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Clinical and laboratory assessment of the application efficacy of antibacterial combinations in the treatment of chronic generalized periodontitis

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Abstract

Aim. To determine the efficacy of the combination of metronidazole and co-trimoxazole in the treatment of chronic generalized periodontitis.

Methods. The studies included patients with slight and moderate chronic generalized periodontitis without concomitant pathology. Patients were divided into two groups with similar age and severity of periodontal diseases. In the first group, metronidazole was administered into the periodontal pocket; in the second group co-trimoxazole and metronidazole combination was used. Oral fluid testing was used to detect ureolytic and glycolytic activity, malondialdehyde (MDA) content, conjugated dienes, catalase activity, Salivary Secretory Immunoglobulin (SIgA) and Lysozyme. Changes in periodontal disease were assessed before and after treatment. The duration of treatment was 12 days.

Results. Co-trimoxazole and metronidazole combination more effectively stimulated ureolytic activity and reduced glycolytic effect. It had a more effective antioxidant effect that manifested in: a statistically significant decrease in malondialdehyde levels by 32.8% ($p < 0.01$) and by 36.6% ($p < 0.01$) in patients with slight and moderate periodontitis, respectively; decrease in diene conjugates by 25.0% ($p < 0.001$) and 37.7% ($p < 0.001$); and increased catalase activity 2.6 and 2.9 times ($p < 0.001$). After treatment, it was revealed an increase in lysozyme activity by 11.3% and 17.6% ($p < 0,001$) in patients with slight and moderate periodontitis, respectively, and increase secretory IgA levels by 37.4% ($p < 0.001$) and 53.2% ($p < 0.001$). In the first group, the amount of SIgA in the oral fluid increases by 35.8% ($p < 0.001$), and by 45.6% ($p < 0.001$) compared to the value before treatment in patients with slight and moderate periodontitis, and in the second group by 37.4% ($p < 0.001$) and 53.2% ($p < 0.001$), respectively.

Conclusion. The combined treatment with co-trimoxazole + metronidazole leads to the positive changes in the studied parameters causes rapid disappearance of the symptoms characteristic of chronic generalized periodontitis; this 2-drug combination is recommended to be included in the complex therapeutic measures for inflammatory periodontal diseases.

Keywords: chronic generalized periodontitis, metronidazole, co-trimoxazole, malondialdehyde, diene conjugates, catalase, lysozyme.

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Background

At present, the treatment of periodontal diseases is still important. On average, 44% of the population needs treatment for chronic generalized periodontitis (CGP) [1]. The current trend in the treatment of periodontitis is to maximize the utilization of conservative methods using effective anti-inflammatory agents [2, 3].

The combined use of metronidazole and long-acting sulfonamides makes it possible to decline antibiotic therapy, because of its side effects, including allergic reactions, formation of microflora resistant to antibiotic agents, dysbacteriosis, and immunosuppression [4].

In periodontics, studies recommended the use of metronidazole and co-trimoxazole separately [4, 5], but the possibility of combining these agents for local use, in particular for CGP, has not been considered.

Biochemical studies of the oral fluid of patients with CGP have an important diagnostic nature and are quite informative in evaluating the treatment

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Table 1. General characteristics of patients with CGP

Group	Number of patients	Age, years	Severity of periodontitis	Treatment
Group 1	16	30.3 ± 2.84 [22; 40]	Mild, n = 10 Moderate, n = 6	Metronidazole
Group 2	17	29.6 ± 1.92 [20; 39]	Mild, n = 10 Moderate, n = 7	Co-trimoxazole + metronidazole

measures since biochemical indicators clearly reflect the depth of changes in the metabolic processes in the oral cavity of patients [6]. In this aspect, the inflammatory process in the periodontium, which is influenced by bacterial endotoxins and proteolytic enzymes that initiate pathomorphological changes, contributes to the impairment in free radical oxidation and antioxidant protection, which ultimately increases the concentrations of malondialdehyde (MDA) and diene conjugates (DC) and decreases the activity of the antioxidant enzyme catalase [4].

Taking into account the importance of free radical oxidation and impairment of antioxidant protection in the development of periodontal inflammation, changes in the concentrations of the end products of passing reactions MDA [7] and DC [8], as well as catalase activity [9], are helpful in assessing the inflammatory process in the periodontium.

