

Gastric acid secretion in typhoid fever

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Summary: Gastric acid secretion was studied in 20 patients with typhoid fever (Group A), ten patients with fever other than typhoid (Group B), and ten healthy adults of matched age and sex (Group C). Patients with typhoid showed reduced acid secretion at the time of fever and one week after subsidence of fever as compared to Group C. In uncomplicated patients (Group A₁), these values rose thereafter but in complicated patients (Group A₂) they remained low even 12 weeks after subsidence of fever. This suggests that these patients had pre-existing hypochlorhydria which predisposed them to a severe form of disease. There may be many factors playing a significant role in making typhoid patients more prone to develop complications but the importance of gastric acid levels has also to be considered.

Introduction

It has been suggested that gastric hypochlorhydria or achlorhydria increases both susceptibility as well as severity of bacterial and orally transmitted enteric infections.^{1,2} In patients with gastric resection, there is an increased occurrence of salmonellosis as compared to subjects with normal acid levels.³ Depressed gastric secretion has also been observed in patients of typhoid fever.⁴ It is, however, uncertain whether low acid levels are the cause or the result of enteric infection. To assess this relationship, a prospective study of gastric acid secretion in patients with typhoid fever was carried out.

Materials and methods

Three groups of subjects were studied. Group A consisted of 20 patients with blood culture proven infection with *Salmonella typhi*, group B of ten patients with fever due to infection other than typhoid fever, and group C of ten healthy subjects matched for age and sex with patients in groups A and B.

Patients in group A were divided into two subgroups on the basis of severity of infection. Group A₁ comprised 13 patients with typhoid fever without any associated complications. In group A₂

there were seven patients with complications – three with encephalopathy, one meningism, one high-grade fever with toxæmia and two relapsed cases. Patients with peripheral circulatory failure, intestinal bleeding or perforation were excluded from the study. Group B comprised four patients with malaria, two with pneumonitis, one with lung abscess, two with urinary tract infection and one with viral fever.

After an overnight fast, a nasogastric tube was passed in the stomach and its tip placed in the most dependent part as assessed by the water recovery test,⁵ and was fixed to the side of the face by means of adhesive tape. The overnight gastric contents were aspirated and discarded. Cotton pledgets were placed under the tongue to prevent contamination by saliva. Basal secretions were collected at intervals of 15 minutes for one hour and acid values were measured. An intramuscular injection of pentagastrin (6 µg/kg body weight) was given. The stimulated secretions were collected at 15 minute intervals for one hour. The acid output was measured by titrating 5 ml of gastric juice with freshly prepared N/10 sodium hydroxide solution. Phenolphthalein was used as an indicator.

Basal acid output (BAO) and maximal acid output (MAO) after pentagastrin were measured in group A, at the time of fever, and one week, 6 weeks and 12 weeks after subsidence of fever, respectively. In group B, BAO and MAO were measured at the time of fever and 4 weeks after subsidence of fever. Group C subjects were investigated only once. Results were evaluated statistically by Student's *t*-test.

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Results

Group A₁ consisted of 13 patients (ten male) with ages ranging from 16 to 40 years (mean 27 years). Group A₂ consisted of seven patients (six male) with ages ranging from 16 to 47 years (mean 27 years). Group B included ten patients (seven male) with ages ranging from 16 to 32 years (mean 25 years). Group C comprised ten subjects (eight male) with ages ranging from 16 to 36 years (mean 24 years).

In group A₁, BAO and MAO at the time of fever and one week after subsidence of fever, were significantly low ($P < 0.01$) as compared to Group C. However, these values rose thereafter and at 6 weeks and 12 weeks after subsidence of fever, were not significantly different from group C ($P > 0.01$) (Table I).

In group A₂, the values of BAO and MAO were significantly lower ($P < 0.01$) than group C at the time of fever and one week after subsidence of fever as well as at 6 weeks and 12 weeks after subsidence of fever. The values of BAO and MAO of group A₂ were also significantly lower than those of group A₁ at 6 weeks and 12 weeks after subsidence of fever ($P < 0.01$).

