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RESEARCH ARTICLE

CHANGING THE MUCOSAL MICROFLORA OF THE STOMACH IN PATIENTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT

Aim: The aim of the study was to assess mucosal microflora of the stomach of patients with RA according to the degree of disease activity.
Materials and Methods: We analyzed 159 people aged 19 to 83 years. Among the patients, mostly women were 128 and men were 31. The ratio of women to men - 4.13:1. The mean of age is 55+0.86 years of all patients. RA was diagnosed in all cases by using the criteria of the American College of Rheumatology. In this study we used for determining RA that routine clinical and radiographic examination, microbiological examination of feces and urine, endoscopy (used machine company "Olympus") of stomach and duodenum with biopsy of the mucosa; it was carried out a microbiological study of the stomach and gastric juice biopsies of mucosa.
Results: In the study of biopsy results showed that RA patients' microflora of stomach insulated Peptostreptococci – 78.5% patients; Streptococci, Staphylococci and Bacillus – 28.5% patients; Escherichia coli and yeast-like fungi of the genus Candida – 21.4%; Clebsiella, Pseudomonas, Enterococci – 8.3% patients in number of cultures from 103 to 3.6x107lg CFU/ml and the combination of microorganisms are from 1 to 7. Escherichia coli were inoculated in an amount of 4.1x107lg CFU/ml; Streptococci – 3.6x107lg CFU/ml; Clebsiella and Pseudomonades – 106lg CFU/ml; Peptostreptococci – 7.6x103lg CFU/ml; staphylococci – 6x103lg CFU/ml; Candida – 1.7x103lg CFU/ml; Enterococci – 103lg CFU/ml.
Conclusion: In patients with RA are marked dysbiotic changes in the stomach. The severity of dysbiosis is directly dependent on the activity of joint pathology.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease that primarily affects the joints. Approximately 0.5% of the adult population worldwide suffer from RA. The functional disability that results from progressive joint destruction is associated with substantial cost, significant morbidity and premature mortality (Arnett *et al*., 1988).

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The immune system is closely linked with the function of normal microflora, which are currently under consideration as a kind of organ of the immune system. Therefore, it is so important to maintain micro-ecological balance in gastro-intestinal tract (GIT). It is known that the loss of functions of normal microflora with subsequent activation of conditionally pathogenic microorganisms are caused violations by both local and systemic immune response (Bevz *et al*., 1990; Vorob'ev *et al*., 1996; Vorobyev *et al*., 2004). The possible role of conditionally pathogenic flora, as a causal or trigger factor was discussed in a number of autoimmune diseases: rheumatoid

arthritis (Loginov and Tsaregorodtsev, 1986; Manelis,, 1986), ankylosing spondylitis (Osipov and Demina, 1996), systemic vasculitis (Tsoy *et al*., 1994), etc. The majority of authors of the greatest importance attached to infections exogenous, ignoring the role of conditionally pathogenic flora, can serve as a source of endogenous infection and potent antigenic stimulation (Chernin *et al*., 2011; Sheveleva, 1999; Shenderov, 1998; Shiraliyev, 1987; Daugelat and Kaufman, 1995). Several studies showed that the condition of the intestinal microflora is related immune disorders in patients with rheumatoid arthritis (RA). Therefore, development of immune disorders in patients with RA is relevant to identifyrole of the microflora of stomach.

PATIENTS AND METHODS

Patient's data

Surveyed 159 people aged 19 to 83 years. Among the patients, mostly women consisted 128 and men were 31. The ratio of women to men equaled 4.13:1. The average age was 55±0.86 years of all patients. The diagnosis of RA in all cases was accurate in accordance with the criteria of the American College of Rheumatology (13, 14). In 23 (22.12%) cases were included 1st degree of activity of rheumatoid process, in 63 (60.58%) cases were 2nd and in 14 (13.46%) – 3rd degree. The nature of the disease, patients was distributed as follows: slowly progressive course in 94 (90.38%) patients and rapidly progressive in 10 (9.62%). The articular form of RA was diagnosed in 95 (100%). Radiologically, stage I RA was detected in 31 (29.81%) patients, stage II in 46 (44.23%), stage III in 26 (25.00%) and stage IV was considered in 1 (0.96%) patients.

