

Gastrointestinal motility disorders in patients with anorexia nervosa – a review of the literature

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Summary

Anorexia nervosa is a disease carrying havoc on many levels of the body functioning. The presence of numerous somatic complications as a consequence of starvation is an important part of the clinical picture of this disease. Symptoms of the gastrointestinal tract are one of the most common complaints reported by patients, especially in the initial period of realimentation. Most common symptoms are associated with gastrointestinal motility disorders. The available data show that as many as half of patients suffering from anorexia nervosa manifest significant gastrointestinal motility disorders (incomplete relaxation of the upper and lower oesophageal sphincter, impaired compliance of the stomach, delayed gastric emptying, intestinal transit extension, decreased motility of the rectum and anus). These disorders along with gastrointestinal tract ailments may impede the restoration of proper diet, if not detected early and treated. There are relatively few studies on gastrointestinal motility disorders in patients suffering from anorexia nervosa, which do not clearly answer the question whether these disorders are genetic, or result from cachexia and whether they disappear along with the restoration of the normal body weight. No reference of research results to the clinical practice, and the lack of standard procedures for diagnosis and treatment of gastrointestinal disorders in patients with anorexia nervosa are significant problems for specialists in the field of psychiatry and gastroenterology.

Key words: motility disorders of the oesophagus, manometry, gastric emptying

Introduction

Anorexia nervosa is a disorder whose essence is intentional weight loss through the use of qualitative and/or quantitative dietary restrictions, supported by a number of measures aimed at reducing body weight, such as excessive physical activity, induced vomiting, the use of laxatives, diuretics, chilling of the body, fluid restriction, and others. Usually, girls at puberty are affected. The incidence among teenage girls amounts to 0.5–2% [1]. The insufficient intake of food, which is incompatible with the needs of the body, carries a number of negative consequences manifested both in terms of physical, mental and social functioning. This has been confirmed by the first research on starvation conducted in the Warsaw Ghetto in 1942, or Key's experiment "The Great Starvation Experiment" published in 1950 [2]. These studies clearly showed that as a result of fasting there is a change in the functioning of virtually all organs and systems of the human body, including gastro-intestinal tract disorders.

Symptoms of the gastrointestinal tract, such as the feeling of fullness after meals, epigastric pain, bloating, constipation, the feeling of regurgitation, nausea and others are usually among the first reported in the course of anorexia nervosa. They may indicate malfunction of the digestive tract, but we should bear in mind the need to differentiate the symptoms resulting from eating disorders (e.g. vomiting in patients suffering from bulimia, or a bulimic form of anorexia) from those which appeared secondarily to the primary disease. The decrease in body weight and the associated symptoms of the gastrointestinal tract may result from primary motility disorders, such as achalasia or diffuse oesophageal spasm. Gastrointestinal motility disorders can significantly hinder the process of recovery and raise a lot of anxiety on the part of patients and their families. So far, no standards have been developed, which would aim at the qualification to broaden the diagnosis of gastrointestinal motility disorders in patients with anorexia nervosa, and reported symptoms do not always correlate with the real problems in the functioning of the gastrointestinal tract [3]. There are relatively few studies on gastrointestinal motility disorders in patients suffering from anorexia nervosa.

The pathophysiology of gastrointestinal tract motility disorders

The cerebrospinal-intestinal (cerebrospinal-visceral) axis plays a key role in the regulation of gastrointestinal tract functioning [4]. Its bi-directional action has been confirmed in many studies. On the one hand, stimuli such as stress and emotions may affect the gastrointestinal tract and modify its motor activity and visceral hypersensitivity, on the other hand, visceral stimuli relating for example to the immune response to the digestive system infection may affect mood, behaviour and pain response at the level of the central nervous system (CNS) [5, 6]. The limbic system and paralimbic structures (the cortex of the island, hypothalamus) play a special role in the regulation of the gastrointestinal tract at the level of the CNS. The emotional state, dependent on the activation of the limbic system, has a direct effect on the gastrointestinal motility and the perception of painful stimuli [7]. Enteric nervous

