

UDC [616.314.17-008.1:616.516]-08:612.017.1

EFFECTIVENESS EVALUATION OF COMPREHENSIVE TREATMENT OF PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS ASSOCIATED WITH ORAL LICHEN PLANUS BY MONITORING OF LOCAL IMMUNITY INDICES

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Relevance. Changes in the oral mucosa, parodontium tissues are in most cases clinical and sometimes only signs of disorders in functioning of different organs and systems. Lichen planus is one of the most wide-spread and manifest as for clinical implications diseases of the oral mucosa.

In this regard the goal of our research is assessment of sIgA in the oral fluid, C3 components of the complement, activity of lysozyme and beta-lysins in patients suffering from CGP and lichen planus before and after treatment, as indices of positive influence of suggested complex therapy on the immunological course of CGP pathogenesis.

Object and methods of the research. 72 patients were examined and divided into 4 groups. The first group (20 people) comprised patients with CGP of initial and mild severity without lichen planus. 32 patients with conjoint course of CGP (initial and mild severity) associated with planus (typical form) were divided into 2 groups (2 and 3). The fourth observational group comprised patients with intact parodontium (20 people).

Results of the research and their consideration. After conservative treatment firm increase of lysozyme activity in the oral fluid of the patients of all observational groups after two weeks of treatment and while control measurement of lysozyme intake in 3 months is noted. However, only in the patients, who were undergoing treatment according to elaborated scheme, indices of lysozyme activity achieved the level of control ones and corresponded to it during the whole period of observation (from 34,86% до 36,38%).

Conclusions. With reference to the foregoing it is possible to draw a conclusion that CGP as well as conjoint course of CGP and lichen planus are accompanied by significant changes of local immunity of the oral cavity which become apparent in the form of sharp decrease of lysozyme and beta-lysins activity, reduction of the amount of C3 components of complement and increase sIgA level in the oral fluid.

Key words: chronicle generalized periodontitis, oral lichen planus, local immunity characteristics, lysozyme containing medicine.

ОЦЕНКА ЭФФЕКТИВНОСТИ КОМПЛЕКСНОГО ЛЕЧЕНИЯ БОЛЬНЫХ С ХРОНИЧЕСКИМ ГЕНЕРАЛИЗОВАННЫМ ПАРОДОНТИТОМ НА ФОНЕ КРАСНОГО ПЛОСКОГО ЛИШАЯ МОНИТОРИРОВАНИЕМ ПОКАЗАТЕЛЕЙ ЛОКАЛЬНОГО ИММУНИТЕТА

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Введение. Изменения слизистой оболочки полости рта и тканей пародонта зачастую являются первыми клиническими, а иногда и единственными признаками нарушений функционирования различных органов и систем. Красный плоский лишай - одно из самых распространенных и манифестных по клиническим проявлениям заболеваний слизистой оболочки полости рта.

В связи с этим целью нашего исследования стало определение в ротовой жидкости IgA, C3 компонента комплемента, активности лизоцима и бета-лизинов у больных ХГП и КПЛ до лечения и после его окончания, как показателей позитивного влияния предложенной комплексной терапии на иммунологическое звено патогенеза ХГП.

Объект и методы исследования. Нами было обследовано 72 пациента, которые были разделены на 4 группы. В 1 группу (20 человек) вошли пациенты с ХГП начальной и легкой степенями тяжести без КПЛ. 32 пациента с сочетанным течением ХГП (начальная и легкая степени тяжести) на фоне КПЛ (типичная форма) были разделены на две группы (2 и 3). Контрольную 4-ю группу составили пациенты с интактным пародонтом (20 человек).

Результаты исследования и их обсуждение

После проведенной консервативной терапии отмечается достоверное увеличение активности лизоцима в ротовой жидкости пациентов всех групп, как через две недели от момента начала лечения, так и при контрольном осмотре через 3 месяца. Однако только у пациентов, получивших лечение по разработанной нами схеме, показатели активности лизоцима вернулись к уровню контрольных и остались таковыми во время всего срока наблюдения (от 34,86% до 36,38%).