Assessment of microflora status

Patients were observed routine clinical and radiographic examinations, microbiological examination of feces and urine, endoscopy (used machine company "Olympus") of stomach and duodenum with biopsy of the mucosa; it was carried out a microbiological study of the stomach and gastric juice biopsies of mucosa. Isolation, identification microorganisms (MOs) were performed according to standard techniques. Disbacteriosis of gastroduodenal zone characterised according to the criteria proposed by Chernin *et al*. (De Freitas *et al*., 1986).

RESULTS

In the study of biopsy results showedthat RA patients' microflora of the stomachinsulated and was determined Peptostreptococci – 71.4% patients; Staphylococci and Escherichiacoli – 50% patients; Clebsiella – 42.8%; Streptococci – 35.7%; Enterococci and Micrococci – 21.4%; Pseudomonas, Bacilli – 14.2%; yeast-like fungi of the genus Candida – 8.3%patients in number of cultures from 2.77 to 10 lg CFU/ml and the combination of microorganisms are from 2 to 5. Figure 1 presents data concerning quantitative characteristics of parietal microflora. In assessing contamination from the stomach in patients with RA, quantitative aspects were obtained the following results.

In Table 1 was showed inoculated amount of cultures of the stomach.

Table 1.

Cultures	Inoculated amount(lg CFU/g)
Clebsiella	10
Pseudomonades	8
Escherichia coli	7.47
Streptococci	5.7
Enterococci	4.33
Bacilli	4.14
staphylococci	3.87
Peptostreptococci	3.68
Micrococci	3
Candida	2.77

Therefore, all the patients examined quantitatively and were high level representatives of both typical and conditional pathogenic microflora, which indicates the development of Disbacteriosis of mucosal microflora (V. V. Chernin and Soave, 2011). The results of the study the spectrum and frequency of occurrence of microorganisms depends on the degree of activity of articular syndrome wasshown in Figure 2. In patients with RA, I degree of activity in the gastric juice reveals the following frequency of occurrence of microorganisms: peptostreptococci – 100%,staphylococci – 80%, Streptococci and Escherichia coli – 40%, Enterococci, Bacilli Clebsiella and Candida were 20% patients. II degree of activity in (CO) of the stomach revealed the following frequency of occurrence of microorganisms approximately equal proportions of Escherichia coli, Clebsiella and peptococci – 55.5%, Staphylococci and Streptococci – 33.3%, Enterococci and Pseudomonades – in 22.2%, Bacilli –in 11.1%. Therefore, in patients with RA, the frequency of occurrence of microorganisms peculiar to the mucosal flora and conditionally pathogenic microorganisms decreases with increase in the degree of the disease activity.

We also analyzed the quantitative aspect of the mucosal flora in patients with RA depending on the degree of activity of inflammatory process in the joints, the data presented in Fig. 3. As can be seen from figure 3, in patients with RA of level achieves were inoculated Clebsiella in the number of crops 12 lg CFU/g; Streptococci – 5.03 lg CFU/g; staphylococci – 4.02lg CFU/g; enterococci – 4 lg CFU/g; peptostreptococci – 3.39 lg CFU/g; Bacilli – 3.14 lg CFU/g; Candida – 2.77 lg CFU/g; Escherichia – 2.15 lg CFU/g. At the II degree of disease activity were inoculated Escherichia and Clebsiella in the number of cultures of 9.6 lg CFU/g, pseudomonads - 8 lg CFU/g Streptococci – 6,15 lg CFU/g, Bacilli – 5,14 lg CFU/g, enterococci is 4.5 lg CFU/g, peptostreptococci -3,98 lg CFU/g, staphylococci – 3.66 m lg CFU/g.

Therefore, overall in patients with RA with the increase of the degree of disease activity in a quantitative sense was characterized by the increase in the number of crops characteristic of the mucosal microflora, as well as unusual (representatives of anaerobic gram-positive cocci, opportunistic flora) microorganisms, keeping within the concept of syndrome dysbiosis of the mucosal microflora. The authors estimated the degree of dysbacteriosis of mucosal microflora, is presented in Fig. 4.

