

Wiadomości Lekarskie Medical Advances



VOLUME LXXVI, ISSUE 9, SEPTEMBER 2023

Official journal of Polish Medical Association has been published since 1928

ISSN 0043-5147
E-ISSN 2719-342X



INDEXED IN PUBMED/MEDLINE, SCOPUS, EMBASE, EBSCO, INDEX COPERNICUS,
POLISH MINISTRY OF EDUCATION AND SCIENCE, POLISH MEDICAL BIBLIOGRAPHY

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fajne.work

Publisher:

ALUNA Publishing

ul. Przesmyckiego 29,

05-510 Konstancin – Jeziorna

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DIFFERENTIAL DRUG CORRECTION CYTOKINE AND PROSTAGLANDIN CONTENT IN BLOOD AND GINGIVAL FLUID IN GENERALIZED PERIODONTITIS AGAINST THE BACKGROUND OF DIFFERENT RESPONSIVENESS OF THE ORGANIZATION

DOI: 10.36740/WLek202309121

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ABSTRACT

The aim is to study the dynamics of prostaglandins and cytokines in the blood and gingival fluid against the background of differential drug correction in patients with generalized periodontitis with different body reactivity.

Materials and methods: 216 people aged 45 between 55 years with a diagnosis of generalized periodontitis of II, III degree of severity, chronic course were examined. Depending on the state of reactivity of the organism, the patients were divided into three groups: the first one consisted of people with normoreaction; the second group included patients with hyperreaction; the third group was made up of people with hyporeaction. The patients underwent patch surgery after the initial therapy. Initially, on the 1st, 2nd, 4th, 6th and 9th day after the operation, the content of prostaglandins (PG) E, E₂, F₂alpha and cytokines (IL-1 β , IL-6, TNF, IL-4) in the blood and gingival fluid was performed. Patients with impaired body reactivity were treated with the proposed differential drug correction of cytokines and prostaglandins. Statistical processing of the obtained digital data was performed using the computer program Statistica 8.0.

Results: The proposed differential drug correction in patients with generalized periodontitis against the background of hyper- and hyporeactivity of the body brings the content of IL-1 β , IL-6, TNF, IL-4 to that of normal body reactivity, which ultimately restores the disturbed balance of pro- and anti-inflammatory cytokines in the blood and gingival fluid. On the 9th day, the content of all proinflammatory cytokines in the main groups was normalized and was commensurate with that of the body's normal response ($p > 0.05$). Differential drug correction led to normalization of the prostaglandin balance index on day 9 after flap surgery ($p > 0.05$), indicating the establishment of a normal balance of eicosanoids in the blood and approximating the values of pro- and anti-inflammatory fractions of prostaglandins to those of normal body reactivity.

Conclusion: Correction of altered parameters in patients with generalized periodontitis accompanied by impaired (hyper- and hypo-) reactivity of the body with bringing them to values that are typical for normoreactivity is considered to be a condition for optimizing mucosal wound healing after surgery and further stabilization of periodontal tissues.

KEY WORDS: periodontitis, reactivity of the organism, drug treatment, cytokines and prostaglandins

Wiad Lek. 2023;76(9):2047-2053

INTRODUCTION

General and local drug treatment of generalized periodontitis has an etiologic, pathogenetic and symptomatic focus [1-3]. Pathogenetic drug correction is aimed at relieving the leading links in the development of the disease [4, 5]. The prescription of nonsteroidal anti-inflammatory drugs (NSAIDs) (mainly selective COX-2 inhibitors to reduce prostaglandin E₂ levels) is justified. There is experience in the use of 3% acetylsalicylic ointment, 3% orthophene ointment, 1% Voltaren emulsion (Switzerland) as part of periodontal dressings, diclofenac sodium medicated paste, flubiprofen gel, mouthwash with 0.1% ketorolac solution

and 1.5% dexibuprofen solution, toothpaste containing 1% and 3% ketoprofen. Selective COX-2 inhibitors have been used in the complex treatment of generalized periodontitis. These are drugs such as etoricoxib, rofecoxib, celecoxib, meloxicam, nimesulide, etodolac, etc. [6]. Schemes of local (immobilization on the sorbent «Enterogel») and general use of a selective COX-2 inhibitor - meloxicam (Melbek, Turkey, have been proposed [7]. Immunocorrective therapy is used, which stimulates immune processes, specifically activates immunocompetent cells (T and B lymphocytes) and additional immune factors (macrophages, secretory immunoglobulins, cytokines, etc.) [8]. High therapeutic

