Gastric potential difference and pH in ulcer patients and normal volunteers during Stroop's colour word conflict test

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SUMMARY Whether mental stress is important in the pathogenesis of gastric mucosal disorders is not clearly established. This study investigated the relationship between sympathetic activation caused by the Stroop's colour word conflict test and gastric mucosal function, monitored by measuring the gastric mucosal electrical potential difference (PD). In 13 healthy volunteers and 12 duodenal ulcer patients gastric PD, pH, and heart rate were measured continuously during basal conditions, during mental stress evoked by the Stroop's colour word conflict test, and after return to basal conditions. The volunteers fell into two groups: In seven no sympathetic activation was elicited as no changes in heart rate were demonstrated. Gastric pH was unchanged, and PD increased slightly. Sympathetic activation was elicited in the other six with increased heart rate by 18 (6) beats per min. Potential difference declined significantly during sympathetic activation ($\Delta PD = -5$ (2) mV, $p < 0.05$). Gastric pH increased. Eleven of 12 ulcer patients had sympathetic activation accompanied by a decline in PD, and an increased pH. Sympathetic activation in ulcer patients and volunteers impaired gastric mucosal function, as shown by a decline in gastric PD.

The pathogenesis of chronic gastric mucosal diseases is still under debate, but its relationship to mental stress has gained support.¹ Several studies have shown that duodenal ulcer patients do not experience more severe or more stressful life events than controls,² but the ulcer patients may have a lower threshold for perceiving situations as stressful.³ A relationship has been found between experimentally induced centrally mediated autonomic stimulation ('stress') and changed gastrointestinal functions in terms of motility⁴ and intestinal transit.⁵ The aim of this study is to investigate whether mental activation induced by the Stroop's colour word conflict test⁶ had a direct effect on the gastric mucosal function evalu-

ated by measuring the gastric potential difference (PD) and pH.⁷

Methods

PATIENTS AND VOLUNTEERS

Thirteen healthy volunteers, six women, with a mean age of 27 years (range 22 to 47) served as controls. None had a history of gastrointestinal disease or dyspeptic symptoms. Twelve patients with chronic duodenal ulcer disease, four women, with a mean age of 36 years (range 21 to 54) were also examined. Duodenal ulcer disease had been diagnosed by upper gastrointestinal endoscopy. The stress test was carried out within one week after endoscopy had proved that the ulcer had healed. The patients were not receiving any medication. The volunteers and ulcer patients were untrained in laboratory stress, and the two groups were comparable in this respect. The study protocol was approved by the local ethical

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committee, and all subjects gave informed consent according to the Helsinki II declaration.

GASTRIC PD AND pH MEASUREMENTS

Gastric PD and pH were measured with a newly developed intragastric microelectrode as described previously,⁷ but only one nasogastric microelectrode (GK2801C, Radiometer, Copenhagen) was used. The PD signal was taken from the Ag/AgCl reference part of the stomach glass electrode.

In six of the volunteers PD results were correlated with results obtained by use of the previously described gastric PD probe.⁷ Regression analysis ($n=6$) showed: $y=x$, $r=0.99$, $p<0.05$.

The stomach electrode was placed with the tip in the corpus of the stomach at the greater curvature within 8–10 cm from the cardia. The position was controlled by fluoroscopy (the total exposure was less than 1 mSv on a 15.2 cm abdominal field⁸). The liquid junction PD (PD_{lj}) between the PD measuring probe and the gastric juice was estimated from the gastric pH values by use of a nomogram previously described.⁷ The PD value corrected for the pH induced liquid junction potentials could thereby be assessed. Potential difference is recorded with gastric lumen negative, and all PD values given are corrected values. The PD/pH electrode was calibrated⁷ with buffer pH 1.09 and 7.38 before and after measurements, and no drift was found.

MENTAL STRESS INDUCTION

Mental activation was induced by a filmed version of the Stroop's colour word conflict test, which is a stress test thoroughly investigated in healthy young men.⁶ The test situation causes a 'flight and flight reaction' with a subjective feeling of stress, and a 'defence-reaction' haemodynamic response with marked cardiac stimulation, and increased arterial noradrenaline levels.⁶ A relation between heart rate and arterial plasma noradrenaline has previously been demonstrated, and an increase in heart rate thereby equals sympathetic activation.⁶ The test lasts for 20 minutes with 25 situations appearing every minute. On the last page of the stress questionnaire the subjects noted whether they had had a feeling of stress during the test. The response was graded as no stress, stress present, severe stress.

STUDY PROTOCOL

The test was carried out in the morning after a light breakfast. Caffeine containing beverages were not allowed. The PD and the reference electrodes were placed in position, and the heart frequency was measured from a single lead electrocardiogram. The subjects were placed in a half sitting position, and PD, pH, and heart frequency were measured con-

Fig. 1 Gastric potential difference (PD) and pH in six healthy volunteers during basal conditions, mental activation evoked by the Stroop's test, and after return to basal conditions. The heart increase was recorded during mental activation.

tinuously. After a basal period of 60 minutes the stress test was performed, and after a rest period of further 60 minutes the investigation was terminated.

STATISTICAL ANALYSIS

Results are presented as mean (SD). The Wilcoxon's non-parametric pair analysis and the Friedman test were used to evaluate statistical hypothesis. $p<0.05$ was considered significant.

