

## THE VALUE OF VASCULAR ENDOTHELIAL GROWTH FACTOR IN PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS ASSOCIATED WITH METABOLIC SYNDROME

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### ABSTRACT

**Background:** Endothelial dysfunction (ED) is one of the key independent risk factors for the development of diabetes mellitus, inflammatory, autoimmune and tumoral diseases. **Purpose:** to study the relationship between the expression of vascular endothelial factor and the number of desquamated endothelial cells in patients with chronic generalized periodontitis (CGP) associated insulin resistance syndrome. **Methods:** 14 practically healthy persons (control) and 72 patients with moderate BPH (24 patients without concomitant diseases, 48 patients with CHP in combination with MS) were examined. Immunoenzymatic methods were used to determine the number of desquamated cells and vascular endothelial growth factor in blood plasma. **Findings:** In patients with CGP associated MS, an increase in the level of desquamated endothelial blood cells was revealed against a background of a significant increase in the vascular endothelial growth factor, which is caused by dysfunction of the carbohydrate, lipid and hormonal systems.

**KEYWORDS:** Periodontitis, endothelial dysfunction, metabolic syndrome.

### INTRODUCTION

Modern scientific studies suggest that endothelial dysfunction (ED) is one of the key independent risk factors for the development of diabetes mellitus, inflammatory, autoimmune and neoplastic diseases.<sup>[1,2,4]</sup> The above listed diseases Kovalenko L.V., Belova Y.A., Verzhnikova L.N.<sup>[5]</sup> refers to diseases of the vascular endothelium. Endothelium is involved in the regulation of vascular tone, hemostasis processes, in ensuring the barrier-transport function of the vascular wall, in the immune response of the organism, in the formation/remodeling of blood vessels.<sup>[6,7,10]</sup> Endothelial deficiency of NO-derivatives is believed to be the primary link that binds insulin resistance and endothelial dysfunction.<sup>[9,11]</sup> The complex interaction between endothelial dysfunction, impaired blood flow in skeletal muscles and a decrease in insulin-mediated absorption of glucose may be key to the relationship between insulin resistance, increased blood pressure, impaired glucose tolerance and the risk of cardiovascular diseases.<sup>[3,8]</sup> Endothelial dysfunction is a multifaceted process, the main manifestation of which is considered a violation of the bioavailability of NO and increased production of endothelin-1 cells and other vasoconstrictor substances by cells.<sup>[12]</sup>

One of the factors of endothelial dysfunction is vascular endothelial growth factor (vascular endothelial growth factor - VEGF).

The expression of this cytokine increases with hypoxia, the production of anti-inflammatory cytokines. Activated macrophages, endothelial cells and smooth muscle cells of the vascular wall take part in the formation of VEGF. VEGF is involved in the formation of metabolic syndrome at the nosological level, which includes the development of atherosclerosis, hypertension, type 2 diabetes and other diseases.<sup>[12]</sup>

Isolation of VEGF facilitates the process of monocyte migration, followed by transformation into macrophages. VEGF stimulates the expression of matrix metalloproteinases, which causes the dissolution of the extracellular matrix and the migration of the endothelium into the collagen gel to form endothelial tubes. Newly formed vessels contribute to the nutrition and growth of plaque, followed by its rupture and the development of vascular complications.

**The purpose of the research** is to study the relationship between the expression of vascular endothelium factor and the number of endothelial cells desquamated in patients with chronic generalized periodontitis (CGP) associated insulin resistance syndrome.

## MATERIALS AND METHODS

We have conducted a prospective study of the state of carbohydrate and lipid metabolism, the expression of VEGF and the number of desquamated cells. To achieve this goal, under our supervision there were 72 patients with moderate CGP and 14 healthy individuals. Of these, 24 patients with CGP without concomitant diseases; 48 patients with CGP in combination with metabolic syndrome (MS). Patients were on outpatient treatment at the clinic of the Tashkent State Dental Institute (TSDI). Patients with MS at the age of 40–65 years were mainly contingents suffering from metabolic disorders, in particular, insulin resistance syndrome, and were on outpatient observation. In 86.8% of patients, concomitant arterial hypertension and obesity were noted.

As an indicator of endothelial damage, the number of desquamated cells was determined by the method of J. Iadovec. The amount of VEGF was determined by the ELISA method using a set of the company "Vector-Best". All clinical and biochemical studies were carried out in the laboratory of the Scientific and Practical Center for Dentistry and Maxillofacial Surgery, TSDI. Statistical processing of the results was performed using the STATISTICA for Windows software package,

version 6.0. In the case of a normal distribution, Student's t-test was used. Differences were considered statistically significant at  $p < 0.05$ .

