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Research Article

Crohn's Disease as a Polymorbid Disease

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Abstract

Introduction: Crohn's disease (CD) is a chronic, recurrent disease of the gastrointestinal tract (GI tract) of unclear etiology, characterized by transmural, segmental, granulomatous inflammation with the development of local and systemic complications. In a number of diseases, for example, Crohn's disease, the presence of changes in the patient's organs and tissues of the oral cavity makes a certain contribution to their diagnosis.

Aim: The aim is to investigate the motor function of the smooth muscles of the gastrointestinal tract and identify damage to the oral mucosa in Crohn's disease.

Materials and Methods: The study included 30 CD patients, 15 women aged 43 ± 10.7 years, 15 men aged 38.5 ± 13.4 years, who made up group 1. The main manifestations of CD were the presence of abdominal pain, frequent - up to 15 times a day - stools with blood, changes in the condition of the oral cavity organs. The comparison group consisted of 15 patients suffering from functional dyspepsia.

Results: In CD with lesions of the oral cavity, there is an increase in both phase and tonic contractile activity of all muscle layers of the stomach with a slight increase in propulsive activity, in CD with lesions of the oral cavity, there is a decrease in both phase and tonic contractile activity of all muscle layers of the small intestine with a slight increase in propulsive activity. in CD with the presence of pathology of the oral cavity organs, contractions of the circular muscles of the left and right parts of the colon are sharply reduced with an increase in the motor activity of the longitudinal muscles, which ensures the rapid passage of contents through the colon as a whole.

Conclusion: In the system of relationships between a gastroenterologist and other specialists, the aspects of their interaction with a dentist are the least studied. This is due to the mutual underestimation of changes on the part of organs and tissues of the oral cavity in various diseases of internal organs and under the influence of drug therapy of these diseases. The presence of certain changes on the part of the organs and tissues of the oral cavity and the appropriate dental advice can help the gastroenterologist in the diagnosis and adequate treatment of the patient.

Keywords: *Crohn's Disease; Dental Manifestations; Disorders of the Motor Function of the Gastrointestinal Tract*

Introduction

Crohn's disease (CD) is a chronic, recurrent disease of the gastrointestinal tract (GI tract) of unclear etiology, characterized by transmural, segmental, granulomatous inflammation with the development of local and systemic complications [1].

The etiology of inflammatory bowel diseases (IBD), including CD, has not been established: the disease develops as a result of a combination of several factors, including genetic predisposition, defects in innate and acquired immunity, intestinal microflora and various environmental factors. About 100 single nucleotide polymorphisms associated with CD have been described. This genetic background predisposes to changes in the innate immune response, autophagy, mechanisms of recognition of microorganisms, endoplasmic reticulocyte stress, epithelial barrier functions and adaptive immune response. A key immune defect predisposing to the development of IBD is a violation of the recognition of bacterial molecular markers (patterns) by dendritic cells, which leads to hyperactivation of signaling proinflammatory pathways [2-4]. IBD also shows a decrease in the diversity of intestinal microflora due to a decrease in the proportion of anaerobic bacteria, mainly *Bacteroidetes* and *Firmicutes*. In the presence of these microbiological and immunological changes, IBD develops under the influence of triggering factors, which include smoking, nervous stress, vitamin D deficiency, a diet with a low content of dietary fiber and an increased content of animal protein, intestinal infections, especially infections associated with Clostridioides difficile. The result of the mutual influence of these risk factors is the activation of Th1 and Th17 cells, overexpression of proinflammatory cytokines, primarily tumor necrosis factor alpha (TNF-alpha), interleukins 12 and 23, and cell adhesion molecules [5-8]. A cascade of humoral and cellular reactions in CD leads to transmural inflammation of the intestinal wall with the formation of sarcoid granulomas characteristic of CD, but not for ulcerative colitis (UC), consisting of epithelioid histiocytes without foci of necrosis and giant cells. CD can affect any part of the gastrointestinal tract - from the mouth to the anus. Nevertheless, in the vast majority of cases, CD affects the ileocecal department. BC, unlike UC, cannot be cured by either therapeutic or surgical methods [9].

