ВЛИЯНИЕ ЭЛЕКТРОСТИМУЛЯЦИИ МЫШЦ БЕДРА НА УРОВЕНЬ ИНТЕРЛЕЙКИНА-6 ПРИ ТРАВМАТИЧЕСКОМ ПОВРЕЖДЕНИИ ПЕРЕДНЕЙ КРЕСТООБРАЗНОЙ СВЯЗКИ КОЛЕННОГО СУСТАВА

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Резюме. Травматическое повреждение передней крестообразной связки приводит к нарушению опороспособности и механической нестабильности конечности. Одним из частых осложнений после травмы, является артрогенное мышечное торможение, вследствие ингибирования четырехглавой мышцы и развития функциональной контрактуры. Напротив, одним из показателей высокой мышечной активности является достаточный уровень в крови функциональных мышечных белков-миокинов, в частности интерлейкина-6, экспрессирующихся и высвобождающихся мышечными волокнами. Целью исследования явилось изучение уровня интерлейкина-6 у мужчин с повреждением передней крестообразной связки в динамике электромиостимуляции четырехглавой мышцы бедра.

В исследовании принимали участие 23 мужчины, средний возраст 34,8±2,2 года, с травматическим повреждением передней крестообразной связки, которым за 10 дней до оперативного вмешательства проводилась электромиостимуляция четырехглавой мышцы бедра на аппарате INTELECT® Advanced (Chattanooga (DJO), США). Контрольную группу составили 12 здоровых мужчин, средний возраст 32,2±2,4 года. Уровень IL-6 определяли в сыворотке крови до электромиостимуляции, и в динамике с помощью набора для иммуноферментного анализа («Вектор-Бест», г. Новосибирск). Обработку полученных данных проводили с применением пакета лицензионных программ Statistica. vers. 10.0.

Базальный уровень IL-6 в основной группе составил 1,28 (0,87-1,72) пг/мл, что значимо ниже в сравнении с показателем здоровых лиц 5,2 (3,8-6,1) пг/мл и обусловлено низким уровнем физической активности, вследствие функциональной контрактуры четырехглавой мышцы. В динамике электромиостимуляции на 5-е сутки уровень IL-6 значимо увеличился в 3,2 раза от базального уровня, на 10-е сутки в 4,6 раз, при этом не превышая показателя группы здоровых лиц. При сокращении мио-

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цитов, в цитоплазме клеток повышалась концентрация миокина – интерлейкина-6, способствующая накоплению в мышечной клетке макроэргов, вследствие миокин-зависимой активации гликогенолиза. Репаративные и противовоспалительные свойства IL-6 реализуются в стимулируемых поперечно-полосатых мышцах по механизму классического сигналинга, способного блокировать активацию универсального внутриклеточного фактора транскрипции NF-κB, в отношении продукции провоспалительных цитокинов. Таким образом, электромиостимуляция до начала оперативного лечения приводит к повышению концентрации в крови миокина – IL-6, что способствует увеличению противовоспалительного и репаративного потенциала поврежденных тканей.

Ключевые слова: мужчины, повреждение передней крестообразной связки, электромиостимуляция, миокины, IL-6, репарация

EFFECT OF ELECTRICAL STIMULATION OF THE THIGH MUSCLES ON THE LEVEL OF INTERLEUKIN-6 IN TRAUMATIC INJURIES OF THE ANTERIOR CRUCIATE LIGAMENT OF THE KNEE JOINT

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Abstract. Traumatic damage to the anterior cruciate ligament leads to impaired support and mechanical instability of the limb. One of the frequent complications after injury is arthrogenic muscle inhibition due to inhibition of the quadriceps muscle and the development of functional contracture. On the contrary, one of the indicators of high muscle activity is a sufficient level in the blood of functional muscle proteins – myokines, in particular interleukin-6, which are expressed and released by muscle fibers. The aim of the study was to study the level of interleukin-6 in men with damage to the anterior cruciate ligament in the dynamics of electromyostimulation of the quadriceps femoris.

The study involved 23 men, mean age 34.8±2.2 years, with traumatic injury of the anterior cruciate ligament, who, 10 days before surgery, underwent electromyostimulation of the quadriceps femoris using the INTELECT® Advanced device (Chattanooga (DJO), USA). The control group consisted of 12 healthy men, mean age 32.2±2.4 years. The level of IL-6 was determined in the blood serum before electromyostimulation, and in dynamics using a kit for enzyme immunoassay (Vector-Best, Novosibirsk). The obtained data were processed using the Statistica licensed software package v. 10.0.

