CLINICAL-DIAGNOSTIC STUDIES

SIGNIFICANCE OF SALIVARY POLY (ADP-RIBOSE)-POLYMERASE IN THE ASSESSMENT OF AGE-RELATED PATHOLOGICAL PROCESSES IN THE ORAL CAVITY

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Age-related changes in the oral cavity are accompanied by the development of age-related pathology, such as chronic periodontitis (CP). Although apoptosis plays a certain role in its pathogenesis, this fact, however, has not been evaluated clinically, and the diagnostic information content of biomarkers of apoptosis and aging has not been determined. The aim of the study was to evaluate the content of cleaved poly-(ADP-ribose)-polymerase (cPARP) and caspase-3 (Casp3) in mixed saliva of elderly patients with age-related dental diseases and in mature patients with mild to moderate CP. The study included 69 people. The control group included 22 healthy young volunteers aged 18 to 44 years. The main group included 22 elderly patients aged 60 to 74 years. They were divided into subgroups according to clinical manifestations: occlusion (comparison group), periodontal, and dystrophic syndromes. Additionally, a group of 25 patients of mature age from 45 to 59 years old with mild to moderate CP was analyzed. The content of salivary Casp3 in patients with occlusion syndrome was lower than in healthy young people (p=0.014). In patients with the periodontal syndrome, the content of cPARP was higher than in the comparison group (p=0.031). The group with dystrophic syndrome had the highest level of Casp3 in comparison with the control group and the comparison group (p=0.012, p=0.004, respectively). There were no statistically significant differences between patients of different age groups with mild to moderate CP. Evaluation of the correlation between cPARP and Casp3 levels revealed a direct relationship in the group of elderly patients and in patients with mild CP (r=0.69, r=0.81, respectively). We assessed the effect of Casp3 levels on changes in the cPARP levels by means of a simple linear regression analysis. The cPARP level correlated with the content of Casp3 (r^2=0.555). According to the results of the ROC analysis, it was found that using the cPARP indicator it would be possible to distinguish between groups of elderly patients with periodontal and occlusion syndromes (AUC=0.71), while using Casp3 it would be possible to distinguish patients with the occlusion syndrome and the control group (AUC=0.78). Since the level of Casp3 in young people is significantly higher than in the elderly patients, its decrease can be considered as a potential salivary biomarker of aging. The level of studied cPARP in the elderly has clinical value in periodontal syndrome and low age dependence.

Key words: biomarker; saliva; aging; poly(ADP-ribose) polymerase; caspase-3; apoptosis

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INTRODUCTION

The increase in the proportion of the elderly population worldwide remains one of the leading demographic trends. Aging is characterized by complex, unevenly developing changes in various structures of the body. These include dysregulation of programmed cell death: in some types of cells, apoptosis activity exceeds the physiological level, in others it becomes lower [1]. The most important role in aging is attributed to impaired DNA methylation, impaired telomere size, etc. Proteins of the poly-(ADP-ribose) polymerase (PARP) family are involved in the mechanisms of DNA repair and genome stability. Their function is to respond to DNA single-strand breaks by forming a bond with break sites and formation of poly(ADP-ribose), which serves as a signal for DNA repair [2]. The substrate for this reaction is nicotinamide adenine dinucleotide (NAD^+). After DNA strand repair, PARP is destroyed. Multiple damage to the DNA molecule leads to increased PARP activity. A rapid depletion of the substrate NAD^+ develops and this causes a decrease in the ATP level, followed by subsequent development of lysis and cell death [3]. Thus, in the case of local DNA damage, PARP contributes to the restoration of its structure, and in the case of extensive damage, it accelerates cell death. This determines association of this enzyme with apoptosis.