efficacy of immunomodulators has been shown. A special place among immunomodulatory drugs is occupied by phytoadaptogens. Clinical and immunological studies have revealed a pronounced immunomodulatory effect of biotritol-based adaptogen on the parameters of both local and systemic immunity in patients with generalized periodontitis [9]. Cytokine therapy is used, which includes the administration of drugs of specific cytokines or drugs of cytokine antagonists of IL-1, TNF, interferon drugs (laferon, immuneron), interferon inducers (amizon, amixin) [10-13]. Thus, modern approaches to the medical treatment of patients with generalized periodontitis are based on the relief of the leading links in the etiopathogenesis of the disease. The correct orientation of this tactic is confirmed by numerous literature data on the high clinical efficacy of the proposed and implemented drug treatment regimens for generalized periodontitis. However, the issues of clarification of the key mechanisms of development and course of the disease in each specific clinical case and the development of differentiated approaches to the choice of a complex of medications for general and local use, depending on exo- and endoparodontic pathogenic factors that most affect the pathogenesis of generalized periodontitis, remain relevant.

THE AIM

The aim of this study was to investigate the dynamics of prostaglandins and cytokines in blood and gingival fluid against the background of differential drug correction in patients with generalized periodontitis with different body reactivity.

MATERIALS AND METHODS

216 patients (82 men and 134 women), aged 45 between 55 years, with the diagnosis of generalized periodontitis of II, III degree of severity, chronic course were examined. The diagnosis was made on the basis of clinical examination, radiography, determination of periodontal samples in accordance with the International Classification of Diseases ICD-10. Depending on the state of reactivity of the body, the patients were divided into three groups: the first one included patients with normoreaction (132 people, 61%); the second group consisted of patients with hyperreaction (46 people, 21%); the third one contained patients with hyporeaction (38 people, 18%). The division of patients into groups depending on the state of reactivity of the organism was performed on the basis of the identified clinical and laboratory differences. All the patients underwent comprehensive treatment of generalized periodontitis in the amount recommended by the Ministry of Health of Ukraine - Order №566 of 23.11.04.

"On approval of the Protocols for the Provision of Medical Care". All the patients with generalized periodontitis of II, III degrees of severity after completion of the complex of initial therapy, according to the indications, underwent patch surgery. Immediately after the surgical intervention, differential medication support was started for patients of the main groups with hyper- (2A) and hypoergic (3A) types of inflammation. Patients with normoergic type of inflammation (comparison group and control groups 2B and 3B) were not additionally offered drug therapy. Since in case of hyperreactivity of the body there is an increased content of proinflammatory prostaglandins E, E2, it is advisable to use an appropriate complex of pathogenetically adequate medications to normalize these parameters. The increased content of proinflammatory prostaglandins determines the validity of the use of nonsteroidal anti-inflammatory drugs (NSAIDs) with the active ingredient nimisulide (UA/9855/01/01 of 17.07.2019; Order 1625(2) of 17.07.2019). The universal mechanism of action of NSAIDs is considered to be the blockade of COX (prostaglandin endoperoxide synthetase) synthesis, a key bifunctional enzyme involved in the regulation of prostaglandin synthesis. The drug containing nimisulide was administered orally in 1 sachet (the sachet contains granules for the preparation of a suspension) 2 times a day (200 mg per day) for 5-7 days. Significant activation of cytokines in case of hyperreaction and reduced levels in case of hyporeaction determine the expediency of using immunocorrective drugs. We opted for the high molecular weight chemically pure immunomodulator Liasten with the active ingredient glucosaminylmuramylpentapeptide (UA/14212/01/01 of 13.05.2020; Order 1128(2) of 13.05.2020). The drug stimulates the production of proinflammatory cytokines only at their initially low levels, and reduces them at initially elevated levels. We used the tablet form of the drug (2 mg) immobilized on a sorbent as a periodontal dressing.