Results

NORMAL VOLUNTEERS WITH 'STRESS RESPONSE'

Six of the normal volunteers showed a response with sympathetic activation and a significant increase in the heart frequency (Δ HF=18 (6) beats/min, $p<0.05$). They all reported a subjective feeling of

Fig. 2 Gastric potential difference (PD) and pH in seven healthy volunteers during basal conditions, during mental activation evoked by the Stroop's test, and after return to basal conditions. The unchanged heart rate applies to the period of mental activation.

stress. Their gastric PD and pH responses are shown in Figure 1. Potential differences declined significantly during the stress test (Δ PD = -5 (2) mV, $n=6$, $p<0.05$), and recovered after the resting period. (A change – for example, from -40 mV to -20 mV is described as a reduction in PD). The gastric pH increased during the stress test, and only partly recovered during the rest period. The magnitude of the change in PD and pH did not correlate.

NORMAL VOLUNTEERS WITHOUT 'STRESS RESPONSE'

In seven of the normal volunteers Stroop's test did not elicit sympathetic activation. The heart frequency was unchanged, and they reported no subjective feeling of 'stress'. The gastric PD and pH responses are shown in Figure 2. Potential differences increased (Δ PD = 4 (1) mV, $n=7$, $p<0.05$), and remained at this level throughout the rest of the study period. The gastric pH values did not change.

For all the normal volunteers the baseline PD values recorded 30 minutes after the PD probe had been placed was -45 (6) mV. This value is within the normal range for a comparable age matched population.⁷

ULCER PATIENTS

The gastric PD and pH responses for the ulcer patients are shown in Figure 3. Sympathetic activation was elicited in all but one patient. Heart frequency increased (Δ HF = 16 (6) beats/min, $n=11$, $p<0.05$), and they reported either 'stress' or 'severe stress'. The one patient with unchanged heart frequency reported a feeling of disorientation. As seen in Figure 3 the 11 patients showed a significant reduction in gastric PD during Stroop's test (Δ PD = -6 (2) mV, $n=11$, $p<0.05$). Potential differences recovered during the rest period. For some patients the gastric pH increased during the 'stress period', and recovered partly after rest ($n=6$). For seven patients no changes in the intragastric pH were observed.

The initial basal PD values: -35 (10) mV were significantly lower than that of a matched normal population: PD = -45 (8) mV.

Discussion

The Stroop's colour word conflict test caused sympathetic activation in 11 of 12 ulcer patients and in six of 13 healthy volunteers. A significantly reduced gastric PD was found during sympathetic activation often together with an increase in gastric pH. Gastric PD measurements describe the gastric mucosal integrity and function, and a decline in PD indicates a hampered gastric mucosal 'health state'; either

Fig. 3 Gastric potential difference (PD) and pH in 12 chronic duodenal ulcer patients, where endoscopy had proven the ulcer to be healed: during basal conditions, during mental stress evoked by the Stroop's test, and after return to basal conditions. The heart rate increase was recorded during mental activation.

because of a low resistance or a low active ion transport.^{7-9,11} Thus, mental stress with sympathetic activation caused a direct change in the gastric mucosal function.

This gastric PD and pH response with a decline in PD and an inhibited acid secretion is similar to the response found during gastric hypoxia and ischaemia¹² in animals. The possible relationship between mental stress and gastric mucosal ischaemia was described in 1833 by William Beaumont, who observed that Alexis Sct Martin had a pale and dry stomach during 'fear, anger, or whatever depresses or disturbs the nervous system'.¹³

The ulcer patients in this study had a low gastric PD value compared with controls despite a normal upper gastrointestinal endoscopy. Ulcer patients were previously reported to have a significantly increased resting plasma catecholamine level,¹⁴ and in another study ulcer patients were reported to have a low gastric mucosal blood flow.¹⁵ Thus, during stress episodes blood flow may further decline, and this would enhance the effects of the noxious substances usually present in the stomach (acid, bile, pepsin, etc). It has been claimed that ulcer patients do not experience an increased number of stressful life situations compared with controls, but without being more stressful everyday life in these patients may provoke an increased number of stress episodes.¹ These frequent stress episodes could be a cofactor in the pathogenesis of gastric mucosal disease.

It can only be hypothesised that the gastric PD and pH changes during mental stress are caused by ischaemia. Unfortunately, only a few suitable methods for gastric mucosal blood flow determinations are available for *in vivo* human studies, as the

measurements are often influenced by changes in the acid secretory state.¹⁶ Duodenal bile reflux during mental stress would cause the same PD and pH response,¹⁷ and it cannot be excluded that the PD and pH response could be the result of bile reflux.

Sympathetic activation in patients and volunteers was assessed by the increase in heart frequency, as a relation between arterial plasma noradrenaline and heart rate was previously shown.⁶ We did not measure the arterial plasma catecholamine concentrations, as we thought it unjustified to perform arterial catheterisations in this study. Unfortunately, venous blood sampling is only misleading in this context.⁶

In some of the normal volunteers Stroop's test did not cause sympathetic activation. The increase in PD found during Stroop's test might be caused by an initially reduced PD in the study period because the intubation procedure may have been unpleasant. Such a stress related initial PD reduction has been previously described in healthy volunteers.⁷

In summary, sympathetic activation evoked by Stroop's colour word conflict test caused a changed gastric mucosal function in terms of a reduced gastric PD. This stress response could be elicited in nearly all the ulcer patients and in half the volunteers.

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