Beta-glucuronidase activity in gastric aspirate in gastric carcinoma

A Ramani, G N Kundaje, A R Agor, K Nalini

Departments of Medicine and Clinical Biochemistry, Kasturba Medical College, Manipal 576 119, Karnataka

Abstract

β-glucuronidase activity was measured in the resting gastric juice of 25 patients presenting with dyspepsia and 10 normal subjects. All patients were investigated by double-contrast barium meal, endoscopy and when appropriate by biopsy. Ten patients had chronic duodenal ulcer and 25 had biopsy proven carcinoma of the stomach. Twenty one (84%) patients with carcinoma had markedly elevated levels of β-glucuronidase whereas patients with chronic duodenal ulcer had normal values.

β-glucuronidase activity in gastric aspirate could be used as a biochemical marker for the diagnosis of carcinoma of the stomach and in differentiating malignant from benign gastric lesions.

Key words: β-glucuronidase, gastric aspirate, pH range, gastric carcinoma.

Introduction

Malignant transformation of cells is often accompanied by enzymatic changes which can be demonstrated histochemically and which may be useful markers of malignancy. β-glucuronidase is a hydrolytic, non-proteolytic enzyme found within intracytoplasmic sub-cellular particles called lysosomes, which are especially abundant in the mammalian liver, spleen, adrenal gland, breast and gastrointestinal mucosa.1,2 The optimum pH for activity of this enzyme in gastric aspirate is 4.0 to 5.5.3-5 Studies on various human body fluids have revealed elevated β-glucuronidase activity in association with neoplastic processes.6-8 Fishman and Anhalt3 reported a 200% to 300% elevation of β-glucuronidase activity in gastric cancer tissue as compared to normal gastric mucosa. The present study was conducted to estimate β-glucuronidase activity in gastric aspirate in gastric carcinoma.

Material and Methods

Thirty five patients presenting with dyspepsia and ten clinically normal, asymptomatic subjects were studied. All patients were investigated by double contrast barium meal and endoscopy and biopsy whenever indicated. Normal subjects were not investigated by these methods. Cimetidine (800 mg) was administered orally at 10 PM and resting fasting gastric juice was aspirated the next morning under sterile conditions and without salivary or biliary contamination. Its pH was noted using a pH meter. β-glucuronidase activity was estimated in the gastric aspirate using paranitrophenyl β-glucuronide as substrate.6 The results were expressed in units/litre.

Results

The values of β-glucuronidase in 25 patients with carcinoma of the stomach, 10 patients with chronic duodenal ulcer and 10 normal subjects are shown in the Table. Statistically significant (P<0.005) elevation in levels was found in patients with gastric carcinoma, when compared with those in patients with duodenal ulcer and normals.

Table: β-glucuronidase activity (expressed in units/litre) in gastric juice in different diagnostic subgroups.

<table>
<thead>
<tr>
<th>Group</th>
<th>No</th>
<th>Range</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>0.03 — 0.38</td>
<td>0.338 ± 0.173</td>
</tr>
<tr>
<td>Duodenal ulcer</td>
<td>10</td>
<td>0.05 — 1.62</td>
<td>0.543 ± 0.50</td>
</tr>
<tr>
<td>Carcinoma: stomach</td>
<td>25</td>
<td>0.11 — 9.8</td>
<td>1.28 ± 0.868*</td>
</tr>
</tbody>
</table>

*p<0.005 as compared to controls

The β-glucuronidase enzyme activity was below 0.70 units/litre in the gastric juice of normal subjects and patients with chronic duodenal ulcer. Twenty one (84%) patients with carcinoma had values higher than this level. Of four patients with carcinoma of the stomach, who had values below 0.70 units/litre, three had anaplastic carcinoma.

Discussion

Markedly elevated levels of β-glucuronidase were found in patients with gastric carcinoma: 21 (84%) of the 25 patients with gastric carcinoma had elevated levels. Other workers have reported elevated levels in 76% to 100% of these patients.3-5,7,8,10 No relationship between the size of the malignant lesion and the extent of elevation of β-glucuronidase levels was observed in these studies.3-5,8,10 Although it is known that the elevated enzyme activity is due to enzyme loss into the stomach, the underlying mechanism is not clear.3-5

A pH range of 4.0 to 5.5 is required for maximum activity of β-glucuronidase. The enzyme is unstable below pH 3.8 and the activity rapidly declines above pH 5.5.1,3,4,5 pH alteration of activity is irreversible in that restoration of pH to a more favourable range does not result in return of activity.3-4 In this study cimetidine was used orally to obtain the optimum pH for the enzyme activity in gastric secretion.

Raport represents: Dr Anup Bharatram, Ramani, Assistant Professor, Department of Medicine.

© 1987 Indian Society of Gastroenterology
In this study, four (16%) patients with carcinoma of the stomach (including 3 with anaplastic carcinoma) had normal enzyme activity. The possible explanations for this include: (a) inhibition of enzyme activity by bilirubin diglucuronide and bile acids; (b) bile acids especially deoxycholate and chenodeoxycholate at concentrations as low as 5 μmol/ml inhibit β-glucuronidase activity; (c) elevations of enzyme activity in anaplastic carcinoma of the stomach are lower than in adenocarcinoma; (d) inadequate neutralization of gastric juice, which may result in acid inactivation and peptic digestion of the enzyme; and (e) gastric protein secretory abnormality.

In conclusion, estimation of β-glucuronidase activity in resting gastric aspirate obtained without contamination and in the pH range of 4.0 to 5.5 may be of considerable value as a biochemical tool in the clinical diagnosis of gastric carcinoma.

References