

The saliva levels of interleukin – 1 receptor antagonist (IL-1 Ra) and soluble receptor type I of tumor necrosis factor (sTNF RI) in chronic periodontitis

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STĘŻENIE W ŚLINIE ANTAGONISTY RECEPTORA INTERLEUKINY 1 (IL-1 Ra)
I ROZPUSZCZALNEGO RECEPTORA CZYNNIKA MARTWICY NOWOTWORU (sTNF RI)
W PRZEWLEKŁYM ZAPALENIU PRZYŻĘBIA

Streszczenie

Wprowadzenie: Zapalenie przyzębia powoduje reakcję immunologiczną gospodarza na antygeny bakteryjne. W tej odpowiedzi istotną rolę pełnią cytokiny i ich receptory.

Cel pracy: Celem prezentowanej pracy była ocena występowania w ślinie antagonisty receptora interleukiny 1 (IL-1 Ra) i rozpuszczalnego receptora czynnika martwicy nowotworu (s TNF RI) u osób z przewlekłym zapaleniem przyzębia.

Metody: Stężenie w ślinie antagonisty receptora interleukiny 1 (IL-1 Ra) i rozpuszczalnego receptora czynnika martwicy nowotworu (s TNF RI, p55) oceniono za pomocą immunoenzymatycznej metody ELISA, przy użyciu fabrycznie gotowych testów (Quantikine, R&D System).

Wyniki: Stężenie w ślinie antagonisty receptora interleukiny 1 (IL-1 Ra) było statystycznie istotnie wyższe ($p < 0,05$) u osób z przewlekłym zapaleniem przyzębia w porównaniu z grupą kontrolną.

Wniosek: Należy rozważyć ocenę stężenia w ślinie antagonisty receptora interleukiny 1 (IL-1 Ra) w diagnostyce przewlekłego zapalenia przyzębia.

Słowa kluczowe: przewlekłe zapalenie przyzębia, antagonisty receptora interleukiny-1 (IL-1 Ra), rozpuszczalny receptor czynnika martwicy nowotworu (sTNF RI)

INTRODUCTION

The key role in the destruction of periodontal tissues play interleukin-1 β and TNF- α . It is known that the interleukin-1 level in the blood serum and gingival fluid correlates with the clinical parameters of periodontal status (1, 2). It has been proved that some bacteria, such as *Porphyromonas gingivalis* and *Actinobacter* (*Actinobacillus*) *actinomycetemcomitans* have the ability to stimulate monocytes and macrophages to produce interleukin-1 (IL-1) and TNF – tumor necrosis factor (3, 4, 5). These cytokines induce the activity of osteoclasts, causing bone resorption. There are numer-

ous macrophages in the periodontal tissues producing considerable amounts of IL-1, which favors inflammatory processes in periodontium, destroys periodontal connective tissue and bones (6, 7). It is believed that both the IL-1 receptor antagonist and soluble s TNF RI receptor are physiological protections against the potential overproduction of IL-1 and TNF and against undesirable effects of excessive activity of these cytokines (8, 9). We still do not know everything about immune and inflammatory response to infections in the course of periodontitis. Periodontitis is a disease always accompanied by a bacterial infection. IL-1 ra and s TNF RI are one of the most important anti-inflammatory mediators.

The increase in the levels of these cytokines in systemic fluids statistically correlates with the disease activity (10, 11). The results of latest research on the significance of the above listed cytokines in periodontitis are not univocal and we still need more data concerning this subject. The aim of the presented paper was to examine the occurrence in saliva interleukin – 1 receptor antagonist (IL-1 Ra) and soluble receptor type I of tumor necrosis factor (sTNF RI) in patients with chronic periodontitis.