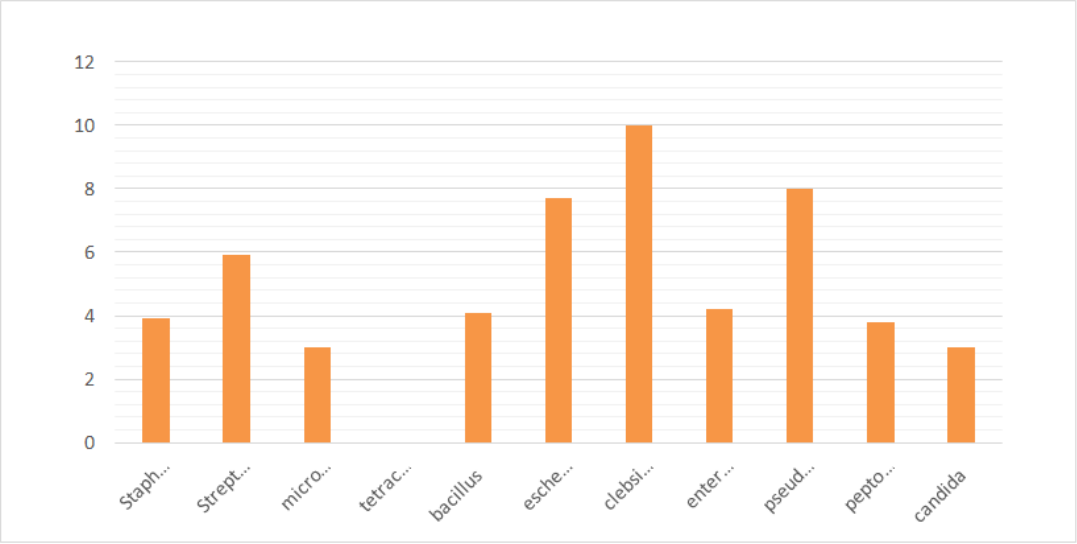

Fig. 1. Quantitative characterization of the stomach parietal Microflora in patients with RA

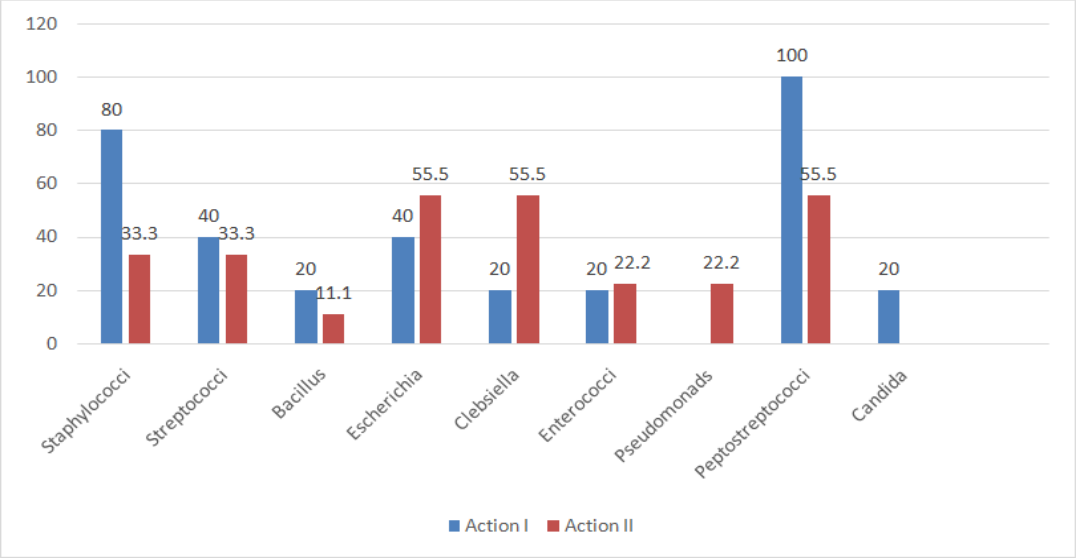

Fig. 2. Range and frequency of occurrence of microorganisms in the mucosal layer in patients with RA, depends on disease activity

