てんかん患者におけるバルプロ酸の消失速度及びバルプロ酸グルクロナイドの尿中排泄

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Urinary Metabolites of Valproic Acid in Epileptic Patients

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ABSTRACT We previously encountered a patient with epilepsy who exhibited rapid elimination of sustained-release valproic acid (VPA) administered at the dose of 2.8g/d as a sodium salt. The purpose of this study was to clarify the relationship between the VPA elimination rate and the proportion of the dose excreted in urine as its glucuronide conjugate(VPA-G) in epileptic patients. Twenty-four-hour urine was collected from four epileptic patients who had taken VPA orally (age:16–39 y, weight:50–63 kg, dose:1.0–2.8 g/d). VPA and its metabolites were detected by gas chromatography-mass spectrometry. The amounts of VPA, VPA-G, 3-keto-VPA, and 3-OH VPA excreted in the 24-h urine were 1.8–13.2, 178–2158, 125–320, and 8.6–18.7 mg (converted into VPA), respectively. The dose of VPA correlated well with the proportion of the dose excreted in urine as VPA-G in each patient, and the patients administered a high dose excreted a large amount of VPA-G in the urine. Thus, differences in the VPA-G production rate may be one of the major variable factors affecting the elimination of administered VPA. We also present a dynamic model of VPA in the kidney which may explain the VPA elimination pheomena in humans on the basis of the data obtained here regarding the concentrations of VPA and its metabolites in plasma and their urinary excretion levels.

抄録　バルプロ酸（VPA）の体内からの消失が速い患者について、尿中に排泄されるグルクロン酸代謝物（VPA-G）の寄与を検討した。その結果、そのような患者ではVPA-Gの尿中排泄率がかなり高いことが明らかとなった。今回の結果を説明しうるVPAの腎での動態モデルを提案した。

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