The content of prostaglandins (PG) E, E2, F2alpha and cytokines (IL-1 β , IL-6, TNF, IL-4) was determined in the blood serum. The corresponding cytokines were determined in the gingival fluid. In the morning, blood and gingival fluid were collected on an empty stomach. Venous blood was taken from the ulnar vein (5 ml). Gingival fluid was collected with standard paper pins (#25) by immersing them without force into the gingival sulcus or periodontal pockets for 30 seconds in the upper canines. The state of cytokine regulation was determined by enzyme-linked immunosorbent assay (ELISA) using commercial reagent kits ProCon IL-1 β , ProCon IL-6, ProCon TNF, ProCon IL-4. The optical density at a given wavelength was measured using a spectrophotometer. The radioimmune method was used to determine GH. The dynamics of the studied laboratory parameters was evaluated on the 1st, 2nd, 4th, 6th and 9th days after surgical treatment.

Statistical processing of the obtained digital data was performed using the computer program Statistica 8.0 (STA862D175437Q).

RESULTS

The results of determining the cytokines IL-1 β , IL-6, TNF α , IL-4 in the blood of patients with generalized periodontitis against the background of normal, hyper- and hyporeactivity of the body after surgery are presented in the table (Table I).

As can be seen from this table, in patients with generalized periodontitis of the main groups, the dynamics of the content of these cytokines against the background of the proposed drug support was unidirectional in the direction of increasing their concentration. This dynamics of indicators is similar to that of normal body reactivity. On the 1st day after surgery in groups 2A and 3A, the greatest

increase in proinflammatory cytokines was noted ($p < 0.05$). The content of these cytokines significantly exceeded the control values on the 2nd day, but to a lesser extent compared to the 1st day. On days 4 and 6, a decrease in the content of all proinflammatory cytokines in the blood serum was recorded. On the 9th day, the content of all proinflammatory cytokines in the main groups was normalized and was commensurate with that in patients with AP with normal body reactivity.

The dynamics of the anti-inflammatory cytokine IL-4 in the blood of patients of groups 2A and 3A differed from that of IL-1 β , IL-6, and TNF α . The content of IL-4, gradually increasing from the 1st day of observation, reached a peak on the 6th day (the content, respectively, was 1.8 and 1.7 times higher compared to the baseline, $p < 0.05$). It should be noted that during this observation period, the values of the indicator differed significantly from those in the control and were, respectively, 2.1

Table I. Cytokine content of IL-1 β , IL-6, TNF α , IL-4, IRC in the blood of patients with generalized periodontitis in normal, hyper- and hyporeactivity after surgical treatment ($M \pm SE$)

