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**Content of mediators of trophotropic systems at psoriatic patients with different degree of severity of clinical event**

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**Abstract**

Psoriasis as one of the most widely-spread dermatosis is still an urgent problem of modern dermatology.

*Aim*. To assess, on the different levels of psoriasis’ clinical event, condition of trophotropic system by the detection serotonin’s, histamine’s and histidine’s content in the daily urine.

*Materials and methods*. 97 patients were examined, by the PASI classification: I-35 patients with light degree of severity, II – 32 with mean, III – 30 with severe. Control group – 30 relatively healthy people. Serotonin’s, histamine’s and histidine’s detection were made in one test of daily urine according to the guideline of C.I. Gerasimova. On the first stage their partition were made with the method of column chromatography. Contest was calculated by the fluorescence standard.

*Results*. Received results indicate about considerable participation of histamine reactive system on the psoriasis’ pathogenesis. Implementation of last is connected with strong psycho-emotional stress, which develops at psoriasis patients in the response, first of all, for itching. Discovered trophotropic mediators’ response: histamine and serotonin in the process of psoriasis’ development has adaptive character. Indirect predominance of histamine reactive system above serotonergic system was marked. In psoriasis’ pathogenesis a leading part play disturbances of vegetative mediators’ balance, in the conditions of its progress lead to the deadaptation and development of pathological reaction, which hook up regulative and metabolic processes.

*Conclusions*. Progressing of psoriasis if followed by gradual activation at transition from light to severe degree of clinical event of trophotropic functions. Given results put up a question about modern correction of condition and trophotropic systems at psoriatic patients with the aim of slowing down its progression.

**Key words**: serotonin, histamine, histidine, trophotropic system.

 Psoriasis, as one the most widespread dermatosis, is still an urgent problem of modern dermatology. Prevalence of psoriasis in the world, due to the data of International Federation of Psoriasis Associations, varies within 1,2 – 5% and the mean value is 3% from general population [9]. For today, psoriasis is characterized by resistance to generally accepted treatment regimens, more severe clinical event and disturbance of psychosocial adaptation of patients. All these induce to find new, pathogenetic well-grounded methods of treatment [12,13, 20]. The letter, as a rule, are based on the correction of key pathogenetic links [ 1, 3, 6, 7, 11,15, 16, 23]. A significant role in pathogenesis of psoriasis appropriates to stress mechanisms. At psoriatic patients are discovered essential differences in resistance abilities to stresses and overcoming with their consequences, which points out on the necessity to discover the role of stress as a starting factor of psoriasis [19, 8, 21, 4, 10, 17]. To define a condition of regulatory process, against the background of stress development, allows the analysis of ergo and trophotropic systems, in which are involved vegetative, active, sensitive and psychic components [22, 14]. This way, trophotropic functional system is in charge, first of all, for anabolic processes in the organism, supplies a nutritive function and promotes supporting of homeostatic balance. In the realization of trophotropic reactions takes part cranial division and leading mediators, in particular, serotonin and histamine. Researches, devoted to the condition of trophotropic system at psoriasis with different levels of severity of clinical event are limited. From the recording, it is also essential, for the comprehensively disclosure of pathogenesis and development of new modern complex therapeutic steps.

**Objective.**  Assess the psoriasis condition at different stages of the clinical course for trophotropic system by determining serotonin, histamine and histidine coherency content in urine.