The basal level of IL-6 in the main group was 1.28 (0.87-1.72) pg/mL, which is significantly lower than in healthy individuals 5.2 (3.8-6.1) pg/mL and is due to a low level of physical activity due to functional contracture of the quadriceps muscle. In the dynamics of electromyostimulation on the 5th day, the level of IL-6 significantly increased by 3.2 times from the basal level, on the 10th day by 4.6 times, while not exceeding that of the group of healthy individuals. With the reduction of myocytes, the concentration of myokine interleukin-6 increased in the cytoplasm of cells, which contributes to the accumulation of macroergs in the muscle cell, due to myokine-dependent activation of glycogenolysis. The reparative and anti-inflammatory properties of IL-6 are realized in stimulated striated muscles by the classical signaling mechanism that can block the activation of the universal intracellular transcription factor NF-κB in relation to the production of pro-inflammatory cytokines. Thus, electromyostimulation before the start of surgical treatment leads to an increase in the concentration of myokine IL-6 in the blood, which contributes to an increase in the anti-inflammatory and reparative potential of damaged tissues.

Keywords: men, anterior cruciate ligament injury, electromyostimulation, myokines, IL-6, repair

Introduction

Traumatic injuries of the anterior cruciate ligament (ACL) are leading with an incidence of 4 cases per 1000 people [1]. Traumatic ACL injury occurs 20-30 times more often than ruptures of the posterior cruciate ligament, more often in women than in men [7], presumably due to the peculiarities of the hormonal background [2]. ACL is the most important component of knee joint stabilization, which has an extensive proprioceptive field, which is the primary link of the kinematic apparatus. The impulses coming from the proprioceptors limit and mechanically stabilize the muscle response. Rupture of the ACL leads to impaired support ability and mechanical instability of the limb [4]. Most often, the ACL is damaged by a sharp deviation of the lower leg outward and torsion of the thigh inward. One of the classic complications that occurs after a knee injury is arthrogenic muscular inhibition (AMT), diagnosed by difficulty or absence of limb extension due to inhibition of the quadriceps muscle and the development of functional contracture of the hamstring. The prolonged course of the AMT phenomenon leads to atrophy of the quadriceps muscle, constant pain in the knee, dynamic instability of the knee joint and has a negative impact on the outcome of surgical treatment [11].

At the same time, one of the indicators of high muscle activity during intensive motor mode is a sufficient level in the blood of functional muscle proteins – myokines, which are expressed and released by muscle fibers and have a polymodal effect on target organs and tissues [10]. In recent years, numerous data have been accumulated on the effect of myokines on the main homeostatic systems: nervous, immune, endocrine. By exerting a local paracrine effect, myokines, in particular IL-6, can affect the signaling pathways involved in muscle metabolism [10].

In connection with the above, the aim of our work was to study the dynamics of the level of myokine IL-6 in men with ACL damage in the dynamics of static electrical myostimulation (EMS) of the quadriceps femoris muscle.

Materials and methods

The main study group consisted of 23 men, whose average age was 34.8±2.2 years, with a verified diagnosis according to ICD-10 S83.5. Stretching, rupture and overstrain of the anterior cruciate ligament of the knee joint with an injury less than 4 months old, admitted for reconstructive surgery. The main complaints of patients: a feeling of instability in the damaged knee joint (87%), moderate pain (64%), muscle hypotrophy of the limb (43%). To verify the diagnosis, an orthopedic examination and X-ray examination were performed. All patients 10 days before surgery underwent EMS of the quadriceps femoris muscle daily, working cycle 10 s stimulation/10 s relaxation, for 20 min on the INTELECT® Advanced combination therapy device (Chattanooga (DJO), USA). The current strength was increased every 2-3 cycles after the start of exposure, until noticeable muscle contractions appeared.

The control group consisted of 12 healthy men with an average age of 32.2±2.4 years. The level of IL-6 was detected in the venous blood serum of healthy individuals and patients with ACL damage in dynamics before EMS, on the 5th and 10th days using a set of reagents for enzyme immunoassay (Vector-Best, Russia) in the concentration range 0-300 pg/

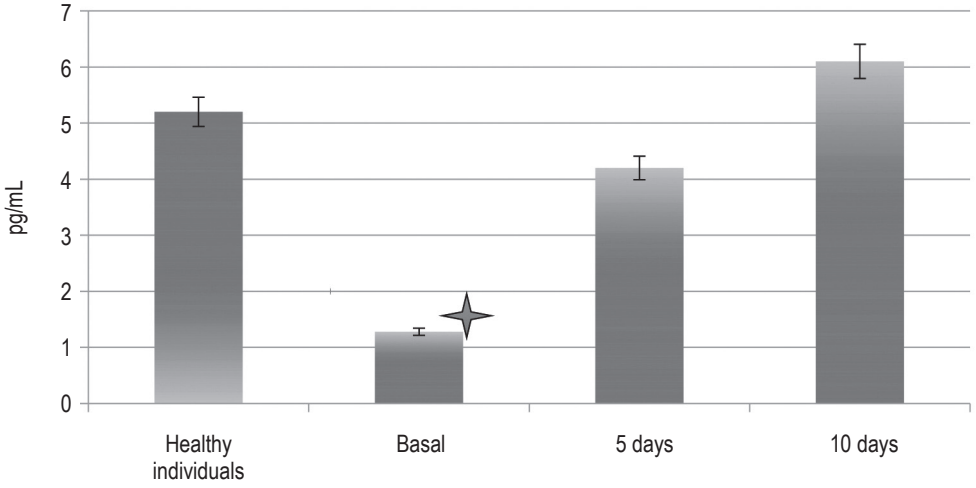

Figure 1. Level of IL-6 in the blood of healthy individuals and in the dynamics of electromyostimulation

