Alcohol and absorption from the small intestine

1. Impairment of absorption from the small intestine in alcoholics


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SUMMARY An absorption screen was performed in 10 chronic alcoholic patients within a few days of admission due to an acute alcoholic episode. Impaired absorption of d-Xylose was noted in three patients and low leucocyte ascorbic acid and serum folate levels in five. No abnormality was detected in jejunal histology. The absorption of water and electrolytes from the jejunum was studied in these patients using a triple-lumen tube perfusion system. The mean rate of absorption of water in the alcoholic subjects (50-0 ± 2.3 ml/h) was significantly lower (p < 0.001) than the mean value in 14 healthy control subjects (205 ± 15.9 ml/h). A significant reduction in Na⁺ and Cl⁻ absorption was also demonstrated in the alcoholic subjects. These results indicate that patients with acute-on-chronic alcoholism may have a functional impairment of water and electrolyte absorption from the jejunum. This may, in part, account for some of the nutritional deficiencies in such patients and for symptoms such as diarrhoea which may be present.

Several abnormalities of intestinal absorption have been observed in chronic alcoholic subjects. Separate studies by various groups have shown impaired absorption of thiamine (Tomasulo et al., 1968; Thomson et al., 1970), vitamin B₁₂ (Lindenbaum and Lieber, 1969), and folic acid (Halsted et al., 1967; Halsted et al., 1971) and low blood levels of ascorbic acid (O'Keane et al., 1972). In some individuals, impaired absorption of d-Xylose (Small et al., 1959) and dietary fats (Mezey et al., 1970) has been demonstrated, and impaired absorption of amino acids in rats has also been noted (Israel et al., 1968). It has been suggested that subclinical protein malnutrition is one of the underlying causes of malabsorption in chronic alcoholics (Mezey et al., 1970). However, alcohol may well exert a direct toxic effect, since recent studies by Halsted et al. (1973a) showed that, even in moderate drinkers, significant concentrations of ethanol are present in the small intestine after recent ingestion.

Absorption of electrolytes from the intestinal lumen to blood involves, predominantly, the process of active transport. Energy for cellular metabolism derives from the splitting of the high energy phosphate bond of adenosine triphosphate (ATP) by the enzyme adenosine triphosphatase (ATPase). (Brooks, 1973). Ethanol has been shown to affect the ATP content in several tissues and it also inhibits the active transport of Na⁺ and K⁺ and the (Na⁺ and K⁺) activated ATPase (Israel et al., 1965; Israel et al., 1969). It seems possible, therefore, that intestinal dysfunction in alcoholics may result, at least in part, from a direct enterotoxic effect of ethanol.

The purpose of the present study was to attempt to define the abnormalities of intestinal absorption which may occur in chronic alcoholic subjects.

Methods

Ten patients conforming to the World Health Organisation definition of chronic alcoholism (1952) agreed to be investigated. Two main groups of tests were carried out. First, a series of standard screening tests were performed. Haemoglobin, serum iron, serum folic acid, and vitamin B₁₂ were measured. Biochemical analysis included serum calcium and phosphate levels, liver function tests (including serum proteins), leucocyte ascorbic acid (Denson and Bowers, 1961), d-Xylose absorption, and faecal fat estimations in some subjects. In addition, a jejunal biopsy was performed as well as a barium
meal and follow-through examination, and pancreatic function tests. The latter included one or a combination of a pancreatic scan using $^{75}$Se selenomethionine measurement of radioselenium in the duodenal aspirate (Youngs et al., 1971), and measurement of tryptic activities after stimulation with a Lundh test meal (Lundh, 1962).

These tests were all performed in the first two to three days after admission to hospital. Secondly, studies of jejunal absorption were undertaken using a small intestinal perfusion system (Cooper et al., 1966; Russell et al., 1972). A triple lumen polyvinyl tube, weighted with a mercury bag, was swallowed by the patient and screened into position in the jejunum.

The test solution consisted of iso-osmotic glucose saline containing glucose in a concentration of 56 mM with phenol red and $^{51}$Chromium EDTA as water-soluble, non-absorbable markers. The solution was infused at a constant rate of 20 ml per minute and a period of 45 minutes was allowed for equilibration. Samples were collected 10 cm and 40 cm distal to the infusion point, and the absorption of water, sodium, and chloride was calculated over the 30 cm test segment. The perfusion was performed within seven days of admission to hospital. Each patient had been consuming large quantities of alcohol until the day of admission. Absorption studies were also performed in 14 healthy volunteers, matched for sex and age (within five years), who acted as a control group.

