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Kydyrmoldina Ainur Shaimuratovna
Candidate of Biological Science (PhD), Associate Professor Kazakh Humanitarian Juridical Innovative University, Semey
e-mail: a_kydyrmoldina@mail.ru

CHANGE OF IMMUNOLOGICAL PROCESSES AND METABOLISM OF THE STUDENTS FROM SOUTH ASIA UNDER ACUTE STRESS

Зерттеудің мақсаты жедел стресстік әсер кезінде Семейде оқитын шетелдік Пәкістандық студенттердің иммундық жүйесінің және зат алмасу процестерінің бейімделуін зерттеу болды.

Осы мақсатқа жету барысында Семейдегі жедел климаттық қоршаған орта жағдайында Оңтүстік Азиядан келген 30 студенттің иммундық, липидтердің асқын тотығу күйі, антиоксиданттық жүйелері мен энергия алмасуы зерттелінді.

Зерттеулердің нәтижесі көрсеткендей, Пәкістандық студенттерде стресс әсерінен 1 ай барысында ФГА митогенімен инкубациядан кейін МИФ өндіру қабілеті бойынша Т-лимфоциттер қызметінің бәсеңдеуімен супрессорлы белсенді Т-жасушаларының санын жоғарыласа, хелперлі белсенді Т-жасушалардың төмендеген. В-лимфоциттердің және IgG мөлшерінің көбеюімен, сондай-ақ нейтрофильді фагоцитарлық белсенділіктің компенсаторлық өсуімен көрінетін иммунитеттің В-жүйесінің белсенділігі анықталған. Жедел стресс перифериялық қан лимфоциттеріндегі биоэнергетика сарқылуын, бастапқы өнім (ДК) деңгейінің жоғарылауымен липидтердің асқын тотығуының активациясын, сондай-ақ антиоксидантты қорғаныстық көрсететін, энергетикалық алмасу ферменттері белсенділігінің төмендеуін тудырған.

Түйін сөздер: *Иммундық жүйе, энергия алмасу, жедел стресс, бейімделу, липидтердің асқын тотығуы, антиоксиданттық жүйе.*

Целью исследования явилось изучение адаптации иммунной системы и обменных процессов у иностранных студентов-пакистанцев, обучающихся в г Семей при действии острого стресса.

Для реализации поставленной цели изучали состояния иммунной, перекисного окисления липидов и антиоксидантной систем и энергетического обмена у 30 студентов из Южной Азии при остром воздействии климатоэкологических условий г. Семей.

Результаты исследований показывают, что при действии острого стресса у студентов-пакистанцев в течение 1 месяца повышаются числа Т-клеток с супрессорной активностью, снижением клеток с хелперной активностью, подавлением функции Т-лимфоцитов по способности к продукции МИФ после инкубации с митогеном ФГА. Выявлена активация В-системы иммунитета, проявляющаяся увеличением числа В-лимфоцитов и содержания IgG, а также компенсаторное усиление фагоцитарной активности нейтрофилов. Острый стресс вызывает снижение активности ферментов энергетического обмена, что свидетельствует о истощении биоэнергетики лимфоцитов периферической крови, активацию перекисного окисления липидов с повышением уровня первичных продуктов (ДК), а также антиоксидантной защитой.

Ключевые слова: *Иммунная система, энергетический обмен, острый стресс, адаптация, перекисное окисление липидов, антиоксидантная система.*

The aim of the study was to study the adaptation of the immune system and metabolic processes in foreign Pakistani students studying in Semey under the action of acute stress.

To achieve this goal, we studied the state of immune, lipid peroxidation and antioxidant systems and energy metabolism in 30 students from South Asia under acute climatic and environmental conditions in Semey.

