Topics in Gastroenterology 12

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Preface

The Annual Postgraduate Course in Gastroenterology in Oxford is now in its twelfth year, and this volume represents the proceedings of the 1984 Course. As usual it provides a series of reviews on different aspects of gastroenterology and is designed to be of benefit for both the specialist and the non-specialist.

We are grateful to all our contributors and to Blackwell Scientific Publications Ltd. who ensure that publication is always within a year of the Course. We thank Mr Per Saugman and Mr John Robson for their unstinting support and, once again, the organization of the Course and the compilation of manuscripts is largely due to the untiring efforts of our Secretaries, Miss Diana Wilson and Mrs Zena Jennings.

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Chapter 1
Alcohol and the small intestine

A.D. THOMSON, P.R. RYLE, M.J. WORLD

The major function of the small intestine is the net absorption of nutrients at a rate sufficient to sustain energy and reparative needs. Chronic alcohol ingestion may render rates of absorption inadequate in two ways. Firstly, it can adversely affect a number of processes upon which the net rate of absorption is normally dependent including nutritional intake and the rate of digestion. Secondly, it can increase the metabolic requirements of the body so that normal rates of nutrient absorption may become inadequate.

The effect of alcohol on the gastrointestinal tract has been the subject of several recent reviews (Beck and Dinda, 1981; Langman and Bell, 1982; Lieber *et al.*, 1982; Thomson and Majumdar, 1981). This review will concentrate on the effects of alcohol on the small intestine in chronic alcoholic patients (Table 1.1).

Table 1.1. Mechanisms whereby chronic alcohol ingestion may render nutrient absorption inadequate

1. Reduction in the normal rate of nutrient absorption
   - (i) Nutritional intake inadequate in quantity and/or quality
   - (ii) Deficient digestion
   - (iii) Delayed gastric emptying
   - (iv) Structural small gut changes
   - (v) Functional small gut changes
   - (vi) Altered splanchnic circulation
   - (vii) Altered lymphatic drainage
2. Increased nutritional requirements secondary to metabolic changes.

Symptoms of gastrointestinal disease

When questioned in hospital, as many as 31% of female and 26% of male alcoholics had symptoms of anorexia, nausea, epigastric or less

well localized abdominal pain, flatulence and diarrhoea which resolved following abstention from alcohol (Morgan and Sherlock, 1977). Weight loss may occur in a third of chronic alcoholic patients. There is no good correlation between symptoms and impaired absorptive function (Roggin *et al.*, 1969)

Dietary history

Combustion data indicate that the energy content of alcohol is considerable (7.1 kcal/g) but the evidence suggests that alcohol provides no net contribution of energy to human metabolism. Therefore, alcohol-derived calories may be disregarded as an energy source. Thus, malnutrition is a common problem in alcoholics although the incidence of this may vary from one group of alcoholics to another. The diets of these patients can be deficient in quality and quantity (Hillman, 1974).

Body weight

Weight changes are commonly seen. In one study, a mean weight loss of 4.1 kg was observed in 8 poorly nourished alcoholics who had consumed at least 1420 kcal (200 g) ethanol daily for at least 3 weeks before admission to hospital while an average weight gain of 3.2 kg was recorded after 2 weeks of abstinence from alcohol and provision of a nutritious diet (Halstead *et al.*, 1971). The question which then arises is whether it was the abstinence from alcohol or provision of the diet that caused the weight gain. Evidence from another study indicates that it was the diet, for when 56 alcoholic patients were admitted to hospital and all were given a normal diet (2600 kcal), no additional weight gain was observed in the 17 of these patients who received a further 1800 kcal (256 gm) as alcohol compared with the other 39 patients who remained abstinent (Mezey and Faillace, 1971).

In a recent study 50 chronic alcoholics with alcohol-related liver disease were observed over a period of 6 months (World *et al.*, 1984). Seven of these patients had compensated cirrhosis but none had persistent or recurrent cholestasis or diarrhoea. On admission to the study, there was no difference between the body weights of these patients and those of the normal population. By the end of 6 months, no statistically significant change in the mean weight of the whole group occurred,

although the patients claimed to have reduced their alcohol consumption. Nevertheless, patients who really did abstain (as suggested by improving laboratory results) gained weight. There was a significant inverse correlation between the change in mean corpuscular volume (MCV) and the change in body weight over the 6 month period. A fall in body weight was the best indicator of continuing alcohol abuse over this period. Direct correlations were also found between changes in MCV and changes in serum alkaline phosphatase, total bilirubin, aspartate aminotransferase, γ-glutamyl transpeptidase, total triglycerides and high density lipoprotein concentrations. Similarly, a significant inverse correlation was noted between the change in MCV and the change in serum albumin concentration.

