Galician medical journal 2017
Vol. 24, Issue 4, E2017412
DOI: 10.21802/gmj.2017.4.12

Research Article

Changes in the Levels of Pro-Inflammatory Cytokines in Patients with Generalized Periodontitis and Hypertension, Depending on the Method of Treatment

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Abstract
Inflammatory mediators have an important role in the pathogenesis of periodontal disease. One of the leading mediators of the initiation of the pathological process is interleukin-1 (IL-1) – an endogenous pyrogen, a lymphocyte-activating factor. Numerous pro-inflammatory effects of interleukin-1β (IL-1β) occur in synergy with tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), effects on hematopoiesis, participates in nonspecific anti-infective defense.
The objective of the study is to determine levels of interleukin-6 and tumor necrosis factor alpha (TNF-α) in patients with hypertension II stage and generalized periodontitis of the II degree depending on the treatment method.
There were examined 30 patients with hypertension of the II stage and with generalized periodontitis of the II degree. Patients' age ranged from 35 to 54 years. These patients were divided into two groups. The control group included 10 patients without general somatic pathology and with healthy periodontitis of the same age.
The result of the analysis of tumor necrosis factor alpha (TNF-α) in patients in the first group before the treatment was 10.69$\pm$2.33 pg/ml. After the treatment this indicator was 6.97$\pm$1.57 pg/ml ($p>0.1$) in patients of the first group.
In patients of the second group the tumor necrosis factor alpha (TNF-α) was 9.49$\pm$2.2 pg/ml; after the treatment according to the offered scheme this figure decreased up to 2.77$\pm$0.9 pg/ml ($p<0.01$). The level of tumor necrosis factor alpha (TNF-α) in the control group was 1.5$\pm$0.77 pg/ml.
Interleukin-6 was 9.91$\pm$2.04 pg/ml before the treatment in the first group. After the treatment according to the standard scheme, the level of interleukin-6 was 6.33$\pm$0.97 pg/ml ($p>0.1$). In the second group, before the treatment the level of interleukin-6 was 9.65$\pm$2.41 pg/ml; after the treatment according to the offered scheme it was 2.62$\pm$0.5 pg/ml ($p<0.01$). In the control group the interleukin-6 level was 2.24$\pm$0.51 pg/ml.
Analyzing the obtained results after the treatment in both groups we can conclude: after the treatment of generalized periodontitis of the II degree in patients with hypertension of the II stage, indices of pro-inflammatory cytokines decreased and ranged in normal limits; in patients from the second group (who received the offered scheme of treatment -including medicines) indexes of pro-inflammatory cytokines were significantly lower than in patients with the standard treatment scheme; the proposed scheme of treatment is more effective for treatment patients with generalized periodontitis of the II degree and hypertension of the II stage.

Keywords
generalized periodontitis; tumor necrosis factor alpha; interleukin-6

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Problem statement and analysis of the recent research

Inflammatory mediators play an important role in the pathogenesis of periodontal disease. One of the leading mediators of the initiation of the pathological process is interleukin-1 (IL-1) – an endogenous pyrogen, a lymphocyte-activating factor that has 2 forms: interleukin-1α (IL-1α) and interleukin-1β (IL-1β) encoded by different genes [1, 11]. Interleukin-1 (IL-1) is produced by activated macrophages, epithelial cells (lymphocytes, fibroblasts, macrophages), endothelial cells, glial cells, fibroblasts, keratinocytes [2, 3, 6, 8]. Cells of the body cannot spontaneously synthesize interleukin-1 (IL-1), but correspond to its production during the infection, the action of microbial toxins, inflammatory agents, other cytokines, activated components of the complement or blood coagulation system. The value of interleukin-1 (IL-1) in the inflammatory response is extremely important. Interleukin-1 (IL-1) stimulates the production of adhesive molecules by endothelial cells that promote the attachment of polymorphonuclear granulocytes and monocytes, as well as the mobilization of these cells in the inflammatory site. Interleukin-1 (IL-1) induces

synthesis of collagenase in fibroblasts. Interleukin-1 (IL-1) stimulates bone resorption and delays the formation of collagen and bone [12]. The level of interleukin-1 (IL-1) increases significantly during the progression of chronic generalized periodontitis in saliva and gum fluid [13].

Interleukin-1β (IL-1β) is a strong cytokine that causes bone resorption and is a mediator in the destruction of soft tissue by stimulating the production of prostaglandins, induction of collagenase, and other proteases. This cytokine has the ability to activate the synthesis of other cytokines: interleukin-2 (IL-2), interleukin-3 (IL-3), interleukin-5 (IL-5), interleukin-6 (IL-6), interleukin-7 (IL -7), interleukin-8 (IL-8), tumor necrosis factor alpha (TNF-α).

Numerous pro-inflammatory effects of interleukin-1β (IL-1β) occur in synergy with tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), effects on hematopoiesis, participates in nonspecific anti-infective defense [3, 8].

Interleukin-6 (IL-6) is a multifunctional cytokine produced by macrophages, T- and B-lymphocytes, fibroblasts, endothelial, epidermis and microglial cells, chondrocytes, and osteocytes. Interleukin-6 (IL-6) stimulates the formation of B-cells, labrocytes, produces both lymphoid and non-lymphoid cells, regulates acute-phase inflammatory response and hematopoiesis [5, 8]. Interleukin-6 (IL-6) takes part in activation of T-lymphocytes, regulates the synthesis of proteins, which appear during acute phase of inflammation (fibrinogen, α-antichymotrypsin, acid glycoprotein, haptoglobin, C-reactive protein) [7, 8, 9, 10].

