КЛИНИКО-ИММУНОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА СТУДЕНТОВ МЕДИЦИНСКОГО ВУЗА В ЗАВИСИМОСТИ ОТ ДЛИТЕЛЬНОСТИ И ПРОГРАММЫ ОБУЧЕНИЯ

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Резюме. Хронический психоэмоциональный стресс может стать причиной дисфункции нейроиммуноэндокринной дисрегуляции с последствиями в виде нарушения функционального потенциала иммунной системы. Адаптация к новым условиям жизни при старте учебы в медицинском вузе – одно из неизбежных обстоятельств, которое преодолевают первокурсники. Обучение по программе военной подготовки в медицинском вузе несет в этом аспекте дополнительную стрессорную нагрузку. Исследования, посвященные механизмам формирования адаптивных реакций иммунной системы при обучении по программе военной подготовки офицеров медицинской службы, представляют несомненный интерес. Целью проведенного исследования стала сопоставительная характеристика клинической манифестации иммуноопосредованной патологии и параметров адаптивного и врожденного иммунитета студентов медицинского вуза в зависимости от стажа и программы обучения. Под наблюдением находились 104 студента-медика, все – мужчины, из которых 37 первокурсников и 67 – студенты третьего курсов медицинского университета. Обследуемые каждого курса разделены на две подгруппы в зависимости от программы обучения. Группа первокурсников состояла из 18 человек военного учебного центра (ВУЦ) и 19 – лечебно-профилактического факультета (ЛПФ). Среди третьекурсников студентов ВУЦ – 31, ЛПФ – 36. Для клинической характеристики заболеваемости в течение года обучения использовали регистрационные карты анализа иммуноопосредованной патологии, параметры иммунной системы в конце весеннего семестра исследовали с использованием стандартных методологических подходов. Полученные данные указывают, что на первом курсе адаптация к обучению у студентов, имеющих дополнительную нагрузку в виде программы военной подготовки, проходит более тяжело в сравнении с первокурсниками лечебного факультета. Эти различия состоят в более частой и значимой клинической манифестации инфекционной патологии и отражаются на функциональном потенциале клеточных показателей врожденного иммунитета. Констатация признаков угнетения функциональных потенций клеток макрофагального ряда и натуральных киллеров у первокурсников военного учебного центра является настораживающим фактором возможного срыва адаптационных резервов системы иммунного реагирования, что, вероятно предполагает необходимость разработки программ превенции негативного влияния стрессообразующих факторов. К третьем году обучения у студентов военного учебного центра в сравнении со студентами

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стандартной образовательной программы врачей-лечебников клинические и иммунологические показатели функционирования иммунной системы лучшие. Вероятно предположение, что в этот период завершается процесс психологической адаптации военных студентов-медиков.

Ключевые слова: психоэмоциональный стресс, адаптация, студенты, натуральные киллеры, иммунная дисрегуляция, стрессообразующие факторы

CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF MEDICAL STUDENTS DEPENDING ON THE DURATION AND PROGRAM OF STUDY

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Abstract. Chronic psycho-emotional stress can cause dysfunction of neuroimmunoendocrine dysregulation with consequences in the form of a violation of the functional potential of the immune system. Adaptation to new living conditions at the start of studies at a medical university is one of the inevitable circumstances that first-year students overcome. Education under the military training program at a medical university carries an additional stress load in this aspect. Research on the mechanisms of formation of adaptive reactions of the immune system during training under the military training program for officers of the medical service is of undoubted interest. The purpose of the study was to compare the clinical manifestations of immune-mediated pathology and the parameters of adaptive and innate immunity of medical students depending on the length of service and training program. Under observation were 104 medical students, all men, of which 37 were first-year students and 67 were third-year students of a medical university. The subjects of each course were divided into two subgroups depending on the training program. The group of first-year students consisted of 18 people from the military training center (VTC) and 19 people from the medical and preventive faculty (LPF). Among the third-year students of the VUC – 31, LPF – 36. For the clinical characterization of the incidence during the year of study, registration cards for the analysis of immune-mediated pathology were used, the parameters of the immune system at the end of the spring semester were studied using standard methodological approaches. The data obtained indicate that in the first year students with an additional load in the form of a military training program have a more difficult time adapting to learning in comparison with first-year students of the medical faculty. These differences consist in a more frequent and significant clinical manifestation of infectious pathology and are reflected in the functional potential of cellular parameters of innate immunity. The statement of signs of inhibition of the functional potencies of macrophage cells and natural killers in first-year students of a military training center is an alarming factor in the possible disruption of the adaptive reserves of the immune response system, which probably suggests the need to develop programs to prevent the negative impact of stress-forming factors. By the third year of study, the students of the military training center have the best clinical and immunological indicators of the functioning of the immune system in comparison with the students of the standard educational program of general practitioners. It is likely that during this period the process of psychological adaptation of military medical students is completed.

Keywords: psycho-emotional stress, adaptation, students, natural killers, immune dysregulation, stress-forming factors

Introduction

The educational process in a medical university is characterized by high intensity, which affects the psycho-emotional status of students and can lead to the formation of chronic stress [8]. In turn, stress causes a change in the functional activity of the homeostatic systems of the body, including the immune system, contributing to a decrease in immunocompetence and the development of clinical manifestations of immune dysfunction [2, 3, 4, 7]. Education under the military training program carries an additional stress load to the standard educational process in a medical school [9]. On the other hand, military medical students initially have higher health requirements than civilians. Is the combination of the above factors reflected in the change in the functional resources of the immune system of medical students? Studies on the aspects of the formation of adaptive reactions of the immune system during training under the military training program for officers of the medical service are fragmentary and are extremely poorly covered.

