

## CHANGES IN BIOCHEMICAL INDICATORS OF BLOOD SERUM, CHARACTERIZED THE STATE OF THE LIVER, DYNAMICS OF EXPERIMENTAL EXTRAHEPATIC CHOLESTASIS IN RATS

Yuldashev N.M., Ahmedov K.H., Akbarhodzhaeva H.N., Mirahmedov F.K., Ismailov N.

*Tashkent Pediatric Medical Institute, Tashkent, e-mail: y\_nosir@rambler.ru*

Biochemical blood indexes of 69 white male rats with experimental extrahepatic cholestasis were studied to reveal the involvement of liver in pathologic process. Substantial changes were revealed in biochemical parameters of experimental animals blood serum which showed hyperenzymemia, hyperbilirubinemia and hypercholesterolemia in dynamics of extrahepatic cholestasis development. If cytolytic process marked on the 3<sup>rd</sup>, and especially on the 7<sup>th</sup>-15<sup>th</sup> day then the increase of activity of alkaline phosphatase, the level of cholesterol and bilirubin on the 3<sup>rd</sup> day of experiment. The indicated changes prove the involvement of liver in pathologic processes that naturally make the course of the main pathology worse.

**Keywords:** experimental extrahepatic cholestasis, rats, biochemical blood indexes, liver

Diseases of the gall bladder and bile ducts, especially cholelithiasis, often (16–23 %) leads to a fatal course of study [2, 4, 6, 7]. Anatomical and physiological relationship of the gall bladder to the liver is likely to affect the function of the latter standing in diseases of the former. However, the publications on the morpho-functional state of the liver in pathology data are contradictory. Some authors do not find specific violations of liver function or believe their transient [8, 9], while others show a profound change in its activity [1, 3].

Based on the above, the **purpose** of the present study was to evaluate blood biochemical parameters characterizing the functional and metabolic condition of the liver, in the dynamics of experimental extrahepatic cholestasis in rats.

### Materials and methods of research

The experiments were performed on 69 white mongrel male rats mixed by populations with initial weight of 180–200 g, containing on a laboratory diet under vivarium conditions. In 37 rats under hexenal anesthesia (100 mg/kg, ip), extrahepatic cholestasis by ligation of the common bile duct was reproduced [9]. The mortality rate was 32,4%. Controls were 24 sham-operated animals who received only laparotomy under aseptic conditions. Intact group included 8 rats. The research was performed at 1, 3, 7 and 15 days after the play models. Selection of research period was related to the development there significant morphological changes in the liver on in the experimental cholestasis [9]. In these periods the animals under ether anesthesia were killed by decapitation and the blood serum assents transaminases, alkaline phosphatase (ALP), cholesterol and bilirubin on biochemical analyzer Aytolumalyzer Human (Germany) was identified.

The obtained digital data was statistically processed by package of application program statistical analysis Excel – 2000.

### Results of research and their discussion

The results showed that in 1 day after reproducing extrahepatic cholestasis significant changes in the activity of alaninaminotranferazes (ALT) in serum of experimental rats were not observed (figure). However, after 3 days activity of the enzyme increased dramatically, exceeding the normal and indexes of previous research period by 2,7 times. Hyperenzymemia by the 7<sup>th</sup> day of the experiment has increased even more. Its significance statistically increased over the previous period in 2,4 and the value of intact rats by 6,9 times. However, by the end of the experiment (15 days after reproducing cholestasis) a decrease of ALT was observed as compared to the previous period (1,7 times). It should be noted that despite the decrease, the activity of serum ALT in experimental animals remained significantly higher than normal ratio for 4,0 times.

Unlike ALT, the activity of aspartateaminotransferase (AST) in all terms of research was significantly more than the rates of the control group (2,4, 2,4, 2,6, and 2,4 – times) (figure).

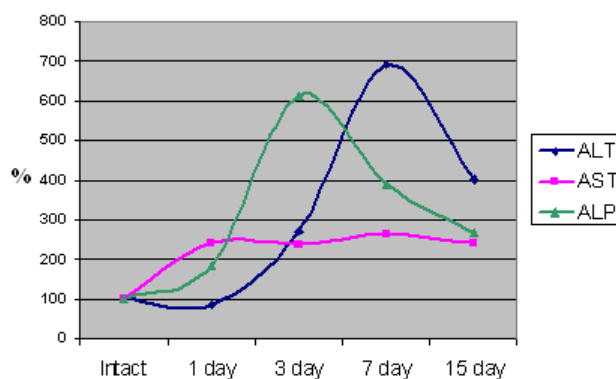
ALP activity increased sharply. For example, 1 day after reproducing of extrahepatic cholestasis ALP activity in serum was significantly exceeding control for 1,8 times (figure). In the future, this number has grown even more, exceeding the previous period and the control, 3,6 and 6,1 times respectively. On the 15<sup>th</sup> day pathology of ALP activity decreased approximately 2 times. However, despite this, the value of it remained high, exceeding indicator of intact rats by 4 times. In the future tendencies to lower serum ALP activity were maintained, and studied figure exceeded the normal value for only 2,7 times.

Increased ALT levels can be explained by the involvement in the pathological process of the liver, since usually in mechanical jaundice the activity of transaminases is normal or slightly increased [5] in our case, the increase of ALT registered already on the third day,

and on the 7<sup>th</sup> day of observation was given the maximum increase. These changes of ALT activity suggest secondary involvement of the liver in the pathological process.

It is more difficult to explain the increase in the activity of AST. We believe that the sharp increase of AST activity is a consequence of surgery in the modeling of this disease, as in muscle tissue the activity of AST was the high-

est. However, the high activity of AST is preserved in more long-term period of the research. One can only assume that the increase in of the enzyme activity is the result of haemolytic – for disturbances of the permeability of red blood cells, hepatocytes cells and of muscle cells due to increased pressure within the gall bladder and the biliary duct. Increased activity of ALP clearly shows the development of cholestasis.