Выводы. На основании вышеизложенного можно сделать вывод, что ХГП, а также сочетанное течение ХГП и КПЛ сопровождается существенными изменениями показателей местного иммунитета ротовой полости, которые проявляются в резком снижении активности лизоцима и бета-лизинов, снижении количества C3 компонента комплемента и возрастании в ротовой жидкости IgA. Данные изменения варьируют в зависимости от степени повреждения пародонта, сопутствующей патологии, микробной обсемененности и отражают процессы местного воспаления и локальных иммунных механизмов.

Ключевые слова: хронический генерализованный пародонтит, красный плоский лишай, показатели местного иммунитета, лизоцимсодержащие средства.

ЛОКАЛДЫ ИММУНИТЕТ КӨРСЕТКІШТЕРІН МОНИТОРЛАУМЕН ЖАЛПАҚ ҚЫЗЫЛ ТЕМІРЕТКІ ФОНЫНДА СОЗЫЛМАЛЫ ГЕНЕРАЛИЗДЕНГЕН ПАРОДОНТИТПЕН НАУҚАСТАРДЫ КЕШЕНДІ ЕМДЕУДІҢ ТИІМДІЛІГІН БАҒАЛАУ

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Кіріспе. Ауыз қуысы сілемейлі қабығындағы және және пародонттың тіндерінің өзгерістері көбінесе бірінші клиникалық, ал кейде әртүрлі ағзалардың және жүйелердің қызмет етуінің бұзылуының жалғыз ғана белгілері болып табылады. Жалпақ қызыл теміреткі - ауыз қуысы сілемейлі қабығы ауруларының клиникалық анықтамалары бойынша ең таралған және манифестілерінің бірі.

Осыған байланысты біздің **зерттеу мақсаты** емдеуден бұрын және оны аятаған кезде, СГП патогенезінің иммунологиялық звеносына ұсынылған кешенді терапияның оңды әсерінің көрсеткіштері ретінде IgA, C3 компоненті комплементінің ауыз ішілік сұйықтығын, СГП және ЖҚТ-мен ауыратын науқастарда лизоцимді және бета-лизиннің белсенділігін анықтау болды.

Зерттеу нысаны және әдістері. Біз 72 пациентті тексердік, ол 4 топқа бөлінді. 1 топқа ЖҚТ жоқ СГП бастапқы және жеңіл дәрежедегі (20 адам) кірді. 32 пациент ЖҚТ фонында (қарапайым түрі) СГП үйлескен ағымымен (бастапқы және жеңіл дәреже) екі топқа бөлінді (2 және 3). 4 –ші бақылау тобын интактілі пародонтпен ауыратын науқастар құрады.

Зерттеу нәтижелері мен оларды талқылау. Консервативті терапия өткізгеннен кейін емдеу басталған сәтінен бастап екі аптадан кейін, сол сияқты 3 ай өткеннен кейін бақылау тексеруі

кезінде барлық топтардағы пациенттердің ауыз сұйықтығында лизоцимнің белсенділігінің нақты артуы белгілі болды. Бірақ тек қана біз әдістеген схема бойынша емдеу алған пациенттерде ғана лизоцимнің белсенділігі көрсеткіштері бақылау деңгейін қайта келді және бақылаудың барлық мерзімінде сондай болып қалды (34,86% - 36,38%).

Қорытындылар. Жоғарыда айтылғандар негізінде, СГП, сол сияқты СГП үйлескен ағымымен ауыз қуысының жергілікті иммунитеті көрсеткіштерінің біршама өзгерістерімен ілеседі, олар лизоцимнің және бета-лизиндердің белсенділігін күрт төмендетуде, компонентті комплименттің С3 санының төмендеуімен және IgA ауыз сұйықтығының көбеюімен айқындалады. Осы өзгерістер пародонтаның зақымдануы дәрежесінен, патологияның, микробты ұрықтануының ілесуіне байланысты өзгереді және жергілікті қабынулар және локалды иммундық механизмдер процесстерін білдіреді.

