SOME ASPECTS OF «CAPICOR» HARMLESSNESS ON PRECLINICAL RESEARCH RESULTS

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One of the main causes in the pathogenesis of chronic ischemia is endothelial dysfunction. The most «typical» manifestations of this condition in clinical practice is ischemic heart disease and cerebrovascular disorders. Combined use of carnitine precursors and carnitine analogs (Meldonium and γ-butyrobetaine (GBB)) is an interesting decision in terms of the modern anti-ischemic therapy optimization by combining of metabolic and hemodynamic concepts.

Purpose of research was a comparative experimental study of «Capicor» safety as the original endothelial corrector with binary mechanism of action in acute experiment.

Materials and methods. Comparative experimental study of the Capicor toxicological properties in single-dose has been conducted. «Capicor» production of JSC «Olainfarm» (Latvia) has been used as the basic sample in this study. The drug has the following composition (per 1 capsule): Meldonium dehydrate 180 mg and GBB dehydrate 60 mg. «Mildronate» 500 mg production of JSC «Grindeks» (Latvia) as the original Meldonium drug has been used as the reference sample. The study of acute toxicity of «Capicor» in compared with «Mildronate» has been conducted by the method of the least-squares for probit-analysis of mortality curves by V.B. Prozorovsky. 60 white nonlinear rats of both sexes weighing 150-180 g were used in the experiment. Rats were divided on 10 experimental groups (1-10) for 6 animals in each group. Capicor was introduced of the 1-5 animal groups, Mildronate was introduced of the 6-10 animal groups one time intragastric (i/g) at doses of 1000, 2000, 3000, 4000, 5000 mg / kg respectively for each group. Class toxicity has been determined according to the generally accepted classification by K. K. Sidorov.

Results and Discussion. During the study of acute toxicity of Capicor at i/g introduction in rats the following picture of intoxication has not been registered in doses of 1000-3000 mg/kg. In the early hours of observations some weakness, languor, decreased motor activity, decreased appetite has been observed on Capicor introduction in doses 4000 and 5000 mg/kg. For the next 3-5 hours general condition and behavior of animals was returning to the physiological norm, and all the manifestations of intoxication was disappearing. On the next day general functional state of the animals was completely in line with the physiological norm. During the study in the experimental groups any case of mortality of animals has not been registered. A similar pattern has been observed in the study of the Mildronate toxicological properties. The negative impact on rat body weight gain at this stage of the research has not been observed. In the study of pathological examination of the internal organs has been carried out after the rat euthanasia on day 14 of the experiment. In the analysis of significant abnormalities has not been observed. All mass coefficient indicators has been within of the physiological norm. The absence of mortality in laboratory animals at i/g introduction of the test and reference products does not allow to calculate the values of average lethal dose by probit analysis. This leads to the conclusion that the LD_{50} value for each of the studied products exceeds the maximum dose, which was used in the experiment. Thus we can say that at i/g introduction of Capicor and Mildronate in rats LD_{50} is more than 5000 mg/kg.

Conclusions. Capicor is practically non-toxic agent to the human body and allow to take it to the V class of toxicity by K. K. Sidorov standard classification. There are practically non-toxic substances. All of the above can serve as a basis for further reserch of «Capicor» in order to implement in clinical practice as a cytoprotective drug for the treatment of diseases in the pathogenesis of which endothelial dysfunction takes a leading place.