**Results**

**SCREENING TESTS FOR ABSORPTION**

Table 1 summarizes the results of the standard tests for intestinal absorption. Previous studies indicated that $18 \mu g/10^8$ WBC is the lower limit of normal for leucocyte ascorbic acid in our laboratory. Subnormal leucocyte ascorbic acid levels were found in five of the 10 subjects and a similar number also had low serum folate levels. D-Xylose absorption was impaired in one-third of those investigated. Of interest was the failure to demonstrate any abnormality on jejunal histology using light microscopy. Excluding elevated aspartate and alanine aminotransferase levels and elevated serum iron levels which do not *per se* represent abnormalities of absorption, only isolated abnormalities were noted in the remainder of the absorption tests.

**INTESTINAL PERFUSION STUDIES**

The results of the studies on intestinal perfusion are shown in Table 2. Water absorption is measured as millilitres per hour per 30 cm test segment. Each figure represents the mean of five or six readings from collections over 10 minute periods. Taking the alcoholic and control groups as a whole, it was found that statistically significant reduction of water, Na$^+$, and Cl$^-$ was present in the alcoholic groups ($p < 0.001$ for each index). In patient 4 a net secretion of water and electrolyte was demonstrated. This patient and one other (patient no. 8) had diarrhoea at the time of the study.

**Discussion**

The demonstration of impaired absorption of d-Xylose in chronic alcoholism corresponds to the findings of Small et al. (1959). Reduced blood levels of ascorbic acid and folic acid are also in agreement with previous studies (Halsted et al., 1967; Halsted et al., 1971; O'Keane et al., 1972). Folate deficiency

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**Table 1** Clinical and investigative data obtained in 10 chronic alcoholic subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Serum iron (80-150 $\mu g/\text{dl}$)</th>
<th>Serum folate (&gt;3 ng/ml)</th>
<th>AST (11-42 IU/l)</th>
<th>ALT (13-55 IU/l)</th>
<th>Ca++ (8-7 mg/100 ml)</th>
<th>PO$_4$(2-5 mg/100 ml)</th>
<th>Leucocyte ascorbic acid (&gt;18 $\mu g/10^8$ WBC)</th>
<th>D-Xylose absorption (&gt;5 g/25 g dose)</th>
<th>Faecal fats (&lt;5 g/day)</th>
<th>Pancreatic function</th>
<th>Jejunal biopsy</th>
<th>Barium meal and follow-through</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 38 M</td>
<td>82 2.7</td>
<td>260 49</td>
<td>37 10.0</td>
<td>29.3</td>
<td>1.0</td>
<td>Normal</td>
<td>NP</td>
<td>Normal</td>
<td>Dilated loop of duodenum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 37 M</td>
<td>175 3.5</td>
<td>100 62</td>
<td>22 9.0</td>
<td>15.1</td>
<td>6.5</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 58 M</td>
<td>150 8.0</td>
<td>300 84</td>
<td>44 9.8</td>
<td>9.4</td>
<td>7.9</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 62 M</td>
<td>170 1.3</td>
<td>900 60</td>
<td>84 10.3</td>
<td>6.8</td>
<td>6.7</td>
<td>Normal</td>
<td>NP</td>
<td>Normal</td>
<td>NP</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5 53 M</td>
<td>65 2.9</td>
<td>1000 58</td>
<td>20 9.8</td>
<td>8.6</td>
<td>6.3</td>
<td>NP</td>
<td>Normal</td>
<td>Normal</td>
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<td></td>
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</tr>
<tr>
<td>6 49 M</td>
<td>150 4.0</td>
<td>300 23</td>
<td>19 10.4</td>
<td>21.2</td>
<td>NP</td>
<td>NP</td>
<td>Normal</td>
<td>Normal</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>7 33 M</td>
<td>325 1.6</td>
<td>250 94</td>
<td>63 10.9</td>
<td>3.9</td>
<td>36.0</td>
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<td></td>
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<tr>
<td>8 32 M</td>
<td>152 3.1</td>
<td>203 74</td>
<td>101 9.0</td>
<td>15.9</td>
<td>11.5</td>
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<tr>
<td>9 44 F</td>
<td>50 10.0</td>
<td>540 26</td>
<td>28 9.3</td>
<td>25.6</td>
<td>3.4</td>
<td>NP</td>
<td>Acute pancreatitis</td>
<td>Normal</td>
<td>Duodenal ulcer</td>
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<tr>
<td>10 50 M</td>
<td>120 2.6</td>
<td>290 42</td>
<td>63 9.7</td>
<td>5.8</td>
<td>2.8</td>
<td>NP</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
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</tbody>
</table>

AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; NP = Not performed; Normal levels in parentheses.

