EFFECTS OF GENDER, AGE AND ETHNICITY ON HUMAN CYTOCHROME P450 ACTIVITY

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INTRODUCTION

It has been well documented that the expression of CYP enzymes is influenced by endogenous factors, such as genetic polymorphisms and hormone levels, and by exogenous factors, such as diet, exposure to drugs, alcohol consumption, cigarette smoking and various environmental factors (Parkinson, et al., 2004). For this study, we examined the effects of factors that influence the expression of CYP activity in human liver microsomes, specifically gender, age, ethnicity and smoking. The aim of this analysis was to evaluate whether the age, gender, or ethnicity of the donor should be taken into account when selecting human liver microsomes for drug metabolism studies, as well as whether cigarette smoking and alcohol consumption are reliable indicators of elevated CYP1A2 and CYP2E1 activity, respectively.

MATERIALS & METHODS

The sources of human liver tissue (obtained at cardiac arrest, cadaveric donation, and autopsy) were obtained from the department of Murphy Medical Center, University of Oklahoma Hospital, and St. Mark's Hospital. All samples were maintained in liquid nitrogen and stored at −80°C prior to analysis.

RESULTS

The results of this study are presented in Table 1 and Figures 1 through 4, which show the effects of age, gender, ethnicity, and smoking on CYP enzyme activity in human liver microsomes.

CONCLUSION

The results of the study consistently point to the same conclusion, namely that CYP enzyme activity in human liver microsomes can be significantly different based on the patient’s age, sex, and ethnicity, and that smoking and drinking are strong predictors of CYP2E1 and CYP2A6 activity. There is a need for further studies to determine the causes of these inter-individual differences and to establish consistent methods for routine drug metabolism studies.

REFERENCES


Figure 1: Effects of gender on CYP activity in human liver microsomes. The statistically significant differences were determined by t-test analysis with the exception of CYP2D6, p<0.05.

Figure 2: Effects of age on CYP activity in human liver microsomes. The statistically significant differences were determined by ANOVA analysis with the exception of CYP1A1 and CYP450, p<0.05.

Figure 3: Effects of ethnicity on CYP activity in human liver microsomes. The statistically significant differences were determined by ANOVA analysis with the exception of CYP2D6, p<0.05.

Figure 4: Apparent effects of smoking cigarettes on CYP1A2 activity in human liver microsomes. The statistically significant differences were determined by t-test analysis, p<0.05.