Негізгі сөздер: созылмалы генерализденген пародонтит, жалпақ қызыл теміреткі, жергілікті иммунитет көрсеткіштері, құрамында лизоцим заттар.

Библиографическая ссылка:

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Yeliseyeva O. V., Sokolova I. I. Effectiveness evaluation of comprehensive treatment of patients with chronic generalized periodontitis associated with oral lichen planus by monitoring of local immunity indices. *Nauka i Zdravooxranenie* [Science & Healthcare]. 2015, 5, pp. 19-25.

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Relevance

The periodontological aspects of oral lichen planus (OLP), especially OLP of the oral cavity mucous membrane (OCMM), relate to the number of those poorly explored, although its autoimmune genesis presupposes the involvement of the most important morphofunctional complex of the oral cavity – the parodontium, with a subsequent development of a graver and generalised combined pathology. According to expert data [3, 8, 9], the frequency of the parodontium specific diseases detection in the presence of the oral cavity oral lichen planus varies from 13,0 to 48,0 per cent. One of such diseases is chronic generalised periodontitis (CGP). CGP is an immune destruction microbe-induced periodontal complex with a high probability of a genetic and general somatic predisposition, proceeding with a free-radical mechanisms disorder in tissues, characterised by a progressing course resulting in the resorption of the alveolar process bone stock [1, 7]. Therefore the problem of the creation of medioprophyllactic methods of CGP and OLP treatment is still urgent.

Changes in the oral mucosa, parodontium tissues are in most cases clinical and sometimes only signs of disorders in functioning of different organs and systems. At the same time disorders, which appear in the oral cavity, can increase

severity of the background disease. Lichen planus is one of the most wide-spread and manifest as for clinical implications diseases of the oral mucosa [1, 3].

One of the most important causes, which determine the possibility of conjoint contraction of chronic generalised periodontitis (CGP) and lichen planus and define their course, is the state of local mechanisms of defense of the oral cavity [1, 2, 3, 8]. Therefore, estimation of immune competence of the oral cavity in patients with CGP and lichen planus can be one of possible objective criteria of treatment quality.

In this regard the goal of our research is assessment of IgA in the oral fluid, C3 components of the complement, activity of lysozyme and beta-lysins in patients suffering from CGP and lichen planus before and after treatment, as indices of positive influence of suggested complex therapy on the immunological course of CGP pathogenesis.

Object and methods of the research. 72 patients were examined and divided into 4 groups. The first group (20 people) comprised patients with CGP of initial and mild severity without lichen planus. 32 patients with conjoint course of CGP (initial and mild severity) associated with planus (typical form) were divided

into 2 groups (2 and 3). The second group (16 people) was represented by patients with CGP and lichen planus without involvement of the oral mucosa; the third group (16 people) was represented by patients with involvement of the oral mucosa. The fourth observational group comprised patients with intact parodontium (20 people). On the basis of treatment methods groups 2 and 3 were divided into subgroups 2a, 2b, 3a 3b (8 patients in each one).

The mouth rinse Perio-Aid 0.12% (Dentaid, Spain) was administered to group 1, 2a, 3 patients twice a day after toothbrushing with "Lacalut Active" tooth paste (Germany). Sea buckthorn oil on affected areas of the oral mucosa was administered to group 3a patients: 8-10 procedures per 1 course. In such a way group 1, 2a and 3a patients underwent standard treatment. A new therapeutic regimen, which included "Lizomuroid" mouthwash (Production Research Association "Odessa Technology", Ukraine), "Lacalut Active" tooth paste (Germany) and "Lysobact" antiseptic tablets (Bosnalijek d.d., Bosnia and Herzegovina), was elaborated for group 2b and 3b patients. The therapeutic regimen of group 3b also included lysozyme-containing films (Production Research Association "Odessa Technology", Ukraine) applied on affected areas of the oral mucosa and marginal parodontium.