**Materials and methods.** The study involved 97 patients with psoriasis of different severity in the age range 30-50 years, selected for the purpose of authenticity and uniformity of the study results. According to the psoriasis severity classification, Psoriasis Area Severity Index – PASI, patients were divided into three groups. At group I were 35 patients with mild psoriasis flow, II group - 32 patients with moderate psoriasis flow and III group - 30 patients with severe psoriasis. The control group included 30 relatively healthy people. Serotonin, histamine and histidine determination in a urine sample carried out according to guidelines of C.I. Gerasimova [5]. At the first stage, samples separated by using of column chromatography; serotonin and histamine eluted by 0.1N NaOH, histidine - 0.1M phosphate buffer. Determination was carried out in part serotonin alkaline elute by adding 1% of cysteine, 0.1% orthophthalic aldehyde and concentrated HCl, with following boiling. Measuring by fluorescence at 440 nm, activation at 355 nm. To determine the proportion of histamine alkaline elute was mixed with 1N NaOH, 0.1% sodium orthophthalic aldehyde and 3N HCl, after which the fluorescence was measured at 440/355 nm. In histidine buffer elute was determined at 440/375 nm, after adding 1N NaOH 0.1% solution of orthophthalic aldehyde and 3N HCl. Content calculation was from the standard fluorescence. Statistical analysis was performed by using the computer application package for the processing of statistical information Statistica 6.1 (StatSoft, Inc., USA).

**Results and discussion.** The results showed (P <0.004) increase in comparison with the control, the level of serotonin in urine excretion in all the experimental groups of patients (Table. 1). In the case of mild level of psoriasis, it was only 26%. For moderate psoriasis serotonin levels increased more clearly in relation to the control group of patients - 89%, while remaining significantly (p <0.001) increased by 50% in comparison with I group. For severe course of the disease was noted most significant increase in the urinary excretion of serotonin: 137% (p <0.001) compared to the control, by 88% (p <0.001) compared with the mild and 25% (p = 0.005) compared to an average degree.

Serotonin synthesis occurs mainly in enterochromaffin cells of the gastrointestinal tract, deposition - in secretory granules of these formations and release - in portal blood stream under the action of various stimuli, indirect noradrenergic and cholinergic innervation of corresponding tissues. It should be noted that circulating serotonin is mainly localized in platelets, but also in the blood plasma pool is formed by its free molecules, relatively independent of platelet [2, 18]. Separately, it should emphasize that the blood-brain barrier is impermeable for monoamines, resulting leads to independence of metabolic processes in the CNS and the periphery. Therefore, serotonin, which excreted in urine, has largely peripheral origin. Further active metabolism of this neurotransmitter occurs over the periphery. The results suggest that quantitative changes in the level of serotonin in urine correlates with the clinical symptoms severity of psoriatic manifestations for the examined patients. Increasing of the serotonin excretion rate can show an increase in the release of the neurotransmitter system trophotropic primarily with peripheral chromaffin cells. On the other hand, the gradual increase in the level of serotonin excretion in the transition from mild to severe psoriasis flow may indirectly indicate a gradual activation of trophotropic adaptive-compensatory reaction.

Table1

**Serotonin, histamine and histidine in the urine of patients with psoriasis depending on the severity of the clinical course**

**(Pmol / day M [25%; 75%] or M ± s)**

|  |  |  |
| --- | --- | --- |
| Index | Group of patients | Control (n=30) |
| I (n=35) | II (n=32) | III (n=30) |
| Serotonin | 1,2 [0,9; 1,4]\*р=0,004 | 1,8 [1,6; 2,05]\*р<0,001\*\*р<0,001 | 2,25 [1,7; 3]\*р<0,001\*\*р<0,001#р=0,005 | 0,95 [0,7; 1,2]  |
| Histamine | 0,9 [0,6; 1,1]\*р=0,088 | 1,7[1,6; 1,9]\*р<0,001\*\*р<0,001 | 2,4 [2; 2,9]\*р<0,001\*\*р<0,001#р<0,001 | 0,7 [0,5; 1,1] |
| Histidine | 1864[1706; 2396]\*р<0,001 | 1509[1192; 1807]\*р<0,001\*\*р<0,001 | 651[555; 704]\*р<0,001\*\*р<0,001#р<0,001 | 1030,5±242,5 |

Note: \* - compared with the control; \*\* - compared with I group; #- compared with II group

