Novel Depots of Ketorolac Esters Have Long-acting Antinociceptive and Anti-inflammatory Effects

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摘要

Abstract

No long-acting nonsteroidal antiinflammatory drug is clinically available for the treatment of pain. In this study, we evaluated the antinociceptive and antiinflammatory effects and duration of action of several novel depots of ketorolac esters, such as ketorolac propyl ester, pentyl ester, heptyl ester, and decyl ester, and observed whether they had a long-acting effect. Four studies in Sprague-Dawley rats were performed. In Studies 1–3, the antinociceptive and antiinflammatory effects of IM ketorolac tromethamine and its base and propyl ester were evaluated. In Study 4, the antinociceptive and antiinflammatory effects of several other ketorolac esters were evaluated. We found that ketorolac tromethamine 24, 80, and 240 μmol/kg (in saline) produced significant antinociceptive and antiinflammatory effects with duration of action of approximately 6–8 h. The four ketorolac esters at a dose of 240 μmol/kg (in oil) produced significant long-acting antinociceptive and antiinflammatory effects, with duration of action of approximately 52–76 h. We concluded that IM injection of novel depots of ketorolac esters in rats produce long-acting antinociceptive and antiinflammatory effects that are 6.5- to 9.5-fold longer than the traditional dosage form of ketorolac tromethamine.