МЕДИЦИНСКИ УНИВЕРСИТЕТ - ВАРНА "Проф. д-р Параскев Стоянов"

Ул."Марин Дринов" 55, Варна 9002, България Тел. : 052/ 65 00 57, Факс: 052/ 65 00 19 e-mail: uni@mu-varna.bg, www.mu-varna.bg



MEDICAL UNIVERSITY - VARNA "Prof. Dr. Paraskev Stoyanov"

55, Marin Drinov Str., 9002 Varna, Bulgaria Tel.: +359 52/ 65 00 57, Fax: + 359 52/ 65 00 19 e-mail: uni@mu-varna.bg, www.mu-varna.bg

Fund "Nauka" Project № 18022 Resume – Competitive-based Session 2018: "Some modern diagnostic aspects of inflammatory intestinal diseases in children and adolescents"

Project leader: Prof. Miglena Dimitrova Georgieva MD, PhD

The purpose of the study is to quantify the expression levels of strictly selected microribonucleic acids (miRNAs) as biological markers of prognostic significance in socially significant inflammatory bowel diseases (chronic ulcerative colitis / UC/ and Crohn's disease /CD/) in children and adolescents.

As a result of the analysis of the available foreign literature, 11 miRNAs were selected, considered suitable for examination in patients with these two diseases. The subject of the study are 35 sick children hospitalized during the period between 01.01.2018 and 31.12.2019, incl. in the Second Children's Clinic of the University Hospital "St. Marina" - Varna at the Department of Pediatrics of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna. In 13 children, it is about UC and 22 children had CD. The control group included 20 children without disease, 12 girls and 8 boys aged between 4 and 17. The serum expression of the following miRNAs was studied: miRNA122, miRNA142-3p, miRNA196-b, miRNA642-b3, miRNA155, miRNA131-a, microRNA125-a, microRNA16-a, microRNA21, microRNA223 and microRNA195. This expression was analyzed using a real-time polymerase chain reaction in the Laboratory of Nutrigenomics, Functional Foods and Nutraceuticals at the Department of Biochemistry, Molecular Medicine and Nutrigenomics of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna. Commercial kits of these miRNAs were used. The values of this expression were calculated by the 2- $\Delta\Delta$ Ct method.

The obtained data were processed by the methods of variation and correlation analysis with the software product IBM SPSS v. 23.

The results of the conducted researches and the data from the modern foreign literature on this issue are formed as manuscripts of three articles, sent for publication in two Bulgarian scientific medical journals (see Appendix N_{2} 1 - Appendix N_{2} 3).

They can be summarized in a concise form as follows:

The expression of all miRNAs is higher in children with Crohn's disease than in healthy children. Statistically significant differences between sick and healthy children were found in two miRNAs - miRNA142-3p (t = 2.05; p <0.05) and miRNA642-b3 (t = 2.00; p <0.05). The borderline statistical significance of the difference between the two groups of children was for miRNA131-a (t = 1.88; p> 0.05) and for miRNA223 (t = 1.80; p> 0.05). Due to the small sample size and the presence of a significant variance between the lowest and highest expression values of the remaining seven miRNAs, no statistically significant differences were observed between children with Crohn's disease and healthy children.

All miRNAs are characterized by higher expression in children with chronic ulcerative colitis than in healthy children. Due to the small number of patients studied and the significant variance between the lowest and highest values of these 11 miRNAs, no statistically significant differences were observed between sick and healthy children. The average value of the expression of mikroRNK122 is 3.76 times higher in children with chronic ulcerative colitis than in healthy children, but the difference was not statistically significant (t = 1,73; p> 0,05).

A correlation analysis is to be performed in order to identify possible relationships between the dynamics of the expression values of these 11 miRNAs and the clinical features of children with chronic ulcerative colitis and Crohn's disease in the course of the diseases.

Achieved results:

Microribonucleic acids (microRNAs) regulate gene expression by acting at the site of interaction between the environment and inherited molecular and cellular phenotypes in a large number of diseases. The expression of 11 different serum miRNAs was examined using a real-time polymerase chain reaction in 22 children with Crohn's disease (CD) and 13 children with ulcerative colitis (UC) hospitalized in UMHAT "St. Marina" – Varna during the period between 01.01.2019 and 31.08.2020, as well as in 20 clinically healthy children. MicroRNA131 has a very high expression in children with CD and very low expression in children with UC, and microRNA16-a has a very high expression in children with UC and very low expression in children with CD. The value of miRNA195 was statistically significantly (2.70 times) higher in children with UC than in those with CD (t=2.03; p<0.05). The expression values of all miRNAs were higher in patients than in healthy children, but statistically significant differences were observed only between children with BC and healthy children in miRNA142-3p and miRNA642-b3 (respectively t=2.05; p<0.05 and t=2.00; p<0.05). There is both a positive weak statistically significant correlation between the values of miRNA16a, on the one hand, and patients with UC versus those with CD (r=0.27; p=0.043), and a negative considerable statistically significant correlation between the values of hemoglobin concentrations in patients with UC, on the one hand, and microRNA122 (r=-0.662; p=0.014), microRNA131a (r=-0.632; p=0.02) and microRNA223 (r=-0.642; p=0.018), on the other hand. The expression of microRNA195, microRNA142-3p and microRNA642-b3, microRNA 131-a may have diagnostic and differential diagnostic value in children with inflammatory bowel disease.