## RESULTS AND DISCUSSION

The average age and length of stay of patients in the region did not have significant differences. Evaluation of the state of carbohydrate metabolism began with the determination of the fasting blood glucose level. In the control group, the glucose level was within the normal range. At the first stage of the study, an oral load test was performed to determine the state of carbohydrate metabolism. At the same time, immunoreactive insulin was measured in the blood plasma. On the basis of these data, indices were calculated — the Homa homeostasis model — IR and the Caro fasting index IR. When analyzing the data obtained in the group of healthy individuals, we did not observe abnormalities. Changes in carbohydrate metabolism in groups of patients with CGP associated with MS (Table 1) indicated that it was impaired. The glucose level in these groups did not return to baseline. The insulin level after the load and the Homa-IR homeostasis model in relation to the control group were significantly higher.

**Table 1: The state of carbohydrate metabolism in the examined individuals.**

Group	Glucose		Insulin		Caro	Homa-IR
	Empty stomach	120 min	Empty stomach	120 min		
Healthy individuals with intact periodontal, n=12	4,1±0,46	5,39±0,61	15,37±7,81	24,75±16,73	0,35±0,12	2,95±1,6
Patients with CGP, n= 24	4,8±0,43	5,54±0,69	14,92±6,71	27,35±19,86	0,38±0,19	3,11±1,96
Patients with CGP combined MS, n=48	5,9±0,44	7,8±1,88	18,94±12,8	57,8±36,38*	0,36±0,27	4,58±3,94*

**Note:** \* Differences between control and compared groups are statistically significant ( $p < 0.05$ ).

Significant changes occurred in terms of lipid metabolism (Table 2). These shifts concerned mainly CGP patients combined with MS. Characterized by increased cholesterol (CS) and a change in the ratio of LDL cholesterol (low density lipids) to HDL cholesterol

(high density lipids) (CA), which is the most unfavorable prognostic factor for the formation of atherosclerotic changes in the vascular wall. Triglycerides also increased statistically significantly in the combined form of the disease.

**Table 2: Lipidogram of patients with CGP combined with MS.**

Surveyed groups	Cholesterol mmol/L	TG mmol/L	CS HDL mmol/L	CS LDL mmol/L	CA
Healthy individuals with intact periodontal, n =12	5,1±0,49	1,5±0,44	1,49±0,41	2,93±0,66	2,77±0,3
Patients with CGP, n= 24	5,6±0,67	1,33±0,42	1,55±0,45	3,4±0,58	2,6±0,4
Patients with CGP combined with MS, n=48	*6,29±0,93	1,75±0,65	1,18±0,34	3,81±0,69	4,29±0,3

**Note:** \* Differences between control and compared groups are statistically significant ( $p < 0.05$ ).

Endothelial dysfunction was assessed by the content of vascular endothelial growth factor and desquamated endothelial cells (Table 3). A slight increase in the number of desquamated cells in the control group is a

consequence of the renewal of the endothelial lining. Increased desquamation of the endothelium in patients with a combined form of the disease is associated with increased expression of cytokines in patients with MS on

the background of insulin resistance and leptin expression. The number of endothelial cells in this group was more than the control group 9.0 times, respectively ( $p < 0.05$ ).

As can be seen from the presented research results, an increase in VEGF occurs in the presence of concomitant

pathology. A number of authors find an explanation for this fact in stimulating the release of cytokines under the action of leptin. It has also been proven that the stimulation of VEGF secretion is a consequence of an increase in Hypoxia-inducible factor 1, whose production increases with hyperinsulinemia against the background of insulin resistance.<sup>[7]</sup>

**Table 3: Content of vascular endothelial growth factor and desquamated endothelial cells in patients with CGP associated MS.**

Surveyed groups	VEGF (pg/ml)	Count of endothelial cell ( $\times 10^4$ L)
Healthy individuals with intact periodontal, n=12	70,3 $\pm$ 11,2	2,0 $\pm$ 0,28
Patient with CGP, n= 24	131,5 $\pm$ 17,6*	9,3 $\pm$ 0,58*
Patient with CGP combined with MS, n=48	223,4 $\pm$ 29,2*	19,3 $\pm$ 1,48*

**Note:** \* Differences between control and compared groups are statistically significant ( $p < 0.05$ ).

## CONCLUSION

Thus, in patients with CGP associated MS, an increase in the level of desquamated endothelial blood cells is observed against the background of significant growth of VEGF, which is caused by dysfunction of the carbohydrate, lipid, and hormonal systems.

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