mL, at a wavelength of 450 nm. The obtained data were processed using the Statistica licensed software package v. 10.0 (StatSoft Inc., USA). When comparing data, the nonparametric Mann-Whitney test was used, in the dynamics of EMS using the Wilcoxon test. Differences were considered significant at $p \leq 0.05$.

Results and discussion

Prior to the EMS of the quadriceps femoris, the basal level of IL-6 in the main group was 1.28 (0.87-1.72) pg/mL, which is significantly lower than in healthy individuals 5.2 (3.8-6.1) pg/mL (Figure 1). In the dynamics of EMS on the 5th day, the level of IL-6 reached a value of 4.2 (3.4-5.1), on the 10th value 6.1 (4.9-6.8), significantly different from the basal concentration. At the same time, the values of IL-6 on the 5th and 10th days did not exceed the values obtained in the group of healthy individuals.

When exposed to and propagated by an electrical impulse with a frequency of more than 10 Hz, depolarization of the sarcolemma occurs, associated with a change in the potential difference. Control over the electromechanical conjugation of contraction processes during EMS of the striated fibers of the quadriceps muscle is designed to be carried out by the intracellular T-system and the sarcoplasmic reticulum, causing a directed current of calcium ions in the sarcoplasm. The maximum intensity of the contractile act occurs with the synergy of the frequency ranges of nerve impulses and electrical stimulation. An impulse arriving at a frequency of more than 50 Hz forms and prolongs the excitation of the nerve fiber and induces passive muscle contraction. It is known that pulsed currents of low frequency, acting on the system of blood and lymph capillaries, contribute to the redistribution of the tissue component of the fluid.

With the reduction of myocytes, in the cytoplasm of cells, in addition to an increase in the level and enzymatic activity of macroergs (creatine phosphate, adenosine triphosphate), synthetic activity increases in relation to the production of myokines. Our studies have shown that the baseline level of interleukin-6 before the EMS procedure was significantly reduced in comparison with healthy men, probably due to a low level of physical activity associated with injury and conscious limitation of muscle loads. On the 5th day and then on the 10th day, there was an exponential increase in the level of myokine IL-6 in the blood, however, its level at the end of the EMS course did not exceed the levels of healthy individuals, which suggests the presence of other, in particular, anti-inflammatory and reparative properties. myokine in relation to muscle tissue. Some authors believe that an increased level of IL-6 contributes to the accumulation of macroergs in the muscle cell.

Literature sources state that the role of IL-6 is not limited to participation in the acute-phase systemic inflammatory response, but the upregulation of its concentration in the acceptable physiological range contributes to the supply of actively functioning muscles with a set of energy substrates [3, 6]. A striking example is the myokine-dependent activation of glycogenolysis in hepatocytes with a parallel increase in the expression of type 4 glucose transporter on hepatocytes and myocytes [9]. There is information about the stimulation of lipolysis processes in adipocytes and the oxidation of free fatty acids by subthreshold concentrations of IL-6, which are utilized by actively functioning myocytes [8].

The pleotropic biological properties of IL-6 are realized through the coordinated work of the receptor complex, consisting of the IL-6R monomer, which directly binds the myokine itself, and the active gp130 subunit, which mediates a cascade of proteolytic transformations leading to the launch of the JAK/STAT (janus kinase/signal transducer and activator) signaling cascade. of transcription protein) or MAPK (mitogen-activated protein kinase) [12]. The reparative and anti-inflammatory properties of IL-6 are realized in stimulated striated muscles by the classical signaling mechanism that can block the activation of the universal intracellular transcription factor NF-κB, an inducer of the signaling cascade responsible for generating an inflammatory response [13, 14].

Relatively recently, it was shown that IL-6 promotes the formation of an alternative phenotypic transformation of macrophages into the M2 form, which, through the production of a number of anti-inflammatory cytokines, IL-10 and TGF-β, is involved in the processes of repair and remodeling, including in damaged muscle tissue. It has also been shown that IL-6 exhibits the properties of an inducer of the expression of the alpha chain of the IL-4 receptor (IL-4R) in M2 macrophages, sensitizing these cells to IL-4-mediated activation [5].

Conclusion

Thus, EMS before the start of surgical treatment of traumatic ACL injury leads to an increase in the blood concentration of myokine IL-6, within the range of healthy individuals, which contributes to an increase in the anti-inflammatory and reparative potential of damaged tissues.

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