EXPERIMENTAL STUDIES OF THE INFLUENCE OF MIX OF THE CALCIUM AND MAGNESIUM SALTS OF INOSITOLHEXAPHOSPHATE ACID ON BILIATION FUNCTION OF A LIVER AT THE ACUTE HEPATITIS

Z. Z. KHAKIMOV, S. S. KASIMOVA, B. M. ASCAMOV, J. Z. AKRAMOVA
2nd Tashkent State Medical Institute, Pharmacology Department

Abstract For white pubertal male-rats was reproduced the model of acute necrosis a hepatitis by way of hypodermic inoculation of the acetothioamide and investigated the influencing a mix of calcium and magnesium salts of the inositolhexaphosphate acid on the excretive function of a liver and elemental composition of bile. It is established that the mix of salts of the inositolhexaphosphate acid at an acute hepatitis is remove considerable disturbance on excretive function of a liver and elemental composition of bile. The studied compound has a cholagogic, hypobilirubinic and hepatoprotective properties and present the important interest as a drug for treatment of acute and chronic defects of a liver.

INTRODUCTION

The last decade is characterized by significant growth of frequency of liver diseases, which takes first place in the general structure of man pathology. In the common sense, it is connected to adverse influence of negative consequences of scientific and technical progress. Thus, first of all, it is necessary to mean the consequences of a unusual high level of chemization of manufacturing, mode of life, medicine, irrational nutrition, increase of various medical manipulations connected to risk of transfer of pathogens of virus hepatitis. The aggravation of gravity of flow, development of complications of hepatitis in many respects is connected with absence of etiotrope and with low efficiency of available pathogenetic remedy of treatment. All of this introduces serious problems for medical science and health services. Accordance with the plan of the increase of the treatment results, it is presented as essential to apply drugs challenging metabolic, bio-energy processes and combination in anti-oxidation, membrane-stabilizing properties. Theoretically, such requirements should be responded with derivatives of inosite and phosphoric acid, as the ions of phosphorus plays a key role in the energy exchange, and inosite – in the exchange of phospholipids of
the essential component of cell and sub-cell biological membranes. Thus, inositol renders braking influence on the dystrophy of a liver$^{2-4}$.

By the purpose of the present activity was the experimental research of influencing of connections representing a mix calcium and magnesium salts of the inositolhexa- phosphate acid on a functional condition of cages of a liver at an acute hepatitis. The selection of research bile forming of a function of a liver was conditioned by that bile is the particular product developed by hepatocytes finely reflecting their functional activity$^{5-6}$.

**MATERIALS AND EXPERIMENTAL**

The tests were conducted on pubertal white male-rats with initial mass of body 190-220 g, which were parted into three groups on 8-10 individual in each. The first group consisted of intact rats and served as a control on the rest. On animals of second and third groups reproduced an acute toxic hepatitis in the way of hypodermic applying once per day, within four days of tetrachlormethane in a dose of 0.25 ml on 100 g of the body mass. After 24 hours after the last injection of hepatotoxine to animals of the third group were injected inside gastric the water suspension of a mix of calcium and magnesium salts of inositolhexaphosphate acid in a dose of 200 mg/kg daily, once within 6 days. Animal second group received only corresponding volume of water (untreated group). About a functional condition of a liver was judged on intensity biliation and excretion of a bilirubin, cholesterol and cholic acids in a structure of bile. The bile, collected within four hours under ethaminal by a narcosis (50 mg/kg, intraperitoneum) through polyethylene cannulas, introduced in a common bile duct. The speed of a biliary secretion, it’s total in each hour and in the sum for 4 hours of observation was accounted. In hour portions of bile were determined concentration (in mg%) and total of isolated bilirubin (in mcg on 100 g of mass of a body animal)$^4$, of cholic acids and cholesterol (in mg on 100 g of mass of a body animal)$^5$. The digital data processed by a method of variational statistics.

**RESULTS AND DISCUSSION**

The results of the conducted researches have shown, that at the acute toxic hepatitis, which has been reproduced by a tetrachlormethane, the considerable depressing of an exocrine function of a liver is watched. So, as contrasted to healthy, for animal with a hepatitis the biliation for 4 hours of experience in count on 100 g of weight a body of rats in 3 day from a beginning of reproduction a pathology, is reduced on 54%, and in 6 day, though is slightly improved, but it is remain statistically significantly diminished on 26.7% (Table 1).
The considerable changes thus are undergone with an elemental composition of bile, which was exhibited in decreasing the contents in it of cholic acids by 47.6 and 27%, cholesterol by 62.1 and 44%, and also bilirubin on 55.2 and 26.2% accordingly through 3 and 6 days from a beginning of disease. It is visible, that at an acute hepatitis described by development of fatty a dystrophy of hepatocytes is watched not only decreasing of a biliation, but also the depressing of an secretion of it components, that testifies to the expressed depressing of a functional state of a liver 5-6. The similar disturbance of exocrine function of a liver are watched and at acute hepatitis’s called and other hepatotoxins, by such as acetothioamide 9, geliotrin 10, tetracycline 11. By the main reason of the detected disturbance, accordingly to the literary data 12, at an acute hepatitis called by tetrachlormethane is the disorganization of membrane connected ferment systems of hepatocytes, developing under influencing of high reactive metabolites, forming from CCl4 at its biotransformation by a system of microsomal monooxygenases. Thus the products of free radical processes are result in considerable modification of molecules of membrane phospholipids, forming the peroxide clusters and the spherical micelles and accordingly upset normal liquid-crystalline structure of the membrane. On it the weakening the inside membrane hydrophobic protein-lipid interaction is conducts to disturbance of catalytic activity of membrane connected ferment complexes, and specially monooxygenases and oxygenases. All it results in a decrease of synthesizing of primary cholic acids from cholesterol and processes of their conjugation by a taurine and glycine.

