46. Biliary Amylase Output in Rats with Pancreatic Duct Obstruction and CCl₄-Intoxication

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Introduction. It has been noted that amylase metabolism takes place not only in the pancreas but also in the liver. Amylase synthesis in the liver was experimentally demonstrated by perfusion method in vitro. This evidence suggests that the liver plays some role in the regulation of circulating amylase. However, very few reports have been published with reference to this mechanism in vivo. In our previous report, we have demonstrated a direct correlation between hepatic excretory function and the level of circulating amylase. For further clarification of the mechanism of hepatic excretion of amylase, we have studied biliary amylase output using rats with hyperamylasemia caused by the pancreatic duct obstruction and rats with liver injury by CCl₄-intoxication. The results showed a positive correlation between the amylase level in the bile and that in the plasma and their increases were quantitatively estimated.

Materials and methods. Fifty-six male albino rats (250-350 gm) were used. The bile was collected through a polyethylene tube inserted into the common bile duct using the method described previously. Blood was taken from the abdominal aorta after the collection of bile. Amylase activities were measured by “Blue Starch (Pharmacia AB, Sweden)” method and expressed by international unit. Amylase output in the bile or urine was calculated as the product of amylase activity (units per L) by excreted bile or urine flow (ml/Hr), respectively.

Experiments were carried out under four different conditions: (1) As a control, the bile was collected for 30 or 60 minutes from thirty-two rats without any treatment. (2) The effect of hyperamylasemia created by obstruction of the pancreatic duct was examined in twelve rats. The tube was inserted into the common bile duct above the openings of pancreatic ducts and its outer end was kept open out of the abdominal wall. In six rats of this group, the common bile duct was also ligated at the opening in the duodenum. The bile collection through the inserted tube was started 24 hours after the operation. (3) The effect of acute CCl₄-intoxication was examined in two subgroups; five control rats were given 1.5 ml/Kg of olive oil,
and other six rats were given the same dose of CCl₄ through a stomach tube. The bile was collected 48 hours thereafter. (4) The effect of chronic CCl₄-intoxication was also studied in two subgroups; six control rats were given 0.5 ml/Kg of olive oil twice a week for 4 weeks, other six rats being given the same dose of CCl₄.
Results and discussions. (A) Biliary amylase output in the control group. In thirty-two rats, the bile samples were collected for 30 or 60 minutes starting from ten minutes after the operation. Amylase output in the bile was 0.275±0.0480 units per hour (Mean ± Standard Error). Twenty-seven of thirty-two rats were chosen as controls whose biliary amylase output fell within Mean ± 1 S.D. (0.007–0.543 u/Hr), and their values were plotted in Fig. 1. Amylase output in the bile (Y u/Hr) revealed a positive correlation with amylase activity (X u/L); Y = 0.0003 X + 0.106 (p<0.01). However, it had no correlation with plasma amylase activity or bile flow. Also, no correlation was found between amylase activity in the plasma and that in the bile.

(B) Effect of obstruction of the pancreatic duct on biliary amylase output (Table I, Fig. 2). Parenchymal damage of the pancreas was confirmed histologically in the treated subgroup of rats after each experiment. Slight elevation of plasma transaminase level was observed in both the control and the treated subgroups. This might indicate that the liver was slightly damaged by the external bile fistula kept for 24 hours. Plasma amylase levels in the treated rats were significantly higher than those in the controls (p<0.01). No significant difference in bile flow was noted between the two subgroups. Both amylase activity in the bile (Y₁ u/L) and biliary amylase output (Y₂ u/Hr) had a positive correlation with plasma amylase level (X u/L); Y₁ = 0.047 X + 210 (p<0.01) and Y₂ = (0.035 X + 7) × 10⁻³ (p<0.01).

These evidences might suggest that biliary amylase output was increased by an elevation of amylase level in the bile due to the high plasma amylase level.

![Graphs showing correlation between plasma amylase activity and biliary amylase output](image)

Fig. 2. Interrelation of bile amylase activity and biliary amylase output to plasma amylase activity in control rats (×) and in rats with pancreatic-duct-obstruction (●).
(C) Effects of acute CCl₄-intoxication on biliary amylase output (Table I). Plasma transaminase level in the CCl₄-treated subgroup was much higher in the mean value than that in the control subgroup, although no statistical significance was obtained because of large dispersion of the observed values in the treated subgroup. There was no significant difference in amylase level in the bile and biliary amylase output between the two subgroups.

(D) Effects of chronic CCl₄-intoxication on biliary amylase output (Tables I, II, Fig. 3). Plasma transaminase level in the CCl₄-treated subgroup was significantly higher than that in the control subgroup (p<0.05). Amylase levels in both the plasma and the bile in the treated subgroup were significantly higher than those in the control subgroup (p<0.01). In the both subgroups, plasma amylase level was positively correlated with plasma transaminase level (p<0.01). On the other hand, bile flow tended to decrease and biliary amylase output tended to increase in the treated subgroup as compared to the control subgroup. However, these difference were not statistically significant. Urinary amylase output in the CCl₄-subgroup was significantly smaller than in the control subgroup (p<0.01), although no
significant difference was found in urine volume.

These evidences in the CCl₄-treated subgroup suggested that biliary amylase level was elevated secondarily to the high plasma amylase level which was probably due to the decrease in urinary output. The increase in biliary amylase output, which was most probably due to the decrease in bile flow, revealed no statistically significant difference from that in the control subgroup.

**Summary.** Effects of hyperamylasemia *in vivo* on biliary amylase output were examined with special attention to the interrelation among bile flow, plasma amylase level and biliary amylase. Experimental hyperamylasemia was produced by pancreatic duct obstruction and by CCl₄-intoxication.

Amylase level in the bile was elevated with a positive correlation to plasma amylase level in rats with pancreatic duct obstruction or chronic CCl₄-intoxication. Biliary amylase output was increased with a positive correlation to amylase level in the bile in untreated rats and in rats with pancreatic duct obstruction. However, in rats with chronic CCl₄-intoxication, no significant increase in biliary amylase output was found, although amylase level was significantly elevated both in the bile and in the blood plasma.

Amylase level in the bile was elevated by chronic CCl₄-intoxication, and it had a positive correlation with plasma levels of transaminase. A significant decrease in urinary excretion of amylase was also observed in rats with chronic CCl₄-intoxication.

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**References**