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Patients with headache and functional dyspepsia present meal-induced hypersensitivity of the stomach

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Abstract Headache is a frequent feature of functional gastrointestinal disorders but there is no data on the responsible pathophysiological mechanism. The aim of this study was to verify whether alteration of post-prandial gastric tone or sensitivity might explain this association. Fourteen patients affected by functional dyspepsia (7 migraine without aura) and 7 healthy volunteers (HV) underwent gastric tone measurement in fasting condition and after the administration of a liquid meal by barostat. Gastric volume (GV) and accommodation were calculated as difference between mean post-prandial and mean fasting volume. Mean post-prandial GV increase and fasting perception and discomfort threshold (DTh) were similar among the 3 groups. DTh after meal was lower in dyspeptic headache patients than in HV and dyspeptic without headache patients. Patients with migraine and functional dyspepsia may be characterised by meal-induced hypersensitivity of the stomach.

Key words Functional dyspepsia • Migraine • Visceral sensitivity • Discomfort threshold • Barostat test

Introduction

Functional gastrointestinal disorders are frequently characterised by the presence of extra-intestinal symptoms. A survey on irritable bowel syndrome showed that gynaecological, urinary, psychological, dermatological and neurological symptoms were significantly more prevalent in patients than in controls [1]. Headache, in particular, was present in more than 30% of patients suffering from this condition. Although there is no similar evaluation for functional dyspepsia, the presence of headache also in patients suffering from this functional disorder is a common finding in day-to-day clinical practice. To our knowledge no data are available on the responsible pathophysiological mechanism.

A new instrument recently became available, the barostat, which allows the evaluation of both tone modifications of large viscera, such as the stomach and colon, and the evaluation of visceral sensitivity, by the study of sensitivity thresholds to mechanical distention [2]. The application of this new technology to the study of the pathophysiology of functional dyspepsia has made it possible to identify several mechanisms at the basis of the onset of dyspeptic symptoms: for example, it was shown that the onset of post-prandial epigastric pain, belching and weight loss is due to gastric hypersensitivity to distention [3]; early satiety was associated with impaired gastric accommodation to a meal [4] and unsuppressed phasic contractility of the gastric fundus is associated with bloating [5].

The aim of this study was, therefore, to verify whether an alteration of post-prandial gastric tone or sensitivity in patients suffering from dyspepsia and headache can explain this association.

Patients and methods

Patients

Fourteen patients (12 F, 2 M, mean age 32±8 years) affected by functional dyspepsia with (7 patients) and without (7 patients) migraine without aura took part in the study. Diagnosis of migraine was made according to ICHD-II criteria [6] and diagnosis of functional dyspepsia was made according to Rome II criteria [7]. As a control group, seven age- and sex-matched healthy volunteers were also enrolled. All subjects underwent gastric tone measurement and sensitivity threshold evaluation both during fasting and after the administration of a meal by barostat.

Barostat test

The aim of the gastric barostat test was to measure fasting and post-prandial gastric tone. After an overnight fast, a double lumen polyvinyl tube (Salem sump tube 14 Ch., Sherwood Medical) with an adherent, infinitely compliant plastic bag (1200 ml capacity, 17 cm maximal diameter), finely folded, was inserted in the stomach through the mouth and secured to the subject's chin with adhesive tape. The polyvinyl tube was connected to a computer-driven programmable volume-displacement barostat device (G & J Electronics Inc., Toronto, Ont., Canada). The barostat device maintains a constant preselected pressure within the bag, changing the bag volume of air, by an electronic feed-back mechanism. The barostat monitors gastric motor activity (contraction or relaxation) as changes in intraballoon volume (reduction or increase, respectively) at a constant intrabag pressure [2]. To initially unfold the balloon, it was inflated with a fixed volume of 250 ml of air for 2 min with the subject in a recumbent position, and then deflated completely. After a 10-min equilibration period, the patients were then positioned in a comfortable sitting position with the knees bent (80°) and the trunk upright in a specifically designed bed. After minimal distending pressure (MDP) determination [8], intra-balloon pressure was set at MDP+2 and fasting gastric tone was measured for a 30-minute period; a liquid caloric meal (1 kcal/ml, 19% fat, 41% carbohydrate, 40% protein) was then given orally. A total of 200 ml (200 kcal) was administered. Gastric tone measurement continued for a further 60 min to evaluate meal-induced modifications of tone.

Isobaric distentions were also performed during fasting and post-prandially, in stepwise increments of 2 mmHg starting from MDP, each lasting for 2 min. Subjects were instructed to score their perception of upper abdominal sensations at the end of every distention step, using a graphic rating scale that combined verbal descriptors on a scale graded 0–6 [8]. The end point of each sequence of distentions was established at an intrabag volume of 1000 ml or when subjects reported discomfort or pain (5 or 6).

