Salivary secretion in duodenal ulcer disease

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SUMMARY Salivary response to stimulation with citric acid was higher in patients with duodenal ulcer disease than in patients with other diseases of the upper gastrointestinal tract. This increase was proportional to an increase of histamine-stimulated gastric acid secretion. In duodenal ulcer disease, the increase in parietal cell mass may therefore be associated with the growth of other exocrine organs such as the salivary glands.

The only consistent and persisting changes in duodenal ulcer disease, apart from the ulcer and its scar, are thought to be an enlargement of the parietal cell mass and an increase in gastric secretion (Grossman, 1960). In the present study it is shown that in ulcer patients the secretion rate of the salivary glands is increased in proportion to the rate of gastric acid secretion. It is suggested that duodenal ulcer disease is characterized by an enlargement of several exocrine glands, such as the parietal cell system, salivary glands, and pancreas while only the enlargement of one gland—the stomach—is related to ulcer symptoms.

Material and Methods

Patients
Seventy hospitalized male veterans who were scheduled for gastric analysis in 1969 and 1970 fulfilled the following criteria: (1) A barium meal had been interpreted independently by two examiners. (2) A disease of the upper gastrointestinal tract was the only major pathological finding at the time of study. Specifically excluded from this study were patients with complications of ulcer disease, such as bleeding and obstruction. (3) No gastric surgery had been performed except in three patients who had previously undergone simple suture for perforated duodenal ulcer. For at least one week before secretion tests the patients had not received anticholinergics and other drugs which might have a lasting effect on gastric or salivary secretion.

 Patients with duodenal ulcer disease, including four in whom ulcer was inactive at the time of admission, formed the duodenal ulcer group. All other patients formed the control group. In patients with gastric ulcer and gastric cancer diagnosis was confirmed by gastroscopy and/or surgery at a later date. Patients with gastrooesophageal reflux had heartburn, reflux of barium following a barium meal, and abnormal histology in an oesophageal biopsy.

In patients with functional disorders, at least two barium meals were performed. Small sliding hiatus hernias were seen in four patients. No abnormal findings were seen in five patients. In all nine patients, epigastric discomfort was nonspecific, and a cholecystogram, a barium enema, and oesophageal histology were normal.

Procedures
Tests were performed eight ± 1.3 days (mean ± SEM) after hospital admission in duodenal ulcer patients and eight ± 1.5 days after admission in control patients respectively. Salivary secretion tests were started at 8.00 am after a 12-hour fast and were followed by gastric secretion tests.

Salivary secretion
For mechanical stimulation the subject was asked to exercise the muscles of the cheek and tongue against the teeth and squeeze the saliva out before voiding it into a preweighed beaker. The process was continued for 10 minutes at the end of which the bottle was weighed again and salivary flow calculated by difference.

For chemical stimulation the subject emptied from the mouth all salivary remnants. At zero time,
0.3 ml of citric acid solution was delivered on the anterior surface of the tongue and tasted by rolling movements of the tongue. At the 30th second, 5 ml of distilled water was delivered rapidly below the tongue. Between the 45th and 60th seconds the patient forcefully emptied the contents of the mouth into a preweighed beaker. The test was performed three times at three to four minute intervals. Salivary flow was calculated by subtracting 5.3 g from the increase in beaker weight.

The response to chemical stimulation was obtained by subtracting from the observed flow rate due to chemical stimulation the flow rate due to mechanical stimulation.

Further details of collection techniques have been reported in previous studies (Blum and Makhlouf, 1971; Makhlouf and Blum, 1971).

**Gastric secretion**

A 14 Fr radiopaque nasogastric tube was positioned in the antrum under fluoroscopic control. During the test the patient was recumbent, usually on his left side. Fasting juice was aspirated manually with a syringe. For further collections, suction pulses of 40 to 45 mm Hg were applied by a modified Gomco intermittent suction apparatus. Every five minutes, patency of the tube was checked by injecting 5 ml of air. Basal secretion was collected for 60 minutes. At the 30th minute, 20 mg of Benadryl (Parke Davis & Co) was injected into the deltoid muscle. At the 60th minute, histamine phosphate (Lilly) was injected subcutaneously at a dose of 40 μg/kg body weight. Stimulated secretion was collected for 60 minutes. During the entire test cotton rolls were inserted into the sulci of the cheeks and under the tongue in order to prevent contamination of gastric juice by saliva. In each 15-minute sample acidity was measured by titration with 0.1 N NaOH to pH 7 in an automatic titrator (Radiometer, Copenhagen). Unstimulated and stimulated acid output were calculated by adding 15-minute outputs during the pre- and post-histamine hour respectively.

**Results**

Characteristics such as age, body weight, and race, duration and type of subjective symptoms were similarly distributed among the two groups (Tables I and II). On palpation, the salivary gland area did not show abnormal findings in any patient.

