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Impact of the genes UGT1A1, GSTT1, GSTM1, GSTA1, GSTP1 and NAT2 on acute alcohol-toxic hepatitis

Research Article

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Abstract: Alcohol metabolism causes cellular damage by changing the redox status of cells. In this study, we investigated the relationship between genetic markers in genes coding for enzymes involved in cellular redox stabilization and their potential role in the clinical outcome of acute alcohol-induced hepatitis. Study subjects comprised 60 patients with acute alcohol-induced hepatitis. The control group consisted of 122 healthy non-related individuals. Eight genetic markers of the genes *UGT1A1*, *GSTA1*, *GSTP1*, *NAT2*, *GSTT1* and *GSTM1* were genotyped. *GSTT1* null genotype was identified as a risk allele for alcohol-toxic hepatitis progression (OR 2.146, P=0.013). It was also found to correlate negatively with the level of prothrombin (β= –11.05, P=0.037) and positively with hyaluronic acid (β=170.4, P=0.014). *NAT2* gene alleles rs1799929 and rs1799930 showed opposing associations with the activity of the biochemical markers γ-glutamyltransferase and alkaline phosphatase; rs1799929 was negatively correlated with γ-glutamyltransferase (β=–261.3, P=0.018) and alkaline phosphatase (β= –270.5, P=0.032), whereas rs1799930 was positively correlated with γ-glutamyltransferase (β=325.8, P=0.011) and alkaline phosphatase (β=374.8, P=0.011). Enzymes of the glutathione *S*-transferase family and NAT2 enzyme play an important role in the detoxification process in the liver and demonstrate an impact on the clinical outcome of acute alcohol-induced hepatitis.

Keywords: *Hepatitis • Alcoholic • Oxidative stress • Pharmacogenetics*

1. Introduction

Acute alcoholic hepatitis develops as a result of toxic additives in unrecorded low-quality alcohol or due to an individual's reduced metabolic ability to convert alcohol into non-toxic substances. The capability for alcohol degradation in humans is mostly genetically determined. Approximately 90% of alcohol is metabolized through the liver. Metabolism occurs predominantly in an oxidative manner, mainly involving the enzymes alcohol dehydrogenase, acetaldehyde dehydrogenase and the cytochrome P405 system enzyme CYP2E1.

The importance of acute alcoholic hepatitis lies in its significantly high morbidity and mortality, with a reported in-hospital mortality as high as 65% [1]. Furthermore, there is an alarmingly high number of people who have died because of alcohol overdose or misuse of unrecorded alcohol ('unrecorded' is an overview category for any kind of alcohol that is not taxed as beverage alcohol or registered in the jurisdiction where it is consumed) [2].

In Latvia, mortality from alcohol-induced liver diseases was 6.9 and 7.3 per 100,000 inhabitants in 2009 and 2011, respectively, but alcohol-induced intoxication mortality was 7.8 and 4.0 per 100,000

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