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Alcohol and absorption from the small intestine

<table>
<thead>
<tr>
<th>Water (ml/h)</th>
<th>Na⁺ (mEq/h)</th>
<th>Cl⁻ (mEq/h)</th>
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<tbody>
<tr>
<td></td>
<td>Alcoholic</td>
<td>Control</td>
</tr>
<tr>
<td>1*</td>
<td>48</td>
<td>159</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>224</td>
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<tr>
<td>3</td>
<td>160</td>
<td>185</td>
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<td>4</td>
<td>75</td>
<td>238</td>
</tr>
<tr>
<td>5</td>
<td>81</td>
<td>200</td>
</tr>
<tr>
<td>6</td>
<td>18</td>
<td>158</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
<td>259</td>
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<tr>
<td>8</td>
<td>4</td>
<td>361</td>
</tr>
<tr>
<td>9</td>
<td>128</td>
<td>142</td>
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<tr>
<td>10</td>
<td>90</td>
<td>172</td>
</tr>
<tr>
<td></td>
<td>224</td>
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<td>243</td>
<td></td>
</tr>
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<td></td>
<td>154</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SEM
50·6 ± 21·3 205 ± 15·9 7·5 ± 2·9 23·1 ± 1·3 7·1 ± 2·4 23·1 ± 1·5

*Patient numbers.

Table 2 Mean absorption of water, sodium, and chloride from the jejunum in chronic alcoholics and control subjects

itself has been shown to contribute to the development of malabsorption in alcoholics and this can be reversed by the administration of folic acid (Halsted et al., 1973b). Several studies have indicated that intestinal malabsorption may occur in the presence of hepatic cirrhosis (Baraona et al., 1962; Sun et al., 1967; Losowsky and Walker, 1969; Marin et al., 1969). Abnormal aspartate or alanine aminotransferase values were observed in seven of the 10 subjects. Faecal fat estimations were undertaken in only three of the 10 subjects. The accuracy of faecal fat testing has been questioned (Blomstrand, 1955; Bouchier et al., 1963). In addition, it was found difficult and in some cases impossible to detain alcoholic subjects, whose cooperation is frequently limited, for the length of time necessary to obtain satisfactory five day stool collections; liver biopsies were not performed on these patients.

The technique of intestinal perfusion measures the net flux of water and electrolytes across the mucosa. The triple-lumen tube system, which incorporates a mixing segment has been studied and validated (Fordtran, 1966; Cooper et al., 1966; Whalen et al., 1966). Results from the present intestinal perfusion studies were more consistent in demonstrating intestinal dysfunction. Only one patient (no. 3) showed a rate of water, sodium, and chloride absorption within the range established in control subjects. Three patients exhibited normal Na⁺ absorption and two patients normal absorption of chloride. It would thus appear that absorption of water and electrolytes from the jejunum in chronic alcoholics is significantly reduced, although standard tests for absorption may show no evidence of, or only minor, disturbance in absorption. It is noteworthy, however, that the one patient with a net secretory state was also found to have one of the lowest levels of serum folate and leucocyte ascorbic acid in the study. Whether the results obtained in these studies can be considered a function of relatively recent acute alcohol ingestion or of chronic alcoholism is debatable, since it is difficult to assess the extent of jejunal mucosal damage or the rapidity with which the damage is repaired. Light microscopy failed to reveal abnormalities of mucosal histology in the patients examined, but Rubin et al. (1972) have demonstrated ultrastructural changes in the small intestine induced by ethanol.

A further clinical implication of impaired water absorption after acute ethanol ingestion relates to the observation that intoxication with alcohol is frequently associated with diarrhoea (Lindenbaum and Lieber, 1969). Impairment of water absorption from the jejunum may be partly responsible for the development of this symptom.

Intestinal disturbances, such as malabsorption and diarrhoea, associated with prolonged ethanol abuse are usually attributed to poor nutritional intake, both qualitative and quantitative. Inhibition of intestinal absorption of nutrients as a direct result of the acute effect of ethanol on the small bowel may play a significant role in the state of malnutrition so frequently encountered among alcoholics and heavy drinkers.

References
Alcohol and absorption from the small intestine. 1. Impairment of absorption from the small intestine in alcoholics.
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