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# The impact of zonisamide on selected central effects of prolonged ethanol consumption in animal experimental models

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New generation of anti-epileptic drugs has complex mechanism of action which is associated with modulatory effects on ion channels and neurotransmission systems. The broad spectrum of pharmacological activity makes opportunities to use them in other conditions besides epilepsy. One of possible, future indication of these drugs alcohol dependence. One of the best-studied drugs in this area is topiramat. Promising results obtain for topiramate draw attention to other drugs from this pharmacological group. The newest drug of this group is zonisamid, which was the subject of my research. The multidirectional mechanism of action of zonisamide which is associated with an influence on neurotransmission involved in the pathogenesis of addiction and neuroprotective activity, confirms the validity of using the drug in the alcohol dependence therapy.

The results of a few experimental studies indicate that zonisamide reduces ethanol intake in rats and mice, and given repeatedly reduces the sensitivity of the hippocampus to an acute dose of ethanol in rabbits.

Previous studies do not explain the beneficial mechanism of action of the drug, hence the aim of the dissertation was to assess the impact of zonisamide on selected central effects of prolonged ethanol consumption in animal experimental models. The study was carried out in two stages. Firstly, the effect of co-administation of zonisamide and alcohol on the bioelectric activity of selected brain structures in rabbits was evaluated. For this purpose, the pharmaco-EEG method was used, which is based on quantitative changes in EEG observed in the midbrain reticular formation, hippocampus and frontal cortex. The EEG traces were recorded after each week of the study.

In the second stage of the study, behavioral models were used to assess the effect of zonisamide on memory processes in rats during long-term ethanol administration and abstinence period. This stages was conducted to verify if the beneficial "anti-alcoholic" action of zonisamide is associated with the impact on memory processes dependent on the hippocampus.

The results of pharmaco-EEG studies indicated that co-administration of zonisamide and ethanol causes a reduction of ethanol-induced alterations in the EEG recordings from the selected brain structures, and changes were most pronounced in the hippocampus and midbrain reticular formation. The beneficial effect of the drug on the course of abstinence should be emphasized. Zonisamide reduced the neuronal hyperactivity characteristic for the abstinence in all examined structures, especially in the hippocampus which is the structure

associated with memory processes. Recently, the impact of memory processes in the pathogenesis of addiction is emphasized. Therefore, this beneficial effect of zonisamide may be an important element of its influence on the development and course of alcohol dependence. In behavioral tests, the effect of the drug on memory processes was assessed but the results were differential. The beneficial effect of the drug on memory processes depended on the research model, dose of zonisamide and the route of administration. However, zonisamide improved hippocampus-dependent emotional memory in the rat during the abstinence. The beneficial effect of zonisamide which was observed during the period of alcohol administration and after discontinuation of ethanol administration, can be an important element of its activity in the treatment of alcohol dependence. However, there is a need to extend research in this area, both experimental and clinical.