The Toxic Effect of Bile Acid on Rat Liver by Bile Duct Obstruction

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INTRODUCTION

The bile juice (the bile) produced in the liver is eliminated through bile duct. The bile is collected and concentrated in gallbladder. The major component of the bile is bilirubin which is the end product of hemoglobin synthesis. The bilirubin metabolism is affected by the prehepatic jaundice, the intrahepatic jaundice and the extrahepatic cholestasis. Epecially, the prolonged extrahepatic cholestasis can induce the biliary liver cirrhosis development. Except bililuibin, procollagen type III and IV may participate in the liver cirrhosis development. In various conditions of the collagen metabolism, we studied the toxic effect of bililuibin in the liver.

METHOD AND MATERIALS

We operated the bile duct obstruction (BDO) to the wistar rats, the development of the biliary liver cirrhosis for 0-4 weeks and observed. After the observation period, the liver and sera were collected, we measured the change of the enzyme activities of procolla-

gen type III and IV in the sera, and hydroxyproline in the liver tissues. Also a piece of the liver was stained by the immunfluorescence and immunhistochemistry.

RESULT

Throughout the observation period, development of jaundice is observed in all the BDO operated rats. Compared with the control rats group, weight ratio of liver/body significantly increased 4 weeks after BDO($p<0.001$). In the BDO group, we observed the significant change of the concentration of collagen type III, IV and total collagen in the liver (Table. 1) In the BDO group, increase of these compounds also is observed by the clinical biochemistry. The concentration of collagen type III and IV in the sera tissue is significantly correlated with the concentration of the total collagen tin the liver tissue ($r=0.81$, $r=0.80$). The liver tissues of the BDO group showed the massive bile duct proliferation (Table. 2) and the formation of thick collagen fiber bundles and the hepatocyte islands in he periportal and strome areas, which were hardly observed in the control rats.

Table 1. The ratio of liver/body weight, total collagen in liver, collagen type III and IV in sera of control rats and BDO rats.of ONO-5046·Na.

Group	LW/BW(%)	Hyp(μ g)/g Liver	PN III P(ng/ml)	PNIVP(ng/ml)
Control Rats	3.447 $\pm$ 0.448	1.225 $\pm$ 0.126	2.660 $\pm$ 1.767	2.950 $\pm$ 1.982
1 Week	4.546 $\pm$ 0.362	2.283 $\pm$ 0.366	4.940 $\pm$ 2.434	4.200 $\pm$ 1.058
B 2 Week	5.196 $\pm$ 0.662	3.250 $\pm$ 0.596	5.183 $\pm$ 1.726	4.517 $\pm$ 1.100
D 3 Week	5.598 $\pm$ 1.030	3.950 $\pm$ 1.675	8.367 $\pm$ 5.792	6.480 $\pm$ 3.363
O 4 Week	5.736 $\pm$ 0.843	5.460 $\pm$ 1.006	8.300 $\pm$ 3.599	7.800 $\pm$ 1.483
5 Week	7.547 $\pm$ 1.826	7.820 $\pm$ 2.531	12.800 $\pm$ 8.818	7.920 $\pm$ 2.582

BDLO: bile duct ligation and scission.

The data shows M $\pm$ SD, ** $p<0.005$, $p<0.05$: significantly different from control.

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CONCLUSION

The rats exposed to the bile stasis for a long time developed the liver fibrosis(cirrhosis). The results suggest that bilirubin acts as a stark stasis in the liver so that it prevents the hepatocytes regeneration. We found that the monitoring of PNIIP and PIVCP in the sera is useful for the screening of the fibrosis(cirrhosis) by the extrahepatic bile duct obstruction.

Table 2. The clinical biochemistry in sera of control rats and BDO rats.

Group	GOT(U/L)	GPT(U/L)	LP(U/L)	G-Bili(mg/dl)
Control Rats	61.2±23.6	17.0±10.8	30.5± 7.9	11.3± 2.3
1 Week	164.8±53.7	25.6± 9.3	414.3±221.0	110.6±53.7
B 2 Week	126.5±63.0	19.5± 7.4	301.7±185.6	108.8±53.3
D 3 Week	123.7±30.7	17.8± 6.0	272.0± 71.4	96.0±46.3
O 4 Week	153.8±30.4	18.8± 2.0	238.0± 56.4	114.2±47.3
5 Week	132.8±45.2	19.6± 7.4	246.4± 56.50	68.2±29.8

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