

from mothers with physiological pregnancy (n=15); II – newborns from mothers whose pregnancy was complicated by preeclampsia of mild severity (n=13); III – newborns from mothers whose pregnancy was complicated by preeclampsia of moderate severity (n=14); IV – newborns from mothers whose pregnancy was complicated by severe preeclampsia (n=13). An immunohistochemical study was performed with monoclonal antibodies to Ki-67.

Results. In groups I-IV in the newborns kidneys Ki-67 expression was detected in the nuclei of cells of the glomeruli, epithelial cells of the tubules and collecting ducts, endothelial cells of the vessels stroma, immune cells and fibroblastic cells located in the organ stroma. In groups II-IV, compared with group I, proliferative activity increased, as evidenced by a significant increase in the number of Ki-67-positive cells (group I – (6.93 ± 0.42) , group II – (22.18 ± 0.58) , group III – (20.36 ± 0.68) , group IV – (19.23 ± 0.45)). Proliferative activity in group I was evenly expressed in the parenchyma and stroma of the organ, but in groups II-IV its predominance was noted in the stroma compared with the parenchyma, which was due to an increase in the number and morphofunctional activity of the fibroblastic cells.

Conclusion. Maternal preeclampsia leads to an increase in the number of Ki-67-positive cells in the kidneys of newborns, while the stromal proliferative activity was increased and the parenchymal decreased. The prospect of further research is to study the processes of apoptosis in these organs.

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CLINICAL DIAGNOSTIC IMPORTANCE OF DETERMINING ANTIMICROBIAL PROTEINS AND CYTOKINES IN THE ORAL FLUID IN PATIENTS WITH PURULENT-INFLAMMATORY DISEASES OF THE ORAL CAVITY

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The applied complex treatment of cancer of the oral mucosa (OM) that is largely determines the development of purulent complications, since the cytostatic effect of radiation exposure and chemotherapy in this group of patients can lead to mucositis with the involvement of all the components of the oral cavity: the mucosa itself, salivary glands, bone structures of the jaws [1]. The presence of pathogenic microflora in the oral cavity, which can at any time lead to serious purulent-inflammatory complications, exacerbated during chemoradiotherapy, is an additional aggravating factor [2]. Radical chemoradiation treatment of patients with cancer of the OM affects the immune status of the body and the problem of the development of purulent complications in the postoperative period, which necessitates special examinations of the oral cavity with diagnostic measures [3]. To solve such practical problems, there is a need for additional molecular diagnostic markers, which could reflect the risk of developing suppurative complications of complex treatment of cancer of the oral mucous membrane disease.

Materials and Methods. The study included 141 patients with cancer of the OM T1-3N0-2M0 stage of the process. The average age of patients was $50,5 \pm 4,4$ years. The patients were divided into 2 groups in which purulent-inflammatory complications developed (necrosis of a muscle or skin-fatty flap used for plasty, osteomyelitis of the mandible, phlegmon of the lower jaw) – the main group (n=96) and the postoperative period leaked in the postoperative period without purulent-septic complications – the comparison group (n = 45). The oral fluid (free unstimulated saliva) was taken in the morning before eating after rinsing the mouth with boiled water. Quantitative determination of interleukin-8 (IL-8) and lactoferrin in the oral fluid was carried out by the method of enzyme-linked immunosorbent assay using the Interleukin-8 kits (Cytokine, Russia), Lactoferrin Strip (ZAO Vector Best Russia) taking into account the instructions. The data were processed using the statistical software package STATISTICA 12.0.

Results. In patients of the main group, purulent complications of the combined treatment were represented by local and systemic reactions. Local wound complications developed in 67 (69,8%) patients and were mainly represented by necrosis of the skin-muscle flap (n=31), necrosis of the skin-fat flap (n=29). Abscesses and cellulitis of the maxillofacial area complicated the healing of the wound in 7 cases. The close connection between the tumor and the mucous-periosteal layer of the mandible led to the development of mandibular osteomyelitis observed in the main group in 28 (29,2%) patients. The levels of lactoferrin and interleukin-8 in the oral fluid in patients of the main group and the comparison group are shown in table 1.