MATERIALS AND METHODS

The tests were performed in the group of 75 persons, aged 20-45, including 42 females and 33 males. The test group consisted of 45 persons suffering from chronic periodontitis, aged 20-45 (25 females, 20 males). The control group consisted of 30 persons with clinically healthy periodontium, aged 23-45 (17 females, 13 males). The samples of mixed non-stimulated saliva were taken 2 hours after breakfast, then refrigerated and stored at -70°C . After defreezing, all samples were centrifuged 1000xg for 20 minutes. The levels of interleukin-1 receptor antagonist and soluble TNF receptor type I (s TNF RI, p55) in saliva were determined with an immunoenzymatic ELISA method using a factory-ready quantitative enzymatic test manufactured by Quantikine, R&D System Europe Ltd., Abingdon, Oxon, United Kingdom, according to the manufacturer's recommendations. The concentration of investigated cytokines were given in pg/ml. The minimum cytokine level that can be detected with these tests amounts to: 22 pg/ml for IL-1 Ra and 3 pg/ml for s TNF RI. Before performing the tests, response specificity was checked. To achieve this, antibodies anti-IL-1 Ra (AF-280-NA) and anti-s TNF RI (AF225) made by R&D Company in concentrations recommended by the manufacturer were added to selected samples. The incubation was carried out at room temperature for 1 h. After this period the concentrations of IL-1 Ra and s TNF RI in the samples with antibodies and without were checked, with the above mentioned enzymatic tests manufactured by R&D Company.

Data were analysed by using Mann-Whitney statistical test. A P-value < 0.05 was considered significant.

RESULTS

Mean concentration values in saliva for interleukin-1 receptor antagonist (IL-1 Ra) and soluble TNF receptor type I (s TNF RI) in persons suffering from chronic periodontitis and in control group are presented in table 1. The level of occurrence for interleukin-1 receptor antagonist (IL-1 Ra) in saliva was statistically significantly higher ($p < 0.05$) in persons with periodontitis and amounted to 28015.15 ± 4921.83 pg/ml as compared with the values for the control group – 21962.48 ± 7159.39 pg/ml. The levels of soluble TNF receptor type I (s TNF RI) in saliva in persons suffering from periodontitis (701.97 ± 511.31) and in the control group (738.29 ± 399.98) did not differ statistically significantly and their values were similar (tab. 1).

Table 1. Mean concentration values in saliva for IL-1 Ra and sTNF RI in persons with chronic periodontitis and in control group.

	Chronic periodontitis	Healthy periodontium
IL-1 Ra (pg/ml)	28015.15 (SD = 4921.83)*	21962.48 (SD = 7159.39)*
sTNF RI (pg/ml)	701.97 (SD = 511.31)	738.29 (SD = 399.98)

* $p < 0.05$

DISCUSSION

The concentration of IL-1 Ra is always higher in the site of inflammation than in peripheral vessels. Kabashima et al. maintain that the presence of IL-1 Ra in gingival fluid confirms an inflammatory process in progress because in their investigations they have not proved the occurrence of IL-1 Ra in the gingival fluid taken both from the persons with clinically healthy periodontium and from the non-inflammatory sites in persons with periodontitis (12). Very low concentration of IL-1 Ra in gingival fluid of persons suffering from advanced periodontitis presented in some papers is probably associated with the fact of hydrolyzing the IL-1 particles by bacteria of a species: *P. gingivalis*. It should be also added that *A. actinomycetemcomitans* bacteria do not have this feature. Thus, it can be assumed that the composition of bacterial flora has a significant and regulating influence on the concentration values in systemic fluids, including gingival fluid and saliva. The elevated concentration of IL-1 Ra in gingival fluid in persons with chronic periodontitis has been noted many times (13). In our own investigations statistically significant ($p < 0.05$) higher concentration values of IL-1 Ra in saliva in patients with periodontitis were noted as compared with the control group. In persons suffering from periodontitis the increase of anti-inflammatory cytokines in gingival fluid is often found. In the case of periodontitis evoked by bacteria of species: *P. gingivalis* and/or *A. actinomycetemcomitans*, antigens coming from these microorganisms induce the production and secretion of both IL-1 Ra, and s TNF RI by the peripheral blood lymphocytes. The role of TNF and its receptors in the etiology of periodontitis is still discussed but there is no univocal opinion about this (14, 15). Our own tests of soluble TNF receptor concentration in saliva have not confirmed the correlation between the occurrence of elevated concentration of the receptor in systemic fluids and the development of periodontitis. In both examined groups i.e. in patients suffering from periodontitis and in control group similar concentration values of soluble TNF receptor in saliva were found.

Any damage to periodontal tissues causes significant changes in the production of pro- and anti-inflammatory cytokines. The balance existing in physiological conditions between pro- and anti-inflammatory immune responses may be disturbed considerably in the course

of periodontitis. The study demonstrated and showed a statistically significant increase of concentration of IL-1 receptor antagonist (IL-1 Ra) in persons suffering from chronic periodontitis as compared with persons with clinically healthy periodontium.

CONCLUSION

We must consider the possibility of some disturbances in course of chronic periodontitis and should remember about it in therapy of this diseases. □

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