Explaining the double peak phenomenon in the absorption kinetics of amisulpride

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ABSTRACT

After oral administration of amisulpride, atypical in vivo kinetics are observed, which are characterized by double peaks in its concentration (C)–time (t) profile, a phenomenon that may be attributed to gastric emptying or variability in absorption. The aim of this study was to investigate the pharmacokinetics of amisulpride using non-linear mixed effect modeling approaches with a special focus on describing the dual peak phenomenon. The model building was based on the concentration-time data of 30 subjects who participated in a two-sequence, two-period, crossover bioequivalence study, after single oral administration of two pharmaceutical products of amisulpride (the Test and Reference). The Stochastic Approximation Expectation-Maximization (SAEM) algorithm was applied for the estimation of the population pharmacokinetic parameters. The objective function value was computed using the sampling method Monte Carlo for the final population parameters. The final best model refers to a two-compartment model with a first-order absorption rate followed by a second first-order absorption rate, with a lag time (Tlag), and first-order elimination. Inclusion of Tlag improved the model, and it was used to express a lag time of the second first-order plasma level time curve due to the physiological factors of amisulpride. Several internal and external validation procedures were deployed to confirm the suitability of the developed amisulpride model. In the next step, the model was used to run simulations that were meant to help make personalized dosing plans that can be used in clinical practice.

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