Research results show that under acute stress, Pakistan students within 1 month increased number of T-suppressor cell activity completely, reducing the helper cell activity, suppression of T-lymphocyte function by their ability to produce MIF after incubation with the mitogen PHA. Spotted B activation of the B immune system, as an increase in lymphocyte number and content of IgG, as well as a compensatory enhancement of the phagocytic activity of neutrophils. Acute stress causes a reduction in enzyme activity of energy metabolism, which indicates depletion of peripheral blood lymphocytes bioenergy, lipid peroxidation with higher levels of primary products (DC) and the antioxidant protection.

Keywords: *Immune system, energy metabolism, acute stress, adaptation, lipid peroxidation, antioxidant system.*

Climatic and ecological situation in each region is unique, has a significant effect on the immune system [1,2]. So immigrants from areas with hot and temperate climate in the north are set increased morbidity due to immune suppression in critical periods of adaptation [3].

Climate of Semey region is continental, with large daily, annual sweep of temperature [4]. Therefore, in the process of adaptation to the formation of resistance to changing factors okruzha6yuschey environment plays a big role the immune system of the body [5,6,7,8]. The state of adaptation to extreme climatic and ecological conditions, a significant effect also has a range of psycho-emotional, genetic, social, and informational factors that reduce the reactivity of the organism.

The action of the various functional load changes occur in the power unit cells and organs. Energetically failure is general pathological manifestation that accompanies most extreme impacts. [9] Thus, when exposed to stress factors are stress and rearrangement of the energy unit cells [10].

Adaptation to different environmental factors and the development of pathological such states in the body occur through modifications of the composition of cell membranes [11,12]. Any form of stress is accompanied by activation of free radical oxidation in violation of oxidative homeostasis and increased antioxidant protection

Therefore, the aim of this study was to examine the state of immunological and metabolic processes in international students from South Asia under the influence of acute stress factor.

Materials and Methods

We examined 30 international students from South Asia who came to study at the Semey Medical Academy, at the time of arrival and 1 month and 25 students of 1-3 courses SGMU residing in the Semey region, who were in the control group. At the time of the survey students Pakistani students and the control group were basically healthy. Total student groups studied - they are exposed to factors specific social group of students (intense mental labor, emotional, and information overload, lack of exercise, working conditions, leisure, food). Survey Pakistani students was designed to clarify the influence of climatic and ecological factors on their health.

Assessment of the immune status was carried out in accordance with the recommendations of the Institute of Immunology from Ministry of Health RF (R.V.Petrov et al., 1982). Blood samples were taken into heparinized tube (25 U / ml). Isolation of lymphocytes from venous blood was performed by the conventional method in a density gradient ficoll-verografin (1,077).

The state of cell-mediated immunity was assessed by the total number of CD3 +, CD4 +, CD8 + and CD19+ with the appropriate monoclonal antibodies by flow cytometry, and mitogen-producing function in the migration inhibition reaction, calculated by counting the immunoregulatory index (IRI). The principle of the method consists in the attachment of human erythrocytes sensitized with monoclonal antibodies LT, to the surface of lymphocytes [13].

The state of humoral immunity was assessed by the number of CD19+, the concentration of circulating immune complexes (CIC) - the method of M. Digeon [14] as modified by Y. Hrynevych and AN Alfyorova [15], immunoglobulins of class A, M and G by the method of Mancini G et al., [16].

The non-specific phagocytic immunity was assessed by phagocytic activity of polymorphonuclear. Contents phagocytic polymorphonuclear (neutrophils, pseudo eosinophiles) were determined as described in [17]. As of phagocytic material we use latex.

In lymphocytes, SDH activity was determined by the method [18], the CCO by RS Krivchenkova [19]. DC level in the blood plasma was determined by the method of VB Gavrilova M. Meshkorudnoy [20], malondialdehyde (MDA) by the modified method [21] was determined SOD activity [22], glutathione reductase (GLR) and glutathione peroxidase (GLPO) [23].

The resulting digital data were processed by

conventional methods of variation statistics as described in [24]. The comparison was performed by t-Student.

