message that a drug commonly used to produce one specific effect has, in fact, a spectrum of similar but different effects. Multiple clinical studies on the analgesic effect of systemic local anesthetics, published over almost 50 yr, may serve as excellent illustrations of the development of our understanding of this effect. Half a century ago, procaine (a local anesthetic) was found to have an analgesic effect when administered systemically (Can Med Assoc J 49:478–481, 1943). The placebo-controlled study demonstrating the analgesic effect of intravenous procaine in postoperative pain was published by Keats *et al.* in 1951 (JAMA 147:1761–1764, 1951). When lidocaine was introduced into medical practice, a similar effect was reported. However, systemic doses of local anesthetics used to relieve postoperative pain were found to be very high. In 1961, Bromage and Robson wrote that “there is a good chance of obtaining analgesia in postoperative pain if the blood concentration of lidocaine reaches 5 $\mu\text{g}/\text{ml}$, that is about half the concentration required to produce toxic manifestations” (Anaesthesia 16:461–478, 1961).

The first convincing study on the analgesic effect of systemic lidocaine in chronic pain syndromes (including central pain) was published in 1982 by Boas *et al.* (Br J Anaesth 54:501–505, 1982). They compared the analgesic effect of intravenous lidocaine on experimental ischemic pain and clinical pain. The analgesic effect of lidocaine on experimental pain was relatively weak and disappeared when the lidocaine blood level was less than 3 $\mu\text{g}/\text{ml}$. At the same time, chronic clinical

pain was suppressed almost totally, and the effect was sustained at a lidocaine blood level of about 1.5 $\mu\text{g}/\text{ml}$. In a controlled study published in 1987, Kastrup *et al.* demonstrated that, in chronic pain of diabetic neuropathy, a single intravenous injection of lidocaine (5 mg/kg) can produce an analgesic effect lasting from 3 to 21 days (Pain 28:69–75, 1987). Marchettini *et al.*, in a controlled study, found that, in patients with chronic neuropathic pain, intravenous lidocaine (1.5 mg/kg) consistently reduced spontaneous pain and mechanical hyperalgesia at a time when direct injection of lidocaine into affected peripheral nerves abolished hyperalgesia but did not relieve spontaneous pain (Pain 48:77–88, 1992). The above-mentioned clinical studies clearly indicated that there might be more than one mechanism for the analgesic effect of systemic lidocaine on various kinds of pain.

The study by Abram and Yaksh provided an experimental basis for the concept that systemic lidocaine produces different analgesic effects. Depending on the type of experimental pain model, lidocaine-induced analgesia may have central or peripheral mechanisms. The lidocaine example of a spectrum of different analgesic effects can be reinforced by the data on multiple mechanisms of analgesia produced by a nonsteroidal antiinflammatory agent (refer to Eisenach, ANESTHESIOLOGY 79:211–213, 1993). Abrams and Yaksh also clearly demonstrated that the nerve compression model can be used successfully for studies of the analgesic effect of systemic local anesthetics in neuropathic pain.

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