According to foreign data, the incidence of CD ranges from 0.3 to 20.2 per 100,000 people, the prevalence reaches 322 per 100,000 people [10]. Data on the prevalence of CD in the Russian Federation are limited. The prevalence of CD is higher in northern latitudes and in the West. The incidence and prevalence of CD in Asia is lower, however, it is increasing. Caucasians suffer from the disease more often than representatives of the Negroid and Mongoloid races. The peak of morbidity is observed between 20 and 30 years of life, and the second peak of morbidity is described at the age of 60 - 70 years. The incidence is approximately the same in men and women.

The severity of the disease is generally determined by the severity of the current exacerbation, the presence of extra-intestinal manifestations and complications, the extent of the lesion, the refractory nature of treatment, in particular, the development of hormonal dependence and resistance.

The most common clinical symptoms of CD include chronic diarrhea (more than 6 weeks), in most cases without blood admixture, abdominal pain, fever and anemia of unknown origin, symptoms of intestinal obstruction, as well as perianal complications (chronic anal fissures, recurrent after surgical treatment, paraproctitis, rectal fistulas). A significant proportion of patients may have extra-intestinal manifestations of the disease [11]. Extra-intestinal manifestations of CD are autoimmune, associated with the activity of the disease; autoimmune, non-activity-related diseases caused by prolonged inflammation and metabolic disorders: arthropathies (arthralgia, arthritis), skin lesions (erythema nodosum, gangrenous pyoderma), mucosal lesions (aphthous stomatitis), eye lesions (uveitis, iritis, iridocyclitis, episcleritis), ankylosing spondylitis (sacroiliitis), primary sclerosing cholangitis, osteoporosis, osteomalacia, psoriasis, psoriatic arthritis, cholelithiasis, liver steatosis, steatohepatitis, peripheral vein thrombosis, pulmonary embolism, amyloidosis.

Autoimmune manifestations associated with the activity of the inflammatory process appear together with the main intestinal symptoms of exacerbation and disappear with them during treatment. Autoimmune manifestations unrelated to the activity of the process

(in English-language literature they are often called "concomitant autoimmune diseases") tend to progress regardless of the phase of the underlying disease (exacerbation or remission) and often determine a negative prognosis of the disease.

Diseases of the digestive system are often accompanied by various changes in the organs and tissues of the oral cavity. This is explained by the morphofunctional similarity of the mucous membrane of the oral cavity and the digestive tract, as well as the presence of a close relationship between various departments of the gastrointestinal tract and its initial department - the oral cavity, carried out through anatomical, physiological and humoral relationships [12-14].

In a number of diseases, for example, gastroesophageal reflux disease (GERD), Crohn's disease, the presence of changes in the patient's organs and tissues of the oral cavity makes a certain contribution to their diagnosis [15].

Inflammatory changes in the oral mucosa can serve as the first clinical manifestations of Crohn's disease or be observed simultaneously with lesions of the ileum and colon [16,17]. Aphthous stomatitis, macrocheilia (lip enlargement) or changes in the relief of the mucous membrane are most often detected. Approximately 10% of patients with ulcerative colitis have aphthae on the mucous membrane of the oral cavity, which disappear as the activity of the underlying disease decreases. Pyostoma with vegetations (Pyostomatitis vegetans) is considered to be practically specific for ulcerative colitis. At the same time, swellings appear on the mucous membrane of the cheeks, lips, and palate, turning into dark slit-like ulcers and papillary growths. According to some researchers [18-20], patients are diagnosed with Crohn's disease and ulcerative colitis for 6 - 7 years, which makes it difficult to prescribe correct treatment and prevention of complications early. The dentist's knowledge of the specific signs of damage to the mucous membrane of the oral cavity, lips, and palate will make it possible to suspect the development of inflammatory bowel diseases, confirm its development with objective studies and prescribe earlier specific treatment. The dynamics of improvement in the condition of the oral mucosa during treatment can be carried out daily, which allows you to navigate the positive dynamics of the course of the process in IBD in the intestine, confirming endoscopically at the end of the course of treatment.

It is important that damage to enterocytes by proinflammatory cytokines and activation of macrophages leads to the release of serotonin and histamine, which affect the motor function of the gastrointestinal tract (GI tract). However, the motor function of the gastrointestinal tract in CD with intestinal and oral lesions has not been sufficiently studied.

Aim of the Study

The aim is to investigate the motor function of the smooth muscles of the gastrointestinal tract and identify damage to the oral mucosa in Crohn's disease.

