Abstract

*The interindividual differences of activity of biotransformation enzymes play an important role in drug´s pharmacokinetics; their are significantly influenced both by external factors (such as age, gender, weight, diet) and genetic disposition. The presence of single nucleotide polymorphisms (SNPs) and mutations at a genes coding drug-metabolising enzymes can cause a major change of the metabolism and drug effects. In this study was evaluated an influence of enzyme CYP2C9 polymorphisms on the pharmacokinetic parameters of Nurofen forte containing racemic mixture of ibuprofen in 20 healthy Czech volunteers (men, Caucasian population, age 21-40 years). The presence of the CYP2C9*1/*1 genotype was found in 17 individuals, the CYP2C9*1/*2 genotype in 2 individuals and the CYP2C9*3/*3 genotype in 1 individual. No statistically significant difference of pharmacokinetic parameters was observed between CYP2C9*1/*1 and CYP2C9*1/*2 genotypes. $AUC_{(0\text{-}inf)}$ and $t_{1/2}$ were higher by 113% and 90%, respectively and clearance was lower by 54% in subject with CYP2C9*3/*3 genotype compared to subjects CYP2C9*1/*1 and CYP2C9*1/*2. The individuals with CYP2C9*3/*3 genotype have increased risk of adverse drug reaction (ulceration, gastroduodenal bleeding) after long time nonsteroidal anti-inflamatory drugs use. The standard dosage of NSAID should be lowered to the half of recommended daily dose with CYP2C9*3/*3 genotype .*