Apoptosis is based on the intracellular proteolytic cascade initiated by cysteine proteases (caspases). This cascade involves initiator caspases (e.g. caspase-9) and executioner caspases (e.g. caspase-3). Cleavage of PARP by caspase-3 (Casp3) is considered a universal sign of apoptotic cell death. This results in formation of two subunits; one subunit, known as cleaved PARP (cPARP), enters the cytosol, while the second one remains in the nucleus, where it binds to DNA and inhibits PARP activity [4]. PARP degradation by Casp3 promotes apoptotic cell death.

Apoptosis plays an important role in the regulation of tissue homeostasis in normal and pathological conditions, particularly, in the development of diseases of the oral cavity [5]. The death of epithelial cells is an important innate mechanism that provides elimination of pathogens and modulates immune-inflammatory responses. Diseases characterized by damage of the oral mucosa, such as leukoplakia, lichen planus, candidal stomatitis, are characterized by impairments of the mechanisms of cell death, as evidenced by altered expression of Casp3 in epithelial cells [6, 7]. In squamous cell carcinoma of the oral mucosa a lower expression of Casp3 compared to moderate dysplasia was reported [8]. An increase in Casp3 activity and PARP cleavage were observed in response to a fungal infection in candidal stomatitis [9].

One of the most common diseases is chronic periodontitis (CP) [10]. A certain role in its pathogenesis is attributed to apoptosis, and also pyroptosis, a type of programmed cell destruction mediated by caspases [11-13]. A significant difference between this process and apoptosis is inflammatory reactions: pyroptosis is accompanied by the release of pro-inflammatory cytokines. It is likely involved in the progression of periodontitis through the release of pro-inflammatory cytokines and increased inflammation [14]. Although the participation of Casp3 is characteristic of the apoptotic pathway of cell destruction, the association of this enzyme with pyroptosis was also shown [15].

Age-related changes in the oral cavity are associated with various dental diseases, particularly, with lesions of the mucous membrane (xerostomia), CP, and loss of teeth. Clinical aspects of oral health in recent years have been actively studied and described in the literature [16]. In the context of the active development of non-invasive “saliva diagnostics”, it seems equally important to search for new biomarkers of aging and apoptosis in mixed saliva in age-related pathology.

The aim of the study was to evaluate the content of cPARP and Casp3 in mixed saliva in elderly patients with age-related dental diseases and in mature patients with mild to moderate CP.

MATERIALS AND METHODS

The open, cross-sectional, non-randomized study involved 69 individuals, of whom 47 suffered from age-related dental diseases. The control group consisted of healthy young volunteers aged 18 to 44 years (n=22); they were selected on the basis of the results of a preventive examination. The age distribution had a median of 28 years (the 25th quartile was 25 years, the 75th quartile was 31 years). Elderly patients from 60 to 74 years old formed the main group. The median age was 67 years (the interquartile range, 61 to 71 years). The main group was divided into the following subgroups according to conventionally identified clinical syndromes [16]: a subgroup of patients with the occlusion syndrome (n=6), a subgroup of patients with the periodontal syndrome (n=10) and a subgroup of patients with the dystrophic syndrome (n=6). Patients with the occlusion syndrome were included in the comparison group; they were characterized by the least pronounced clinical symptoms of damage to the mucous membrane and periodontal tissues. We also formed a group of patients of mature age from 45 to 59 years with the periodontal syndrome. Age (median and interquartile rangeto) was 48 years (45 to 53 years). This group included patients with mild (n=16) and moderate (n=9) CP. There were no gender and age differences between the examined groups. For age periodization, recommendations for the classification of age periods by WHO (1963) were used.

Examination and treatment of patients was carried out on the basis of the Dental Clinic of the Ural State Medical University. All participants included in the study underwent a dental examination according to the protocol adopted in the clinic. X-ray (2D- and 3D-) examination was used to verify the diagnosis.

The occlusion syndrome group included patients with such manifestations as increased tooth wear and wedge-shaped defects and relatively intact periodontium (i.e. without pronounced signs of inflammation). Patients with the periodontal syndrome had CP of moderate severity. Patients with the dystrophic syndrome had diseases of the oral mucosa (non-tumor changes in the epithelium of the oral cavity).

