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CHRONIC PERIODONTITIS AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH ARTERIAL HYPERTENSION

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ABSTRACT — The work offers a view at the data obtained through an examination of 120 patients with chronic generalized periodontitis (CP) and arterial hypertension (AH). The check-up included clinical examination, immunohistochemical, morphometric studies, as well as evaluation of the endothelium vasodilating function. CP in patients with hypertension features more significant changes in the quantitative density of gum cells positive to ET-1, endothelial NO-synthase, if compared to the CP values in patients with no background somatic pathology. Changes affecting vasoactive mediators in the gum are associated with a systemic inflammatory response and a violation of the endothelium vasodilating function. Periodontitis remission can be achieved with the therapy of the neurotransmitter imbalance.

KEYWORDS — periodontitis, arterial hypertension, NO-synthase, endothelin-1, endothelial dysfunction.

INTRODUCTION

Chronic periodontitis, which is the leading cause behind tooth loss, is often associated with cardiovascular health issues [4, 9]. Periodontitis and the circulatory system diseases share risk factors like age, smoking, diabetes and obesity [2, 12–15]. Chronic inflammatory processes, impaired immune response and oxidative stress are believed to be the basis of comorbidity between periodontitis and cardiovascular diseases [8, 10].

An important thing determining timely prevention of cardiovascular events is identifying vascular endothelial dysfunction. Endothelial dysfunction is a common pathway, which is taken by risk factors aiming to affect long-term atherogenesis processes [1]. The triggers of endothelial dysfunction include ischemia/hypoxia of tissues, elevated blood pressure, dyslipidemia, hyperinsulinemia, oxidative stress, chronic systemic inflammation and other factors [5]. Currently, the pathogenetic basis of endothelial dysfunction is viewed as residing in disturbed local production of nitric oxide (NO) and oxidative stress, which stimulate the synthesis of vasoconstrictors, lipid oxidation and damage to endotheliocyte membranes [11].

Endothelin (ET)-1, known as a vascular inflammation mediator and a vasoconstrictor, is expressed in the gum under the effect of pathogenic bacteria, cytokines, hypoxia, ischemia and mechanical stress [3]. The ET-1 levels in the gingival fluid and blood serum of patients with periodontitis exceed the similar indicator in healthy people and decrease following respective treatment [7].

The data on the relationship between periodontitis and endothelial dysfunction, which is to be found in the available literature, is scarce. There are single mentions claiming that severe periodontitis is associated with impaired endothelial function [6]. This study will help expand the understanding of the mechanisms behind the development of combined periodontal pathology and cardiovascular system, and identify the ways to promote prevention.

Aim: to study the vasoactive markers expression in the gum in patients with chronic periodontitis and arterial hypertension through the treatment dynamics, matching that against the specific features of the endothelial functions.

MATERIALS AND METHODS

The study included 120 patients with chronic periodontitis (CP) and arterial hypertension (AH) of Stage I–II (males — 62.5%; median age — 51.5±6.3). Sixty of the patients (50%) had mild CP, while another 60 (50%) featured moderate CP. As for a comparison group, there were 55 patients examined, who had mild and moderate CP with no somatic pathology (median age — 51.0±5.4); the control group included 25 basically healthy individuals. The examination was carried out prior to the treatment and then — 12 weeks into the treatment. As for the treatment, the following was

done: sanation and professional oral hygiene; antibacterial and anti-inflammatory treatment; surgical treatment, subject to respective indications. All patients received antihypertension therapy, with 93.3% of the patients arriving at the target blood pressure values.

The material for the morphological study was based on a biopsy of the gingival mucosa at the interdental papilla. The verification of the gum cells expression relied on the immunohistochemical method with primary monoclonal antibodies to endothelin-1 (ET-1) and to endothelial NO-synthase (eNOS). The immunohistochemical staining outcomes were evaluated through a morphometric study, with the relative expression area estimated.

The functional status of the endothelium was assessed through flow-induced endothelium-dependent vasodilation (EDV) of the right brachial artery with the standard ultrasound approach employed. The C-reactive protein blood levels were identified with the high-sensitivity method (hs-CRP).

All the participants were duly notified of the aims and of the study protocol, with respective written informed consents obtained from them prior to launching the study. The statistical processing of the outcomes results was performed with the IBM SPSS Statistical 21 software package employing the Mann-Whitney and Wilcoxon reliability criteria, the χ^2 Pearson criterion, and the Spearman correlation factor.

RESULTS AND DISCUSSION

The groups of patients with CP were comparable in terms of age and gender, while there were no statistically significant differences observed in the smoking rate, the body mass index and the glycemic level.

