Gastric secretion and basal gastrin concentration in bilharzial hepatic fibrosis

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SUMMARY Gastric secretion and fasting plasma gastrin levels were investigated in 26 patients with bilharzial hepatic fibrosis and 26 controls. The groups did not differ in their basal secretion. When stimulated by intravenous infusion of histamine the maximal acid output in patients with bilharzial hepatic fibrosis was significantly less than in the control group. This was unlikely to be a result of neutralisation by reflux of alkaline duodenal contents as the volumes of reflux were not different from control subjects, but was compatible with a true reduction in gastric secretion as assessed by two-component hypothesis. Neither the lowered gastric acidity nor the liver damage in patients with bilharzial hepatic fibrosis correlated with circulating gastrin. The fasting levels of plasma gastrin in these patients were not different from controls. As in other liver diseases the cause of diminished gastric secretion remains unclear.

Few clinical studies of gastric secretory function in hepatic disease have been reported and the results often appear inconsistent. Studies of gastric secretion in cirrhosis have revealed either a normal (Tabaqchali and Dawson, 1964) or a decreased response to histamine or pentagastrin (Ostrow et al., 1960; Scobie and Summerskill, 1964; Schmidt and Martini, 1969; Lam, 1976).

Bilharzial hepatic fibrosis differs from other types of cirrhosis not only in many well-known clinical features (Reboucas, 1975) but also in the fact that the histological changes are more marked in the periportal tissues, while the normal architecture of the liver parenchyma is maintained. Other than studies in Egypt (Hassab et al., 1972), there is scanty information in the world literature on gastric secretory function in this liver disease.

The purpose of the present investigation was therefore to compare gastric secretion in control individuals and in patients with bilharzial hepatic fibrosis. Moreover, in view of the conflicting results of serum gastrin levels in patients with liver disease (Mazzacca et al., 1974; Pointner, 1975; Lam, 1976; Lauristen et al., 1976), gastrin levels were compared in both groups.

METHODS

SUBJECTS Gastric secretion was studied in 26 male patients, aged 12 to 65 years (mean 33 years), with bilharzial hepatic fibrosis diagnosed by histological examination of hepatic tissue obtained at laparotomy. They all gave a history of gastrointestinal bleeding, and oesophageal varices were demonstrated either by x-ray examination or oesophagoscopy.

The control group consisted of 26 males, whose ages ranged from 15 to 58 years (mean 30 years) and who had had no gastrointestinal symptoms.

The patients’ and controls’ heights were recorded. After an overnight fast, a No. 14 French gauge nasogastric tube was swallowed and its optimal position in the stomach confirmed by the water recovery test (Hassan and Hobsley, 1970). Gastric juice was collected in 15 minute samples under negative pressure aided by hand suction at regular intervals. At the end of a one-hour basal collection period, 0·04 mg kg−1 h−1 histamine acid phosphate and 50 mg mepyramine maleate (Anthisan) were infused at the rate of 5·2 ml/h using a Palmer slow infusion pump until a steady plateau lasting at least 90 minutes was achieved (Lawrie et al., 1964).

The volume of each sample was noted and the concentrations of hydrogen, sodium, potassium, and chloride ions were determined and expressed in mmol/l. The titratable acidity was determined by

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titation against 0.1 N NaOH to pH 7.0. Chloride concentration was determined by an EEL chloride meter (Evans Electroselectum Ltd.), while sodium and potassium concentrations were determined by an EEL flame photometer.

Hydrogen and sodium ion outputs were calculated as follows:

1. Basal output was obtained as the sum of the outputs in two 15 minute samples collected during the second half of the basal period (Faber and Hobsley, 1977) and then expressed as mmol/h.

2. Maximal plateau output was calculated throughout the accepted plateau period and then expressed as mmol/h. Potassium and chloride ion measurements were used in checking total anion-cation differences for consistency of electrolyte measurement.

The volume of duodenogastric reflux was calculated by the formula devised by Hobsley (1974) based on the sodium ion output in the gastric juice. The reflux-corrected volume could then be derived.

Blood samples were collected from all individuals before the start of the test. The specimens were collected in heparin bottles, centrifuged, and the plasma separated for gastrin measurement by radioimmunoassay following the method described by Russell et al. (1977), the concentrations being expressed as pg/ml.

As the data were not normally distributed non-parametric statistics were used. The Mann-Whitney form of the Wilcoxon rank sum test was used to assess significance of differences.

The significance of the results obtained in the two groups of subjects in terms of the two-component hypothesis of gastric secretion was assessed by plotting, for individual maximal plateau averages, the 15 minute hydrogen ion output against the volume secreted (Hobsley and Silen, 1970).

Results

The mean height of patients with bilharzial hepatic fibrosis (168.8 cm, SD 9.9 cm) was not different from the mean height of the control subjects (173 cm, SD 8.6 cm). There was no correlation between the heights and gastric secretion in either group.

In all measured respects, the basal secretion in patients did not differ from that in controls. However, on maximal stimulation the volume of gastric aspirate in patients with bilharzial hepatic fibrosis was significantly less than in controls (p < 0.02). The volumes of duodenogastric reflux in the two groups were nearly the same; therefore the volumes of gastric secretion after correcting for reflux remained significantly less (p < 0.01) in patients with bilharzial hepatic fibrosis (Fig. 1). The maximal acid output was significantly reduced in patients with bilharzial hepatic fibrosis when compared with normal subjects (p < 0.005) (Fig. 2).

The electrolyte concentrations during maximal stimulation are shown in Fig. 3. The concentrations of potassium and chloride ions in the gastric juice did not differ between the two groups of subjects. However, the hydrogen ion concentration was lower and the sodium ion concentration higher in patients with bilharzial hepatic fibrosis than in the controls.

