First-in-Human Safety, Tolerability and Pharmacokinetics of a Novel Drug with Therapeutic Potential for Vascular Dementia, Naoqingzhiming Tablet: Results from Single Ascending Doses studies in Healthy Chinese Subjects

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Abstract

Purpose: The primary aim of this study was to evaluate the safety, tolerability and pharmacokinetics of single ascending doses of Naoqingzhiming tablet after oral administration in healthy Chinese subjects. Methods: This study adopted randomized, double-blind, placebo-controlled dose ascending trial design. Healthy Chinese subjects were sequentially enrolled into one of six cohorts (180, 360, 720, 1080, 1620, 2160 mg). Blood samples were collected at specified time intervals, and the plasma concentrations of echinacoside were determined by a validated LC–MS/MS method. PK parameters were estimated via non-compartmental methods. Tolerability was evaluated by monitoring adverse events (AEs), physical examination, laboratory assays, vital signs, and 12-lead ECG. Results: The single ascending dose of Naoqingzhiming tablet (180-2160 mg) were well tolerated in all enrolled subjects, without serious adverse events and adverse events leading to withdrawal from the study. After single-dose administration of Naoqingzhiming tablet, echinacoside was absorbed with a Tmax at 1.25-1.75 h and declined with a t1/2 of 2.42-3.33 h. However, the proportionality coefficients for Cmax, AUC0-t and AUC0-[?] of echinacoside were not fully contained in the pre-defined 90 % CI criterion (0.91-1.09). As a result, the dose proportionality could not be concluded statistically within the dosage range of this study. Conclusion: Our study provided the initial safety, tolerability and pharmacokinetic profiles of Naoqingzhiming tablet, and could enable further clinical development in vascular dementia patients.

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