Results and Discussion

At the time of the survey among Pakistan students significant changes were observed by the number of cells and CD3 + CD4 +, significantly raised the number of CD8 + and auto-RFC, decreased immuno-regulatory immuno-regulatory index to 1.78 versus 3.12 in the control (P <0.05) . These changes were not accompanied by decreased functional activity of T-cells (Table 1). In the peripheral blood was an increase in the number of B-lymphocytes, the level of the CIC, lower concentrations of IgA and IgM (Table 2).

This is probably due to the adverse impact of environmental factors and the adaptation of the immune system.

Immunological aspects of adaptation of foreign students in Semey within 1 month after arrival are characterized disregulatory immune disorders with rising numbers of T cells with suppressive activity (CD4+) and decrease in the number of cells with helper activity (CD8+), oppression cellular responses to stimulation with PHA.

This allows us to conclude that the climatic conditions in Semey during the first month after the arrival of the students-Pakistanis cause immunosuppression of T-cell immunity.

Table 1. T-cell immunity in acute stress in students-Pakistanis

Parameteres	Begining		1 month	
	I group	III group	II group	III group
Lymphocytes, abs.	2,43± 0,13	2,25± 0,22	2,38± 0,15	2,63± 0,23
CD3+ abs.	0,93± 0,09	0,89± 0,10	0,90± 0,09	1,18± 0,03 °*
CD3+ %	38,4± 4,1	42,0± 0,8	37,6± 4,0	41,6±3,4
CD4+ abs.	0,61± 0,06	0,49± 0,06	0,57± 0,07	0,53± 0,06
CD4+ %	25,1± 1,0	21,7± 1,5	23,9± 1,2	20,1± 1,3 °
CD8+ abs.	0,20± 0,02	0,27± 0,03 °	0,20± 0,02	0,52± 0,04 °° **
CD8+ %	8,2± 1,1	12,0± 1,4 °°	8,4± 1,0	19,7± 2,6 ° *
IRI	3,12± 0,29	1,78± 0,22 °°	2,90± 0,31	1,18± 0,22 °°
IRML	22,4± 2,1	25,6± 3,2	22,4± 2,1	7,3± 1,5 °° **
Auto-RFC, abs.	0,11± 0,02	0,20± 0,01 °	0,10± 0,02	0,12± 0,02*
Auto-RFC, %	5,2± 0,3	9,0± 0,6 °	5,0± 0,3	7,2± 0,2* °°
Notes: 1. Group I - students from Semey (control group), II group - students from South Asia. 2. o - The difference with a control group deemed reliable * - the difference from baseline reliable, (1 sign – p<0,05; 2 – p<0,01).				

A month after the arrival of the Pakistan students absolute number of B lymphocytes remained elevated, whereas the relative abundance was reduced to the level of the control group (Table 2). The content of immunoglobulin IgA was restored to the level of the control group, IgM remained reduced, IgG was increased. CIC concentration in serum dropped to the level of control units. The results show that students month stay Pakistanis in the new climatic and environmental conditions cause phase changes of immuno-globulins to the suppression of the primary immune response to an unaccustomed antigens in adapting to new climatic and ecological conditions.

Students-Pakistanis have phagocytic activity of neutrophils in comparison with those of the control group tended to be lower immediately after arrival and increased sharply after 1 month (p <0,01). Phagocytic number in the experimental group was reduced immediately after arrival (p <0.05), and restored to the level of the control group by the end of the first month of observation.

Table 2. Indicators of humoral immunity in the dynamics of the system of observation

	Begining		1 month	
	I group	II group	I group	II group
CD19+, abs.	0,30± 0,02	0,36± 0,02 °	0,31± 0,02	0,39± 0,03 °
CD19+ %	12,3± 1,7	16,0± 1,6	13,0± 1,7	14,8± 1,0