The examinees were also observed some violations of urinary excretion of histamine and its precursor histidine (Table. 1). In the experimental group I in the overall statistical picture, with connection to the control, tended to not significant (p = 0.088) increase in daily urinary excretion of histamine (an average of 28%) due to a statistically significant (p <0.001) increase in the level of histidine (on average 80%). These results probably reflect the low level of intensity of the decarboxylation of histidine to histamine formation in patients with mild psoriasis. In Group II was observed compared with the control, a significant increase in the excretion of histamine (an average of 143%, p <0.001) due to less distinct than in group I, increased excretion of histidine (46%, p <0.001). It should be noted that the level of histamine in the urine in psoriasis moderate clinical course was statistically significant (p <0.001) increase of almost 90%, compared with the mild level psoriasis, whereas histidine level, on the contrary, was significantly reduced (p <0.001) by an average of 19%. Obtained results suggest that patients with psoriasis in group II is an increase intensity decarboxylation of histidine to produce histamine. In group III patients have the most significant increase (p <0.001), urinary excretion of histamine: 3.4-fold relative to the control, 2.7 times - in relation to group I, 1.4 times - in relation to group II. The detected changes in these patients were marked by a statistically significant (p <0.001) compared to the control, reducing the excretion of histidine in average 37%. Histidine content remained statistically significant reduction by 65 and 57% and in comparison with groups I and II relatively. These results clearly indicate an increase in tone histamine reactive system in case of psoriasis with severe disease level.

In general, the results indicate meaningful participation histamine reactive system in the pathogenesis of psoriasis. Rather, the latter linked to the implementation of strong emotional stress, which develops in patients with psoriasis in response primarily to itch [8]. For its implementation neurotransmitter like histamine plays an important role [24].

On the other hand, the observed reaction trophotropic mediators such as histamine and serotonin in the development of psoriatic process has adaptive coherency. Calculation of the ratio between the histamine urinary excretion level to the level of serotonin excretion showed that, in the case of psoriasis it easy flow compared with the control, almost unchanged (P = 0.757) (Table. 2). At moderate and severe clinical course of psoriasis occurs slight (24%), but statistically significant (p = 0.005 and p = 0.0016, respectively), compared to control, his increase. This indirectly indicates a predominance of the serotonergic system at the histamine reactive. A comparison of the value of the coefficient in the group with an average degree of psoriatic process flow level in the group with severe statistically significant differences were found (p = 0.29).

Table2

**The ratio between the content of histamine and serotonin in the urine of patients with psoriasis based on the severity of the clinical course**

**(std.unit, M [25%; 75%] or M ± s)**

**(std.unit, Me [25%; 75%] or M ± s)**

|  |  |  |
| --- | --- | --- |
| Index | Group of patients | Control(n=30) |
| I (n=35) | II (n=32) | III (n=30) |
| Histamine/serotonine | 0,79±0,3\*р=0,757 | 0,99±0,22\*р=0,005\*\*р<0,001 | 0,98 [0,85; 1,47]\*р=0,00164; \*\*р<0,001#р=0,29 | 0,8[0,6; 1] |

Note: \* - compared with the control; \*\* - compared with I group; #- compared with II group

Thus, in the psoriasis pathogenesis leading role has autonomic disorders of neurotransmitter balance, in terms of its progression leads to maladaptation and development of pathological reactions which cling regulatory and metabolic processes.

**Findings**

1. The psoriasis progression accompanied by the gradual activation of the transition from mild to severe clinical course trophotropic functions indirectly confirmed by an increase in urinary excretion of histamine, histidine, serotonin, histamine/serotonin ratio.

2. The results raise the question of a timely correction of ergo- and trophotropic systems for the patients with psoriasis, to slow its progression. Correction levels investigated indicators trophotropic system is pathogenetically justified and necessary component of therapy for psoriasis.

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Берегова А.А.

