EFFECT OF HISTAMINE ON BILE FORMATION IN ALBINO RATS

I. K. Venger

UDC 615.218.1.015.45:612.357.4

Experiments on adult male rats showed that histamine (100-500 μg/100 g body weight, subcutaneously) retards the rate of bile secretion. The concentration of bile acids in the bile was reduced correspondingly, chiefly on account of taurocholic acid, and the cholesterol level also fell. The concentration of glycocholic acid usually rose. Histamine evidently interferes with the formation of primary bile acids in the liver from cholesterol and inhibits the conjugation of cholic acid with taurine, but facilitates its conjugation with glycine.

Anrep and Barsoum [6] observed that if salts of the bile acids are injected into the hepatic blood vessels or if the common bile duct is ligated the blood histamine concentration is increased by 25-35 times.

It was therefore decided to study the action of histamine on the bile-forming function of the liver. The few observations recorded on this subject were made on dogs [7-9].

EXPERIMENTAL METHOD

Experiments were carried out on 115 male albino rats weighing 120-130 g using a method described earlier [4]. Bile was collected from each animal in hourly portions for 4 h. In all the experiments the rate of secretion of bile was calculated every hour and expressed in mg/min/100 g body weight, and total volume of secretion obtained during each hour and its aggregate during the experiment were determined (in mg/100 g body weight). The concentration (in mg%) and total content (in mg/100 g body weight) of bile acids (total and each individual acid), bilirubin, and cholesterol also were determined in the hourly bile samples. The bile acids were separated by ascending chromatography on paper [1, 2]. The concentration of bile acids was determined by Karbach's method [1], bilirubin by Skakun's modification [3] of Van den Bergh's method, and cholesterol by Drogovoz's method [7].

The basic level of bile formation was determined in the first series of experiments and the effect of histamine, injected subcutaneously in doses of 25, 50, 100, 150, 250, and 500 μg/100 g body weight, was investigated in the rest.

EXPERIMENTAL RESULTS

In doses of 25-50 μg/100 g histamine had no significant effect on the intensity of bile formation, but in larger doses it had an inhibitory action (Fig. 1).

The anticholeretic action of histamine was accompanied by marked disturbances of the chemical composition of the bile. The total concentration of bile acids in the bile usually fell: slightly under the influence of histamine in doses of up to 100 μg/100 g and more considerably if the dose was increased. For example, after injection of histamine in a dose of 150 μg/100 g the concentration of bile acids fell from 1239-878 to 775-595 mg%.

Department of Pharmacology, Ternopol' Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 74, No. 12, pp. 16-18, December, 1972. Original article submitted December 3, 1971.

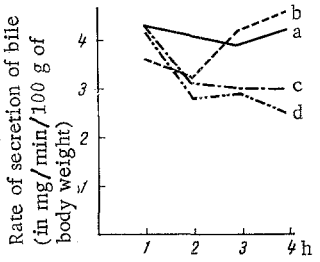

Fig. 1. Effect of Histamine on intensity of bile formation in albino rats: a) control; b) histamine in dose of 100 μg/100 g body weight; c) 250 μg/100 g body weight; d) 500 μg/100 g body weight.

The total quantity of acids secreted with the bile in the control series was 10,461 mg/100 g in 4 h, while after injection of histamines in doses of 100, 150, 250, and 500 μg/100 g it was 6925, 4816, 5696, and 8624 mg/100 g respectively, or 23, 54, 46, and 17% less than in the control. In albino rats histamine thus inhibits the synthesis and secretion of bile acids.

The results of the chromatographic analysis of the bile showed that the decrease in concentration of bile acids took place mainly on account of taurocholic acid. Its concentration was reduced by 1.5-3 times after injection of histamine in a dose of 100 μg/100 g and by 4-10 times if the dose was increased to 150 μg/100 g.

By contrast the concentration of the other conjugated acid (glycocholic) rose under the influence of histamine. Whereas in the bile of the experimental animals its concentration did not exceed 30-16 mg%, after administration of histamine in a dose of 100 μg/100 g it reached 458-81 mg%, in a dose of 150 μg/100 g it reached 326-104 mg%, and after a dose of 250 μg/100 g it reached 88-37 mg%.

Less regular changes were found in the concentration of free deoxycholic acid. In individual hourly portions its concentraion was at the initial level, in others it was zero, and in a few cases it was considerably above normal.

The concentration of free cholic acid, just as in the control, did not exceed 1-2 mg% after administration of histamine.

Under the influence of histamine the total taurocholic acid fell sharply (by 2-10 times or more). This affected deoxycholic acid to a lesser degree, although its concentration also fell significantly. By contrast the total content of glycocholic acid rose in all the experiments. In particular, under the influence of histamine in doses of 100-150 μg/100 g body weight its concentration increased by about 8-9 times.

It can be concluded from the analysis of these results that histamine affects several links in the chain of cholate formation in rats. In particular, it evidently inhibits the synthesis of primary bile acids from cholesterol, with a resulting decrease in the cholate concentration in the bile. Histamine also inhibits the biochemical processes responsible for the conjugation of cholic acid with taurine, but it stimulates the conjugation of cholic acid with glycine.

The concentration of taurocholic acid in the bile accordingly decreases while that of glycocholic acid increases.

Histamine also affected the cholesterol-excretory function of the liver. Through the action of histamine the cholesterol concentration in the bile was reduced, and in particular, the total cholesterol content was reduced on the average by 1.5-2 times. The action of histamine on bilirubin secretion was manifested to a lesser degree. The bilirubin concentration was slightly increased after administration of histamine in a dose of 25-50 μg/100 g, but slightly reduced (on the average from 0.07 to 0.057 mg/100 g) if the dose of histamine was increased.

In albino rats histamine thus reduces the intensity of bile secretion, inhibits the synthesis of bile acids, and reduces the excretion of bilirubin and also of cholesterol with the bile.

LITERATURE CITED

1. S. M. Drogovoz, Vopr. Med. Khimii, 4, 397 (1971).
2. Ya. I. Karbach, Biokhimiya, 2, 305 (1961).
3. Ya. I. Karbach, Lab. Delo, 2, 104 (1967).
4. N. P. Skakun, Probl. Endokrinol., 6, 75 (1956).
5. N. P. Skakun and A. N. Oleinik, Farkamol. i Toksikol., 3, 334 (1967).
6. G. V. Anrep and G. S. Barsoum, J. Physiol. (London), 120, 427 (1953).
7. R. S. Jones and M. I. Grossman, J. Physiol. (London), 216, 335 (1969).
8. R. S. Jones and M. I. Grossman, J. Physiol. (London), 217, 532 (1969).
9. S. Laterka and M. I. Grossman, Gastroenterology, 50, 500 (1966).