The group of young healthy volunteers included individuals without concomitant pathology. Elderly and old patients were characterized by polymorbidity: a combination of 2-3 somatic diseases. In anamnesis these patients had diseases of the cardiovascular system, gastrointestinal tract, respiratory system, etc. (Table 1).

Table 2 shows clinical characteristics of the groups according to objective parameters of the state of the oral cavity (dental indices). The values of the the decayed, missing, and filled teeth (DMFT) index, reflecting the state of hard tissues of the tooth, and the papillary-marginal-attached index (PMA), characterizing the state of the periodontium, differed markedly between groups, thus indicating correct selection of patients according to clinical signs.

The following criteria for inclusion of patients were used: compliance with the requirements of age periodization, clinical confirmation of the diagnosis, patient consent to participate in the study, compliance of clinical diagnoses with signs of the occlusion, periodontal or dystrophic syndromes. The exclusion criteria for patients were: age under 18 years, refusal to participate in the study, the presence of acute injuries of the facial skeleton, the presence

Table 1. Accompanying somatic pathology in the examined patients

Pathology	Occlusion syndrome (n=6)	Periodontal syndrome (n=10)	Dystrophic syndrome (n=6)	Mature patients with CP (n=25)	Control group (n=22)	*p**
Ischemic heart disease	3	5	3	1	0	<0.001
Hypertension	4	7	5	2	0	<0.001
Bronchial astma	0	1	1	0	0	0.120
Gastritis and duodenitis	2	6	4	5	0	<0.001
Metabolic syndrome	3	4	3	7	0	0.013

* – the Kruskal-Wallis test.

Table 2. Clinical characteristics of patients

Index	Occlusion syndrome (n=6)	Periodontal syndrome (n=10)	Dystrophic syndrome (n=6)	Mature patients with CP (n=25)	Control group (n=22)	*p**
DMFT	10.0 (9.0–14.0)	20.0 (19.0–24.0)	21.0 (21.5–23.5)	16.0 (15.0–20.0)	11.5 (10.0–15.0)	<0.001
PMA	27.0 (23.5–31.0)	83.0 (72.0–86.0)	57.0 (51.7–67.5)	32.0 (28.0–37.0)	15.0 (12.2–19.7)	<0.001

* – the Kruskal-Wallis test.

of type 1 and 2 diabetes mellitus in the sub- and decompensation stage, severe somatic pathology in the sub- and decompensation stage in the anamnesis.

The content of the caspase-cleaved form of PARP (cPARP) and Casp3, was determined in mixed saliva by multiparametric fluorescence analysis with magnetic microspheres (xMAP technology, Luminex 200, Luminex, USA) using the ProcartaPlex Human Apoptosis Panel 6-Plex test system (Invitrogen, USA) and following the manufacturer's protocol. This technology is similar to ELISA when pairs of appropriate antibodies are used to identify the protein of interest. It uses magnetic particles with a diameter of 6.45 μm, stained with red and infrared fluorophores, carrying specific antibodies. This complex is visualized with biotinylated antibodies and streptavidin-R-phycoerythrin (RPE) and identified by the Luminex system. The technique included incubation of 25 μl of mixed saliva with a mixture of specially prepared magnetic microspheres in a 96-well flat-bottomed plate. After a series of washes with a washing solution on a magnet, a mixture of detection antibodies specific for the studied parameters and RPE was added to each well. Two lasers were used to detect magnetic particles with the Luminex 200: the reporter laser was green with a wavelength of 534 nm, and the classification laser was red with a wavelength of 635 nm. The red laser was used for spectral signature differences, the green laser was used to determine the RPE fluorescence intensity, which was proportional to the amount of protein present in the sample. cPARP and Casp3 concentrations were calculated from the mean particle fluorescence intensity by using xPONENT and ProcartaPlex software.