There were no differences in fasting plasma gastrin concentrations between patients and control subjects (Fig. 4).

Figure 5 shows the plot of 15 minute outputs of hydrogen ion against 15 minute volumes of secretion in the individual subjects of the two groups. The regression line shown is not that of the present data.
but that found by Hobsley and Silen (1970) in their subjects in San Francisco. The distribution of the secretion data above and below the regression line did not differ from random, whether each group of subjects was considered separately or whether both groups were considered together.

**Discussion**

Basal secretion is variable and non-reproducible (Faber and Hobsley, 1977). It is therefore not surprising that our findings of no difference in basal secretion between controls and patients with hepatic fibrosis due to bilharzia is at variance with other reports in the literature (Scobie and Summerskill, 1964; Tabaqchali and Dawson, 1964).

Our findings of a reduction in maximally stimulated secretion with regard both to volume and to acid output in bilharzial hepatic fibrosis confirm the work of Hassab and colleagues (1972), who also found a reduction in peptic activity. This is similar to the reductions found in liver cirrhosis due to other causes (Ostrow et al., 1960; Scobie and Summerskill, 1964; Schmidt and Martini, 1969; Lam, 1976). While Ostrow et al. (1960) found a reduction in the volume and the hydrogen ion concentration, Scobie and Summerskill (1964) could demonstrate only a reduction in the volume of secretion.

Our results show during stimulated secretion a reduction in hydrogen ion concentration and volume that is consistent with the two component hypothesis of gastric secretion as modified by Makhlof et al. (1966) and Hobsley and Silen (1970). This is demonstrated in Fig. 5 where our results, plotted against the regression line of Hobsley and Silen (1970), clearly show that the electrolytes in gastric secretion follow much the same pattern in Khartoum as in San Francisco and are much the same in bilharzial patients as in controls. The slope of the regression line depends on the hydrogen ion concentrations of the acid component. The similarity of the slope of our data in Fig. 5 with that of Hobsley and Silen (1970) shows that the hydrogen ion concentration of the acid component is the same in subjects in Khartoum as in San Francisco. On the other hand the intercept of the regression line depends on the volume and concentration of the alkali in the apparent alkaline component. The distribution of the secretion data above and below the line in bilharzial patients did not differ from that of the controls, and this fact indicates that the intercepts for each group did not differ and that therefore the alkaline component was substantially the same in both groups. As the apparent alkaline component is the sum of the true component secreted by the stomach and the reflux from the duodenum, this finding of no change in the apparent alkaline component demonstrates that there is no greater reflux than in controls in the bilharzial group. This fact was illustrated mathematically by the reflux formula. Thus the high sodium concentration in bilharzial hepatic fibrosis is completely explicable in terms of a lower output of acid component in combination with an unchanged
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Fig. 3 Electrolyte concentrations during histamine stimulated period in controls and patients with bilharzial hepatic fibrosis.

Gastric hyposecretion in patients with cirrhosis has been attributed to parietal cell damage due to alcohol (Palmer, 1954), though the evidence is conflicting. The frequency of atrophic gastritis in alcoholics is similar to that found in matched control individuals according to Cox (1948), and Stadel et al. (1963). On the other hand, Krentz (1968) reported an increased incidence of atrophic gastritis in patients with chronic hepatitis and liver cirrhosis. None of our subjects in this study consumed alcohol, but nonetheless it may be worth considering the possibility of gastritis in patients with bilharzial hepatic fibrosis.

While Mazzacca et al. (1974), Lauristen et al. (1976) and Lam (1976) reported high serum gastrin levels in patients with liver cirrhosis, Pointner (1975) like ourselves could not find raised serum gastrin compared with normal subjects. This is interesting because, with decreased gastric acidity, the gastrin levels would be expected to rise, unless gastrin was degraded more rapidly or there was a diminished alkaline component.

Although we did not measure pyloric losses, other reported studies show that pyloric losses in control individuals and patients with liver cirrhosis are similar (Bendett et al., 1963; Scobie and Summerskill, 1964).

Maximal gastric secretion is related to body stature (Hobsley et al., 1975), therefore patients with bilharzial hepatic fibrosis should not be labelled as hyposecretors without considering their height. This is particularly so in view of the fact that hepatosplenic bilharziasis may present with variable degrees of dwarfism (Cheng et al., 1959). There was no correlation between the heights and maximal gastric secretion, but this was probably because, in the present series, pyloric losses had not been measured and taken into consideration (Hassan and Hobsley, 1971), and because our two groups were small in number. In any case, the heights of both groups were nearly the same, so stature was unlikely to be the cause of the difference in secretion.
response from the antral mucosa.

As far as the role of the liver in the catabolism of endogenous gastrin is concerned, studies (Temperley et al., 1971; Reeder et al., 1972; Dencker et al., 1973; Debas and Grossman, 1974) indicate that this is unlikely to be of any significance. A potential difficulty is that serum gastrin levels vary greatly from time to time and it may be necessary to obtain multiple samples in order to demonstrate hypergastrinaemia (Thompson et al., 1975).

It seems that the ability of the stomach to secrete water and hydrogen ions is diminished in bilharzial as well as in other forms of cirrhosis. The increased incidence of duodenal ulceration with liver disease (Schnitker and Hass, 1934; Ask-Upmark, 1940; Fainer and Halsted, 1955; Tabaqchali and Dawson, 1964), though disputed (Ratnoff and Patek, 1942; Doll, 1952; Sullivan et al., 1954), is therefore difficult to explain in terms of hypersecretion of acid or gastrin.

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