Statistical analysis

Gastric tone was assessed by monitoring bag volume with intrabag pressure set at MDP+2 mmHg. Barostat measures bag volume and pressure at a frequency of 1/s. Mean balloon volume for consecutive 5-min intervals was considered to calculate the time-volume curve for each patient. Fasting gastric tone was calculated as the mean volume of the 30-min fasting period; post-prandial gastric tone was calculated as the mean volume of the 60-min post-prandial period. The meal-induced gastric tone modification was quantified as the difference between the average volumes during the 30-min fasting period and 60-min post-prandial period.

Data are presented as mean±SD. Pressure-volume curves of patients and healthy volunteers were compared by analysis of variance (ANOVA). Differences were considered significant at the 5% level.

Results

Patients with dyspepsia-migraine showed mean post-prandial gastric volume increase (156±150 ml) similar to patients with dyspepsia without migraine (145±135 ml) and HV (168±121 ml; p=NS, ANOVA).

As far as fasting sensitivity threshold was concerned, no difference was found between the three groups studied,

Table 1 Values obtained in the three groups of patients. Data are presented as mean±SD

	Dyspepsia-migraine	Dyspepsia without migraine	Healthy volunteers
Post-prandial gastric volume increase, ml	156±150	145±135	168±121
Fasting sensitivity perception threshold, mmHg	4.0±1.0	3.8±1.1	3.9±1.1
Discomfort threshold, mmHg	12±5	11±5	12±5
After the meal			
Perception threshold, mmHg	4.4±1.2	3.9±1.2	3.8±1.3
Discomfort threshold, mmHg	7±4 (p<0.01)	11±4	11±6

as mean perception threshold was 4.0±1.0 mmHg in patients with dyspepsia-migraine, 3.8±1.1 mmHg in patients with dyspepsia without migraine and 3.9±1.1 mmHg in HV (p=NS, ANOVA); similarly, discomfort threshold was 12±5 mmHg in dyspeptic-migraine patients, 11±5 mmHg in dyspeptic without migraine and 12±5 mmHg in HV (p=NS, ANOVA).

On the contrary, after the meal a significant reduction of discomfort threshold was evident only in dyspeptic-migraine patients (7±4 mmHg; $p<0.01$), while no difference was shown by HV (11±6 mmHg; p=NS) and dyspeptic subjects without migraine (11±4mmHg; p=NS). Post-prandial perception threshold was similar to fasting value in all studied groups: 4.4±1.2 mmHg in patients with dyspepsia-migraine, 3.9±1.2 mmHg in patients with dyspepsia without migraine and 3.8±1.3 mmHg in HV. Table 1 summarises the results in the three groups of patients as observed in the present study.

Discussion

Using the pressure value needed to induce gastric sensation, we showed that post-prandial hypersensitivity to gastric distention is present in patients with dyspepsia and migraine. In particular, no difference was evident in terms of perception thresholds between the three studied groups, but discomfort thresholds were significantly reduced after a meal only in dyspepsia and migraine patients. As far as gastric accommodation is concerned, no alteration of this reflex was evident between the three groups.

Abnormal processing of gastric stimuli at the level of the central nervous system can be one of the mechanisms for visceral hypersensitivity revealed in functional dyspepsia patients [9], but the brain loci responsible for gastric pain remains unclear.

Recently, neuroimaging studies [10, 11] on the central processing of gastric pain revealed activation of a wide range of cortical and subcortical structures (bilateral thalamus, bilateral insula, anterior cingulated cortex, caudate nuclei, brainstem, amygdala, periaqueductal grey matter, cerebellum and occipital cortex). These results support the hypothesis of a possible common cerebral pain network for both somatic and visceral pain.

Our data are very intriguing on pathophysiological grounds, as they connect gastric tone, which is regulated by serotoninergic pathways, to the onset of a symptom that can be correlated to serotoninergic pathway alterations. In fact, a role for the 5-HT receptor in the pathophysiology of migraine without aura was recently suggested [12]. In particular, in a group of migraine patients the administration of the 5HT1A agonist buspirone induced a significantly higher rise of serum prolactin than in healthy volunteers, suggesting a sort of receptor hypersensitivity.

Serotoninergic pathways regulate gastrointestinal tonic and phasic activity. Oral administration of buspirone improves gastric accommodation [13], accelerates interdigestive gastrointestinal motility in man [14] and increases oesophageal wave amplitude and wave progression velocity and reduces the duration and extent of lower oesophageal sphincter relaxation in healthy volunteers [15], suggesting a wide regulatory effect of this receptor on gastrointestinal motility. Other 5-HT receptors were shown to be important in the regulation of intestinal motility, as 5-HT4 and 5-HT3 are the main receptors involved in gastrointestinal peristalsis [16, 17].

Gastric parietal tension receptors were shown to be involved in symptom generation in men [18, 19] and the modulation of the activity of these receptors by serotoninergic fundus-relaxing drugs decreases post-prandial symptoms in functional dyspepsia patients [20]. It is, therefore, possible to hypothesise that serotoninergic pathways may represent the target for the therapy of migraine associated with dyspepsia.

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