Materials and Methods

The study included 30 CD patients, 15 women aged 43 ± 10.7 years, 15 men aged 38.5 ± 13.4 years, who made up group 1. The main manifestations of CD were the presence of abdominal pain, frequent - up to 15 times a day - stools with blood, changes in the condition of the oral cavity organs. Of the concomitant diseases, fatty liver and pancreatic dystrophy were noted - 28.6% of cases, duodenogastric reflux (DHR) and GERD - 28.6%, diverticulosis, dolichosigma, biliary sludge, GI - 7% each. The comparison group consisted of 15 patients with functional dyspepsia.

Electromotor activity was recorded using bipolar cutaneous silver electrodes with a contact surface area of 0.5 - 0.6 mm^2 placed in the projection area of the organ under study on the anterior abdominal wall, registration was performed for 15 - 20 minutes. The amplitude-frequency characteristics of slow-wave and spike activity were measured on the electromyogram curve, the power of tonic and phase contractions and the propulsive activity of the gastrointestinal tract were calculated using the Conan-M hardware and software complex with a bandwidth from 0.01 Hz to 10 kHz and a noise level of less than 1 - 5 MV, sensitivity of 96% and specificity of 95% [21,22].

Patients (group I, n = 30, comparison group, n = 15) underwent electromyography of smooth muscles of the gastrointestinal tract, endoscopic and ultrasound examination.

The processing of the experimental data obtained was carried out using the Statistics-17 software package, during which the normality of the distribution of quantitative features was first checked according to the Kolmogorov-Smirnov criterion, the degree of reliability was assessed using the Student's T-test ($p < 0.05$).

Results and their Discussion

When examining the oral cavity of patients of group 1, the presence of aphthous stomatitis, macrocheilia (lip enlargement) and changes in the relief of the mucous membrane in the form of a "cobblestone pavement" is noted. Examination of the oral cavity of patients in the comparison group revealed no pathological changes.

Electromyographically, the frequency of slow waves of smooth stomach muscles in patients of group 1 was 10.1 ± 0.8 per minute (an increase of 83.6% $p < 0.05$), the amplitude was 0.19 ± 0.04 mV (an increase of 21.1% $p < 0.05$), the power of tonic contraction was 1.919 ± 0.13 (an increase of 132.5% $p < 0.01$). The spike frequency was 1.9 ± 0.25 (an increase of 89.9% $p < 0.05$), the amplitude was 0.12 ± 0.007 mV (an increase of 20% $p < 0.05$). The power of the phase reduction was 0.228 ± 0.017 (an increase of 128% $p < 0.01$), the propulsive activity was 8.4 ± 0.25 (an increase of 1.9%, $p > 0.1$). That is, in CD with lesions of the oral cavity, there is an increase in both phase and tonic contractile activity of all muscle layers of the stomach with a slight increase in propulsive activity.

Electromyographically, the frequency of slow waves of the small intestine in patients of group 1 was 11.6 ± 0.3 per minute (decrease by 42% $p < 0.05$), amplitude - 0.15 ± 0.05 mV (increase by 50.1% $p < 0.05$), tonic contraction power - 1.740 (decrease by 15.3% $p < 0.05$). The spike frequency was 1.2 ± 0.08 (an increase of 20% $p < 0.05$), the amplitude was 0.06 ± 0.004 mV (a decrease of 40% $p < 0.05$). The power of phase contractions was 0.072 ± 0.005 (decrease by 64% $p < 0.05$), the propulsive activity was 24.2 ± 1.8 (increase by 21%, $p < 005$). That is, in CD with lesions of the oral cavity, there is a decrease in both phase and tonic contractile activity of all muscle layers of the stomach with a slight increase in propulsive activity.

The frequency of slow waves of the right colon in patients of group 1 was 10.5 ± 0.6 per minute (decrease by 4.5% $p < 0.05$), amplitude - 0.16 ± 0.004 mV (increase by 59.9% $p < 0.05$), the power of tonic contractions - 1,680 ± 0.007 (increase by 52.7% $p < 0.05$). The spike frequency was 1.02 ± 0.03 (an increase of 2% $p > 0.1$), the amplitude was 0.06 ± 0.005 mV (a decrease of 40.1% $p < 0.05$), the power of phase contractions was 0.0612 ± 0.0009 (a decrease of 38.8% $p < 0.05$), the propulsive activity was 27.4 ± 2.5 (an increase of 149%, $p < 0.001$). Thus, in CD with pathology of the oral cavity organs, the tone of the longitudinal muscles of the right colon is increased, with a decrease in the contractile activity of the circular muscles, which accelerates intestinal transit through this part of the intestine.