The introducing to animals with a toxic hepatitis a mixes calcium and magnesium salts of the inositolhexaphosphate acid rendered clear recovering influence on a functional condition of a liver. So, after three days of treatment the quantity emanated bile for 4

<table>
<thead>
<tr>
<th>Groups</th>
<th>Quantity of the bile, ml</th>
<th>Cholic acids, mg</th>
<th>Cholesterol, mg</th>
<th>Bilirubin, mcg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>1.20±0.064</td>
<td>6.15±0.534</td>
<td>0.31±0.041</td>
<td>94.8±8.88</td>
</tr>
<tr>
<td>No treated</td>
<td>0.533±0.071&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.22±0.370&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.114±0.007&lt;sup&gt;a&lt;/sup&gt;</td>
<td>42.5±4.77&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>0.880±0.069&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.50±0.310&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.202±0.014&lt;sup&gt;a&lt;/sup&gt;</td>
<td>70.0±5.09&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Treated</td>
<td>0.920±0.051&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>5.03±0.290&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.212±0.016&lt;sup&gt;*&lt;/sup&gt;</td>
<td>95.0±5.85&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>1.03±0.055</td>
<td>6.20±0.415&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.270±0.018&lt;sup&gt;*&lt;/sup&gt;</td>
<td>115.1±8.83&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

The notice: In numerator the data of a three-day time, and in a denominator – of six-day time research
a - statistically significant results as contrasted to healthy,
* - statistically significant results as contrasted to no treated animal.
experiences as contrasted to by control increases on 66%, and in 6 days the marked effect is
growth and volume excreted bile is statistically significant did not differ from the applicable
values healthy animals. It is remarkable, that the increase of quantity of emanated bile is
accompanied by ascending of the contents of cholic acids in it on 56.2% and 38%, and also
cholesterol on 86 and 33.7% accordingly in the indicated terms of observation. The mix of
calcium and magnesium salts of the inositolhexaphosphate acid was boosted also a bilirubin
an excretory function of a liver on 123.5% in 3 days and on 64.4% in 6 days from a beginning
of treatment of a hepatitis. Thus quantity of the excreted bilirubin already after three-day
time treatment has achieved a level of the healthy rats, and increase of term of treatment
result in ascending of the marked effect and quantity of a bilirubin, emanated by treated
animals was exceeded the indexes of healthy animals on 21.4%.

Therefore, the mix of calcium and magnesium salts of the inositolhexaphosphate acid
renders the expressed recovering influence on particular functions of a liver – bile extraction
and bile forming at an acute hepatitis of a toxic etiology. Allowing that circumstance, that
at acute hepatitis the decrease of a chelate emanated function of a liver is conditioned by a
decrease of synthesizing of primary cholic acids, and also depressing of processes of a
conjugation by their taurine and glycine. It is possible to suspect the strengthening
under effect of an investigated drug of the inositolhexaphosphate acid of synthesizing of
primary cholic acids. As it is visible from the cited data the given drug is increase
considerably an excretion of a bilirubin. Last, as it is known, in a composition of bile was
emanated basically as glucuronides of a bilirubin. As the process of its conjugation
with a glucuronic acid depends on activity of the uredinediphosphateglucuronil transferase,
it is necessary to consider, that the mix of calcium and magnesium salts of the
inositolhexaphosphate acid increases an activity of this enzyme of a liver.

CONCLUSION

Thus, the mix of the calcium and magnesium salts of the inositolhexaphosphate acid
for animals with an acute hepatitis calls intensification of synthesizing of primary cholic
acids and internal liver exchange of a bilirubin, owing to what the intensity of bile extraction
and emanation of a bilirubin in a composition of bile is boosted. The results of toxicological
researches conducted on white mice and rats have shown a hypo toxicity of investigated
derivative of the inositolhexaphosphate acid and absence of side effects. Allowing it and
the expressed positive influencing on a particular function of a liver it is possible to
recommend applying of a mix of calcium and magnesium salts of the inositolhexaphosphate
acid in practical medicine as a means for treatment of hepatitises.
REFERENCES

7. N.P.Skakun. Problems of endocrinology and endocrinotherapy. 2, No.6, 75 (1956)