system is characterized by a high degree of autonomy, and neurotransmitters that occur here are not different from neurotransmitters of the central nervous system (e.g. serotonin – one of the main neurotransmitters of the enteric nervous system [8], substance P, corticotropin-releasing hormone, thyrotropin-releasing hormone, cholecystokinin, calcitonin gene-related peptide, oxytocin, somatostatin, vasopressin, tachykinin, opioids or cannabinoids) [4]. It is well known that anxiety and depression (and the potentially associated dysregulation of neurotransmission) accompany the symptoms of anorexia nervosa in 50–75% of cases [9]. The gastrointestinal symptoms may exacerbate the symptoms of anxiety, which in turn adversely affect the already disturbed function of the digestive tract.

Motility disorders of the gastrointestinal tract

Gastrointestinal motility disorders are not identical with functional disorders. Functional disorders include pathological symptoms, in which no organic or metabolic cause is identified [10], so most commonly a diagnosis is made on an “exclusion” basis and imaging and biochemical tests show no morphological changes [4]. Gastrointestinal tract motility disorders instead, have their cause in dysfunction of the muscle that form the gastrointestinal tract, or in the nervous or endocrine systems, closely related to the functioning of the digestive tract. Often, it is difficult to unambiguously differentiate whether we deal only with functional disorders, or they co-exist with motor problems. Symptomatology of functional and motor disorders is similar. The typical symptoms include dysphagia, vomiting, regurgitation, heartburn, chest pain or pain when swallowing [10]. The diagnostic methods that evaluate functional disorders, including motility disorders of the upper gastrointestinal tract include: radiology, endoscopy, scintigraphy, ultrasound, pH-metry, breathing tests and newer and more precise examinations, such as high-resolution manometry and pH-impedance. Anorectal manometry is used to evaluate the motility of the distal gastrointestinal tract; we apply radiological techniques using contrast markers to assess the intestinal transit time.

The state of knowledge on the functioning of the upper gastrointestinal tract in anorexia nervosa

In 1986 the first studies on motility disorders of the oesophagus were published. Stacher et al. [11] described the use of manometry technique in patients with anorexia nervosa. They examined 30 patients aged 14–43 years, and showed changes in motility in 50% of them. Seven enrolled patients with primary anorexia nervosa had achalasia, thus contradicting the initial diagnosis. In six patients the wall motion abnormalities of the distal oesophagus predominated, one patient suffered from diffuse oesophageal spasm and one from gastro-oesophageal reflux.

This study also recorded gastric emptying. In 12 out of 15 patients with the normal result of oesophageal manometry, and 4 subjects with abnormal motility, gastric emptying was examined after ingestion of a semi-liquid meal – showing delayed emptying

in as many as 13 cases. These patients usually complained of postprandial fullness, bloating, belching, abdominal pain and vomiting. Emptying half-time was significantly shorter after the intravenous administration of domperidone, especially in patients with clear delay in gastric emptying, but this procedure was used only in 8 patients.

The conclusions on the extension of gastric emptying time are consistent with the previously conducted studies on gastric emptying in anorexia nervosa after water loading [12]. Disorders of gastric emptying were also examined using the isotopic technique; and although most studies indicate delayed gastric emptying [11–19], the results are different from each other. McCallum et al. and Saleh et al. observed emptying of the stomach only from the solid content, which can be partially reversed by the administration of metoclopramide [14, 15], while Holt et al. and Hutson showed that the gastric emptying rate is much lower in patients suffering from anorexia nervosa than in healthy subjects and it concerns both liquid and solid food [16, 17]. Also, the matter of maintaining delayed gastric emptying after reaching the normal body weight in anorexia nervosa is controversial. Dubois showed that gastric emptying disorders persist even after obtaining the proper weight [12] and the studies conducted by Szmukler and Rigaud revealed that gastric emptying rapidly improved after normalization of the diet standard [18, 19]. There are also studies which did not show delayed gastric emptying in any of the examined patients suffering from anorexia nervosa [20]; however, they found impaired compliance of the stomach, measured as a postprandial diameter of the antral part assessed by ultrasound.