Auto-RFC, abs.	0,11± 0,02	0,20± 0,01 º	0,10± 0,02	0,12± 0,02*
Auto-RFC, %	5,2± 0,3	9,0± 0,6 º	5,0± 0,3	7,2± 0,2* º º
IgA, mg%	200,0± 19,0	138,7± 18,9 º	198± 16,53	167,3± 12,9
IgM, mg%	150,0± 14,0	115,6± 6,9 º	143,0± 12,3	109,3± 3,3 º
IgG, mg%	1190± 113	1116± 66,8	1236± 119	1475± 72,6*
CIC, y.e.	0,98± 0,07	2,60± 0,23 º º	0,96± 0,08	2,04± 0,58
Phag., %	45,2± 4,3	37,4± 2,2	44,3± 5,2	76,2± 4,0 º º ***
Ph.n.	3,25± 0,31	2,02± 0,38 º	3,12± 0,29	2,80± 0,12*
Notes: 1. Group I - students from Semey (control group), II group - students from South Asia. 2. o - The difference with a control group deemed reliable * - the difference from baseline reliable, (1 sign – p<0,05; 2 – p<0,01; 3– p<0,001).				

Thus, the immunological aspects of adaptation of foreign Pakistan students in regarding the climatic and ecological conditions of Semey within 1 month after arriving in the city of Semey correspond to an adaptive response of the body at an early stage of the adaptation syndrome.

Stress influences determine the directivity of the same changes in the energy metabolism. Found that non-specific stress loads derive energy metabolism in low-energized state. The enzyme activity of the energy exchange is changing under the influence of various stimuli in different periods of observation in various organs [25,26].

To assess the bioenergetics processes in students-Pakistanis that adapt to changing environmental conditions habitat, we studied the activity of the mitochondrial enzyme succinate dehydrogenase and cytochrome oxidase in peripheral blood lymphocytes for 1 and 6 months after their arrival (Table 3). The results showed that of the initial level of SDH activity in students-Pakistanis of reliable lower than the control group (by 33,3%, p <0,05); CCO - on the contrary, higher by 55,8% (p <0 , 05). After 1 month of stay in the subjects under the influence of stress factors happened significant increase in SDH activity at 28,6% (p <0,05) with the approach to the level of the control group, a significant reduction of CCO regarding control of 23%, (p <0,05). After 6 months noted further increase SDH activity relative to the baseline level decreased 67,8%, (p <0,05), has reached the level of control. CCO activity remained reduced.

Thus, the state of the energy metabolism of Pakistan students is immediately after arriving at Semey, in comparison with the control group, characterized by a decrease in the initial activity of SDH and higher initial activity of CCO.

Table 3. Energy metabolism in Pakistani students studying in the SGMU

Time	SDH		CCO	
	Control	Pakistani students	Control	Pakistani students
Begining	4,2±0,5	2,8±0,30^{0}	30,2±3,4	47,2±6,2^{0}
1 month	4,3±0,4	3,6±0,14*^{0}	28,8±3,1	22,3±1.8*^{00}
6 month	5,0±0,5	4,7±0,37*	24,5±2,8	23,6±4,0*
Note: ^{0} - significantly to group 2 (control), * - authentically to the original				

Later, after 1 month of activity of SDH and CCO has been suppressed, but after 6 months of SDH activity rose to the level of the control group, and remained reduced CCO. The high activity of SDH to the effects of extreme climatic and ecological factors while reducing the activity of the terminal respiratory chain enzyme (CCO) at 1 and 6 months after arrival that the restructuring of bio-energy cells and replenish the energy in these conditions is mainly due to the oxidation of succinic acid.

Table 4. Lipid peroxidation and antioxidant protection in Pakistani students studying in the SGMU

Time	DC (c.u. /ml)	MDA (micromol/ ml)	GLR (micromol/ ml)	GLPO (micromol/ ml)	SOD (c.u., ml)
Begining	1,4±0,15	3,9±0,17	0,29±0,02	39±1,6	2,34±0,13
1 month	3,0±0,34^{0}	2,1±0,32^{0}	0,57±0,08^{0}	41±2,2	4,78±0,02^{00}
6 month	1,5±0,11	4,5±0,58	0,28±0,02	33,1±3,8	1,63±0,15^{0}
Note: ^{0} – significantly to the original (P <0,05)					