The frequency of slow waves of the left colon was 9.8 ± 0.4 per minute (an increase of 63.3% $p < 0.05$), the amplitude was 0.09 ± 0.0023 mV (a decrease of 10% $p < 0.05$), the power of tonic contractions was 0.882 ± 0.004 (an increase of 47% $p < 0.05$). The spike frequency was 1.2 ± 0.03 (an increase of 20% $p < 0.05$), the amplitude was 0.044 ± 0.005 mV (a decrease of 56% $p < 0.05$). The power of phase contractions was 0.0528 ± 0.003 (decrease by 47.2% $p < 0.05$), the propulsive activity was 16.7 ± 1.4 (increase by 178.3%, $p < 0.001$). That is, in CD with the presence of pathology of the oral cavity organs, contractions of the circular muscles of the left colon are sharply reduced with an increase in the motor activity of the longitudinal muscles, which ensures the rapid passage of contents through the colon as a whole.

That is, in Crohn's disease, hypermotor dyskinesia of the gastrointestinal tract is observed progrediently increasing distally, which correlates with diarrhea observed in patients.

Endoscopic examination of group 1 patients reveals terminal ileitis, contact vulnerability of the mucous membrane, a characteristic change in the relief of the mucous membrane due to submucosal nodes, which is confirmation of the development of CD. In patients of the comparison group, the mucous membrane of the ileum and colon of the usual color and relief, contact bleeding was not detected.

Ultrasound examination of group 1 patients reveals a thickening of the intestinal wall characteristic of the inflammatory process and swelling of the surrounding tissues. These signs are absent in patients of the comparison group.

A comparison of the condition of the mucous membrane of the oral cavity, ileum and colon makes it possible to identify earlier manifestations of oral lesions.

Conclusion

Diseases of the digestive system are often accompanied by various changes in the organs and tissues of the oral cavity. This is explained by the morphofunctional similarity of the mucous membrane of the oral cavity and the digestive tract, as well as the presence of a close relationship between various departments of the gastrointestinal tract and its initial department - the oral cavity, carried out through anatomical, physiological and humoral relationships [23-26].

Over the past 20 years, the incidence of Crohn's disease (CD) has increased significantly, and mainly in developed countries. The prevalence of CD ranges from 20 to 150 cases per 100,000 population, reaching maximum levels in the Scandinavian countries, North American countries, and Israel. Men and women suffer from CD with approximately equal frequency [27]. At the same time, the time of the diagnostic period for CD, despite the possibility of a multilateral examination by means of modern medicine, often takes several years.

It is known that the gene responsible for the predisposition to the development of CD - nod2 (or card 15) has been identified on the long arm of the IG chromosome at the IBD1 locus. This gene is expressed by macrophages and Pannet cells and is involved in the regulation of the immune response, factor Nf-kB, macrophage apoptosis and intestinal barrier permeability by bacterial lipopolysaccharides. It is assumed that the locus associated with the early onset of Crohn's disease is present on 5 oncogenes infecting a variety of cytokine receptors [28].

Damage to enteral cells by proinflammatory mediators IL-2, IFN-γ cytokines of macrophage origin (TNFa, IL-1, IL-12) leads to the development of inflammatory infiltration of all layers of the intestinal wall. The morphological substrate of inflammatory bowel diseases (IBD) is a nonspecific immune inflammation of the intestinal wall with dense infiltration by lymphatic plasma cells and macrophages [29]. The latter also secrete serotonin and histamine, which, in turn, regulate the contractile function of the smooth muscles of the intestine.

In the system of relationships between a gastroenterologist and other specialists, the aspects of their interaction with a dentist are the least studied. This is due to the mutual underestimation of changes on the part of the organs and tissues of the oral cavity in various diseases of internal organs and under the influence of drug therapy of these diseases. The presence of certain changes on the part of the organs and tissues of the oral cavity and the appropriate dental advice can help the gastroenterologist in the diagnosis and adequate treatment of the patient.

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