Indicators.	Terms. observation	Patient groups		
		norm-reaction (n = 132)	overreaction (n = 23)	Hyporesponse (n = 19)
IL-1 β , pkg/mL	initially	73,6 \pm 16,4	74,2 \pm 28,0	71,8 \pm 28,8
	1st day	142,1 \pm 20,8 *	165,0 \pm 32,1 *	115,8 \pm 30,0
	2nd day	130,6 \pm 18,2 *	148,2 \pm 26,0 *	110,0 \pm 30,5
	4th day	125,9 \pm 18,0 *	134,4 \pm 25,8	106,9 \pm 28,5
	6th day	94,5 \pm 17,2	103,5 \pm 25,4	96,6 \pm 25,4
	9th day	74,2 \pm 16,0	88,8 \pm 24,4	77,8 \pm 25,0
IL-6, pkg/mL	initially	86,1 \pm 14,4	87,0 \pm 32,4	85,2 \pm 33,5
	1st day	126,4 \pm 18,0 *	130,9 \pm 34,9	119,7 \pm 35,0
	2nd day	115,2 \pm 17,6 *	123,6 \pm 32,6	117,0 \pm 34,3
	4th day	104,1 \pm 16,8	112,8 \pm 30,0	105,8 \pm 36,0
	6th day	96,5 \pm 15,0	108,2 \pm 30,2	97,1 \pm 34,8
	9th day	84,9 \pm 14,2	99,0 \pm 29,7	85,0 \pm 30,2
FNPa, pkg/mL	initially	75,9 \pm 12,8	76,2 \pm 34,4	74,5 \pm 35,7
	1st day	111,8 \pm 17,4 *	136,1 \pm 34,4	128,0 \pm 34,2
	2nd day	106,4 \pm 16,7 *	130,4 \pm 34,0	108,6 \pm 34,0
	4th day	104,8 \pm 16,5	122,1 \pm 30,4	118,2 \pm 30,3
	6th day	82,6 \pm 13,4	97,0 \pm 28,2	86,9 \pm 28,9
	9th day	77,1 \pm 12,6	82,9 \pm 28,0	79,8 \pm 28,5
IL-4, pkg/ml	initially	42,1 \pm 8,4	43,8 \pm 15,8	41,6 \pm 18,8
	1st day	50,6 \pm 8,8	62,8 \pm 22,0	56,7 \pm 18,8
	2nd day	54,4 \pm 9,2	58,8 \pm 16,9	55,1 \pm 18,0
	4th day	68,9 \pm 9,7 *	69,5 \pm 17,8	64,5 \pm 19,4
	6th day	74,5 \pm 10,0 *	77,5 \pm 16,5 *	70,6 \pm 19,1 "
	9th day	48,2 \pm 8,0	53,2 \pm 15,6	54,0 \pm 16,0
CPI	initially	1,06 \pm 0,04	1,08 \pm 0,13	1,09 \pm 0,15
	1st day	2,34 \pm 0,07 *	2,38 \pm 0,20 *	2,37 \pm 0,19 *
	2nd day	2,01 \pm 0,07 *	2,14 \pm 0,26 *	2,02 \pm 0,17 *
	4th day	1,68 \pm 0,06 *	1,69 \pm 0,19 *	1,73 \pm 0,16 *
	6th day	1,22 \pm 0,05 *	1,38 \pm 0,18	1,28 \pm 0,15
	9th day	1,16 \pm 0,05	1,24 \pm 0,16	1,23 \pm 0,15

Note: * - $p < 0.05$ vs. initial values

"- $p < 0.05$ vs. values at normal body reactivity

Table II. The content of cytokines IL-1 β , IL-6, TNF α , IL-4 in the gingival fluid of patients with generalized periodontitis in normal, hyper- and hyporeactivity after surgical treatment (M \pm SE)

Indicators.	Terms. observation	Patient groups		
		norm-reaction (n = 132)	overreaction (n = 23)	Hyporeponse (n = 19)
IL-1 β , pkg/mL	initially	27,3 \pm 1,4	28,2 \pm 2,4	26,9 \pm 2,4
	1st day	68,1 \pm 2,8 *	76,8 \pm 4,4 *	62,0 \pm 4,6 *
	2nd day	59,0 \pm 1,8 *	62,0 \pm 4,2 *	58,2 \pm 4,1 *
	Day 4	52,9 \pm 1,9 *	54,4 \pm 3,8 *	49,8 \pm 3,8 *
	6th day	34,5 \pm 1,5 *	38,5 \pm 2,9 *	32,7 \pm 2,8 *
	9th day	28,2 \pm 1,4	26,8 \pm 2,7	25,9 \pm 2,70
IL-6, pkg/mL	initially	123,6 \pm 5,4	124,2 \pm 9,7	122,8 \pm 9,6
	1st day	264,4 \pm 8,0 *	271,2 \pm 10,2 *	244,8 \pm 11,0 *
	2nd day	189,5 \pm 7,3 *	194,5 \pm 9,8 *	168,5 \pm 10,8 *
	Day 4	134,1 \pm 6,1	139,6 \pm 8,8	131,2 \pm 9,8
	6th day	128,6 \pm 5,0	132,0 \pm 8,5	123,8 \pm 9,6
	9th day	124,9 \pm 4,8	126,4 \pm 8,4	122,4 \pm 8,6
FNPa, pkg/mL	initially	45,4 \pm 4,8	46,1 \pm 9,0	44,8 \pm 8,8
	1st day	116,2 \pm 7,1 *	126,7 \pm 10,5 *	108,8 \pm 10,0 *
	2nd day	101,0 \pm 6,7 *	107,9 \pm 9,2 *	96,5 \pm 9,2 *
	Day 4	85,9 \pm 5,1 *	92,0 \pm 9,0 *	81,9 \pm 9,0 *
	6th day	62,7 \pm 4,4	56,8 \pm 8,9	56,9 \pm 8,7
	9th day	47,3 \pm 4,2	49,4 \pm 8,5	45,8 \pm 8,5
IL-4, pkg/mL	initially	16,9 \pm 2,4	17,2 \pm 5,1	16,7 \pm 5,3
	1st day	21,8 \pm 2,8	27,7 \pm 6,1	20,2 \pm 6,2
	2nd day	24,9 \pm 2,2	26,8 \pm 6,0	22,8 \pm 6,9
	Day 4	48,1 \pm 3,7 *	52,2 \pm 6,4 *	44,7 \pm 8,2 *
	6th day	54,5 \pm 3,8 *	57,8 \pm 6,2 *	52,8 \pm 6,1 *
	9th day	18,1 \pm 2,2	19,6 \pm 5,6	17,6 \pm 5,8

