Weight loss in primary biliary cirrhosis

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SUMMARY Duodenal bile salt concentrations were measured throughout one day in six patients with primary biliary cirrhosis while they were eating a normal ward diet. Five of them had lost weight; none had ascites. Each patient had a radiologically normal small bowel and a normal jejunal biopsy. No clear relationship between high faecal fat excretion and abnormally low duodenal bile salt concentration was found. Xylose absorption was abnormal in five patients. If weight loss in primary biliary cirrhosis is due to malabsorption, factors other than a reduced small intestinal bile salt concentration must be important.

Weight loss in chronic liver disease, including primary biliary cirrhosis, is often attributed to malabsorption, which is presumed to be due to a failure to achieve adequate bile salt concentrations in the small intestine. Van Berge Henegouwen and colleagues showed that duodenal bile salt concentrations were diminished in primary biliary cirrhosis but were still significantly above the critical micellar concentration. In this study, cholecystokinin was used to stimulate the gallbladder and this procedure may not have produced duodenal bile salt concentrations similar to those which would be present in response to a normal diet. Westergaard used a standardised fatty meal as a stimulus to gallbladder contraction in patients with chronic liver disease and found that critical micellar concentrations of bile salts were not exceeded.

The purpose of this study was to further examine the proposal that malabsorption in primary biliary cirrhosis is due to inadequate duodenal bile salt concentrations. The duodenal bile salt concentrations were measured after ingestion of the normal hospital diet. The intestinal absorption of xylose was also studied.

Methods

Patients Six patients (five female and one male) with primary biliary cirrhosis were studied. Five had lost weight. Diagnosis was based on clinical features, biochemical cholestasis (Table 1), positive serum antimitochondrial antibody tests, and liver biopsy appearances compatible with primary biliary cirrhosis.

Each patient had a radiologically normal small bowel, a normal jejunal biopsy, and a normal creatinine clearance. Schilling tests were performed on five of the patients and were normal in four of these. In one, patient A, the urinary excretion of vitamin B₁₂ was only 2.7% of the administered dose. The peripheral blood film was normal.

Procedure Jejunal and liver biopsies were performed on all patients before admission to hospital. All patients had taken oral cholestyramine before the study and this was discontinued seven days before admission.

On the day of admission, patients were started on a diet containing at least 70 g of fat per day, and a five day collection of faeces was begun. Blood was taken for estimation of plasma bilirubin, alkaline phosphatase (EC 3.1.3.1.), alanine aminotransferase (EC 2.1.6.1.), albumin, and creatinine. These measurements were carried out on a Technicon Sequential Multiple Analysis with Computer System (Technicon Instruments Company Ltd., Basingstoke, UK).

In the afternoon of the next day a single lumen tube was passed into the duodenum and its position checked by x-ray screening. Patients were fasted from 2200 h.

At 0800 h on the next morning and every hour thereafter for approximately 14 hours, duodenal aspirate (2 ml) was withdrawn for bile salt analysis. Patients ate the diet described above in the form of meals taken at recorded times. A 24 hour urine collection was carried out for creatinine clearance studies.
The urinary excretion of xylose over five hours was measured after an oral dose of xylose (5 g) on the fifth day.\(^5\) The faecal fat collection was concluded.

**Duodenal Bile Salt Concentrations**

Duodenal bile salt concentrations were measured by thin-layer chromatography followed by densitometry.\(^6\) This method separates the taurine and glycine conjugates of the dihydroxy and trihydroxy bile acids but does not differentiate conjugated chenodeoxycholate from conjugated deoxycholate.

**Results**

**Duodenal Bile Salts**

In four patients duodenal bile salt concentrations were below the lower limit of the reference range of 5-4 mmol/l\(^4\) but three of these never exceeded 1 mmol/l at any time during the day. Of the remaining two patients one achieved a maximal concentration of only 5-5 mmol/l (Figure).

**Faecal Fat and Xylose Tests**

The faecal fat excretion was increased in five of the six patients, although in one (E) it was only marginally increased. The faecal fat excretion was normal in the one patient (D) who had not lost weight (Table 2).

There was no correlation between faecal fat excretion and duodenal bile salt concentrations. Two patients had normal duodenal bile salt concentrations and increased faecal fat excretions, and one patient had low duodenal bile salt concentrations and a normal faecal fat excretion. Xylose excretion was diminished in five patients.

**Discussion**

The formation of mixed micelles by conjugated bile salts, monoglycerides, and fatty acids is generally considered an essential step in the efficient absorption of dietary fat. The amount of lipid solubilised in micelles is proportional to the conjugated bile salt concentration, and this obtains even when the critical micellar concentration has been exceeded; the amount of fat which can be solubilised increases by 40% as the concentration of bile salt rises from 4 mmol/l to 6 mmol/l.\(^7\)\(^8\) It would therefore be reasonable to attribute the steatorrhoea commonly found in cirrhosis to inadequate duodenal bile salt concentrations, as bile salt synthesis is impaired and the bile salt pool size is reduced.\(^9\) In addition, there is a particular failure of bile flow in primary biliary cirrhosis...

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**Table 1  Liver function tests in patients with primary biliary cirrhosis**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Bilirubin (µmol/l)</th>
<th>AP (IU/l)</th>
<th>ALT (IU/l)</th>
<th>Albumin (g/l)</th>
<th>Cholecystogram</th>
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<tr>
<td></td>
<td></td>
<td>Presentation</td>
<td>During study</td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td>55</td>
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<td>1910</td>
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</tr>
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<td>78</td>
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<tr>
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<td>55</td>
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</tr>
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<td>61</td>
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</tr>
</tbody>
</table>

The table shows plasma concentrations of bilirubin, alkaline phosphatase (AP), alanine aminotransferase (ALT), and albumin in six patients with primary biliary cirrhosis. The reference ranges are bilirubin 2-17 µmol/l, AP 40-100 IU/l, ALT 10-40 IU/l, and albumin 36-47 g/l.
candidaemia may explain the steatorrhoea observed in primary biliary cirrhosis, two of our patients (A and F) had a normal duodenal bile salt concentration and yet both of them had abnormal faecal fat excretion. Abnormal faecal fat excretion was also found in two of the remaining patients (B and C) and in these cases there were low duodenal bile salt concentrations. Our investigations indicate therefore that in patients with primary biliary cirrhosis accompanied by weight loss there is abnormal faecal fat excretion but the theory that this is solely attributable to a failure of lipid solubilisation by duodenal bile salts has not been confirmed.

Xylose absorption tests were performed in our patients and in five cases the absorption of this pentose was abnormal. In four of these the faecal fat excretion was also abnormal. A possible renal explanation for the abnormal xylose tests was apparently excluded by the observation that creatinine clearance was normal in each case. Ascites or massive bacterial overgrowth in the proximal small intestine are also recognised causes of abnormal xylose tests. None of our patients had clinically recognisable ascites and the radiological appearances of the small intestine failed to reveal features associated with bacterial overgrowth: none of our patients received antibiotic therapy as a confirmatory test to rule out bacterial overgrowth in a definitive manner. Each of our patients had a histologically normal jejunal biopsy and an albeit uncommon association between normal biopsy appearances and abnormal xylose absorption has been previously reported, but not in patients with biliary cirrhosis. Xylose absorption is generally found to be normal in most cases of liver disease associated with hyperbilirubinaemia but studies in primary biliary cirrhosis do not appear to have been reported previously. The mechanism of the abnormal xylose absorption is not clear but it may be an important contributing factor to weight loss in primary biliary cirrhosis.

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References


