

Pharmacokinetics of olanzapine in Chinese male schizophrenic patients with various smoking behaviors.

盧孟良

Wu TH;Chiu CC;Shen WW;Lin FW;Wang LH;Chen HY;Lu ML

摘要

Abstract

Tobacco consumption has been recognized as a factor mediating the interindividual variations in olanzapine's pharmacokinetics and pharmacodynamics. The primary objective of this study was to describe the dose effect of smoking on the dose-plasma concentration relationship and the pharmacokinetics of oral olanzapine in male schizophrenic patients using high-performance liquid chromatography coupled with electrochemical detector. Twenty-seven male schizophrenic inpatients were recruited and were stratified into the following groups according to smoking behaviors: non-smokers (n=9), light-smokers (1-4 cigarettes per day; n=9), and heavy-smokers (≥ 5 cigarettes per day; n=9). Plasma olanzapine concentrations were determined up to 120 h following a single oral dose of 10 mg olanzapine. The pharmacokinetic parameters were calculated by the non-compartment method using WinNonlin software. Results show that there was a significant correlation among non-smokers (n=9; 0.79; $p=0.01$) or combined with light-smokers (n=18; 0.62; $p<0.01$) between peak plasma olanzapine concentrations (C_{max}) and their individual dose-corrected by body weight, but this correlation did not appear in heavy-smokers. There were no significant differences between non-smokers and light-smokers except for significant decreased $AUC_{0\rightarrow 120}$ by 45.1% in light-smokers. The mean C_{max} and the mean area under the plasma concentration-time curve from time zero to 120 h ($AUC_{0\rightarrow 120}$) of the heavy-smoking patients was 9.3 ± 4.3 ng/ml (65.2% reduction compared to the non-smokers) and 302.4 ± 167.8 h ng/ml (67.6% reduction compared to the non-smokers), respectively. In summary, a daily consumption of 5 cigarettes is probably sufficient for induction of olanzapine metabolism. Smoking cessation is recommended for olanzapine therapy to have better prediction for therapeutic dosages particularly in heavy-smokers. Compared to non-smokers, heavy-smokers therefore require a 50-100% increase in olanzapine doses. Therapeutic drug monitoring will need to be considered when schizophrenic patients change their smoking behaviors.