題名:Optimal dose regiments of esomeprazole for gastric acid suppression with minimal influence of CYP2C19 polymorphism.

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摘要:In this pilot study, we attempted to determine the optimal dosage regimens of esomeprazole for treatment of GERD with minimal influence of the CYP2C19 polymorphism through a study of the pharmacokinetics and pharmacodynamics of esomeprazole given at 3 different dosage regimens with the same total daily dose. METHODS: Each of the 3 genotypes of CYP2C19, homozygous extensive metabolizers (homEMs), heterozygous EMS (hetEMs), and poor metabolizers (PMs) were recruited in this clinical trial. Subjects were given a placebo followed by the administration of esomeprazole, at a dose of 40 mg once daily (40QD), 20 mg twice daily (20TD), or 10 mg 4 times daily (10Q4D) for 7 days. Twenty-four-hour and nocturnal intragastric pH and plasma esomeprazole concentrations were all determined on day 7. RESULTS: The pharmacokinetic parameters and dynamic characteristics differed among the 3 CYP2C19 genotype groups. With esomeprazole 40QD, gastric acid suppression was insufficient to achieve a therapeutic effect, while 20TD and 10Q4D were found to be effective in controlling both daytime and nocturnal gastric acidity for all 3 genotype groups. CONCLUSIONS: It was confirmed that intragastric pH values and plasma esomeprazole concentrations potentially depended on the CYP2C19 genotype status for treatment with esomeprazole. Dosage regimens of divided doses of 20TD or 10Q4D esomeprazole yielded improved antisecretory effects with a minimal influence of CYP2C19 polymorphisms.