Intranasal midazolam in piglets: pharmacodynamics (0.2 vs 0.4 mg/kg) and pharmacokinetics (0.4 mg/kg) with bioavailability determination.

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Intranasal midazolam was studied in two series of piglets: series 1, n = 20 (18 +/- 3 kg), a randomized double blind pharmacodynamic study to compare doses of 0.2 mg/kg and 0.4 mg/kg; series 2, n = 9 (42 +/- 8 kg), a pharmacokinetic study with a 0.4 mg/kg dose administered either intravenously (i.v.) or intranasally (i.n.) in a cross-over protocol with a one-week wash-out period between each. In series 1, midazolam caused significant anxiolysis and sedation within 3 to 4 min, without a significant difference between 0.2 and 0.4 mg/kg doses for any of the studied parameters. In series 2, after intranasal midazolam administration of 0.4 mg/kg, plasma concentrations attained a maximum (Cmax) of 0.13 +/- 0.04 mg/l at 5 min (median Tmax) and remained higher than 0.04 mg/l until 60 min. The bioavailability factor (F) in this study was F = 0.64 +/- 0.17 by the intranasal route. The terminal half-life (T1/2 lambda z) = 145 +/- 138 min was comparable with the i.v. administration half-life (158 +/- 127 min). In conclusion, optimal intranasal midazolam dose in piglets was 0.2 mg/kg, which procures rapid and reliable sedation, adapted to laboratory piglets.