

A Randomised, Crossover, Assessor-Blind Study of the Pharmacokinetics of Parenteral Nimesulide versus Placebo in Healthy Indian Volunteers

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ABSTRACT

Objective: The primary objective of this study was to investigate the pharmacokinetics of nimesulide 1 mg/kg administered intramuscularly in healthy Indian volunteers. The secondary objective was to compare the tolerability of the formulation versus placebo (vehicle only).

Design: A randomized, crossover, assessor-blind study in 13 healthy Indian volunteers.

Setting: The study was conducted in a clinical pharmacology ward at the KEM Hospital, a tertiary referral centre, in Mumbai (Bombay), India.

Subjects: Healthy male Indian volunteers who satisfied in inclusion/exclusion criteria were enrolled for the study.

Interventions: All subjects received a 1 mg/kg single dose of both the active drug (a light yellow-colored, particle-free liquid with a pH between 3.5 and 5.5) and placebo with a 2-week washout period in between. The intramuscular route was used to obtain rapid onset of action. Blood samples for pharmacokinetic analysis were collected at 0, 15, 30, 45, 60, 75 & 90 minutes and 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 6.0, 7.0, 8.0, 10.0, 12.0, 18.0, 24.0, 36.0 and 48.0 hours. Safety was measured by pre-and post-drug biochemical investigations, ECG and physical examination, while tolerability was assessed by pain as perceived by the subject.

Outcome measures: The pharmacokinetics of nimesulide and its metabolite were calculated by maximum plasma concentration (C_{max}), time to reach C_{max} (t_{max}), area under the concentration versus time curve from time zero to 48 hours (AUC_{0-48}) and from time zero to infinity ($AUC_{0-\infty}$), clearance and volume of distribution.

Conclusion: The 1 mg/kg dose gave a mean C_{max} of 2.36 ± 0.94 mg/L, and t_{max} was 2.73 ± 1.07 h. The AUC_{0-48} was 22.57 ± 7.67 μ g·h/ml and $AUC_{0-\infty}$ was 23.96 ± 7.59 μ g· h/ml. For the 4-hydroxy-nimesulide metabolite, C_{max} was 0.76 ± 0.33 mg/L and t_{max} was 5.04 ± 1.34 h. All 13 subjects experienced pain with the active drug, while 12 of 13 subjects had pain when receiving placebo. This difference was not statistically significant. Parenteral NSAIDs have shown good analgesic efficacy in general surgery coupled with the advantage of an opioid-sparing effect. The 1 mg/kg dose of this nimesulide formulation can be used as the starting dose for phase II clinical studies.