In the first consecutive 25 subjects of this study (11 duodenal ulcer patients and 14 control subjects respectively) dose response curves were constructed by using the following concentrations of citric acid: 2.5%, 5%, 7.5%, 10%, and 20%. The response to 10% citric acid was a constant fraction of the calculated maximal secretion rate (64 ± 2% in duodenal ulcer patients and 63 ± 2% in control subjects respectively, mean ± SEM). These observations corresponded to values previously obtained in young healthy volunteers (Makhlouf and Blum, 1971). In subsequent patients, therefore, the response to 10% citric acid was used as an estimate for the secretory capacity of the salivary glands.

Of the three consecutive salivary secretion tests with 10% citric acid, the response in the second and in the third test was 101 ± 0.6% and 99 ± 0.6% (mean ± SEM) of the first response respectively. This good reproducibility corresponds to observations in previous studies (Blum and Makhlouf, 1971; Makhlouf, 1971).

Results of secretion tests are summarized in Table III. Salivary secretion in response to citric acid...
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Fig. 1 Gastric acid output during histamine stimulation (upper graph) and salivary output during stimulation with citric acid (lower graph). Results for patients below and above 50 years of age are given on left and right side of each graph respectively. Closed symbols represent patients of duodenal ulcer group and open symbols represent patients of control group. A small divided box indicates mean ± SEM.

in patients with duodenal ulcer was 34% higher than in controls, and gastric acid output in response to histamine was 41% higher.

The effect of age on secretion rate is shown in Figures 1 and 2. A reduction of salivary secretion with old age was seen in controls, but not in patients with duodenal ulcer. In an analysis of covariance, both age and duodenal ulcer were significantly

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Rate of Salivary Secretion (ml/min)</th>
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<tbody>
<tr>
<td></td>
<td>Duodenal Ulcer Group</td>
</tr>
<tr>
<td></td>
<td>&lt;50 Years</td>
</tr>
<tr>
<td>All patients</td>
<td>5.40 ± 0.40 (n = 20)</td>
</tr>
<tr>
<td>Smoking</td>
<td>5.38 ± 0.41 (n = 15)</td>
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<tr>
<td>Drinking</td>
<td>5.45 ± 0.38 (n = 7)</td>
</tr>
<tr>
<td>Dentures</td>
<td>5.01 ± 0.65 (n = 6)</td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td>5.61 ± 0.72 (n = 5)</td>
</tr>
<tr>
<td>Gastroesophageal reflux</td>
<td>6.72 (n = 1)</td>
</tr>
</tbody>
</table>

Table IV Rate of stimulated salivary secretion1

1mean ± SEM, n = number of patients.
and drinking or to other factors such as wearing of dentures but it appears to be related to the rate of gastric acid secretion. It could be shown that in duodenal ulcer disease the rate of salivary secretion was increased in proportion to the rate of gastric secretion. Furthermore, the fall in secretion rate of exocrine glands which usually occurs beyond the age of 50 (Garrett, 1962; Baron, 1963a and b; Waterhouse, 1963; Blackman, Lambert, and Thayer, 1970) was not observed in patients with duodenal ulcer. The rate of both gastric and salivary secretion remained high in older ulcer patients. This observation confirms previous studies on this subject (Baron, 1963b; Blackman et al., 1970). It is well established that the rate of gastric secretion is related to the parietal cell mass and that both gland size and secretion rate depend upon body weight (Boyd, 1941; Brody, 1945; Card and Marks, 1960; Crean, 1967; 1969; Blackman et al., 1970). In duodenal ulcer disease, an increase in gastric secretion is caused by an increase in parietal cell mass. It is likely therefore that the parallel increase in salivary secretion is caused by an increase in salivary gland mass. This postulate is supported by our previous observation of a relationship between salivary secretion and body weight (Blum and Makhoul, 1971) and by the well-established relationship between salivary gland size and body weight (Boyd, 1941). In this context it is interesting to note that pancreatic secretion is also increased in duodenal ulcer disease (Petersen, 1970). It may well be that duodenal ulcer disease is characterized by an enlargement of several exocrine glands such as the parietal cell system, salivary glands, and pancreas while only the enlargement of one gland—the stomach—is related to ulcer symptoms.

Increased salivary secretion in patients with duodenal ulcer might be of some practical importance. The value of gastric secretion tests for the diagnosis of duodenal ulcer disease is low since there is a broad overlap of secretion rates between duodenal ulcer and control populations (Baron, 1963a and b; Blackman et al., 1970). The results of the present study suggest that combined tests of gastric and salivary secretion might improve diagnostic accuracy—at minimal additional costs of time and discomfort.

Discussion

The results of the present study demonstrate that patients with duodenal ulcer disease have a higher rate of salivary secretion than matched control patients without duodenal ulcer. This difference in secretion rate is not due to habits such as smoking

References

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