Statistical processing of the results obtained was carried out on the basis of the principles of variation statistics. The critical significance level was set at 0.05 (p=0.05). A one-sample two-tailed Kolmogorov-Smirnov test was used to determine the closeness of the obtained data to the normal distribution law. Since the hypothesis that the data were normally distributed was rejected, nonparametric statistical tests were used for statistical data processing. The research results are presented as median (25th; 75th quartile) — Me (Q1; Q3). The two-tailed Mann-Whitney test was used to evaluate the differences between two independent datasets. The nonparametric Kruskal-Wallis test was used to perform a one-way analysis of variance. A two-tailed Spearman test was performed to find correlations between the studied parameters. Tightness of relationships was evaluated using the Chaddock scale. The coefficient values below 0.3 were considered as a sign of weak correlation, the values from 0.3 to 0.5 suggested moderate correlation, the values from 0.5 to 0.7 were considered as marked correlations, the values from 0.7 to 0.9 suggested high correlation, and the values above 0.9 were considered as very high correlation. A simple linear regression analysis was performed to evaluate the linear relationship between biomarkers. To assess the diagnostic characteristics of the studied parameters, diagnostic sensitivity and diagnostic specificity were calculated. ROC analysis was used to assess the diagnostic efficiency; it included construction and determination of the area under the ROC curve — (AUC). The AUC value from 0.5 to 0.7 was interpreted as a test with low accuracy, the values ranged from 0.7 to 0.9 indicated moderate accuracy, and the values from 0.9 or more suggested high accuracy. The optimal cutoff point was selected using the Youden index (J). Statistical analysis was carried out using the Python programming language (version 3.9.12), open libraries SciPy (version 1.7.3), Statsmodels (version 0.13.2), Scikitlearn (version 1.0.2).

RESULTS AND DISCUSSION

Age-related changes in the oral cavity are characterized by a certain polymorphism. In this study, the level of salivary cPARP and Casp3 was determined in elderly people with various gerontostomatological syndromes (Table 3).

The lowest level of the studied parameters was noted in patients with the occlusion syndrome. In these patients salivary Casp3 concentrations were statistically significantly lower than in healthy young people. In patients with the periodontal syndrome, an increase in mixed saliva cPARP was found in comparison with occlusion syndrome patients (comparison group). In the group of patients with the dystrophic syndrome, the highest level of Casp3 was detected; it significantly differed from control group individuals and comparison group patients.

The content of Casp3 determined in occlusion syndrome patients most likely reflects the absence of pronounced DNA damage and apoptosis. A higher content of Casp3 in young people is probably due to a higher rate of cell turnover, and, accordingly, apoptosis [1]. The more cells are renewed, the higher the probability of various disorders leading to apoptosis is.

The content of the studied biomarkers in the periodontal syndrome was lower than in dystrophic, but higher than in occlusion syndromes. This seems logical, since CP is characterized by progressive inflammation of periodontal tissues. Early studies of the mechanisms of cell death in this disease were focused on investigation of apoptosis [17, 18]. Recent studies suggest that the processes of apoptosis and pyroptosis occur simultaneously and in interaction with each other in CP [19]. Casp3 is a common key protein in the mechanisms described above [20]. Certain evidence exists that PARP cleavage is a common feature of pyroptotic and apoptotic processes [21, 22]. This explains the differences in the cPARP content; the lower content of Casp3 (as compared with the dystrophic syndrome) indicates that apoptosis is not the dominant mechanism of cell destruction. A high concentration of Casp3 in mixed saliva in patients with the dystrophic syndrome may be associated with severe damage of the oral mucosa epithelium and predominance of apoptosis [23, 24].

In order to determine the diagnostic value of biomarkers in two age groups — in elderly people with the occlusion syndrome who do not have pronounced signs of inflammation in the oral cavity (comparison group), and in the control group — we performed a ROC analysis. The ROC analysis consists in constructing a ROC curve and determining AUC, which reflects the diagnostic efficiency of the test (Table 4).