Degranulation of cytokines and immunoglobulins in periodontal tissues lead to destructive changes. Increased levels of interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) provoke processes and biochemical reactions that destroy periodontal tissues. Interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF-α) activate osteoclasts, interleukin-1 (IL-1) provokes synthesis of collagenase, interleukin-6 (IL-6) activates differentiation of B cells into plasma cells and the development of Ig G, which promotes the fixation of the complement. Increased production of interleukin-6 (IL-6) and interleukin-8 (IL-8) play an important role in the pathogenesis of inflammation and resorption of bone tissues [4]; chronic suppression of the production of interleukin-2 (IL-2) lead to the development of autoimmune disorders.

The objective of the study. The objective of the study is to determine levels of interleukin-6 and tumor necrosis factor alpha (TNF-α) in patients with hypertension of the II stage and generalized periodontitis of the II degree depending on the treatment method.

1. Materials and methods

There were examined 30 patients with hypertension of the II stage and with generalized periodontitis of the II degree. Patients' age ranged from 35 to 54 years. These patients were divided into two groups.

The first group received treatment according to the following scheme: irrigation of the oral cavity with solutions of antiseptic agents (0.1% solution of chlorhexidine digluconate), removal of soft plaque, ultrasonic removal of calculus, use of "Metrogyl-denta" gel. The second group received the same treatment as the first group, but with the inclusion of the following medicines (offered scheme): "Ca-D3 NICOMED" – 2 tablets per day (morning and evening, during 12 months); Electrophoresis "Calcium Gluconate" for 10 sessions; "Pentoxifylline" – 1 tablet 3 times a day (during 30 days. The medicine is prescribed as a course one time for three months – 4 courses per year).

The control group included 10 patients of the same age without general somatic pathology and with healthy periodontitis. The diagnosis of periodontal diseases was made according to the anamnesis, clinical dental examination and generally accepted additional methods of examination; and it was classified according to M.F. Danylevsky (1994).

The obtained results were subjected to the variation-statistical processing using statistical package "StatSoft 6.0", classical methods of variation statistics using averages and assessment of their authenticity.

2. Results of the research and their discussion

The result of the analysis of tumor necrosis factor alpha (TNF-α) in patients of the first group before treatment was 10.69 ± 2.33 pg/ml. After the treatment this indicator was 6.97 ± 1.57 pg/ml ($p>0.1$) in patients of the first group.

In patients of the second group the tumor necrosis factor alpha (TNF-α) was 9.49 ± 2.2 pg/ml; after the treatment according to the offered scheme this figure decreased up to 2.77 ± 0.9 pg/ml ($p<0.01$).

The level of tumor necrosis factor alpha (TNF-α) in the control group was 1.5 ± 0.77 pg/ml.

After the performed treatment the tumor necrosis factor (TNF-α) decreased and ranged in the normal level in both groups. The second group (where the improved scheme of the treatment was used) the level of tumor necrosis factor (TNF-α) was significantly lower than in the first group (standard treatment).

Interleukin-6 before the treatment in the first group was 9.91 ± 2.04 pg/ml. After the treatment according to the standard scheme, the level of interleukin-6 was 6.33 ± 0.97 pg/ml ($p>0.1$). In the second group, before the treatment the level of interleukin-6 was 9.65 ± 2.41 pg/ml; after the treatment according to the offered scheme – 2.62 ± 0.5 pg/ml ($p<0.01$).

In the control group the interleukin-6 level was 2.24 ± 0.51 pg/ml.

Levels of pro-inflammatory cytokine interleukin-6 after the treatment in both groups also returned to the normal levels; the second group (with the offered scheme of treatment) level of interleukin-6 was lower than in the first group (the standard treatment) (table 1).

In the control group both indices were in the normal range.

Table 1. Indeces of pro-inflammatory cytokines before and after the treatment

	Group 1		Group 2		Control group
	Before treatment	After treatment	Before treatment	After treatment	
TNF-α	10.69±2.33 pg/ml	6.97±1.57 pg/ml	9.49±2.2 pg/ml	2.77±0.9 pg/ml	1.5±0.77 pg/ml
IL-6	9.91±2.04 pg/ml	6.33±0.97 pg/ml	9.65±2.41 pg/ml	2.62±0.5 pg/ml	2.24±0.51 pg/ml

Notes: In the Group 1 the reliability of the results of TNF-α (the factor of tumor necrosis alpha) before and after the treatment was $p>0.1$; in the Group 2 the reliability of the results of TNF-α before and after the treatment was $p<0.01$; in the Group 1 the reliability of the results of IL-6 (interleukin-6) before and after the treatment was $p>0.1$; in the Group 2, the reliability of the results of IL-6 before and after treatment was $p<0.01$.

3. Conclusions

Analyzing the results after the treatment in both groups we can conclude:

1. After the treatment of generalized periodontitis of the II degree in patients with hypertension of the II stage the indeces of pro-inflammatory cytokines decreased and ranged in normal limits.

2. In patients of the second group (who received the offered by us scheme of treatment – including medicines) these indexes of pro-inflammatory cytokines were significantly lower than in patients with the standard treatment scheme.

3. The offered scheme of treatment is more effective for treatment of patients with generalized periodontitis of the II degree and hypertension of the II stage.

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Received: 27 Nov 2017

Revised: 26 Dec 2017

Accepted: 26 Dec 2017