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Application of tritium labeled drotaverine and furosemide for estimation of drug/binding capacity of blood transport system

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For labeling of pharmacological preparations of furosemide and drotaverine we used the method of labeling by thermally activated tritium. Furosemide and drotaverine were labeled by thermally activated tritium in apparatus for tritium labeling. The optimum regime of labeling was selected. The systems of purification of tritium-labeled furosemide and drotaverine by thin layer chromatography (TLC) has been developed. Tritium-labeled furosemide was purified by TLC on silicagel in system hexane:acetone (1:1). Tritium-labeled drotaverine was purified by TLC in system iso-propanol:ammonia:water (8:1:1). Application of TLC for purification of tritium-labeled furosemide and drotaverine allows to purify completely furosemide and drotaverine from by-products. The output of purified tritium-labeled furosemide was 12 %, with specific radioactivity 202 MBq/mmol. The output of purified tritium-labeled drotaverine was 36%, with specific radioactivity 1.39 GBq/mmol.

We have investigated the drug-binding capacity of serum proteins of patients with the help of the tritium-labeled pharmacological drugs of furosemide and drotaverine (no-spa). Series of groups of pediatric patients in the age of 3 to 14 years with acute and chronic hepatitis A and B have been investigated. Control group includes the conditionally healthy children of same age. The binding capacity of serum proteins was determined by binding of tritium-labeled drotaverine and furosemide with serum proteins in vitro. The micromethod consists in incubation in vitro samples of 20 microliter of serum with tritium-labeled drotaverine and with tritium-labeled furosemide. After incubation serum proteins were fractionated by chromatography and tritium radioactivity bound with fraction of serum proteins was measured.

It was found, that at the severe form of virus hepatitis B the binding capacity of serum proteins actually of all investigated patients in a stage of peak of disease was reduced in comparison with control group. At the moderate form of acute virus hepatitis B the decrease of binding capacity of serum proteins was observed at 69 % of patients.

We have also investigated dynamics of changes of binding capacity of serum proteins during standard therapy of hepatitis A and B. We found, that during convalescence at application of standard therapy the binding capacity of serum proteins comes nearer to values of control group. Thus dynamics of changes of binding capacity of serum proteins at patients with hepatitis B differed from dynamics at patients with hepatitis A. It was found that children with an acute virus hepatitis B after basic treatment have an increased level of binding of tritium-labeled drotaverine by serum proteins, and at children with acute virus hepatitis A it does not occur.

Obtained results in the whole indicate the reducing of binding capacity of serum proteins at virus hepatitis that allows to determine the optimal strategy of a pharmacological load on patient organism and thus to optimize the treatment of patients.

Primary author: Mr DADAKHONOV, Jakhongir (Institute Nuclear Physics of academy of sciences of Uzbekistan)

Co-authors: Dr KIM, Andrey (Institute Nuclear Physics of academy of sciences of Uzbekistan); Dr SHUKUROV,

Bahtiyor (Tashkent Medicine Academy, Tashkent, Uzbekistan.); Ms DJURAYEVA, Gulnora (Institute Nuclear Physics of academy of sciences of Uzbekistan); Prof. MAVLYANOV, Iskandar (Tashkent Medicine Academy, Tashkent, Uzbekistan.)

Presenter: Mr DADAKHONOV, Jakhongir (Institute Nuclear Physics of academy of sciences of Uzbekistan)

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