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论著

UGT2B7基因多态性对丙戊酸血药浓度的影响

马虹英[1], 张婷[1], 龚志成[1], 周伯庭[1], 邹明[1,2], 肖珊[1,2], 朱武[3]

1. 中南大学湘雅医院药剂科, 长沙410008;
2. 中南大学药学院, 长沙410078;
3. 湘雅医院皮肤科, 长沙410008

摘要：

目的: 探讨UGT2B7 A268G和UGT2B7 G211T基因多态性对丙戊酸血药浓度的影响。方法: 用限制性片段长度多态性聚合酶链反应(polymerase chain reaction restriction fragment length polymorphism,PCR-RFLP)的方法分别对248名癫痫患者检测UGT2B7 A268G和UGT2B7 G211T两个位点的基因型,并收集患者的基本流行性病学资料和相关临床信息,如癫痫类型、病史、服药剂量、疗效和肝肾功能等。采用SPSS 13.0软件分别对资料进行多元线性回归、单因素方差分析、卡方检验和配对T检验等方法的数据统计。结果: 多元线性回归分析显示,性别、年龄和体质量指数与丙戊酸血药浓度无明显相关,而浓度剂量比率则与血药浓度相关。在被纳入的248名患者中,UGT2B7 A268G和UGT2B7 G211T的基因型均符合哈迪温伯格平衡定律。UGT2B7-268A等位基因频率为30.05%,而G等位基因频率为69.95%,且携带AA,AG,GG不同基因型的患者服用丙戊酸后血药浓度的比较差异有统计学意义(F=5.477,P=0.005),AA基因组显著高于GG基因组(P=0.048),其他两组间比较差异无统计学意义(P>0.05).UGT2B7 211G等位基因频率为77.24%,T等位基因频率为22.58%;而携带该位点GG,GT和TT不同基因型的患者服用丙戊酸后,三者血药浓度间比较,差异无统计学意义(P>0.05)。结论: 本研究揭示了UGT2B7A268G和UGT2B7G211T的基因多态在中国汉族癫痫人群中的分布,UGT2B7 A268G基因多态参与体内丙戊酸代谢并进而影响其血药浓度。临床上针对癫痫患者给予丙戊酸药物时,需要考虑患者携带UGT2B7A268G位所产生的影响而适当调整患者用药剂量。

关键词： UGT 基因多态性 丙戊酸 癫痫

Effect of UGT2B7 genetic variants on serum valproic acid concentration

MA Hongying[1], ZHANG Ting[1], GONG Zhicheng[1], ZHOU Boting[1], ZOU Ming[1,2], XIAO Shan[1,2], ZHU Wu[3]

1. Department of Pharmacy, Xiangya Hospital, Central South University, Changsha 410008;
2. School of Pharmaceutical Sciences, Central South University, Changsha 410078;
3. Department of Dermatology, Xiangya Hospital, Central South University, Changsha 410008, China

Abstract:

Objective: To investigate the effect of UGT2B7 A268G and UGT2B7 G211T genetic polymorphism on serum drug concentration of valproic acid(VPA). Methods: Genetic polymorphisms of UGT2B7 A268G and UGT2B7 G211T were tested in 248 epileptic patients by polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP).Data including basic information,epilepsy type,times and doses of drug,treatment response and liver and kidney functions were collected.Statistical analysis was performed by SPSS 13.0 through multivariate linear regression,one-way ANOVA,χ^2 test,and paired T-test. Results: Based on multivariate linear regression,there was no significant difference between gender,age,or body mass index and VPA,but concentration-to-dose ratios(CDRs)were positively correlated with VPA.The genetic polymorphisms of UGT2B7 A268G and UGT2B7 G211T were consistent with Hardy-Weinberg equilibrium.UGT2B7-268A>G allele frequency distribution A was 30.05%,and G was 69.95%.Variance analysis showed that serum drug concentration was significantly different in the genotype of AA,AG,or GG(F=5.477,P=0.005).Further analysis of paired T test showed that AA type was significantly different from GG type(P=0.048),and that serum concentration of AA type was much higher than that of GG type,while no significant difference between AA type and AG type,GG type and AG type.UGT2B7 G211T allele frequency distribution G was 77.24%,and T was 22.58%.There was no significant difference in standardized serum concentration among genotypes of GG,GT,and TT. Conclusion: This study reveals UGT2B7 A268G genetic polymorphism distribution in Chinese epilepsy population.UGT2B7 A268G plays an important role in VPA's metabolism,and has certain effect on VPA's serum concentration.Epilepsy patient with this genotype should be adjusted the dose of VPA to make a therapeutic effect.

Keywords: UGT genetic polymorphism valproic acid epilepsy

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通讯作者: ZHU Wu,Email:zhuwu1970@hotmail.com

作者简介: MA Hongying,master degree,associate professor,mainly engaged in the research of pharmaceutical science.
作者Email: zhuwu1970@hotmail.com

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