

UDC [616.211:616.216]-002.2-006.5-078:57.083.6'152.34

## **THE CONTENT OF MCP-1 AND MMP-9 IN BLOOD SERUM OF PATIENTS WITH CHRONIC POLYPOID RHINOSINUSITIS**

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The content of MCP-1 and MMP-9 in blood serum of patients with chronic polypoid rhinosinusitis was studied. It was found that this pathology led to a significant increase in MCP-1, which is a marker of fibrosis, in blood serum. The compensatory increase in MMP-9, serving as an antifibrotic factor, is much weaker. Such imbalance between profibrotic MCP-1 and antifibrotic MMP-9 indicates a lack of compensatory adaptation mechanisms of fibrolysis activation and contributes to the development of fibrosis in chronic polypoid rhinosinusitis.

**KEY WORDS:** chronic polypoid rhinosinusitis, monocyte chemoattractant protein-1, MCP-1, matrix metalloproteinase-9, MMP-9

### **ВМІСТ MCP-1 ТА MMP-9 У СИРОВАТЦІ КРОВІ ПАЦІЄНТІВ З ХРОНІЧНИМ ПОЛІПОЗНИМ РИНОСИНУСИТОМ**

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Вивчено вміст MCP-1 і MMP-9 у сироватці крові пацієнтів з хронічним поліпозним риносинуситом. Встановлено, що дана патологія призводить до значного підвищення маркера фіброзу MCP-1 у сироватці крові. Компенсаторне підвищення MMP-9, яка виступає в якості антифібротичного фактора, виражене набагато слабше. Подібний дисбаланс між профібротичним MCP-1 і антифібротичною MMP-9 вказує на недостатність компенсаторних адаптаційних механізмів активації фібролізу і сприяє розвитку фіброзу при хронічному поліпозному риносинуситі.

**КЛЮЧОВІ СЛОВА:** хронічний поліпозний риносинусит, моноцитарний хемоаттрактантний протеїн-1, MCP-1, матриксна металопротеїназа-9, MMP-9

### **СОДЕРЖАНИЕ MCP-1 И MMP-9 В СЫВОРОТКЕ КРОВИ БОЛЬНЫХ С ХРОНИЧЕСКИМ ПОЛИПОЗНЫМ РИНОСИНУСИТОМ**

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Изучено содержание MCP-1 и MMP-9 в сыворотке крови пациентов с хроническим полипозным риносинуситом. Установлено, что данная патология приводит к значительному повышению маркера фиброза MCP-1 в сыворотке крови. Компенсаторное повышение MMP-9, выступающей в качестве антифибротического фактора, выражено намного слабее. Подобный дисбаланс между профибротическим MCP-1 и антифибротической MMP-9 указывает на недостаточность компенсаторных адаптационных механизмов активации фибролиза и способствует развитию фиброза при хроническом полипозном риносинусите.

**КЛЮЧЕВЫЕ СЛОВА:** хронический полипозный риносинусит, моноцитарный хемоаттрактантный протеин-1, MCP-1, матриксная металлопротеиназа-9, MMP-9

## **INTRODUCTION**

Chronic rhinosinusitis is one of the most common diseases in otorhinolaryngology that covers up to 11% of the population of European countries. The disease negatively

affects the quality of life of patients. It has an impact on both physical and mental health and leads to a decrease in working efficiency, insomnia [1]. Negative social aspects of chronic rhinosinusitis imply significant costs of the public health system spent on the treatment

of patients with rhinosinusitis. All of the factors mentioned above contribute to the investigation of the pathogenesis of this disease and the development of new treatment strategies.

It has been known that inflammatory pathology of various etiologies is accompanied by changes in the cytokine serum spectrum and activation of enzymes involved in degradation of the extracellular matrix – matrix metalloproteinases (MMPs) [2–5]. One of such cytokines whose expression increases in inflammatory processes is called monocyte chemoattractant protein-1 (MCP-1). In addition to its ability to stimulate the recruitment of new monocytes into the inflammation zone, MCP-1 is capable of inducing the expression of collagen molecules, acting as a profibrotic factor. Thus, it can serve as a marker of fibrosis [6].

MMPs, in particular matrix metalloproteinase-9 (MMP-9), have collagenase activity and, accordingly, are involved in breakdown of connective tissue structural components [7]. Thus, MMP-9 is considered to be an antifibrotic factor. Chronic inflammatory processes are known to be accompanied by proliferation of the connective tissue whose intensity depends primarily on the balance between pro - and antifibrotic factors. Features of the content of the abovementioned factors in chronic polypoid rhinosinusitis should be elucidated.

