Therapeutic Drug Monitoring of Levetiracetam – preliminary study of clinical usefulness

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Introduction: Therapeutic drug monitoring (TDM) is a common clinical practice aimed at individualizing therapy and optimizing dosage regimens to increase clinical efficiency. Arguments for TDM include among others, non-linear pharmacokinetics and polytherapy. Levetiracetam (LEV) introduced on the drug-market recently, is currently used as an anti-epileptic drug. Available medical data report limited evidence to monitor this drug, but it may be recommended in cases where the pharmacokinetics change.

Aim of the study: This work aimed to develop a method for LEV determination for therapeutic use. The presented procedure allowed to detect LEV with high efficiency, which confirmed its usefulness in clinical practice.

Matherial and methods: The available guidelines for the determination of levetiracetam were used for the analysis. Biological material from patients treated with LEV was secured for researches. A method of drug isolation via liquid chromatography with UV detection was developed. During the research, the usefulness of various extraction methods, separation conditions and factors affecting the analysis were examined. The relationships between drug levels and dose, gender, age, drug form and possible interactions with other medicaments were evaluated.

Results: Twenty patients between 18-40 years old have been qualified for research. Determined drug concentrations ranged from 1.2 to 45 µg/ml in blood collected at various time intervals from the last dose to the collection time. Significant dependence was observed during polytherapy with lamotrigine and valproic acid.

Conclusions: It seems reasonable to monitor blood LEV levels in groups of epileptic patients undergoing polytherapy. Increasing the size of the research group by introducing routine determination of blood levetiracetam level will give more data to control therapy effects. The developed method is characterized by practical aspects and it may show potential for future usage in clinical laboratories.

Oxidative stress in patients treated and intoxicated with valproic acid

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Introduction: Valproic acid (VPA) belongs to the group of anticonvulsants and it has a wide application in many types of paroxysms treatment. Its usage is generally safe, but it can marginally cause liver damage. The mechanism of VPA activity is complex and hasn't been completely recognized yet. One of active metabolites is 2-propyl-4-pentenoic acid (4-en VPA) which can be responsible for hepatotoxic effects of the drug enhanced by generated oxidative stress (OS). To monitor, the OS specific markers are used, such as lipid peroxidation as well as the ones allowing to assess antioxidative status.

Aim of the study: The aim of this study was to examine the influence of the VPA and its active metabolite, 4-en VPA both in therapeutic doses and in poisoning on the formation of OS in patients.

Matherial and methods: For the OS assessment there have been applied quantitative markers such as total glutathione concentration and the level of antioxidant potential (FRAP) in the patients' plasma. The concentration of VPA and 4-en VPA have been determined in plasma by the HPLC method.

Results: 29 patients treated with VPA due to epilepsy (VPA 71±11 μg/ml, 4-en VPA 4,1±0,8 μg/ml) and 28 poisoned ones (VPA 332±435 μg/ml, 4-en VPA 11,3± 10,0 μg/ml) were qualified for the study, of which 12 were monitored at the time of admission (VPA 740±609 μg/ml, 4-en VPA 19,9±12,4 μg/ml) and after a certain time, reaching drug lower levels (VPA 203±192 μg/ml, 4-en VPA 10,3±8,0 μg/ml). Together with the VPA concentration increase, lower FRAP values (by 37% in the poisoned group and 23% in treated ones) and the decrease in total glutathione (by 38% in the poisoned group and 33% in treated ones) were observed.

Conclusions: Valproic acid generated oxidative stress which could condition its toxic effects in therapy as well as in the course of intoxication.