Note: * - $p < 0.05$ vs. initial values

" - $p < 0.05$ vs. values at normal body reactivity

and 2.3 times lower ($p < 0.05$). On day 9, the value of IL-4 in the main groups remained higher than the initial value and became commensurate with that in the comparison group. As can be seen from this table, the dynamics of the cytokine balance index in the main groups coincided with that of the normoreactivity of the body and was monophasic with a peak on the 1st day. The increase in the balance index on the 1st day after surgery against the background of the proposed medical support testifies in favor of a shift in balance towards the predominant activation of proinflammatory cytokines. Starting from day 2, in groups 2A and 3A, as well as in the comparison group, the equilibrium began to level off - the index decreased with a minimum value by the end of the observation. At the same time, the IRC was, respectively, 1.24 ± 0.16 and 1.23 ± 0.15 , which did not differ significantly from the initial values and those of the normal body reactivity ($p > 0.05$). Thus, the proposed targeted drug correction in patients with generalized periodontitis against the background of hyper- and hyporeactivity of the body approximates the values of cytokines to those of normal body reactivity, which ultimately restores the disturbed balance of pro- and anti-inflammatory cytokines in the blood.

The results of determining cytokines (IL-1 β , IL-6, TNF α , IL-4) in the gingival fluid of patients with generalized periodontitis in normal, hyper- and hyporeactivity after surgery are presented in the table (Table II).

As can be seen from this table, the dynamics of the content of these cytokines in the gingival fluid of patients with generalized periodontitis of the main groups was similar to that in the blood serum and was characterized by their increase with maximum values of proinflammatory cytokines on day 1, anti-inflammatory cytokines - on day 6 and subsequent normalization of indicators by the end of the observation. The differences concerned the amplitude of changes in these parameters: in the gingival fluid, the changes were significantly more pronounced compared to those in the blood at all follow-up periods ($p < 0.05$). On the 1st day after surgery, the greatest increase in proinflammatory cytokines was noted in groups 2A and 3A ($p < 0.05$). The content of these cytokines significantly exceeded the control values on day 2, but to a lesser extent compared to day 1. On days 4 and 6, a decrease in the content of IL-1 β , IL-6, and TNF α in the gingival fluid was recorded. On the 9th day, the content of all proinflammatory cytokines in the main groups was normalized and was commensurate with that in patients with HP with normal body reactivity.

Table III. The content of prostaglandins F2 α and E2, the ratio of PG F2 α / PG E2, the value of the prostaglandin balance index (PBI) in the blood of patients with generalized periodontitis in normal, hyper and hyporeactivity of the body after surgical treatment (M \pm SE)