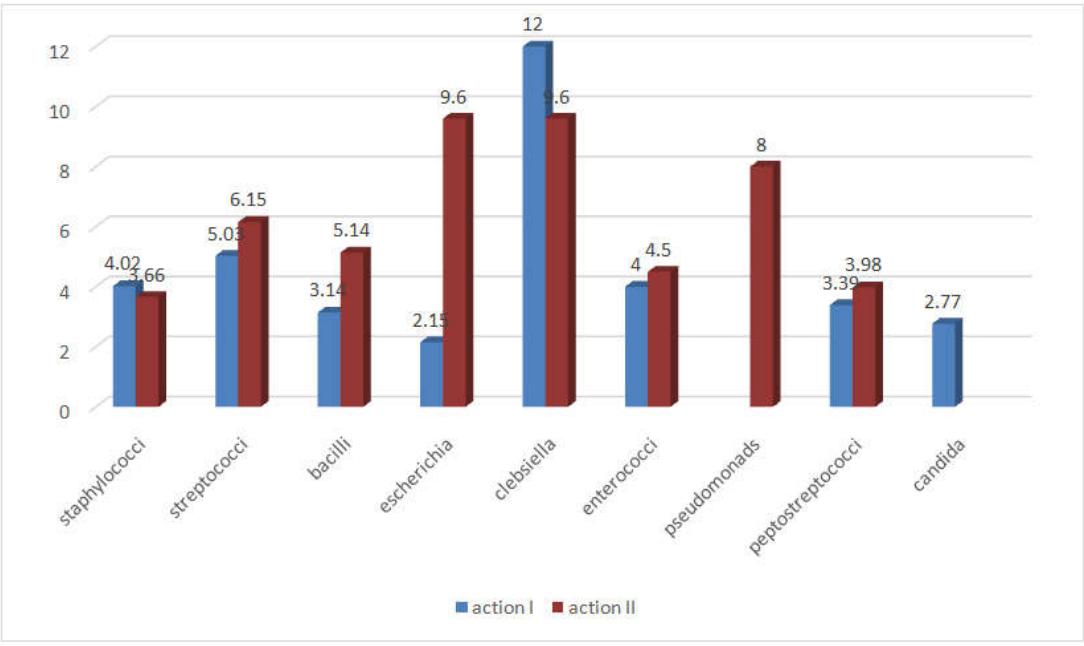

Fig. 3. Quantitative characterization of the parietal Microflora of the stomach of patients with RA, depending on disease activity

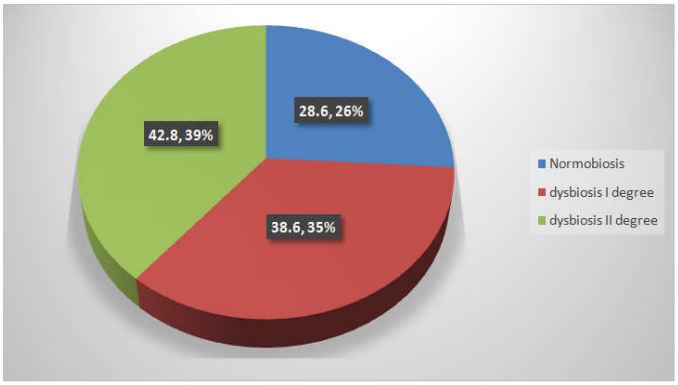

Fig. 4. Dysbiosis of the mucosal flora in patients with RA

As can be seen in 71.4% of patients with RA was revealeddysbacteriosis of mucosal microflora of different severity (according to the classification of intraluminal syndrome of gastroduodenal dysbacteriosis in Beyul E. A. and KuvaevaI. B.). the following table presents data of severity degree of dysbacteriosismucosal microflora depending on the disease activity. It is established that in patients with RA in parietal microflora there has been an increasing severity of dysbiotic shifts with increasing degree of inflammatory activity in the joints. So when I degree of dysbiosis achieves the RA III degree revealed 20% of patients, II degree of activity of RA dysbiosis of III degree was detected in 55.5% of patients.

Development of dysbiosis of the stomach is manifested in the change of protective barrier potential of this zone as biotope microflora has a protective function - colonization resistance (4). One of the important functions of the normal microflora is maintenance of immune protection (8). It is likely that in conditions of dysbiosis there are changes in the immune protection of the organism in consequence of which disturbances occur in immune inflammatory response of the body. Thus, it becomes obvious that the development of dysbiosis GDZ should have some influence on the course of our study of rheumatoid arthritis. Indeed, as the results of our studies between the severity of the dysbiosis and the degree of activity of joint pathology and definite dependence. The higher activity of the joint disease, the more marked becomes the dysbacteriosis of stomach and Vice versa

Conclusion

In patients with RA are marked dysbiotic changes in the stomach. The severity of dysbiosis is directly dependent on the activity of joint pathology.

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