## **OBJECTIVE**

The aim of the study was to study the content of the profibrotic factor MCP-1 and the antifibrotic protease MMP-9 in blood serum of patients with chronic polypoid rhinosinusitis.

## **MATERIALS AND METHODS**

Forty individuals who were treated in the department of otorhinolaryngology at Kharkiv Regional Clinical Hospital were examined. Polypoid form of chronic rhinosinusitis was diagnosed in twenty patients. Their diagnosis was verified using scrupulous clinical and anamnestic examination, as well as laboratory and instrumental tests using criteria proposed by the WHO expert committee. The control group consisted of twenty conditionally healthy individuals with deviated nasal septum without signs of pathology of other organs and systems.

The research was carried out in accordance with *The Code of Ethics of the World Medical Association (Declaration of Helsinki)* and *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (ETC 164)*. The informed consent of patients was obtained for the research. The privacy rights of patients were taken into account.

Samples of venous blood were collected for biochemical tests on an empty stomach in representatives of both groups. The blood was centrifuged for 15 minutes at 3,000 rpm to obtain blood serum. The MCP-1 concentration in blood serum was determined by enzyme-linked immunosorbent assay kits manufactured by eBioscience (Vienna, Austria). To study the content of MMP-9 in the blood serum, the ELISA kit produced by eBioscience (Vienna, Austria) was used. The optical density of the solutions was determined using the Awareness Technology Stat Fax 303 Plus Microstrip Reader.

The data obtained as a result of our research were statistically processed by the GraphPad Prism 5 application using the Student's t-test. Difference between groups was considered to be statistically significant at  $p < 0.05$ .

## **RESULTS AND DISCUSSION**

Determination of blood serum MCP-1 levels in patients with chronic polypoid rhinosinusitis demonstrated a more than sevenfold increase in this parameter compared to the control group (Table). It has been known that this chemokine is involved in fibrillogenesis of collagen [8, 9] and, therefore, is able to promote proliferation of the extracellular matrix. Thus, the increase in MCP-1 concentrations in the serum of patients with polypoid rhinosinusitis indicates the activation of fibrotic processes.

Given that the intensity of fibrotic changes depends on the balance between profibrotic and antifibrotic factors, we studied the blood serum MMP-9 levels in patients for a complex evaluation of the fibrosis-fibrololysis system in chronic polypoid rhinosinusitis. The choice of MMP-9 can be explained by the ability of this proteolytic enzyme to degrade various types of collagen, thereby mediating fibrololysis [10] and leveling the profibrotic effect of MCP-1.

It was established that MMP-9 blood serum concentrations in patients with the polypoid form of chronic rhinosinusitis were 1.5-fold

higher compared to the same parameter of the control group (Table). Similar changes in the serum content of MMP-9 can be due to its compensatory activation in response to an increase in MCP-1 levels and subsequent intensification of MCP-1-dependent fibrosis. The shift of equilibrium in the fibrosis-fibrolysis system towards the former leads to the corresponding adaptive overproduction of

antifibrotic factors. However, we can notice insufficient activation of the metalloproteinase-mediated link of the antifibrotic system in patients with chronic polypoid rhinosinusitis, which indicates a near exhaustion of compensatory capabilities and the shift of equilibrium towards the development of sclerosis.

Table

**The content of MCP-1 and MMP-9 in blood serum of patient's chronic polypoid rhinosinusitis (M ± m)**

Indices, units	Control group	Patients with chronic polypoid rhinosinusitis
	n = 20	n = 20
Monocyte chemoattractant protein-1 (MCP-1), pg/ml	50.74 ± 0.74	351 ± 40.98 p < 0.001
Matrix metalloproteinase-9 (MMP-9), ng/ml	3.28 ± 0.47	4.81 ± 0.19 p < 0.05

Note: *p* is a significance value compared to the control group

## CONCLUSIONS

1. Chronic polypoid rhinosinusitis is accompanied by an increase in blood serum MCP-1 levels in patients, which indicates the involvement of this chemokine in the proliferation of connective tissue in this pathology.

2. High levels of the antifibrotic proteolytic enzyme MMP-9 are observed in blood serum of patients with chronic polypoid rhinosinusitis, which can serve as a sign of the activation of compensatory

adaptive mechanisms aimed at inhibiting the extracellular matrix proliferation.

3. The pronounced increase in MCP-1 levels against the background of a slight activation of MMP-9 in the blood serum of patients with chronic polypoid rhinosinusitis indicates insufficiency of compensatory mechanisms and activation of fibrosis.

## PROSPECTS FOR FUTURE STUDIES

It seems to be promising to study other factors that affect the intensity of proliferation of connective tissue in chronic polypoid rhinosinusitis.

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