Using Casp3 we were able to differentiate with moderate accuracy elderly people with intact periodontium and the control group individuals. However, the use of Casp3 as a salivary biomarker of aging remains problematic due to the high variability of this parameter in patients.

Since the most common gerontostomatological disorder was the periodontal syndrome, it seemed important to assess the change in biomarker levels depending on the age and severity of CP. The content of cPARP and Casp3 was compared in mature patients with mild and moderate CP, as well as in elderly patients with moderate CP (Table 5).

Table 3. The content of cPARP and Casp3 in elderly patients

Parameter	Occlusion syndrome (n=6)	Periodontal syndrome (n=10)	Dystrophic syndrome (n=6)	Control group (n=22)
cPARP, pg/ml	0.34 (0.34–0.83) p_1=0.240	1.00 (0.76–4.16) p_1=0.330 p_2=0.031	1.79 (0.34–3.24) p_1=0.750 p_2=0.360	0.62 (0.34–10.09)
Casp3, pg/ml	22.80 (12.49–26.86) p_1=0.014	85.31 (43.79–132.89) p_1=0.420 p_2=0.056	175.85 (100.48–251.23) p_1=0.012 p_2=0,004	48.95 (34.44–99.42)

p_1 value – comparison with the control group; p_2 value – comparison with the group of patients with the occlusion syndrome (comparison group).

Table 4. ROC-analysis of the salivary parameters in the occlusion syndrome

Parameter	cut-off	AUC	sensitivity, %	specificity, %	J
cPARP, pg/ml	<0.36	0.67	100.00	42.90	0.41
Casp3, pg/ml	<22.80	0.78	75.00	92.30	0.67

This study found no differences between these parameters in patients of different age groups with mild to moderate CP. However, it can be noted that the median values of cPARP and Casp3 levels were higher in the group of elderly people and in the group of mature age with moderate CP. At the same time, the results obtained roughly corresponded to each other in the group of patients with mild periodontitis and in healthy young volunteers. It can be assumed that the obtained results reflect the dependence of the levels of the studied biomarkers on the severity of CP rather than on age.

Currently, diagnostics of CP is based on a dental clinical examination and computed tomography, which has limitations in its use. At the same time, non-invasive salivary biomarkers could be used as tools for early diagnostics of CP, assessing the activity of the pathological process, predicting the development of the disease, and response to therapy [25, 26]. In particular, the value of cPARP may be of some interest in the laboratory monitoring of CP.

The pathophysiological mechanisms of cPARP formation suggest a close relationship with the level of Casp3. As described above, in diseases related to the dystrophic syndrome, the apoptotic process predominates, as evidenced by the highest levels of Casp3 and cPARP. CP is characterized by more complex mechanisms of cell death; apoptosis can be combined with pyroptosis [12, 20]. Some authors report that PARP is not a key enzyme in pyroptosis [13]. However, the association of cPARP with the level of Casp3 in CP assessed using correlation analysis is of interest (Table 6).

The correlation analysis of relationships between cPARP and Casp3 levels revealed a statistically significant direct relationship in the group of elderly patients with the periodontal syndrome and mature age with mild CP. However, correlation does not mean causality. It is known that the cleavage of PARP and formation of cPARP in periodontitis can be associated with caspase-1 [11, 13, 14, 21, 22]. Therefore, we assessed the effect of Casp3 levels on changes in cPARP levels using a simple linear regression analysis, combining groups of elderly and mature patients with CP (figure).