The enzyme activity in the blood serum of rats with experimental hepatic cholestasis is in dynamics

Significant changes occurred in the content of cholesterol in the blood serum. Thus, after 1 day of reproducing extrahepatic cholestasis the level compared to the control increased significantly by 1,4 times (Table). In the future, the content increased even more, exceeding the previous term

of 1,5 and control animals by 2,1 times. In the following periods of total cholesterol content in the blood serum gradually decreased. However, despite of this its value after over 7 and 15 days after reproducing cholestasis was still above the control for 1,64 and 1,2 times, accordingly.

Cholesterol and bilirubin fractions in serum of experimental animals in mg/dl

| Groups      | Indexes       |                                |                             |                             |                             |
|-------------|---------------|--------------------------------|-----------------------------|-----------------------------|-----------------------------|
|             | Cholesterol   | Bilirubin                      |                             |                             |                             |
|             |               | Total                          | Direct                      | Indirect                    |                             |
| Intact      | 134,75 ± 6,26 | 0,57 ± 0,04                    | –                           | 0,57 ± 0,03                 |                             |
| Obturation: |               |                                |                             |                             |                             |
| 1 day       | Experiment    | 205,83 ± 2,06 <sup>a, b</sup>  | 2,43 ± 0,06 <sup>a, b</sup> | 1,36 ± 0,05 <sup>a, b</sup> | 1,03 ± 0,07 <sup>a, b</sup> |
|             | Control       | 147,3 ± 1,89                   | 0,68 ± 0,06                 | –                           | 0,67 ± 0,06                 |
| 3 day       | Experiment    | 313,83 ± 10,29 <sup>a, b</sup> | 8,22 ± 0,10 <sup>a, b</sup> | 5,56 ± 0,08 <sup>a, b</sup> | 2,66 ± 0,16 <sup>a, b</sup> |
|             | Control       | 151,50 ± 1,59 <sup>a</sup>     | 0,73 ± 0,05 <sup>a</sup>    | –                           | 0,62 ± 0,05                 |
| 7 day       | Experiment    | 232,50 ± 6,19 <sup>a, b</sup>  | 2,05 ± 0,05 <sup>a, b</sup> | 1,35 ± 0,05 <sup>a, b</sup> | 0,77 ± 0,03 <sup>a, b</sup> |
|             | Control       | 141,77 ± 1,53                  | 0,73 ± 0,05 <sup>a</sup>    | –                           | 0,62 ± 0,05                 |
| 15 day      | Experiment    | 166,67 ± 11,79 <sup>a, b</sup> | 2,10 ± 0,06 <sup>a, b</sup> | 1,75 ± 0,04 <sup>a, b</sup> | 0,36 ± 0,01 <sup>a, b</sup> |
|             | Control       | 138,33 ± 1,26                  | 0,63 ± 0,04                 | –                           | 0,61 ± 0,03                 |

Notes: P < 0,05 a – compared to intact, b – compared with the control group.

One of the manifestations of extrahepatic cholestasis in experimental animals was the development of hyperbilirubinemia. It was

manifested by increase in both total, indirect and, especially, direct bilirubin in the blood serum, depending on the duration of the ex-

periment. For example, after 1 day in reproducing extrahepatic cholestasis indirect bilirubin levels rose to  $1,03 \pm 0,07$  mg/dl at its value in the control animals  $0,67 \pm 0,06$  mg/dl (Table). Absent in normal direct bilirubin was  $1,36 \pm 0,05$  mg/dl. This led to increased levels of total bilirubin up to  $2,43 \pm 0,06$  mg/dl at the value it in the control group and at the intact animals  $0,68 \pm 0,06$  and  $0,57 \pm 0,04$  mg/dl respectively. As lengthening the duration of cholestasis the content of bilirubin and its fractions increased sharply. If the content of total bilirubin increased till  $88,22 \pm 0,09$  mg/dl after 3 days, then indirect increased to  $2,66 \pm 0,16$  mg/dl and the direct to  $5,56 \pm 0,08$  mg/dl. However, within 7 days after the reproduction of model value of the general, the indirect and direct bilirubin significantly decreased relative to that of previous period, accordingly, 4,0, 3,5 and 4,1 times. Despite that, this rate remained high in comparison with the norm. Thus, the overall level of bilirubin was equal to  $2,05 \pm 0,05$  mg/dl, indirect to  $0,77 \pm 0,33$  mg/dl, and direct to  $1,35 \pm 0,05$  mg/dl. After 15 days of experiment, total bilirubin level maintained within the range of the previous term, and direct bilirubin tended to increase, accounting for  $1,75 \pm 0,04$  mg/dl.

For jaundice characterized by hypercholesterolemia. A significant increase of content of direct bilirubin in our case is connected to overruns bile tract caused by blockage, their bursting, and the subsequent transfer of bile in the blood stream. Elevated levels of indirect bilirubin is probably due to hemolysis, leading to enhanced formation of bilirubin.

## Conclusions

Thus, the dynamics of extrahepatic cholestasis in the blood of experimental animals, observed significant displacement on the biochemical parameters of the raw manifested hyperenzymemia, hyperbilirubinemia, hypercholesterolemia. If cytolytic processes manifested in the third and, especially, on the 7<sup>th</sup>–15<sup>th</sup> day, the increased activity of alkaline phosphatase, bilirubin and cholesterol levels was manifested on the third day of the experiment. These changes demonstrate the involvement in the pathological process of liver, which naturally exacerbates the main pathology.

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