BREAKDOWN OF PROTHROMBIN AND PROCONVERTIN IN RATS WITH EXPERIMENTAL EXTRAHEPATIC CHOLESTASIS

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Changes in the half-life of prothrombin and proconvertin were studied in rats with experimental extrahepatic cholestasis induced by ligation of the common bile duct. By the end of the second week of cholestasis the prothrombin activity was reduced almost by half and the proconvertin activity by more than two-thirds compared with the control. Meanwhile the half-life of prothrombin after cholestasis for 14 days was increased by 1.5 h and that of proconvertin by 4.7 h compared with the control. The slower breakdown of prothrombin and proconvertin during cholestasis is regarded as a compensatory reaction.

KEY WORDS: prothrombin; proconvertin; extrahepatic cholestasis.

In disease of the liver and biliary tract, especially if accompanied by prolonged jaundice, an increased bleeding tendency is often observed [1, 2, 4, 5], and one of its causes is a decrease in the content of factors of the "prothrombin complex" (factors II, VII, IX, and X) resulting from the vitamin K deficiency and liver damage [7, 8, 10-13]. However, the state of the metabolism of these factors in jaundice has been inadequately studied.

In the investigation described below the breakdown of prothrombin (factor II) and proconvertin (factor VII) was studied in rats at various periods of experimental extrahepatic cholestasis.

EXPERIMENTAL METHOD

The common bile duct was ligated in albino rats of both sexes weighing 170-210 g. The presence of cholestasis was confirmed biochemically and morphologically. The experimental animals were investigated for 2 weeks, for at longer periods after the operation the common bile duct was recanalized.

After the initial prothrombin and proconvertin activity had been determined [3] the thrombin-forming function of the liver was blocked by phenindione (5 mg/100 g body weight by the intragastric route) and the activity of the blood clotting factors was again studied 4 h later. Considering that the breakdown of the substances in vivo obeys the exponential law [4, 6], the half-life $T_{1/2}$, i.e., time after which the quantity of the substance is reduced by half its initial value, was calculated by the equation

$$T_{1/2} = \frac{0{,}3 \cdot t}{\lg M_0 - \lg M},$$

where M_0 is the initial activity of the substance and M its activity a certain time (t = 4 h) after the administration of phenindione.

EXPERIMENTAL RESULTS

The results of the biochemical and morphological tests reflected the liver damage in cholestasis. On the 14th day after ligation of the common bile duct, for instance, the serum bilirubin concentration was increased by more than 9 times and the concentration of bile acids was doubled compared with the control.

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TABLE 1. Activity and Half-Life of Prothrombin and Proconvertin in Rats Depending on Period of Cholestasis (M ± m)

Clotting factor	Control (18)	Expt. (days after creation of cholestasis) 1 (13)	3 (15)	7 (14)	14 (12)
Prothrombin					
activity (in %)	105,0±3,6	84,0±1,4	72,4±1,2	64,0±1,0	58,4±0,9
half-life (in h)	10,1±0,08	11,0±0,07	11,1±0,09	11,4±0.08	11,6±0,09
Proconvertin					
activity (in %)	96,8±6,5	46,8±1,5	41,6±1,6	35,8±0,9	27,4±0,8
half-life (in h)	2,1±0,05	2,9±0,06	3,8±0,07	5,0±0,04	6,8±0,03

Note. All values in cholestasis differ statistically significantly from control ($P < 0.05$). Numbers in parentheses give number of animals.

In the histological sections of the liver dilatation of the biliary passages, degenerative changes in the hepatocytes, and hyperplasia of the connective tissue were observed.

On the first day after ligation of the common bile duct the prothrombin and, in particular, the proconvertin activity were appreciably reduced. This decrease continued throughout the period of observation (Table 1).

By the 14th day after the operation the prothrombin activity was reduced almost by half and its half-life was increased by 1.5 h. The proconvertin activity was reduced by 3.5 times and its half-life was increased by 4.7 h compared with the control.

The results indicate that the decrease in prothrombin and proconvertin synthesis observed in the presence of an extrahepatic block to bile secretion is accompanied by delay in their breakdown. This agrees with the view that not only the rate of synthesis of protein but also the rate of its breakdown is regulated in the cells of higher organisms [6, 9]. Delay in the breakdown of prothrombin and proconvertin in cholestasis is evidently a compensatory reaction of the body which, if disturbed, could be a pathogenetic factor in cholemic hemorrhage.

LITERATURE CITED

1. U. A. Aripov, P. N. Mazaev, É. V. Grishkevich, et al., Mechanical Jaundice [in Russian], Tashkent (1971).
2. É. V. Grishkevich, M. V. Danilov, V. A. Vishnevskii, et al., Klin. Med., No. 2, 74 (1973).
3. Investigation of Blood Clotting Factors (Technical Instructions) [in Russian], Leningrad (1971).
4. I. I. Kal'chenko, P. V. Lys, and V. P. Ishchenko, Khirurgiya, No. 7, 47 (1971).
5. A. I. Krakovskii and T. P. Makovskaya, Khirurgiya, No. 7, 107 (1972).
6. M. I. Lerman, in: Chemical Factors in the Regulation of Enzyme Activity and Biosynthesis [in Russian], Moscow (1969), p. 381.
7. T. Sh. Magdiev, Éksper. Khir., No. 3, 39 (1960).
8. E. Deutsch, Progr. Liver Dis., 2, 69 (1965).
9. A. Grossman and C. Mavridis, Fed. Proc., 25, 285 (1966).
10. H. G. Lasch and A. Linke, Dtsch. Arch. klin. Med., 200, 290 (1953).
11. O. D. Ratnoff, Med. Clin. N. Amer., 47, 721 (1963).
12. H. R. Roberts and A. I. Cederbaum, Gastroenterology, 63, 297 (1972).
13. W. B. Walls and M. S. Losowsky, Gastroenterology, 60, 108 (1971).