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# Pharmacogenetics of uridine diphosphate glucuronosyltransferase (UGT2B7) genetic polymorphism on valproic acid pharmacokinetics in epilepsy

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## Background

Sodium valproate is a widely prescribed broad-spectrum antiepileptic drug. It shows high inter-individual variability in pharmacokinetics and pharmacodynamics and has a narrow therapeutic range [1]. We evaluated the effects of polymorphic Uridine diphosphate glucuronosyltransferase (UGT2B7) metabolizing enzyme on the pharmacokinetics of sodium valproate in the patients with epilepsy who showed toxicity to therapy.

## Materials and methods

Genotype analysis of the patients was made with polymerase chain–restriction fragment length polymorphism (RFLP) with sequencing. Plasma drug concentrations were measured with reversed phase high-performance liquid chromatography (HPLC) and concentration–time data were analyzed by using a non-compartmental approach.

## Results

The results of this study suggested a significant genotypic as well as allelic association with valproic acid toxicity for UGT2B7 polymorphic enzymes. The elimination half-life ($t_{1/2}$=42.2 h) of valproic acid was longer and the clearance rate (CL=947 ml/h) was lower in the poor metabolizers group of UGT2B7 polymorphism who showed toxicity than in the intermediate metabolizers group (t1/2 = 36.5 h, CL = 1,042 ml/h) or the extensive metabolizers group (t1/2 = 27. h, CL = 1,602 ml/h).

## Conclusions

Our findings suggest that the UGT2B7 genetic polymorphism plays a significant role in the steady state concentration of valproic acid, and it thereby has an impact on the toxicity of the valproic acid used in the patients with epilepsy.

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