Indicators.	Terms. observation	Patient groups		
		Normoreaction (n = 132)	overreaction (n = 23)	Hyporesponse (n = 19)
GHG F2 α , ng/ml	Initially	0,534 \pm 0,051	0,553 \pm 0,153	0,509 \pm 0,149
	1st day	0,986 \pm 0,062 *	1,101 \pm 0,160 *	0,912 \pm 0,157 *
	2nd day	1,062 \pm 0,063 *	1,079 \pm 0,168 *	1,039 \pm 0,159 *
	4th day	0,890 \pm 0,054 *	0,920 \pm 0,152 *	0,886 \pm 0,150 *
	6th day	0,740 \pm 0,055 *	0,778 \pm 0,145	0,725 \pm 0,148
	9th day	0,682 \pm 0,050 *	0,695 \pm 0,140 "	0,677 \pm 0,144
GHG E2, ng/ml	Initially	2,296 \pm 0,330	2,352 \pm 0,538	2,090 \pm 0,536
	1st day	2,532 \pm 0,322	2,750 \pm 0,560	2,485 \pm 0,608
	2nd day	2,314 \pm 0,282	2,462 \pm 0,558	2,270 \pm 0,600
	4th day	2,453 \pm 0,290	2,460 \pm 0,558	2,384 \pm 0,614
	6th day	3,006 \pm 0,340 *	3,208 \pm 0,600 *	2,885 \pm 0,626 *
	9th day	2,764 \pm 0,307	2,785 \pm 0,582	2,687 \pm 0,577
GHG F2 α / GHG E2	Initially	0,25 \pm 0,02	0,23 \pm 0,06	0,24 \pm 0,05
	1st day	0,40 \pm 0,03 *	0,40 \pm 0,06 *	0,36 \pm 0,06 *
	2nd day	0,46 \pm 0,03 *	0,44 \pm 0,06 *	0,45 \pm 0,08 *
	4th day	0,38 \pm 0,02 *	0,37 \pm 0,05 *	0,37 \pm 0,07 *
	6th day	0,25 \pm 0,02	0,24 \pm 0,04	0,25 \pm 0,06
	9th day	0,25 \pm 0,01	0,25 \pm 0,05	0,25 \pm 0,06
IRPG	Initially	1,26 \pm 0,09	1,22 \pm 0,15	1,23 \pm 0,16
	1st day	2,03 \pm 0,10 *	1,82 \pm 0,17 *	1,86 \pm 0,17 *
	2nd day	2,46 \pm 0,11 *	2,32 \pm 0,19 *	2,35 \pm 0,19 *
	4th day	1,86 \pm 0,09 *	2,01 \pm 0,19 *	2,04 \pm 0,18 *
	6th day	1,32 \pm 0,08	1,25 \pm 0,14	1,26 \pm 0,16
	9th day	1,00 \pm 0,05 *	1,04 \pm 0,14	1,03 \pm 0,16

Note: * - p < 0.05 vs. initial values

" - p < 0.05 vs. values at normal body reactivity

The dynamics of the anti-inflammatory cytokine IL-4 in the gingival fluid of patients of groups 2A and 3A differed from that of IL-1 β , IL-6, TNF α - the peak of IL-4 content was noted on day 6. This indicator had the same dynamics in the case of normal body reactivity. On the 9th day, the value of IL-4 in the main groups remained higher than the initial value and was commensurate with that in the comparison group. Thus, the proposed targeted drug correction in patients with generalized periodontitis against the background of hyper- and hyporeactivity of the body approximates the values of cytokines in the gingival fluid to those of normal body reactivity, which ultimately restores the disturbed balance of pro- and anti-inflammatory cytokines.

The results of determining the content of different fractions of prostaglandins in the blood of patients with generalized periodontitis against the background of normal, hyper- and hyporeactivity of the body after surgery are presented in the table (Table III).

As can be seen from this table, initially (before surgery), the concentration of anti-inflammatory PG F2 α in the blood of patients with generalized periodontitis with targeted drug correction differed from that in the first group (p > 0.05). Surgical intervention led to an increase in the content of this eicosanoid in the main groups

and the comparison group with monophasic dynamics. The maximum value occurred on day 2 (p < 0.05) with a subsequent decrease until the end of the study. The level of proinflammatory PG E2 in the blood of patients with generalized periodontitis was also initially slightly different from that in the first group (p > 0.05). Surgical intervention caused a similar initial increase in the concentration of PG E2 in the main groups (2A and 3A) and the comparison group (p > 0.05). However, both the amplitude of changes and the dynamics of the index differed from that of PG F2 α : the changes were less pronounced, the dynamics were biphasic with maximum values on days 1 and 6. On the 2nd day, a slight decrease in the concentration of GH E2 was observed - at this point, the different direction of changes in the content of GH F2 α and GH E2 is noteworthy. The former reached maximum peak values, while the latter, on the contrary, was minimal. Subsequently, the second peak in the concentration of GHG E2 was observed in the main groups, which was more pronounced than the first. Its values, on average, were 1.4 times higher than the initial ones (p < 0.05). A similar dynamics of the indicator was recorded in patients with HP with normal body reactivity (comparison group). By the end of the observations, there was a tendency to decrease the content of PG