Acid levels in patients of group B showed no significant difference ($P > 0.1$) from group C either at the time of fever or at 4 weeks after subsidence of fever.

Discussion

In our study of patients with typhoid fever we have observed that both basal and maximal acid output were significantly low at the time of fever and one

week afterwards in both uncomplicated (A₁) and complicated (A₂) groups of patients when compared with a control group. Further, in group A₁ patients, BAO and MAO rose significantly after 6 weeks, while in group A₂ patients it remained depressed and did not show any significant rise even 12 weeks after subsidence of fever.

Apparently gastric acid levels in our patients had an important relationship with the severity of the disease process. Compared to our study, Bhalla *et al.*⁴ observed that both BAO and MAO were decreased during convalescence, in all patients with typhoid with or without complications. When the gastric acid study was repeated 2 months after fever, BAO and MAO returned to normal control levels in patients without complications but in patients with complications a significant rise in acid output over the convalescence values was observed which is contrary to our observations.

There can be two possible explanations for the depressed acid secretions observed in group A₂ patients even 12 weeks after an attack of typhoid. Firstly, the gastric acidity was suppressed more in patients with severe typhoid fever, which would possibly take more time to recover. The other explanation can be that these patients had pre-existing reduced acidity, with the result that they were unable to deal effectively with the ingested organisms. Moreover substances other than acid whose concentration may be decreased in hypochlorhydric gastric juice may affect the survival of salmonella. This seems to be the more likely explanation since no significant rise in acid levels even after 12 weeks of subsidence of fever was observed in patients of typhoid with complications (A₂). Some studies indicate that fever as such rather than the type of infective agent is responsible for

Table I Comparison of basal acid output (BAO) and maximal acid output (MAO) in groups A₁, A₂ and B with that of group C

Group		BAO (total acid) ($\mu\text{mol/s}$)	MAO (total acid) ($\mu\text{mol/s}$)
A ₁	At time of fever	0.75* \pm 0.10	3.94* \pm 0.86
	One week after fever	0.76* \pm 0.10	4.04* \pm 0.82
	6 weeks after fever	1.21 \pm 0.16	5.15 \pm 2.69
	12 weeks after fever	1.22 \pm 0.14	5.16 \pm 0.56
A ₂	At the time of fever	0.57* \pm 0.10	2.73* \pm 0.46
	One week after fever	0.58* \pm 0.13	2.80* \pm 0.54
	6 weeks after fever	0.58* \pm 0.13	3.13* \pm 0.06
	12 weeks after fever	0.58* \pm 0.11	2.76* \pm 0.55
B	At time of fever	1.15 \pm 0.07	5.27 \pm 0.72
	4 weeks after fever	1.15 \pm 0.16	5.13 \pm 0.59
C	Normal control	1.23 \pm 0.14	5.16 \pm 0.62

*Difference statistically significant when compared with group C ($P < 0.01$).

the decrease in gastric secretion.^{6,7} However, we did not find any decrease in gastric secretion in our group B patients with fever due to causes other than typhoid.

From our study it is evident that patients with decreased gastric acidity have a more severe form of salmonella infection. Hypochlorhydria has been observed in patients with cholera where fever is rare.⁸ Many parasitic infestations⁹⁻¹¹ in man cause a decrease in gastric acidity again substantiating the fact that it is the type of infection rather than fever itself which is important in affecting gastric acidity

levels. Since typhoid fever also occurs in patients with normal gastric acid levels, other factors such as buffering action of gastric acid, physical protection afforded to bacteria by food or quick emptying of bolus containing salmonella may nullify the protection given by gastric acid. It may be concluded that, although there may be many factors that play a significant role in making the patients more prone to complications in case of typhoid fever, our study tends to highlight the importance of hypochlorhydria or achlorhydria in this regard.

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