Determination of 3β-Hydroxylated Bile Acids in Human Serum and Liver Tissue

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NAGAKURA, T., SUZUKI, H., MIYAZAKI, Y., OTSUKI, M., GOTO, J., NAMBARA, T. and TOYOTA, T. Determination of 3β-Hydroxylated Bile Acids in Human Serum and Liver Tissue. Tohoku J. Exp. Med., 1989, 159 (2), 165-166 —— 3β, 7α-Dihydroxy-5β-cholanoic acid (3β, 7α-diOH) was detected in serum of 3 patients with intrahepatic cholestasis. 3β, 7β-dihydroxy-5β-cholanoic acid (3β, 7β-diOH) appeared in serum of those patients after treatment with ursodeoxycholic acid (UDC). These bile acids were also detected in only unconjugated fractions of serum of another 7 patients with chronic liver diseases, but not in liver tissue of them. The liver does not seem to form these bile acids itself because they were absent in liver tissue. —— 3β-hydroxylated bile acids; liver tissue bile acids; gas chromatography-mass spectrometry

3β, 7β-diOH is known as 3β-epimer of UDC. As 3β, 7β-diOH was not found in bile, the metabolic site of this bile acid seems to be different from that of another bile acids which have enterohepatic circulation. To clarify the metabolic site of 3β-hydroxylated bile acids, we determined not only 3β, 7β-diOH but also 3β, 7α-diOH in serum and liver tissue using gas chromatography-mass spectrometry as described by Goto et al. (1988).

We orally administered 600 mg/day of UDC to 3 patients with intrahepatic cholestasis. Their fasting serum bile acids were determined before and 2 weeks after administration of UDC (Table 1). Since very small amount of secondary bile acids were detected before UDC administration, bile acids might not have enough enterohepatic circulation. But 3β, 7α-diOH was detected as much as ranging from 1.5% to 4.7% of total bile acids. And after UDC administration, 3β, 7β-diOH was also detected ranging from 2.7% to 32.8% of total bile acids. We performed needle liver biopsies 1-3 months after UDC therapy. Neither 3β, 7α-diOH nor 3β, 7β-diOH was detected in the liver tissue samples.

We also examined serum and liver samples of another 9 patients with liver diseases without UDC administration as control. Bile acids were separated into the unconjugated, glycine- and taurine-conjugated fractions. In 7 serum samples of 9, 3β-hydroxylated bile acids were detected not in glycine- and taurine-conjugated fractions, but in unconjugated fraction (Table 2). These bile acids were not detected in any of the liver tissue samples. Thus the liver does not seem to form 3β, 7α-diOH and 3β, 7β-diOH, because they were not detected in liver tissue. Nevertheless 3β, 7α-diOH was detected in serum of patients with intrahepatic cholestasis, who might not have enough enterohepatic circulation. Not only the liver but also intestinal tract do not seem to be involved to metabolize 3β, 7α-diOH.

Received September 13, 1989; revision accepted for publication September 30, 1989.
among these patients. Recently, dehydroxylation of the keto groups of dehydrocholic acid in blood has been reported (Tamasawa et al. 1987). Our findings suggest 3β-hydroxylated bile acids are formed in other than the liver, for example in blood, like dehydrocholic acid. Further study to confirm the metabolic site of 3β-hydroxylated bile acids should be needed.

References