Patients with CP were found to have higher values of hs-CRP compared to practically healthy individuals (1.32±0.41 mg/l). The hs-CRP levels in patients with mild CP was 2.26±0.85 mg/l ($p<0.001$), whereas in patients with moderate CP these values were at 5.18±2.01 mg/l ($p<0.001$). Patients with CP and AH featured a more significant increase in hs-CRP compared to patients with just CP: 3.71±0.97 mg/l ($p<0.001$) for mild CP cases, and 8.52±4.18 mg/l ($p<0.001$) for patients with moderate CP.

The EDV index in the control group was 15.40±6.58%. Vasoreactivity in patients with mild CP remained unchanged (14.50±2.28%), while in patients with moderate CP it was significantly reduced compared to the control group members (13.07±2.26, $p<0.05$).

Patients with CP and AH revealed a more significant violation of the brachial artery EDV compared to patients with an isolated CP course, which was 12.35±2.14% and 10.93±1.60%, respectively, with mild and moderate CP ($p<0.05$). Disturbed EDV was observed in 41 (68.3%) patients with moderate hypertension and CP, and two times less often – in 21 (35%) patients with mild AH and CP ($\chi^2=30.06$, $p<0.0001$). Following the Spearman correlation analysis, a relationship was established between the PI and the EDV ($r = -0.44$, $p=0.005$); between the blood hs-CRP concentration and the EDV ($r = -0.48$, $p<0.001$).

Morphometric analysis showed that the expression of endothelium-associated markers, such as NO-synthase, ET-1 in patients with mild CP matched the control values, while patients with moderate CP showed a decrease in the expression of cells positive to NO-synthase (see Table 1).

Patients with CP combined with AH were found to feature hyperexpression in gum cells positive to ET-1, as well as a decrease in the expression of cells positive to NO-synthase, if compared to the control group, and patients with moderate CP featured a similar trend even compared to the values in patients suffering from CP with no AH. ET-1 plays an obviously important role in periodontal inflammation. The quantitative density of gum cells positive to ET-1 increased in pursuant to the severity of periodontitis, and correlated with the PI index ($r= 0.61$; $p<0.001$), the depth of periodontal pockets ($r= 0.48$; $p<0.001$).

The expression of endothelial markers, just like ET-1 and NO-synthase in the gingival vessels in case of CP and AH, must reflect some systemic change in the vascular wall, the evidence to that being the correlation of the number of gum cells immune-positive to endothelin-1 and NO-synthase with the EDV index ($r= -0.578$ $p<0.001$, Spearman; and 0.533, $p<0.001$, Spearman, respectively). The detected changes appear to be natural, since the combined effect of hemodynamic factors, as well as the systemic inflammatory response in case of moderate CP and AH can cause changes in the vasoregulatory function of the endothelium. Obviously, ET-1 can be viewed as one of the key mediators involved in the development of the mutual aggravation syndrome in periodontitis and AH.

The remission of periodontitis, when the majority of patients reach the target blood pressure, occurs against a positive dynamics of the gum morphofunctional status. After 12 weeks, the expression of gum cells positive to ET-1 and NO-synthase matched the indicators observed in basically healthy individuals (Table 1).

CONCLUSION

Patients with moderate CP without somatic pathology feature signs of endothelial dysfunction combined with a decrease in the expression of gum cells positive to NO-synthase. In case CP and AH are

Table 1. *Expression of gum cells immune-positive to endothelin-1 and nitric oxide synthesis in patients with periodontitis against AH, through the treatment dynamics*

Groups of patients	Value (expression area)	
	ET-1-positive cells (%)	eNO-synthase-positive cells (%)
Basically healthy, n =25	2.92±2.00	7.92±1.95
Patients with CP		
Patients with mild CP, n=25	3.20±1.65	6.88±2.24
Patients with moderate CP, n=30	3.37±1.77	6.30±2.23*
Patients with CP and AH prior to treatment		
Patients with mild CP combined with AH; n=60	6.08±2.35*&	5.94±2.31*
Patients with moderate CP combined with AH; n=60	7.47±2.76*&#	4.75±1.79*& #
Patients with CP and AH following treatment		
Patients with mild CP combined with AH; n=60	3.53 ±1.76	8.23 ±2.65
Patients with moderate CP combined with AH; n=60	4.03±2.45	7.26±3.19

Note: *the data is presented as M±SD; * — differences compared to the values in basically healthy individuals are statistically significant (p<0.05); & — differences compared to the values in patients with CP with no AH are statistically significant (p<0.05); # — differences compared to the values in patients with mild CP are statistically significant (p<0.05).*

combined, they reveal a mutually aggravating effect, where the endothelium is involved in the pathological process affecting the gum with changes in the gum neurotransmitter balance on the one hand, and a more significant endothelial dysfunction along with the combined effect of hemodynamic factors and a systemic inflammatory response — on the other. A success outcome here will take comprehensive dental treatment in combination with effective antihypertensive therapy.

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