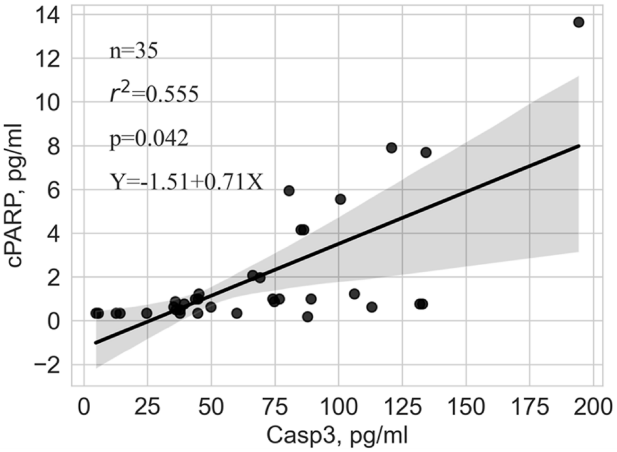

Figure. Linear regression curve with confidence intervals. Casp3 and cPARP are independent and dependent variables, respectively.

Table 5. Mixed saliva cPARP and Casp3 content in patients with mild to moderate CP

Parameter	Elderly patients with moderate CP (n=10)	Mature patients with mild CP (n=16)	Mature patients with moderate CP (n=9)	Control group (n=22)
cPARP, pg/ml	1.00 (0.76–4.16) p_1=0.33 p_2=0.30 p_3=0.39	0.69 (0.35–2.94) p_1=0.92 p_3=0.95 p_4=0.30	0.88 (0.63–1.00) p_1=0.90 p_2=0.95 p_4=0.39	0.62 (0.34–10.09)
Casp3, pg/ml	85.31 (43.79–132.89) p_1=0.43 p_2=0.30 p_3=0.71	44.94 (37.31–82.74) p_1=0.88 p_3=0.18 p_4=0.30	74.73 (69.13–87.80) p_1=0.24 p_2=0.18 p_4=0.71	48.95 (34.44–99.42)

p_1 value – comparison with the control group; p_2 value – comparison with the group of mature patients with mild CP; p_3 value – comparison with the group of mature patients with moderate CP; p_4 value – comparison with the group of elderly patients with moderate CP.

Table 6. Spearman's rank correlations (r) between cPARP and Casp3 levels

Groups	*r*	*p*
Elderly patients with the occlusion syndrome	-0.23	0.65
Elderly patients with the periodontal syndrome	0.69	0.02
Elderly patients with the dystrophic syndrome	0.81	0.06
Mature patients with mild CP	0.81	0.01
Mature patients with moderate CP	-0.12	0.74
Control group	0.76	0.54

The slope was greater than zero, thus indicating an increase in cPARP levels with the Casp3 increase (n=35, r^2=0.555, p=0.042, Y=-1.51+0.71X). The coefficient of determination (r^2) was 0.555. This suggests that the cPARP level was 55.5% explained by the content of Casp3. This result is consistent with the concept of the relationship between the PARP cleavage (by caspase-1 and Casp3) with the cPARP formation in CP. Thus, it seems reasonable to use cPARP as a potential diagnostic biomarker in the diagnostics of CP. To achieve the goal of the study, an ROC analysis was carried out. It was found that the cPARP assay distinguished groups of elderly people with periodontal and occlusal syndromes. At the cut-off level above 4.16 pg/ml, AUC was 0.71, diagnostic sensitivity — 66.6%, diagnostic specificity — 90.0%. This indicates that the diagnostic performance of the saliva cPARP test in gerontostomatological syndromes was moderately accurate.

The changes in two salivary markers in gerontostomatological syndromes recognized in this study are based on examination of healthy volunteers and 4 groups of patients, two of which were small. This is a certain limitation of this study. Although the statistical methods have been adequately selected and applicable for a given group size, we do not exclude that slightly different results will be obtained with an increase in the cohort of patients.

CONCLUSIONS

There is a growing interest in mixed saliva as an accessible, minimally invasive, and informative diagnostic material. Being an organ-specific component, this biological fluid may be of interest in the issue of detecting premature aging of oral tissues, as well as in diagnostics of periodontal diseases. The results of the study suggest that salivary Casp3 may be a potential biomarker of age-related dental pathology. The level of salivary cPARP in the elderly patients is of clinical value in the periodontal syndrome, and an increase in the level of Casp3 reflects the activity of apoptosis in the most severe pathology, the dystrophic syndrome.