Systemic treatment of lichen planus (after specialized medical consultation) consisted in prescribing of Delagil, 1 pill twice a day, Xantinal nicotinate, 1 pill three times a day and vitamin E in capsules, 1 capsule once a day, to the patients of the second and third groups.

Immunology research of the oral fluid included study of lysozyme activity by means of nephelometric method [7] and also assessment of sIgA, C3 components of complement and beta-lysins activity by enzyme linked immunoassay [6, 9, 10].

Table 1.

Change of lysozyme content in the oral cavity of patients with CGP and CGP associated with lichen planus before and after treatment (%).

Groups	Before treatment	In 14 days after treatment	In 3 months after treatment
1 (n=20)	24,88±4,41*	27,01±3,20*	27,97±9,72*
2a (n=8)	12,51±2,80*	23,53±3,40*	22,80±13,40*
2b (n=8)	15,94±3,19*	34,86±8,89	35,35±5,72
3a (n=8)	15,41±2,06*	23,41±6,13*	25,34±2,85*
3b (n=8)	13,42±5,80*	36,22±7,80	36,38±5,15
4 (n=20)	38,77±4,23	-	-

* - index value in comparison with control differences in group were significant at $p < 0.05$

Informed consent for participation in the study from those examined as well as permission from the Kharkov National Medical University Committee on Medical Ethics and Bioethics were obtained.

For statistical data processing, the Statistica version 6.0 for Windows data processing universal program package was used. The Mann-Whitney *U* test was used as a distribution-free method. The trustworthiness of the results received was estimated with the help of the Wilcoxon signed-rank test [4].

Results of the research and their consideration. Efficacy of treatment of the patients representing different groups was assessed through study of indices of local immunity of the oral cavity, of both non-specific (lysozyme, beta-lysins, C3 components of complement) and specific (sIgA) types of immunity.

As Table 1 shows, in patients of all groups with CGP of initial and mild severity associated with lichen planus of typical form (the second and third groups) as well as without lichen planus (the first group) sharp decrease of lysozyme activity in the oral fluid (activity of lysozyme varies depending on degree of CGP and co-morbidity from 12,51% to 24,88%, in case of activity rate of lysozyme in health people of control group – 38,77%) is marked, and in patients of the second and third groups with CGP associated with lichen planus this index is on average decreased by 2,8 times. As the role of lysozyme (acetylmuramidase ferment) as a mycolytic ferment of the oral cavity is hard to be overestimated (lysis of microorganisms, stimulation of phagocytosis, regeneration of biological tissues), development of marked pathological processes in the oral cavity in significant decrease of its activity becomes clear.

After conservative treatment firm increase of lysozyme activity in the oral fluid of the patients of all observational groups after two weeks of treatment and while control measurement of lysozyme intake in 3 months is noted. However, only in the patients, who were undergoing treatment according to elaborated scheme, indices of lysozyme activity achieved the level of control ones and corresponded to it during the whole period of observation (from 34,86% до 36,38%).

Dynamic of control of beta-lysins activity of bactericide factor, which is most active against anaerobic and sporogenous aerobic microorganisms (Table 2), during the whole period of observation has shown that in all patients with CGP and CGP associated with lichen planus of typical form, firm decrease of activity of this bactericide factor of the saliva in comparison with control before treatment and normalization of beta-lysins activity after use of different treatment schemes is identified.

Table 2.

Dynamic of activity of oral fluid beta-lysins in patients before and after treatment (%).

Groups	Before treatment	In 14 days after treatment	In 3 months after treatment
1 (n=20)	39,07±2,20*	25,83±2,91	38,89±2,88*
2a (n=8)	17,55±2,30*	21,45±1,21*	19,30±2,83*
2b (n=8)	17,6±2,12*	32,35±5,05*	27,70±3,48
3a (n=8)	15,47±2,49*	20,95±1,12*	20,01±1,75*
3b (n=8)	14,29±1,88*	27,41±4,83	22,95±4,22*
4 (n=20)	28,43±3,84	-	-

* - index value in comparison with control differences in group were significant at p<0.05.