Table 1 Lactoferrin and interleukin-8 levels in the oral fluid in patients of the main group and the comparison group

Indicator	Main group, n=96	Comparison group, n=45	p
Lactoferrin, $\mu\text{g/ml}$	$2,0 \pm 0,24$	$3,5 \pm 0,38$	<0,05
IL-8, pg/ml	$3328,5 \pm 56,2$	$2895,6 \pm 66,9$	<0,05

In patients of the main group, statistically significant differences in the concentrations in the oral fluid were established for lactoferrin and interleukin-8. In patients of the main group, in contrast to patients in the comparison group, the concentration of the antimicrobial protein lactoferrin was reduced by 42,9% ($p < 0,05$), IL-8 increased by 15% ($p < 0,05$). Thus, with the development of purulent complications locally in biological environments, a decrease in the intensity of antimicrobial protection due to lactoferrin, an increase in the content of pro-inflammatory factors (IL-8), contributing to angiopathy and lymphogenesis, which increase vascular permeability, develops. The high risk of developing inflammatory postoperative complications in patients with cancer of the OM after surgery is pathogenetically caused by a decrease in oral antimicrobial protection due to a low content of antimicrobial proteins in saliva, an increase in the titer of the oral pathogenic microbiota, and the level of pro-inflammatory mediator IL-8. Reduced antimicrobial protection due to low levels of lactoferrin, increasing the concentration of the pro-inflammatory mediator IL-8 contributed to increased vascular permeability, macrophage and granulocyte chemotaxis.

By the method of ROC-analysis, it was found that the decrease in the content of lactoferrin in the oral fluid below $19 \mu\text{g/ml}$, pro-inflammatory cytokine IL-8 above 3335 pg/ml is associated with the development of inflammatory postoperative complications with a diagnostic sensitivity of 83%, diagnostic specificity of 69% and accuracy 76% ($p < 0,001$). This opens up further prospects for their determination in biological media for the formation of a prognosis of inflammatory complications in the oral cavity. .

Conclusion. In the oral fluid as a homeostatic environment for the processes in the oral mucosa in patients with cancer of the suppression of retinal dysprosis with purulent-

inflammatory complications, a decrease in antimicrobial factors and an increase in proinflammatory mediators were noted.

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PLASMA OSTEOPROTEGERIN AS A MARKER OF DOCUMENTED CORONARY ATHEROSCLEROSIS IN TYPE TWO DIABETES MELLITUS PATIENTS

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Osteoprotegerin (OPG) is a member of tumor necrosis factor superfamily, belonging to the class of inhibitors of osteoclastogenesis [1]. OPG is expressed in vivo by osteoblasts, endothelial cells, smooth muscle cells of the arteries and veins media and is a specific receptor for the ligand receptor activation of nuclear transcription factor kappa beta (receptor for receptor activator of nuclear factor kappa-B ligand - RANKL) and TNF-alpha-dependent ligand inducing apoptosis (tumor necrosis factor-related apoptosis-inducing ligand - TRAIL)[2]. Major inducers of synthesis of the latter are proinflammatory cytokines, such as interleukin (IL)-2, IL-6, monocytes chemoattractant protein-1, is produced mainly by mononuclear phagocytes [3]. In this regard, OPG is often seen as an indicator of proinflammatory activation, atherosclerosis and metabolic comorbidities. Universal biological potential of OPG, designed to control the intensity of the processes of ossification, is often used as a predictor of early atherosclerotic lesions of arteries[3]. Also, it has found a strong association between the concentration of OPG, the risk of stroke, ischemic heart disease, stable angina, as well as the severity of coronary atherosclerosis, as measured by the total value of the latter and the severity of coronary calcification [4]. In addition, OPG is likely to have an acceptable predictive value with respect to the onset of death in long-term observation of patients with coronary heart disease, type 2 diabetes, ischemic stroke, hypertension, and in patients with chronic renal failure [4]. Objective of the study: to evaluate the interrelation between circulating OPG and coronary vasculature damage in type 2 diabetes mellitus (T2DM) patients with documented coronary artery disease.

Materials and Methods. 167 subjects with T2DM with previously documented Coronary Artery Disease were enrolled to the study. Osteoprotegerin levels were measured by ELISA technique (Bender Med Systems GmbH, Austria). Concentrations of total and HDL cholesterol were determined and obtained with "AU640 Analyzer" (Olympus Diagnostic Systems Group, Japan).

Statistical analysis was performed in SPSS for Windows v. 17.0 (SPSS Inc., Chicago, IL, USA). All values were given as mean and 95% CI or median and percentiles. An independent group t-test was used for comparisons for all interval parameters meeting the criteria of normality and homogeneity of variance. For interval parameters not meeting these criteria, the non-parametric Mann-Whitney test was used to make comparisons between groups. Comparisons of categorical variables between groups were performed using the Chi² test, and the Fisher exact test. Receiver operating