

## CHARACTERISTICS OF CYTOKINE REGULATION AND CARTILAGINOUS TISSUE METABOLISM AT PRIMARY AND POST-TRAUMATIC OSTEOARTHRITIS

*E.V. Gladkova, A.N. Ivanov*

Scientific Research Institute of Traumatology, Orthopedics and Neurosurgery  
of Saratov State Medical University n.a. V.I. Razumovsky, Saratov, Russia

## ОСОБЕННОСТИ ЦИТОКИНОВОЙ РЕГУЛЯЦИИ И МЕТАБОЛИЗМА ХРЯЩЕВОЙ ТКАНИ ПРИ ПЕРВИЧНОМ И ПОСТТРАВМАТИЧЕСКОМ ОСТЕОАРТРОЗЕ

*Е.В. Гладкова, А.Н. Иванов*

Научно-исследовательский институт травматологии, ортопедии и нейрохирургии  
ФГБОУ ВО «Саратовский государственный медицинский университет им. В.И. Разумовского»  
Минздрава России, Саратов

Cytokine system and cartilaginous tissue metabolism of 27 women affected by 0-1 stage of primary and 19 women affected by 0-1 stage of post-traumatic osteoarthritis (OA) have been studied as well as of 10 healthy persons of the control group. The enzyme-linked immunoassay method was used to determine the content of cartilage oligometric matrix protein (COMP), cartilage glucoprotein (YKL-40), interleukins (ILs) 4 and 1 $\beta$  in blood serum, collagen fragments (CTX II) in urine. It was found that COMP, CTX II, YKL-40 and IL-1 $\beta$  concentrations grew at more intensive rate in case of primary OA compared to post-traumatic OA. The diminution of correlation relationship strength in IL-1 $\beta$  serum concentrations is noted with the system level of cartilaginous tissue degradation products on the background of YKL-40 regulatory influence buildup which is more prominent with primary OA than it is with the post-traumatic one. **Conclusions:** early stages of primary OA are characterized by more prominent degenerative changes in the joint hyaline cartilage due to losses of type II collagen and hyperproduction of proinflammatory link cytokines with the background of YKL-40 regulatory influence buildup and reduction of the IL-1 $\beta$  influence. The changes of cartilaginous tissue metabolism with post-traumatic OA were characterized by preservation of dependence on IL-1 $\beta$  serum concentration with the background of reduction of YKL-40 influence.

**Keywords:** osteoarthritis; cytokines; cartilage degradation products.

Изучена система цитокинов и метаболизм хрящевой ткани у 27 женщин с 0–I ст. первичного, 19 — с 0–I ст. посттравматического остеоартроза (ОА) и 10 здоровых лиц группы сравнения. В сыворотке крови методом ИФА определено содержание олигомерный матриксный белок (СОМР), хрящевой гликопротеин (УКЛ-40), интерлейкинов (ИЛ) 4 и 1 $\beta$ , в моче — фрагментов коллагена (СТХ II). Выявлено, что концентрации СОМР, СТХ II, УКЛ-40 и ИЛ-1 $\beta$  более интенсивно нарастают при первичном ОА по сравнению с посттравматическим. Отмечено снижение силы корреляционных связей сывороточных концентраций ИЛ-1 $\beta$  с системным уровнем продуктов деградации хрящевой ткани на фоне нарастания регуляторного влияния УКЛ-40, более выраженное при первичном ОА, чем при посттравматическом. **Выводы:** ранние стадии первичного ОА характеризуются более выраженными дегенеративными изменениями суставного гиалинового хряща за счет потерь коллагена II типа и гиперпродукцией цитокинов провоспалительного звена на фоне нарастания регуляторного значения УКЛ-40 и снижения влияния ИЛ-1 $\beta$ . Изменения метаболизма хрящевой ткани при посттравматическом ОА отличаются сохранением зависимости от сывороточной концентрации ИЛ-1 $\beta$  на фоне снижения влияния УКЛ-40.

**Ключевые слова:** остеоартроз; цитокины; продукты деградации хряща; хрящевой гликопротеин-39; олигомерный матриксный белок хряща; фрагменты коллагена II типа.

**Introduction.** The late stages of osteoarthritis (OA) are characterized with severe pain syndrome, disorders of skeletal connective tissue remodeling with the background of microcirculatory, cellular and molecular immune disorders leading to depression of reparative chondrogenesis, intraosseous hypertension and changes in osteogenesis of articular surfaces. At this, the prominent imbalance in the system of cytokine regulation has been noted [1]. However, for now the interrela-

tion of cytokine regulation and skeletal connective tissue remodeling processes at early stages of post-traumatic and primary OA are understudied. Objective: Research of characteristics of cytokine regulation and cartilaginous tissue metabolism in patients affected by early presentations of primary and post-traumatic osteoarthritis.