The discrepancies in the results may be related to the small sample size of the study groups. Usually, the studies mentioned above included 10 [17], 12 [16], 16 [11, 14, 20], and the most numerous group 18 [18] patients suffering from anorexia nervosa. This data should be treated with caution.

The oesophageal manometry technique using a 4-channel flow probe was also used by Polish researchers – Kwiecień and Ziora who examined 40 girls aged 15.6 \pm 1.3 years with a diagnosis of anorexia nervosa [21]. The lack of information concerning the duration of the disease, its course, and the age at which symptoms appeared are the limitations of the study. The results of this study clearly indicate the occurrence of gastrointestinal motility disorders, which were found in nearly half of the patients, but the type of abnormalities is not consistent with the previously cited studies conducted by Stacher. 40% of girls (16 subjects) showed incomplete relaxation of the upper oesophageal sphincter (UES). At the level of the trend, a negative correlation was observed between the nutritional status (BMI – body mass index) and the resting pressure of the UES. 12.5% (5 subjects) showed incomplete relaxation of the lower oesophageal sphincter (LES) with swallowing. The increased steady LES pressure was another abnormality that affected 10% of patients (4 girls). In contrast to the study conducted by Stacher et al. [11], none of the patients showed achalasia of the oesophagus. There were no relationships between the test results, the reported gastrointestinal symptoms and the current clinical status. None of the study girls, who manifested variations in UES relaxation, had severe somatic disorders.

The more advanced 8-channel manometric probe was used in the study published by Italian researchers under the leadership of Luigi Benini [3]. The study included 23

adult patients with anorexia nervosa, but 6 of them prematurely withdrew from the participation in the project. The study was completed by 17 patients (8 with a bulimic subtype and 9 with restrictive anorexia nervosa). The control group of the manometry test consisted of 35 subjects. It is the only available study with manometry technique done twice, i.e. at the beginning of hospitalization, and at the follow-up conducted after 22 weeks of nutritional rehabilitation. In the determined in advance period of 22 weeks, the earlier assumed BMI value of more than 18.5 kg/m² was achieved only by 13 out of 17 patients. Initially, the patients mainly complained of the feeling of regurgitation, heartburn, excessive belching and dysphagia. These symptoms were significantly more frequent and more severe in all patients with anorexia nervosa than in the control group. Patients reported that the symptoms appeared secondarily to anorexia nervosa, suggesting that they were the consequence of eating disorders, and not the primary problem associated with motility disorders. The reported gastric and intestinal symptoms along with the duration of hospitalization were significantly minimized. Only oesophageal symptoms did not diminish. The achieved results of manometric tests revealed effective peristaltic waves in more than 80%. The resting LES pressure was increased (but within standards) in patients with the restrictive type of anorexia, and it was normalized after 22 weeks of treatment. No difference was shown in the resting LES pressure between the control group and patients with the bulimic subtype of anorexia. Relaxation of the lower oesophageal sphincter was within normal limits. No correlation was found between the reported symptoms and the results of manometric tests, as well as between the severity of symptoms, the duration of disease, BMI and mental state. So once again, it was confirmed that the gastrointestinal tract symptoms can not be the only criterion of inclusion for diagnostic tests.

A small size of the group is a limitation of the quoted study. In addition, in the assumed in advance period of 22 weeks of rehabilitation, a desirable nutritional status (BMI above 18.5 kg/m²) was achieved only by 13 patients. It is hard to recognize the remaining 4 patients as those that have undergone effective nutritional rehabilitation. As we know, the period of recovery in patients suffering from anorexia nervosa is very different; therefore assuming a predetermined time end point for the control test appears to be wrong.

Data on the motility of the lower gastrointestinal tract in patients with anorexia nervosa

Motility disorders may also involve the distal part of the gastrointestinal tract. Most patients with the symptoms of anorexia nervosa complain of constipation, and treat it as one of the most troublesome symptoms [22, 23]. The symptom is confirmed by 60% of sufferers [22]. So far, two studies were conducted which aimed to evaluate the motility of the distal part of the gastrointestinal tract in patients with anorexia nervosa [24, 25]. They used anorectal manometry and radiological methods with contrast markers.

