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Research Article

Study of systemic inflammation markers and their association with intestinal microbiota in patients with chronic kidney disease

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ABSTRACT
Markers of systemic inflammation and their connection with intestinal microbiota in patients with 2-4 stages of cerebral palsy are studied in the article. The study of markers responsible for proinflammatory effects in the body has shown that such indicators as IL-6, DRB, fibrinogen showed a significant correlation with the severity of changes in the composition of the microbiota in patients with CHF.

Keywords: chronic kidney disease, systemic inflammation, strawberry filtration rate, intestinal microbiota.

INTRODUCTION

Due to the fact that human microbiota varies depending on many factors, including comorbid pathology, it seems reasonable to investigate intestinal microbiota in patients with chronic kidney disease and its probable connection with markers of systemic inflammation. The aim of the study was to reveal the relationship between some inflammatory biomarkers and changes in intestinal microbiota composition in patients with chronic kidney disease. The study included 85 patients with chronic kidney disease. The average age of the patients was 52±4 years (48 men and 37 women). The control group consisted of 30 healthy volunteers aged 50±3 years, 15 men and 15 women, comparable with the main group by sex and age. The results of the study showed that in patients with cerebral palsy the imbalance of intestinal microbiota was combined with increased levels of DRR, IL-6, leukocytes. There is a bi-directional connection, in which inflammation and dysbiosis contribute to the progression of chronic kidney disease. The study of markers responsible for pro-inflammatory effects in the body has shown that such indicators as IL-6, DRR, fibrinogen showed a significant correlation with the composition of the microbiota in patients with CHD.

RELEVANCE

Intestinal microbiota plays an important role in metabolic, nutritional, physiological and immunological processes and represents a real ecosystem. More than 100 trillion microbes (1014) coexist with us throughout our lives, representing 10 times more than our own human cells, and constitute 1.5-2 kg of our weight [6.8]. In patients with chronic kidney disease there is progressive damage to morphology and functions of various systems, and microbiota becomes less diverse and more dynamic, which is characterized by the prevalence of pathogenic or opportunistic strains [1,4,7]. These changes include changes in intestinal transit, reduced protein uptake, reduced fibre consumption, oral iron treatment and frequent use of antibiotics. All this contributes to systemic inflammation and the accumulation of uremic toxins that are absorbed by the intestines and excreted by the kidneys. Inflammation and uremic toxins play a central role in the pathophysiology of atherosclerosis and other complications associated with CBC [1,2,7]. In this connection it seems to be relevant to study the potential value of multi-faceted testing, including various markers of inflammation in patients with CHF reflecting manifestations of inflammatory and metabolic processes, which play a fundamental role in the emergence of cardiovascular complications, on the one hand, and to study the role of changes in intestinal microbiota on the other hand [2,3].

AIM

The aim of the study was to identify the relationship between some inflammatory biomarkers and changes in intestinal microbiota composition in patients with chronic kidney disease.

PATIENTS AND METHODS

The study enrolled 85 patients with cerebral palsy. The average age of the patients was 52±4 years (48 men and 37 women). The control group consisted of 30 healthy volunteers aged 50±3 years, 15 men and 15 women, comparable with the main group by sex and age. Blood tests were taken using standard methods. The SCF was evaluated using the CKD-EPI formula (2011). In addition, biomarkers such as interleukin-6 (IL-6), alpha tumor necrosis factor (TNF-α) were evaluated. Bacteriological study of feces was carried out in the bacteriological laboratory of the 3rd TMA clinic. Markers of systemic inflammation were evaluated on the basis of an increase in the leukocyte level (>11×109/l), C - reactive protein (>5.0 mg/l) by immunoturbodymetric method, fibrinogen (>4.0 g/l), and interleukin-6 by immunoenzyme method. The differences between the groups were considered statistically significant at p0.05, the correlation analysis was carried out using the non-parametric Spirman rank correlation method. The exact Fisher-Irvin method is used to test the null hypothesis of whether the two binary (dichotomous) samples under study were selected from general sets with the same frequency of the studied effect. Then a basic multiple regression model was created including significant factors ($P < 0.05$) found in the single factor analysis.

THE RESULTS OF THE STUDY

The results showed that the percentage of patients with type II diabetes mellitus was 18%, i.e. 15 out of 85 patients. 36 patients appeared to be smokers, 78 patients (92%) received antihypertensive treatment. Myocardial infarction and OMIC were detected in 23 patients. The average rate of strawberry filtration was 29±4 ml/min/1.73 m2. The main demographic, anthropometric, and clinical and biochemical indicators are presented in Table 1.