**Material and methods.** 66 women aged 35 to 50 were examined, 27 were affected by 0-1 stages of primary OA, 19 were affected by post-traumatic

OA and 10 were healthy persons of the control group. The enzyme-linked immunoassay method was used to determine the content of cartilage oligomeric matrix protein (COMP), cartilage glycoprotein (YKL-40), interleukins (ILs) 4 and 1 $\beta$  in blood serum, collagen fragments (CTX II) in urine. The results were processed using Statistica 10.0. Most of the data had no normal distribution and thus the median and interquartile range was calculated. Mann-Whitney U-test was employed to compare the groups and the Spearman correlation coefficient ( $r$ ) to evaluate interrelations between the parameters. The certainty factor ( $p$ ) was considered valuable at  $p < 0.05$ .

**Results and discussion.** Despite the etiological form of OA, its early stages are characterized by the development of cartilaginous tissue extracellular matrix disorganization making itself evident by raising concentrations of COMP in blood and CTX II in urine compared to these of healthy persons whose average values of these parameters constituted 557.34 (513.42; 561.26) ng/ml and 3.48 (1.70; 5.12) ng/ml correspondingly. The rise of the cartilage degradation products system level was of clearer pronounced nature at primary OA compared to post-traumatic one as evidenced by significantly ( $p < 0.05$ ) higher concentrations of COMP in blood (952.13 (884.06; 998.72) versus 744.12 (691.17; 792.23), ng/ml) and CTX II in urine (23.4 (19.6; 26.8) versus 14.7 (9.1; 16.3) ng/ml). At that with patients affected by primary OA the IL-1 $\beta$  concentration constituted 8.96 (7.03; 10.20) pg/ml and YKL-40 68.3 (45.9; 77.1) ng/ml which is higher compared to values in both the control group (3.98 (1.12; 5.77) pg/ml and 23.1 (18.0; 30.2) ng/ml) as well as the level of these cytokines in female patients affected by

post-traumatic OA (5.44 (3.19; 6.37) pg/ml and 37.8 (29.0; 41.6) ng/ml correspondingly). The unidirectional change in concentrations of cartilage tissue degradation products and proinflammatory cytokines was detected which apparently owed to the fact that the latter activated the output of the wide range of proteoclastic ferments including collagenase [2].

When estimating the correlational interrelations, the presence of moderate force relations between concentrations of IL-1 $\beta$  and Urine CTX II ( $r = 0.5$ ;  $p < 0.05$ ) as well as concentrations of COMP ( $r = 0.5$ ;  $p < 0.05$ ) and concentration of YKL-40 with the levels of Urine CTX II ( $r = 0.4$ ;  $p < 0.05$ ) and COMP ( $r = 0.3$ ;  $p < 0.05$ ) in control group persons was detected. With primary OA some reduction of relation force between IL-1 $\beta$  and Urine CTX II ( $r = 0.4$ ;  $p < 0.05$ ) as well as rise of dependence between YKL-40 and Urine CTX II ( $r = 0.5$ ;  $p < 0.05$ ) were detected. With post-traumatic OA the presence of moderate force relations between IL-1 $\beta$  and COMP ( $r = 0.5$ ;  $p < 0.05$ ) as well as Urine CTX II ( $r = 0.4$ ;  $p < 0.05$ ) was established. The relation between YKL-40 and COMP ( $r = 0.3$ ;  $p < 0.05$ ) as well as Urine CTX II ( $r = 0.3$ ;  $p < 0.05$ ) was less prominent.

**Conclusion.** Early stages of primary OA are characterized by more prominent degenerative changes in the joint hyaline cartilage due to losses of type II collagen and hyperproduction of proinflammatory link cytokines with the background of YKL-40 regulatory influence buildup and reduction of the IL-1 $\beta$  influence. The changes of cartilaginous tissue metabolism with post-traumatic OA were characterized by preservation of dependence on IL-1 $\beta$  serum concentration with the background of reduction of YKL-40 influence.

## References

1. Popkov VM. Cytokines: the biologic role in the development of adjustment and damage response under normal and pathological conditions of various genesis: monograph. Saratov State Medical University n.a. V.I. Razumovsky. 2016. 448 p.
2. Varyushina EA. Proinflammatory cytokines in regulation of inflammatory and repair processes. Life Science Ph.D. thesis. Saint Petersburg. 2013. 45 p.