COMPARATIVE ASSESSMENT OF THE ABSORPTION CAPACITY OF THE NEW METAL COMPLEX ANTIHYPOXANT OKAGERM–4 UNDER NORMAL CONDITIONS AND IN HYPOXIA

Lukianchuk Victor
Doctor of Medical Sciences, Professor of the Department of Pharmacy
Pylyp Orlyk International Classical University, Ukraine

Litvinenko Dmitry
Candidate of Medical Sciences, Assistant of the Department of Intensive Care, Emergencies and Anesthesiology
State Establishment “Lugansk State Medical University”, Ukraine

One of the most dangerous forms of exogenous hypoxia is hypoxic hypoxia in combination with hypercapnia, which is better known as confined space hypoxia (CSH).

Unfortunately, existing medical drugs for the treatment and prevention of hypoxia do not meet modern requirements. Therefore, the search for and development of new highly effective and safe antihypoxants is one of the priorities of pharmacological science.

Previously performed screening studies on the model of CSH determined the high antihypoxic activity of the original coordination compound of germanium – (manganese (II) tartrate germanate (IV)) under the laboratory code OKAGERM–4. It is known that, at the preclinical stage of the study of a potential drug, the key is to determine the features of its pharmacokinetic profile, in particular the initial link of passage of the compound within the body, namely – absorption.

The aim of the work is to conduct a comparative pharmacokinetic analysis of the antihypoxant OKAGERM–4 at the stage of its normal absorption and in the modelled CSH.

The experiments were performed on 48 nonlinear white rats weighing 170–200 g. Animals of both groups, without pathology (normal) and experimental (CSH), were administered OKAGERM–4 once intraperitoneally at a dose of 96.8 mg/kg. CSH was modelled by placing rats for 25 min in isolated sealed containers (10 dm³). Determination of germanium content in the central chamber of the kinetic model of distribution (blood serum) was performed in the dynamics: after 45 min; 3; 6 and 24 hours after the introduction of OKAGERM–4. The following pharmacokinetic
parameters characterizing absorption were determined: absorption rate constant ($K_{01}$), absorption half-life ($t_{1/2a}$), maximum concentration of the drug in the blood ($C_{max}$), time of reaching the maximum concentration in the blood ($t_{max}$).

The following values of pharmacokinetic parameters of OKAGERM–4 absorption process were obtained in the framework of two–chamber analysis: $C_{max}$ (normal)=7.54±0.29 mg/l; $C_{max}$ (CSH)=7.13±0.20 mg/l; $t_{max}$ (normal)=1.47±0.04 h; $t_{max}$ (CSH)=1.52±0.06 h; $K_{01}$ (normal)=0.82±0.05 h$^{-1}$; $K_{01}$ (CSH)=0.80±0.05 h$^{-1}$; $t_{1/2a}$ (normal)=0.85±0.07 h; $t_{1/2a}$ (CSH)=0.87±0.05 h.

Thus, against the background of hypoxic damage, occur the most significant changes in the parameter $C_{max}$ ($P <0.05$), which indicates the need to take this into account when developing the dose regimen of OKAGERM–4 in conditions of providing assistance to victims of CSH.