Chun et al. [25] evaluated the transit time in 13 women with anorexia nervosa who complained of constipation. In 6 patients studies were conducted within 3 weeks

of admission to the hospital, in 7, in turn after 3 weeks of nutritional rehabilitation. The extended transit time was observed in 4 out of 6 patients studied during the first 3 weeks of hospitalization and in none of those examined after 3 weeks of treatment. No variations in the manometry test were observed. The exact relationship between results obtained in the research and the persistence of subjective symptoms was not analyzed, although the authors describe in general the persistence of constipation complaints despite normal control test results.

In 67% of patients (8 out of 12) with anorexia, Chiaroni et al. [26] found longer transit time which returned to the normal value after 4 weeks of dietary treatment. Unlike the work described above, this study showed a number of motility disorders within the rectum and anus in patients with anorexia nervosa, which did not change after nutritional rehabilitation. The authors suggest that the weakened anorectal motility may be the cause of constipation, and the abnormal transit time, which returns to the normal value, may result from the improperly balanced diet prior to hospitalization.

The results of both studies described above are divergent in terms of manometric data. They both were carried out in a very small number of patients. In addition, in both designs, all the patients included in the study reported constipation, and as we know merely up to 60% of patients with anorexia nervosa suffer from this complaint [22]. It is not clear whether the study of consecutive patients (also not suffering from constipation) would produce similar results. In addition, the prolonged transit time resulting from the weakening of the propulsive force of the colon, was also observed in women not suffering from anorexia, but using laxatives for a long time. It cannot be excluded that a significant proportion of patients enrolled to the studies applied such a therapy, just because of chronic constipation, and there is no information in the texts on the subject.

Recapitulation and conclusions

Currently available studies are not consistent in terms of the results and their interpretation. Most authors believe that motility disorders are secondary to the dramatic dietary restrictions and that they improve after treatment [3, 18, 19, 22]. Some studies suggest, however, that after nutritional rehabilitation only gastric and intestinal symptoms subside, but the oesophageal symptoms persist [3, 21].

There is still no explicitness whether frequent complaints from the gastrointestinal tract have their roots in motility disorders. Most authors point to the lack of correlation between the reported symptoms and the results of diagnostic tests [3, 17, 21]. It is also unclear why the complaints maintain, which is reported in some studies, despite the normalization of the body's nutritional status [3, 22].

More and more attention is paid to the links between the proper functioning of the digestive tract and the action of neurotransmitter systems or receptors of the CNS. Some authors suggest that the improvement of gastric emptying, as well as other abnormalities of the gastrointestinal tract motility may be more related to the improvement of the mental state [26] and the normalization at the level of neurotransmission,

rather than the equalization of the body weight [21]. Probably the broad diagnosis of the CNS would provide answers to many unsolved questions. For example, studies in patients suffering from Parkinson's disease showed a relatively high proportion of changes in the UES relaxation, not causing any symptoms in patients and associated with the dysfunction of central motor neurons [27].

In the context of developing techniques and improving equipment, which would be capable of diagnosing gastrointestinal motility disorders, significant differences in the type of test deviations, for instance manometric, seem to be less important. There is still very few data in the literature regarding motility disorders in patients suffering from anorexia nervosa using the most modern equipment. To this day, for example, no studies have been published on the use of pH-impedance technique in patients with anorexia nervosa. Paradoxically, this is currently the most modern testing used in the diagnosis of gastroesophageal reflux. The works, which were cited by our study concerning motility disorders in patients suffering from anorexia nervosa, still do not give a clear answer to the fundamental question – whether motility disorders are primary and are a sort of predisposing factor for eating disorders or result from the long-term dietary restriction leading to the destruction of the body? The answer can only be obtained by performing tests twice i.e. in the state of destruction and after reaching the desirable body weight (control test). The research should be done in a larger group of patients, and additionally include data on symptoms, their severity, time of onset, duration and diet. The lack of reference of the study results available in literature to the clinical practice, and hence no standards of management are a big problem for specialists in the field of psychiatry and gastroenterology.

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