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Genetic variability in organic cation transporter OCT1: a variance with clinical implication?

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OCT1 is by far the most strongly expressed uptake transporter of cationic and weekly basic drugs in the human liver. OCT1 is highly genetically variable. Approximately 1 in 11 Europeans and White Americans is a homozygous or compound-heterozygous carrier of loss or reduced function OCT1 alleles. These “poor OCT1 transporter” may have reduced hepatic uptake and/or impaired metabolism of some commonly used drugs like metformin, morphine, codeine, tramadol, sumatriptan, and fenoterol. Consequently, these individuals may have altered drug efficacy and may be at higher risk of toxicities. A recently published opinion paper of the International Transporter Consortium strongly suggested that OCT1 polymorphisms should be considered during drug development (https://doi.org/10.1002/cpt.1098). This talk will review the available data on the effects of heritable OCT1 deficiency on pharmacokinetics, efficacy, and toxicity of some commonly used drugs, will give an overview of the inter-ethnic differences in heritable OCT1 deficiency, and will critically discuss the possible applications of OCT1 genotyping in the clinical praxis.