Table 1: Clinical and biochemical parameters of patients with KhBP

Parameter	HBP patients, n=85.
Age, years.	52±4
Sex, men men (%)	48 (56%)
Diabetes mellitus type II, %	15 (18%)
Myocardial infarction or ONMC, %	(17%)
Patients receiving antihypertensive therapy, %	78 (92%)
Systolic AD, mmHg.	129±13
Diastolic AD, mmHg.	79±9
Hemoglobin, g/l	125±17
Serum creatinine, g/l	283±16
Speed of strawberry filtration, ml/min/1.73 m2	29±4 мл/мин/1,73м^2
Blood glucose on an empty stomach, g/l	9,9±2,4г/л

Fecal analysis showed a deficit of Bifidobacterium (<108COE) bacteria in the examined patients. The composition of normal intestinal microflora includes lactic acid bacteria - bifidobacteria, lactobacilli and propionic acid bacteria with predominance of bifidobacteria, which play the main role in maintaining the optimal composition of biocoenosis and its functions. A fall in the number of bifidobacteria and lactobacteria below the norm indicates the presence of pathological shifts in the body, such as inflammation and reduced immune protection. Drawing. Composition of intestinal microbiota in patients with different stages of cerebral palsy. *-r>0.05 compared to CG. In addition, an increase in Echerichia number (>108 CFU) was observed in the examined patients. It is known that they belong to conditionally pathogenic flora [7,8,11]. Under normal conditions, they do not cause disturbances. However, when the norm is exceeded and/or the immune protection is ineffective, they can cause serious shifts. Competing with beneficial bacteria, conditionally pathogenic flora may enter the microbial film of the intestine and cause functional disorders, inflammatory, and allergic diseases. It is possible to translocation of conditionally pathogenic microflora, i.e. its penetration through the intestinal wall into the blood and its spread throughout the body, which increases uremic intoxication in patients with cerebral palsy, leading also to immunodeficiency.

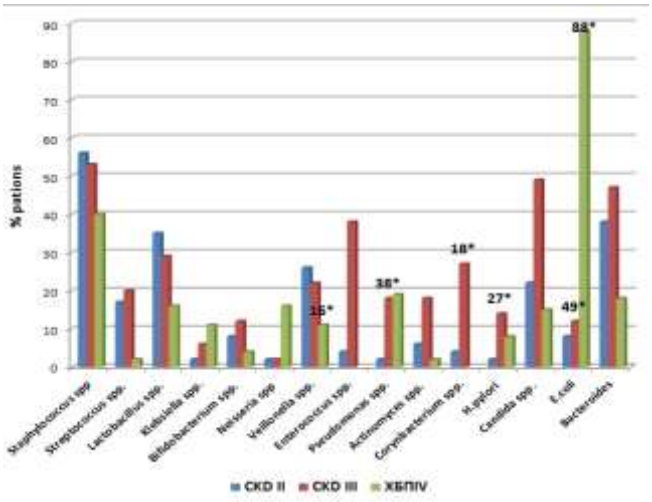

Fig.1:

Table 2: Content of biomarkers in patients with cerebral palsy and in the comparison group.

Indicator	Control group (n=30) Patients with HBP (n=85)	Control group (n=30) Patients with HBP (n=85)	P
Il-6, pg/ml	0,7	0,6	<0.05
FNO-α	11,4	11,1	<0.05
DRB	4,8	6.32	<0.05
Fibrinogen	2,5±0,8	4.36	<0.05

Independent association of IL-6, DRB, fibrinogen biomarkers with severity of intestinal dysbiosis manifestation in patients with cerebral palsy of dodialysis stages was revealed.

DISCUSSION

The study of markers responsible for proinflammatory effects in the body has shown that such indicators as IL-6, DRB, fibrinogen showed a significant correlation with the severity of changes in microbiota composition in patients with cerebral palsy. In men the IL-6 index appeared to be higher than in women. In patients with cerebral palsy with obesity the titer of pathogenic bacteria and their spectrum showed the worst results, though not reliable. Thus, given that uremic toxins are divided into three groups: endogenous, exogenous, and those derived from microbes, it may be assumed that the development of an imbalance in intestinal microbiota will exacerbate the latter type of toxin [9,10,12]. The increased content of urea, creatinine, other uremic toxins and a number of other factors leads to changes in intestinal microbiota with potential biochemical shifts of gastrointestinal tract [5]. As a result, microbial dysbiosis and disturbance of intestinal epithelial barrier develop. Transslocation of endotoxin and uremic toxins of bacterial origin into the bloodstream will promote inflammation and oxidative stress. [9,13]. Therefore, further studies are required, using microbiota studies on a larger cohort of patients, to determine its value in patients with CHD.

CONCLUSION

Thus, the obtained data demonstrated that patients with cerebral palsy combine an imbalance of intestinal microbiota with increased levels of DRR, IL-6, leukocytes. There is a bi-directional connection, in which inflammation and dysbiosis will contribute to the progression of chronic kidney disease. The degree of dysbiosis depends on the stage of cerebral palsy: the higher the stage of cerebral palsy, the more pronounced is the dysbiosis phenomenon.

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