Pirola and Lieber (1972) showed that when the proportion of total calories taken as alcohol by 11 normal subjects was gradually increased to 50%, weight loss occurred (Fig. 1.1). Furthermore, in one subject, the addition of 2000 kcal daily as alcohol to the diet caused no consistent change in body weight whereas the addition of 2000 kcals as chocolate resulted in a consistent gain in body weight. During another controlled metabolic study of 6 healthy adult men, it was noted that weight loss was confined to periods when alcohol accounted for 25% of total calorie intake (McDonald and Margen, 1976).

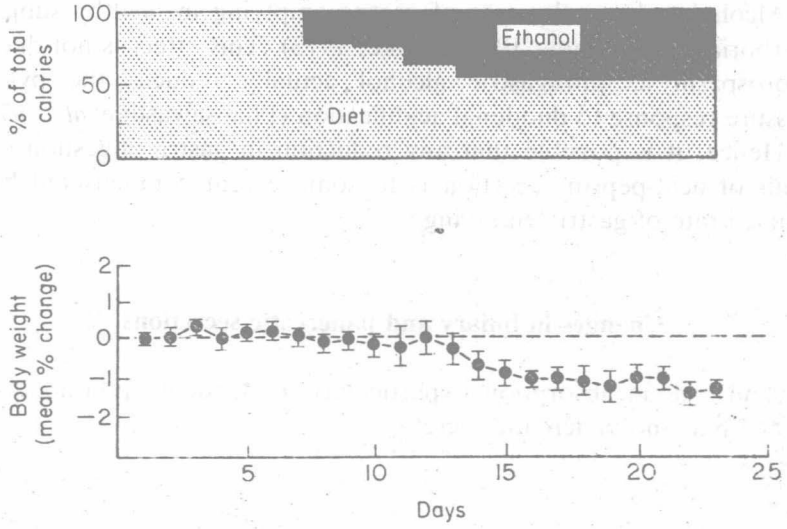

Fig. 1.1. Body weight changes after isocaloric substitution of carbohydrate (50% of total calories) by ethanol in 11 subjects (means ± standard errors). The dotted line represents the mean change in weight in the control period.

The weight loss is largely due to loss of adipose tissue and to generalized muscle wasting. Triceps skin-fold thickness is significantly reduced in malnourished alcoholics and there is a reduced muscle mass as assessed by creatinine: height ratio and arm muscle circumference (Morgan, 1981; Simko *et al.*, 1982).

Maldigestion

Salivary glands

Maldigestion from this source is unlikely as the rate of parotid secretion in response to citric acid stimulation in patients with alcoholic cirrhosis tends to be increased when compared with normal subjects whereas that of alcoholics without cirrhosis shows no change (Durr *et al.*, 1975).

Stomach

In chronic alcoholics without hepatic or pancreatic disease both the mean basal and maximal gastric acid outputs were significantly less than age and sex-matched controls (Chey *et al.*, 1968). Similar findings were obtained in patients with alcoholic cirrhosis (Ostrow *et al.*, 1960; Scobie and Summerskill, 1964).

Alcohol reduces the rate of gastric emptying in healthy subjects (Barboriak and Meade, 1970; Cooke, 1972). This effect is not due to pylorospasm as intragastric alcohol actually reduces the pyloric pressure response to duodenal acidification (Phaosawasdi *et al.*, 1979).

Hence, it is possible that any reduction in gastric digestion as a result of acid-pepsin secretion is to some extent compensated by a reduced rate of gastric emptying.

Changes in biliary and pancreatic secretions

Fat and protein absorption is particularly dependent upon adequate flow of bile and pancreatic secretions.

Bile

Chronic ethanol feeding stimulates bile flow and bile salt secretions in rats (Boyer, 1972; Maddrey and Boyer, 1973). An increased flow of

bile from choledochostomy tubes has been observed in patients with alcoholic cirrhosis who have undergone biliary tract surgery (Lenthall *et al.*, 1970). Therefore it is unlikely that malabsorption is due to inadequate bile flow in alcoholics.

