Studies in obstructive jaundice

W. B. CONOLLY, F. O. BELZER, AND J. E. DUNPHY

From the Departments of Surgery, University of California School of Medicine, and San Francisco General Hospital, San Francisco, California

SUMMARY Acute obstruction of the extrahepatic ducts causes gross proximal duct dilatation, and elevated levels of ornithine carbamyl transferase, bilirubin, and alkaline phosphatase.

Slow progressive obstruction causes variable proximal duct dilatation and in these cases bilirubin, alkaline phosphatase, and ornithine carbamyl transferase return to normal, despite the presence of severe though incomplete obstruction of the common duct and microscopic findings of biliary cirrhosis. In the early phases, ornithine carbamyl transferase is a slightly more sensitive indicator of biliary obstruction than alkaline phosphatase or bilirubin, but the values still return to normal in the face of a persistent stricture.

If a patient who has previously had common duct surgery develops recurrent episodes of fever which suggest cholangitis, it should be assumed that he has a recurrent stricture, even though a cholangiogram and liver function may be normal or only slightly altered. A delay until the liver function studies show consistently raised levels may result in severe biliary cirrhosis and decreased hepatic reserve.

Stricture of the extrahepatic ducts can be difficult to diagnose because the patient may feel well, and the liver enzymes may be normal or only slightly elevated. Delaying operation, however, until the bilirubin and alkaline phosphatase levels are consistently elevated may result in a cirrhotic liver and diminished hepatic reserve.

Ornithine carbamyl transferase is an enzyme found predominantly in the mammalian liver. Reichard (1957) described a method for its estimation and determined its activity in the serum of 695 patients (1962). Jonson and Reichard (1963) compared ornithine carbamyl transferase, alkaline phosphatase, and bilirubin in acute extrahepatic biliary obstruction of dogs and concluded that ornithine carbamyl transferase activity was a more sensitive index of biliary obstruction than that of alkaline phosphatase or bilirubin. Their study consisted of 10-hour experiments.

This study compares ornithine carbamyl transferase values with bilirubin and alkaline phosphatase in extrahepatic obstruction of the biliary tract over a three-month period, and relates them to cholangiograms and liver biopsies.

MATERIALS AND METHODS

Obstructive jaundice was produced in eight 20-kg goats by placing an ameroid constrictor (3.5 mm, internal diameter) around the hepatic or common bile ducts. Venous blood samples were taken from the jugular vein before operation, and three times weekly until the goats became jaundiced. The blood was tested in each sample for bilirubin, alkaline phosphatase, and ornithine carbamyl transferase. Liver biopsies were taken before placing the constrictors during postoperative cholangiography. The goats were divided into three groups. Group 1 (one goat) had bilirubin, alkaline phosphatase, and ornithine carbamyl transferase tests three times a week for five weeks for control studies. Group 2 (four goats, nos. 2, 3, 4, and 5) had water-sterilized ameroid constrictors placed around the common bile duct to produce rapid obstruction. In group 3 (four goats, nos. 6, 7, 8, and 9), slow obstruction was produced by placing an oil-sterilized ameroid constrictor around the common or hepatic ducts.

If the goats became severely jaundiced they were killed and cholangiograms and liver biopsies were performed. In goats without jaundice, re-exploration was performed after eight weeks and cholangiograms and liver biopsies were obtained.

RESULTS

GROUP 1 (CONTROL) The values for bilirubin were consistently less than 0.1 mg/100 ml, alkaline phosphatase ranged between 2 and 4 Bodansky units/100 ml, and ornithine carbamyl transferase between 0.1 and 0.25 Reichard units/100 ml (Fig. 1a).
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**FIG. 1.** Enzyme and bilirubin values: (a) normal goat (group 1); (b) acute obstructive jaundice (group 2); (c) chronic obstructive jaundice (group 3).

**FIG. 1a.**

**FIG. 1b.**

**FIG. 1c.**
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FIG. 2. Liver biopsy one week after acute ameroid constriction of common bile duct. Note cholestasis and cholangitis.

GROUP 2 (RAPID OBSTRUCTION) Jaundice occurred within 10 to 14 days. The bilirubin and the ornithine carbamyl transferase became progressively elevated. The elevation of alkaline phosphatase was slower and showed moderate variation at times (Fig. 1b). Liver biopsies showed substantial dilatation of the intrahepatic ducts and microscopic studies showed cholestasis and cholangitis (Fig. 2).

GROUP 3 (SLOW OBSTRUCTION) These four animals were studied for three months. The bilirubin, alkaline phosphatase, and ornithine carbamyl transferase levels were raised in the early postoperative period (Fig. 1c). They then slowly returned to normal levels, but rose again after cholangiography. Normal enzymes were formed in spite of constricted extrahepatic ducts, and biliary stasis was seen on microscopic examination (Fig. 3). Intrahepatic duct dilatation appeared to be directly related to the rapidity and degree of obstruction.

DISCUSSION

Jonson and Reichard (1963) showed that partial obstruction of the common bile duct resulted in increased ornithine carbamyl transferase levels at lower biliary pressures than were required to elevate the bilirubin or alkaline phosphatase. They concluded that ornithine carbamyl transferase activity appeared to be a more sensitive index of incomplete biliary obstruction than either alkaline phosphatase or bilirubin. In our studies, however, we were unable to show any advantage in the ornithine carbamyl transferase determinations over the routine bilirubin and alkaline phosphatase values. In acute obstruction the ornithine carbamyl transferase increased consistently as did the bilirubin. The rise in alkaline phosphatase was sometimes minimal and delayed. The ornithine carbamyl transferase appeared to have little value in these situations of rapid and complete obstruction; the bilirubin is reliable and far easier to estimate. In slow, progressive obstruction, the ornithine carbamyl transferase showed a progressive rise, but it did not appear to be a more sensitive index than the bilirubin.
Fig. 3. Liver biopsy following three months of chronic ameroid constriction of the common bile duct. Note periportal cholangitis.

Fig. 4. Cholangiogram of goat no. 9 (following three months of chronic ameroid constriction). A clamp was necessary to force dye proximal to the constrictor.
thine carbamyl transferase increased to abnormal levels about three days before the bilirubin or alkaline phosphatase rose but returned to normal in about five weeks. However, it remained normal despite severe, though incomplete, obstruction of the extrahepatic duct.

It is commonly assumed that dilatation occurs proximal to bile duct constriction, either by stricture, neoplasms, stones, or oedema from severe pancreatitis. Radiographs taken during these experiments showed that dilatation occurred only when a constriction was complete enough to prevent free flow of bile. The common bile duct of goat no. 9 (Fig. 4) was constricted from 4 mm to 0.5 mm without proximal dilatation. Dye, however, did not cross the obstruction at the time of cholangiography, until the distal common biliary duct was occluded but microscopic examination of this liver showed changes of early biliary cirrhosis. The pathological sequelae of extrahepatic duct obstruction are cholestasis, cholangitis, portal cirrhosis, and biliary cirrhosis. Early changes can be seen in the liver, even in the presence of normal enzymes, and cholangiographic evidence of ducts of normal size.

REFERENCES

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