The most important component of complement system is C3 fragment, the breakdown of which into C3a and C3b is considered to be a midpoint of each several cascades of activation of complement system which end with formation of membranes of attack complex and lysis of pathogenic bacteria of the oral cavity. Consequently, in all patients with CGP and CGP associated with lichen planus the level of this fragment of complement is reduced in comparison with control by 1,5-2 times (Table 3). The therapeutic regimen, which has been

elaborated and applies by us, regulates this index in patients of groups 2b (923,3 mg/l) and 3b (1002,5 mg/l) in two weeks after beginning of therapy and remains on the level of control data during 3 months of observation (993,5 mg/l and 972,4 mg/l, respectively). When standard schemes of treatment of the patients with CGP (groups 1, 2a and 3a) are used, positive dynamics is also apparent. However, firm normalization of concentration of C3 fragments in the oral fluid is not achieved.

Table 3.

Change of concentration of C3 component in patients with CGP and CGP associated with lichen planus (mg/l).

Groups	Before treatment	In 14 days after treatment	In 3 months after treatment
1 (n=20)	637,8±39,22*	846,9±82,77*	861,9±80,99*
2a (n=8)	460,8±55,51*	696,2±80,86*	634,8±135,43*
2b (n=8)	483,1±66,73*	923,3±151,90	993,5±37,72
3a (n=8)	480,9±55,64*	721,9±85,81*	609,3±117,24*
3b (n=8)	478,3±34,93*	1002,5±54,80	972,4±141,45
4 (n=20)	984,3±102,90	-	-

* - index value in comparison with control differences in group were significant at p<0.05.

In all patients with CGP associated with lichen planus in the oral fluid, increase of concentration of sIgA (Table 4) by 2 times (in comparison with the norm) has been detected, and in patients of the first group this index was tended to sharp decrease. After performed treatment according to

the elaborated scheme normalization of sIgA level in the oral fluid of the patient of groups 2b and 3b during the whole period of observation was accomplished.

In patients with CGP associated with lichen planus, who underwent standard treatment (2a and

3a), reliable changes of this index were absent and in patients of the first group normalization of sIgA

level was observed immediately after end of treatment, but in three months it was the same.

Table 4.

Content of sIgA in oral fluid in patients (g/l).

Groups	Before treatment	In 14 days after treatment	In 3 months after treatment
1 (n=20)	0,13±0,05*	0,31±0,05	0,17±0,03*
2a (n=8)	0,54±0,03*	0,45±0,05*	0,49±0,12*
2б (n=8)	0,60±0,08*	0,39±0,04	0,35±0,04
3a (n=8)	0,60±0,07*	0,52±0,07*	0,48±0,06*
3б (n=8)	0,57±0,09*	0,36±0,03	0,37±0,06
4 (n=20)	0,29±0,05	-	-

* - index value in comparison with control differences in group were significant at $p < 0.05$.

Conclusions

With reference to the foregoing it is possible to draw a conclusion that CGP as well as conjoint course of CGP and lichen planus are accompanied by significant changes of local immunity of the oral cavity which become apparent in the form of sharp decrease of lysozyme and beta-lysins activity, reduction of the amount of C3 components of complement and increase sIgA level in the oral fluid.

Efficiency of our method of treatment of patients with CGP associated with lichen planus is proved through recovery of indices of local non-specific immunity of the oral cavity such as lysozyme and beta-lysins activity and concentration of C3 fragments of complement as well as normalization of sIgA level directly after the course is finished and in 3 months after treatment.

Normalization of indices of local immunity of the oral cavity is accompanied by absence of symptoms of inflammation of parodontium tissue.

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