MEDLINE Abstract

Pharmacokinetics and pharmacodynamics of midazolam after intranasal administration.

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This study aimed to characterize the pharmacokinetics and pharmacodynamics of midazolam after intranasal administration to healthy volunteers. Eight participants were given 0.25 mg/kg intranasally and 2 mg intravenously in a randomized, crossover fashion. Blood samples for determination of plasma concentrations of midazolam and measures of cognitive function (using the digit symbol substitution test) were obtained at baseline and 5, 10, 20, 30, 45, 60, 90, 120, 180, 240, and 360 minutes after administration of study medications. Plasma samples were analyzed by gas chromatography (% coefficient of variation < 10%). Pharmacokinetic data were fitted using iterative two-stage analysis to a two-compartment model. Pharmacodynamic data were fitted by a baseline subtraction Hill-type model. The mean (SD) for total clearance, distributional clearance, volume of distribution in the central compartment, volume of distribution in the peripheral compartment, absorption rate constant, bioavailability, and half-life were 0.57 (0.26) L/hr/kg, 0.31 (0.29) L/hr/kg, 0.27 (0.14) L/kg, 0.67 (0.11) L/kg, 2.46 (1.72) hr-1, 50% (13%), and 3.1 (0.84) hours, respectively. The mean (SD) for the concentration at which the effect is half maximal (EC50) and the maximal effect or the maximal change in effect measure from baseline (Emax) were 63.1 (21.2) ng/mL and 52.8 (21.1) correct substitutions, respectively. After intranasal administration, midazolam concentrations rapidly achieve values considered sufficient to induce conscious sedation and produce predictable changes in digit symbol substitution score.

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