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COMPLIANCE WITH ETHICAL STANDARDS

The study was conducted in accordance with the principles of the Helsinki Declaration of the World Medical Association (Helsinki, 2000). Informed consent to participate in the study was obtained from all patients. The design of the study, its novelty, admissibility and acceptability were approved at the meeting of the Local Ethical Committee of the Ural State Medical University on March 19, 2021 (protocol no. 3).

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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ЗНАЧЕНИЕ САЛИВАРНОЙ ПОЛИ (ADP-РИБОЗА)-ПОЛИМЕРАЗЫ В ОЦЕНКЕ ВОЗРАСТЗАВИСИМЫХ ПАТОЛОГИЧЕСКИХ ПРОЦЕССОВ В ПОЛОСТИ РТА

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Возрастные изменения в полости рта сопровождаются развитием возраст-ассоциированной патологии, например, хронического пародонтита (ХП). В его патогенезе определённая роль принадлежит апоптозу. Однако данный факт не нашёл пока клинической оценки, не определена диагностическая информативность биомаркеров апоптоза и старения. Цель исследования — оценить содержание расщепленной формы поли-(ADP-рибоза)-полимеразы (cPARP) и каспазы-3 (Casp3) в смешанной слюне у пожилых пациентов с возраст-ассоциированными стоматологическими заболеваниями и у пациентов зрелого возраста с ХП лёгкой и средней степени тяжести. В исследование было включено 69 человек. В контрольную группу вошли 22 здоровых добровольца молодого возраста от 18 до 44 лет. В основную группу вошли 22 пациента пожилого возраста от 60 до 74 лет. Их подразделили на подгруппы по клиническим синдромам — окклюзионный (группа сравнения), пародонтальный, дистрофический. Дополнительно анализировали группу из 25 пациентов зрелого возраста от 45 до 59 лет с ХП лёгкой и средней степени тяжести. Содержание саливарной Casp3 у пациентов с окклюзионным синдромом было ниже, чем у здоровых молодых людей (p=0,014). У пациентов с пародонтальным синдромом увеличено содержание cPARP относительно группы сравнения (p=0,031). Группа с дистрофическим синдромом отличалась наиболее высоким уровнем Casp3 в сравнении с контрольной группой и группой сравнения (p=0,012, p=0,004 соответственно). Между пациентами различных возрастных групп с ХП лёгкой и средней степени тяжести не было статистически значимых отличий. Оценка корреляционной связи между уровнями cPARP и Casp3 выявила прямую связь в группе пациентов пожилого возраста и у пациентов с ХП лёгкой степени тяжести (r=0,69, r=0,81 соответственно). Мы оценили влияние уровня Casp3 на изменение содержания cPARP с помощью простого линейного регрессионного анализа. Уровень cPARP коррелировал с содержанием Casp3 (r^2=0,555). По результатам ROC-анализа было установлено, что показатель cPARP позволял различать группы пациентов пожилого возраста с пародонтальным и окклюзионным синдромами (AUC=0,71), а использование Casp3 — пациентов с окклюзионным синдромом и контрольную группу (AUC=0,78). Поскольку уровень Casp3 у молодых людей существенно выше, чем у пожилых, его снижение может рассматриваться как потенциальный саливарный биомаркер старения. Уровень изученной cPARP у пожилых людей имеет клиническую ценность при пародонтальном синдроме и низкую зависимость от возраста.

Полный текст статьи на русском языке доступен на сайте журнала (http://pbmc.ibmc.msk.ru).

Ключевые слова: биомаркер; смешанная слюна; старение, поли (ADP-рибоза)-полимераза; каспаза-3; апоптоз

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