MEDLINE Abstract

Intranasal administration of midazolam in a cyclodextrin based formulation: bioavailability and clinical evaluation in humans.

Pharmazie. 2001; 56(12):963-6 (ISSN: 0031-7144)

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Intranasal administration of midazolam has been of particular interest because of the rapid and reliable onset of action, predictable effects, and avoidance of injections. The available intravenous formulation (Dormicum i.v. solution from Hoffmann-La Roche) is however less than optimal for intranasal administration due to low midazolam concentration and acidity of the formulation (pH 3.0-3.3). In this study midazolam was formulated in aqueous sulfobutylether-beta-cyclodextrin buffer solution. The nasal spray was tested in 12 healthy volunteers and compared to intravenous midazolam in an open crossover trial. Clinical sedation effects, irritation, and serum drug levels were monitored. The absolute bioavailability of midazolam in the nasal formulation was determined to be 64 +/- 19% (mean +/- standard deviation). The peak serum concentration from nasal application, 42 +/- 11 ng ml-1, was reached within 10-15 min following administration and clinical sedative effects were observed within 5 to 10 min and lasted for about 40 min. Intravenous administration gave clinical sedative effects within 3 to 4 min, which lasted for about 35 minutes. Mild to moderate, transient irritation of nasal and pharyngeal mucosa was reported. The nasal formulation approaches the intravenous form in speed of absorption, serum concentration and clinical sedation effect. No serious side effects were observed.

PreMedline Identifier:11802661