E2 in all three groups. Initially (before surgery), the ratio of PG F2 α / PG E2 in the main groups was proportional to that in the first group. Surgical intervention disrupted the balance between these eicosanoid fractions in the main groups and the comparison group. On the 1st day, the ratio of the studied pro- and anti-inflammatory prostaglandins increased, reaching a maximum level on the 2nd day, exceeding the initial values in the main groups, on average, by 1.9 times ($p < 0.05$). This is due to a sharp increase in the content of PG F2 α in the blood of patients with generalized periodontitis against the background of a decrease in the concentration of PG E2. Subsequently, there was an equalization of the primary prostaglandin balance - on the 9th day, the ratio of PG F2 α / PG E2 reached normal values. As can be seen from this table, the dynamics of the prostaglandin balance index in the main groups against the background of the proposed drug support coincided with that of the body's normoreactivity and was monophasic with a peak on day 2. The increase in the balance index on the 2nd day after surgery testified in favor of a shift in balance towards proinflammatory GH. Subsequently, there was a decrease in the IRPG with the achievement of the initial level on the 6th day and the normal level on the 9th day after flap surgery. This indicates the establishment of a normal balance of eicosanoids in the blood of patients with AP after targeted drug correction. Thus, the proposed differential general and local medication support in patients with generalized periodontitis against the background of hyper- and hyporesponsiveness of the body approximates the values of pro- and anti-inflammatory fractions of prostaglandins to those of normal body reactivity, which ultimately restores their disturbed balance in the blood.

DISCUSSION

Drug treatment of generalized periodontitis is based on the identification of the leading pathogenetic links in the development of the disease [4]. The correct focus of this tactic is confirmed by numerous literature data on the high clinical efficacy of the proposed and implemented drug treatment regimens for generalized periodontitis. This is evidenced by the widespread use of COX inhibitors, immunocorrectors, and cytokine therapy in the complex treatment of generalized

periodontitis [7, 8, 10]. However, the issues of clarifying the key mechanisms of the development and course of the disease in each specific clinical case and developing differentiated approaches to the choice of a complex of medications for general and local use, depending on the indicators of the state of the body's reactivity, which have the greatest impact on the pathogenesis of generalized periodontitis, remain relevant. It is known that the intensity and duration of the inflammatory reaction during the healing of a myocardial infarction is determined by the form of the initial reactivity of the body and determines the complicated and uncomplicated consequences [14]. In our study, we have shown that in generalized periodontitis of II and III severity after surgical treatment, the dynamics of prostaglandins (PG) E, E2, F2 α and cytokines (IL-1 β , IL-6, TNF, IL-4) in the blood and gingival fluid is different depending on the initial state of the body's reactivity. Our proposed targeted drug correction in patients with generalized periodontitis against the background of hyper- and hyporeactivity of the body brings the values of prostaglandins and cytokines closer to those of normal body reactivity. As a result, the disturbed balance of indicators in the blood and gingival fluid is restored, which creates optimal conditions for the course of the disease and helps to stabilize the pathological process.

CONCLUSIONS

The complex of drugs for medical support in the treatment of patients with chronic generalized periodontitis should be pathogenetically justified and differentiated depending on the initial state of the body's reactivity, which determines the type of inflammatory reaction and, accordingly, the nature of the healing process and further stabilization of the pathological process. Patients with generalized periodontitis of II, III severity with normal body reactivity should not be prescribed medication correction after surgical treatment. In patients with hyper- and hyporesponsiveness of the body, postoperative drug therapy is appropriate and pathogenetically justified. The complex of means for medical correction should be differential and determined by the nature of the change in the indicators regulating the healing process.

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The work is a fragment of the research initiative of the Department of Stomatology «To develop differential medication support in the complex treatment of generalized periodontitis against the background of different body reactivity». State registration number 0122U000247.

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Conflict of interest:

The Authors declare no conflict of interest.

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Received: 27.04.2023

Accepted: 09.08.2023

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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