Steady-State Effects of Opioids On Normal Volunteers
Louis C Saeger M.D., F.A.C.P.M.

Abstract

We report a method for controlling and adjusting plasma opioid concentration to preselected target values in individual human subjects in order to study analgesic and other effects of opioids at steady state. The method employs a computer-controlled infusion pump and an algorithm that utilizes individual subject pharmacokinetic parameters predetermined with tailoring bolus opioid doses. We used this approach to produce 3-step increases in plasma concentrations of alfentanil, fentanyl and morphine in each of 15 subjects. We maintained each plasma concentration plateau for 70 min, measured plasma opioid concentrations achieved during the infusions and analyzed the results for bias and precision of the individually tailored infusions. Our results show that pharmacokinetically tailored opioid infusions produce stable plasma opioid concentrations within 10 min for alfentanil and morphine; with each drug overall prediction error was 20% or less. Fentanyl was somewhat more difficult to control by this method than were the other 2 opioids. We conclude that individual tailoring of opioid infusions minimizes the impact of individual pharmacokinetic differences on achieving preselected plasma opioid concentrations and provides an accurate means of controlling steady-state drug concentrations for studies of concentration-effect relationships and comparisons of side-effect intensities produced by equianalgesic plasma opioid concentrations.