**Вміст медіаторів трофотропної системи у хворих на псоріаз з різним ступенем тяжкості клінічного перебігу**

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**Резюме**

Псоріаз, як один з найпоширеніших дерматозів, залишається актуальною проблемою сучасної дерматології.
*Мета*. Оцінити на різних стадіях клінічного перебігу псоріазу стан трофотропної системи шляхом визначення вмісту в добовій сечі серотоніну, гістаміну і гістидину.
*Матеріали та методи*. Було обстежено 97 хворих, які розділені за класифікацією PASI на групи: I - 35 хворих з легким ступенем, II - 32 середньої, III - 30 з важким ступенем псоріазу. Контрольна група - 30 відносно здорових людей. Визначення серотоніну, гістаміну і гістидину проводили в одній пробі добової сечі згідно з методичними рекомендаціями Ц. І. Герасимової. На першому етапі здійснювали їх поділ методом колонкової хроматографії. Вміст розраховували за флюоресценциєю стандарту.
*Результати*. Отримані результати свідчать про вагому участь гістамінреактівної системи в патогенезі псоріазу. Реалізація останньої пов'язана з вираженим психоемоційним стресом, що розвивається у хворих на псоріаз у відповідь, насамперед, на свербіж.
Виявлена ​​реакція трофотропних медіаторів: гістаміну і серотоніну в процесі розвитку псоріатичного процесу має адаптивний характер. Відзначено непряме переважання гістамінреактівної системи над серотонинергическою. У патогенезі псоріазу провідну роль відіграють порушення вегетативного медиаторного балансу, що в умовах його прогресування призводить до дезадаптації і розвитку патологічних реакцій, які чіпляють регуляторні та метаболічні процеси.
*Висновки*. Прогресування псоріазу супроводжується при переході від легкого до важкого ступеня клінічного перебігу поступовою активацією трофотропних функцій. Отримані результати ставлять питання про своєчасну корекцію стану трофотропних систем у пацієнтів з псоріазом з метою уповільнення його прогресування.
**Ключові слова:** серотонін, гістамін, гістидин, трофотропная система

Береговая А.А.

**Содержание медиаторов трофотропной системы у больных псориазом с разной степенью тяжести клинического течения**

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**Резюме**

Псориаз, как один из самых распространенных дерматозов, остается актуальной проблемой современной дерматологии.

*Цель*. Оценить на разных стадиях клинического течения псориаза состояние трофотропной системы путем определения содержания в суточной моче серотонина, гистамина и гистидина.

*Материалы и методы*. Было обследовано 97 больных, которые по классификации PASI разделили на группы: I - 35 больных с легкой степенью, II - 32 средней, III - 30 с тяжелой степенью псориаза. Контрольная группа - 30 относительно здоровых людей. Определение серотонина, гистамина и гистидина проводили в одной пробе суточной мочи согласно методическим рекомендациям Ц. И. Герасимовой. На первом этапе осуществляли их разделение методом колоночной хроматографии. Содержание рассчитывали по флюоресценции стандарта.

*Результаты*. Полученные результаты свидетельствуют о весомом участии гистаминреактивной системы в патогенезе псориаза. Реализация последней связана с выраженным психоэмоциональным стрессом, развивающейся у больных псориазом в ответ, прежде всего, на зуд. Обнаруженная реакция трофотропных медиаторов: гистамина и серотонина в процессе развития псориатического процесса имеет адаптивный характер. Отмечено косвенное преобладание гистаминреактивной системы над серотонинергической. В патогенезе псориаза ведущую роль играют нарушения вегетативного медиаторного баланса, что в условиях его прогрессирования приводит к дезадаптации и развитию патологических реакций, которые цепляют регуляторные и метаболические процессы.

*Выводы*. Прогрессирование псориаза сопровождается при переходе от легкой к тяжелой степени клинического течения постепенной активацией трофотропных функций. Полученные результаты ставят вопрос о своевременной коррекции состояния трофотропной системы у пациентов с псориазом с целью замедления его прогрессирования.

**Ключевые слова**: серотонин, гистамин, гистидин, трофотропная система.