Pancreatic secretion

Mezey and Halsted (1979) have reviewed the recent evidence which suggests that impaired pancreatic function may be much more common than previously supposed in chronic alcoholics who have recently been drinking heavily and who have been taking impoverished diets that are particularly poor in protein. Forty-four per cent of such patients have subnormal responses to intravenous secretin. Restoration of a normal protein content in the diet while drinking continued resulted in a return to normal pancreatic function and a reduction in faecal fat excretion (Mezey *et al.*, 1970). Hence, reduced pancreatic function is probably an important cause of maldigestion and malabsorption, particularly that of lipids, but a poor protein content of the diet appears to be more important than heavy alcohol consumption.

Changes in the small intestine

Whereas a number of structural and functional changes have been found in the small intestine of chronic alcoholics, it is difficult to ascribe all of these to alcohol abuse alone in patients who may be malnourished with multiple vitamin and mineral deficiencies. For example, in folate deficiency accompanying alcoholism, subtotal villous atrophy with decreased crypt mitoses has been described (Hermos *et al.*, 1972). Similar abnormalities can occur in the severe protein malnutrition of Kwashiorkor where calorie intake, as carbohydrate, may be adequate. In both these situations, impaired intestinal absorption of several substances has been described (Green and Tall, 1979).

Structural changes

Following the acute ingestion of 0.8 g/kg of alcohol as whisky in an alcoholic patient (approximately 3 double whiskies in a 70 kg man), the concentrations of alcohol in jejunal juice are high (Halsted *et al.*, 1973a) (Fig. 1.2). Similar concentrations produce haemorrhagic erosions of

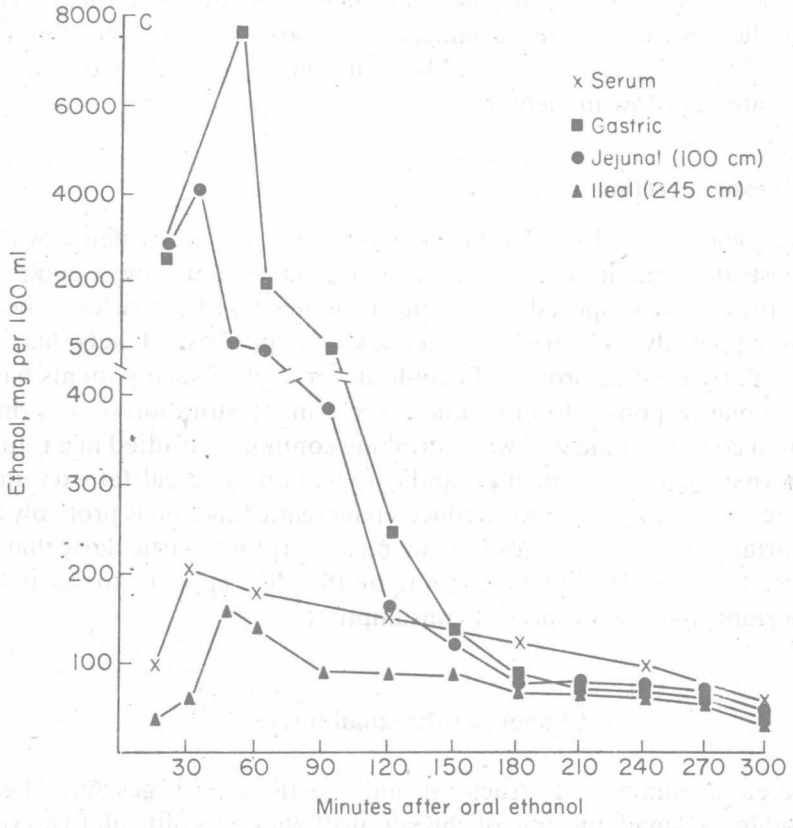

Fig. 1.2. Concentrations of ethanol in the serum, gastric, proximal jejunal and ileal contents of an alcoholic patient at timed intervals after the acute oral ingestion of ethanol, 0.8 g/kg body weight. (Numbers in parentheses refer to distance from the teeth to each aspiration port).

the tips of jejunal villi of rats in a dose-dependent fashion after 10 minutes, with resolution after 4 to 16 hours (Baraona *et al.*, 1974; Krawitt, 1974). Similar changes with a similar time course have been described following the acute ingestion of alcohol by normal human subjects (Millan *et al.*, 1980) and chronic alcoholics (Gottfried *et al.*, 1976). Such changes can be produced in rats by hyperosmolar damage with urea (Baraona *et al.*, 1974) or mannitol (Fox *et al.*, 1978b; Krawitt, 1974). As alcohol, at least in hamster jejunum, has no effective osmotic activity and the intestine is completely permeable to it, the morphological changes produced are more likely to be due to a direct toxic rather than an indirect hyperosmolar effect (Fox *et al.*, 1978a and b). In man,