The purpose of this work was a comparative assessment of the clinical manifestation of immune-mediated pathology and the parameters of adaptive and innate immunity of medical students depending on the length of service and training program.

Materials and methods

The object of the study were 37 first-year and 67 third-year students of the medical and preventive faculty and the military training center of the Federal State Budgetary Educational Institution of Higher Education of the Rostov State Medical University of the Ministry of Health of Russia. The subjects of each course were divided into two subgroups depending on the training program. The group of first-year students consisted of 18 people from the military training center (MTC) and 19 people from the medical and preventive faculty (MPF). Among the third-year students of the MTC – 31, MPF – 36. The study participants were comparable in age (respectively, years: 19±1 and 19±2 in the first year group; 23±3 and 22±2 in the third year), gender (all men), physical condition (corresponded to the I group of health).

All study participants signed an informed consent in accordance with the protocol approved by the Local Independent Ethical Committee of the Federal State Budgetary Educational Institution of Higher Education Rostov State Medical University (No. 15/19 dated October 08, 2019).

The study was conducted at the end of the second and sixth semesters of study.

The work used registration cards for the analysis of immune-mediated pathology (Sizyakina L.P., 2013), reflecting the incidence during the year from the standpoint of assessing the work of the immune system according to the main syndromes: infectious, allergological, autoimmune, lymphoproliferative. The parameters of the immune system were studied using standard methodological approaches [5].

The inclusion criterion for all participants at this stage was the absence of acute or chronic diseases in the acute stage. Statistical calculations were performed using the StatTech v. 1.2.0 and Statistica SPSS v. 26. The description of the results obtained was carried out by calculating the median (Me) and the interquantile range of values in the form of 25 and 75 percentiles, which is presented in the text as Me ($Q_{0.25}$-$Q_{0.75}$). Comparison of two groups on a non-normally distributed score was performed using the Mann–Whitney U test, and groups with a normal distribution were compared using a parametric Student's t-test. Differences were considered significant at $p < 0.05$.

Results and discussion

Processing of data from registration cards of immune-mediated pathology indicates that during the first two semesters of study at the Medical University, there were no lymphoproliferative disorders, as well as manifestations of autoimmune pathology, in both subgroups of first-year students. Allergic syndrome was absent in MTC students and was detected (seasonal allergic rhinitis) in 10% of MPF students. Infectious manifestations were noted in all students of the MTC (100% of cases) and only in 36% of students of the MPF. Clinically, the infectious syndrome was manifested by acute infections of the respiratory tract. Complications that required the use of antibiotic therapy developed in 36% of cases in military students and in 20% of cases in MPF students.

Comparative characteristics of the parameters of the immune system of the two subgroups did not reveal fundamentally significant changes in the parameters of the subpopulation composition and functional characteristics of T and B-lymphocytes, as well as the level of production of serum immunoglobulins. At the same time, a statistically significant difference was noted in the content of a functionally active subpopulation of natural killers in the peripheral circulation. Thus, in MTC students, the proportion of granzyme-containing $CD3^-CD16^+Gr^+$ lymphocytes is 3 (1.9-4.8) %, while in MPF students this figure is 10 (7-13) % ($p = 0, 0001$). Also, in military medical students, in comparison with the MPF group, a smaller number of peripheral blood monocytes express the pattern-recognizing receptor TLR4: $CD14^+CD284^+$ 13.5 (10-18) % and 19 (13-24) %, respectively ($p = 0.03$).

The data obtained indicate that in the first year students with an additional load in the form of a military training program have a more difficult time adapting to learning in comparison with first-year students of the medical faculty. These differences are also reflected in more frequent and significant clinical manifestations and, most importantly, affect the functional potential of cellular parameters of innate immunity. The results obtained are of particular interest because they are in line with the data of studies emphasizing that among all subpopulations of immunocytes, natural killer cells have the highest sensitivity to chronic stress [1, 6].

The analysis of third-year students' survey data revealed that during the 4th and 5th semesters of study, the clinical manifestation of immune-mediated processes was registered in 58% of the students of the MTC and 61% of the students of the LPF. At the same time, no lymphoproliferative disorders and manifestations of autoimmune pathology were noted. Allergosyndrome (seasonal allergic rhinitis) was recorded in 3% of cases of military doctors and in the same ratio (3%) in the MPF group. Infectious manifestation in the form of acute infections of the upper respiratory tract was manifested in 45% of military doctors and 50% of students of the medical faculty. Complications that required the use of antibiotic therapy developed in 28% of cases in military students and in 45% of students of the MPF.

A comparative analysis of the parameters of the immune status of two subgroups of third-year students

showed that statistically significant differences affected only the functional parameters of monocytes. Thus, students of the MTC have a higher relative amount of $CD14^+HLADR^+$ (77.5 (70-79) % and 71 (64-74) %, $p = 0.02$), as well as $CD14^+CD282^+$ (78 (72.25-81.1) and 72 (66-77), $p = 0.006$), respectively. As follows from a generalized analysis of the data obtained from the survey of third-year students, military medical students in this period of study, in comparison with students without an additional training program, have better indicators of the functioning of the immune system. This postulate is confirmed by a fundamentally lower number of complications after ARVI and a more pronounced activation of cells that provide the processes of primary antigenic recognition and regulation of the adaptive immune response.

Conclusion

Thus, the data obtained indicate that at the start of training at a medical university, military medical students, in comparison with students of the medical and preventive faculty, have a more significant infectious manifestation of immune dysfunction against the background of a decrease in the functional parameters of natural killers and monocytes. However, in the third year of study, the trend is reversed; the clinical and immunological characteristics of MTC students exceed the corresponding criteria for students who do not have an additional educational load. Obviously, during this period, the process of psychological adaptation of military medical students is completed.

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