Lipid peroxidation (LPO) is a universal indicator of the sustainability of biological membranes. In low concentrations of primary lipid peroxidation products cause reversible hydrophilic hydrophobic conversion of fatty acid residues of membrane phospholipids, changes in the functional state of membranes, reversible inactivation of many membrane-bound enzymes. The secondary products of lipid peroxidation are already having a damaging effect, and a further increase in lipid peroxidation products can lead to the destruction of biological membranes. The normal processes of free oxidation of lipids are strictly regulated at a relatively constant level of functioning of the antioxidant system (AOS). By enzymatic antioxidant protection system includes superoxide dismutase (SOD), glutathione peroxidase (GLPO), glutathione reductase (GLR), which plays an important role in the stabilization of lipid peroxidation.

Table 4 shows that a month after the arrival of Pakistan students significantly decreased the level of malondialdehyde (MD) and elevated levels of diene conjugates (DC) compared with baseline lipid peroxidation products ($P<0.05$). However, a condition characterized by increased antioxidant activity of glutathione reductase (GLR), superoxide dismutase (SOD). Glutathione peroxidase activity (GLPO) did not change. 6-month observation indicators of primary and secondary products of lipid peroxidation (MDA and DC) met the initial value. Also showed normalization of enzymes GLR and GLPO, whereas SOD activity decreased to 1,63 ± 0,15 standard units / ml vs 4,78 ± 0,02 ($P <0.05$).

Thus, the adaptation of Pakistan students in the new climatic and ecological conditions within a month after his arrival in the city of Semey is accompanied by activation of lipid peroxidation with increased levels of primary products (DC) capable in low concentrations induce reversible changes in the functional state of biological membranes, as well as AOP. After 6 months of follow-content of lipid peroxidation products was restored to the original level, however, significantly reduced the level of the enzyme leading AOP system-SOD.

Conclusion

1. The action of acute stress Pakistan students within 1 month increased number of T-suppressor cell activity completely, reducing the helper cell activity, suppression of T-lymphocyte function by their ability to produce MIF after incubation with the mitogen PHA.

2. Spotted B activation of the B immune system, as an increase in lymphocyte number and content of IgG, as well as a compensatory enhancement of the phagocytic activity of neutrophils.

3. Acute stress causes a reduction in enzyme activity of energy metabolism, which indicates depletion of peripheral blood lymphocytes bioenergy, lipid peroxidation with higher levels of primary products (DC) and the antioxidant protection.

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Қыдырмолдина Айнұр Шаймұратқызы
Лауазымы: Биология ғылымдарының кандидаты, доцент, Ақпараттық технологиялар және экономика факультеті деканы, Қазақ инновациялық гуманитарлық-заң университеті, Семей қ.
Почталық мекен-жайы: 071400, Қазақстан Республикасы, Семей қ., Абай көшесі 107
Ұялы тел: 8 775 342 16 15
Оңтүстік азиялық студенттердегі жедел стресс әсер ету кезіндегі иммунологиялық және алмасу үдерістеріндегі өзгерістер

Кыдырмолдина Айнур Шаймуратовна
Должность: кандидат биологических наук, доцент, декан факультета информационных технологии и экономики, Казахский гуманитарно-юридический инновационный университет, г.Семей
Почтовый адрес: 071400, Республика Казахстан, г. Семей, ул. Абая 107
сот. тел: 8 775 342 16 15
Изменение иммунологических и обменных процессов у студентов из южной азии при действии острого стресса

Kydyrmoldina Ainur Shaimuratovna
Position: Candidate of Biological Science (PhD), Associate Professor, Dean of the Faculty of Information Technology and Economics, Kazakh Humanitarian Juridical Innovative University, Semey city
Mailing address: 071400, Republic of Kazakhstan, Semey, st. Abay 107
cells. ph: 8 775 342 16 15
Change of immunological processes and metabolism of the students from south asia under acute stress