Impaired metabolic processes are accompanied by a weakening immune status, in particular, the local immunity, expressed by a decrease in the concentrations of lysozyme and secretory immunoglobulin class A (sIgA) in oral fluids [4]. Unique changes in local factors of oral resistance reflecting immune imbalance in inflammatory periodontal changes were investigated by analyzing the activity of lysozyme [10] and sIgA [11].

Active growth of pathogenic microflora in periodontitis and consequently impairment of bacterial balance lead to an imbalance, that is, an increase in ureolytic, and a reduction of the glycolytic activity in the oral fluids. In periodontitis, the number of ureolytic microorganisms increases and the activity of glucose-fermenting microorganism decreases, and such changes correlate with the severity of the disease [12].

With treatment, inflammatory changes disappear and metabolic processes recover and normalize, which are expressed in the values of the corresponding biochemical parameters in the oral fluids, a comparative analysis of these biochemical parameters allows us to judge the quality of the therapeutic effect on the pathological process in the periodontium [4,6,12].

The aim of the study was to determine the effectiveness of the combination of metronidazole and co-trimoxazole in the treatment of CGP based on data obtained from clinical and laboratory studies.

Material and methods

This study included patients aged 18–54 (average, 39.3 ± 2.6) years with mild and moderate CGP without concomitant somatic diseases. These patients provided their consent to participate in the study. The study was approved by the ethics Committee of the Azerbaijan Medical University (Report no. 9 of 14.05.2014).

The exclusion criteria were as follows: pregnant and nursing mothers, patients who took antibiotics in the coming months, patients who have a chronic somatic pathology, and patients who decline to participate in the study.

In this study, the patients were divided according to age and severity of periodontal disease depending on the agent used for treatment or their combination (Table 1).

In both groups, conventional treatment measures were performed in the oral cavity, including removal of dental deposits, treatment with an antiseptic agent (0.05% chlorhexidine solution), and curettage of periodontal pockets. In group 1, only turunds with the antibacterial agent metronidazole were placed in the periodontal pocket during the treatment; in group 2, a combination of antibacterial drugs consisting of co-trimoxazole and metronidazole was used.

The effect of the treatment on the periodontal health of patients was assessed using objective clinical criteria, which include hyperemia, edema, pain, periodontal pockets, and tooth mobility. Changes in periodontal health were also evaluated before and after treatment according to the numerical values of the simplified oral hygiene index (OHI-S), papillary marginal alveolar index (PMA), periodontal index (PI), and Mulleman–Cowell index. Treatment was performed until signs of inflammation in the periodontium disappeared. The treatment period was 12 days. The effectiveness of treatment was also evaluated in the long term (6 months after the start of treatment).

The Statistica 8.0 program was used for the statistical processing of the research results. The reliability was evaluated using the $\chi 2$ and Wilcoxon–Mann–Whitney criteria.

Table 2. Frequency of objective clinical appearances of periodontitis before treatment and day 6 of treatment

Indicator	Time of monitoring	Group 1		Group 2	
		Mild (n=10)	Moderate (n=6)	Mild (n=10)	Moderate (n=7)
Hyperemia	Before treatment, n/%	7/70.0	6/100	8/80.0	6/85.7
	On day 6, n/%	5/50.0*	5/83.3	2/20.0*.**	2/28.6*.**
Edema	Before treatment,	9/90.0	6/100	9/90.0	6/85.7
	On day 6	5/50.0*	4/66.7*	5/50.0*	4/57.1*
Pain	Before treatment,	7/70.0	5/83.3	7/70.0	5/71.4
	On day 6	4/40.0*	3/50.0*	4/40.0*	3/42.8*
Periodontal pockets	Before treatment,	6/60.0	6/100	6/60.0	6/85.7
	On day 6	3/30.0*	5/83.3	3/30.0*	3/42.8*.**
Tooth mobility	Before treatment,	—	6/100	—	7/100
	On day 6	—	3/50.0*	—	3/42.8*

Note: * statistical significance between indicators before and after treatment within the group; * * statistical significance of indicators between groups after treatment ($p < 0.05–0.01$).

Results

During the comparative evaluation of the results obtained 6 and 9 days after metronidazole therapy and combined treatment with co-trimoxazole + metronidazole, objective clinical symptoms of patients with both mild and moderate CGP regressed in both groups.

In 6 days from the start of treatment, the observed clinical picture of the disease reflected the advantage of using metronidazole + co-trimoxazole. This was expressed by an active relief of the main objective signs of CGP. Thus, by this period, 20.0% of patients with mild CGP who received the combined therapy have hyperemia versus 50.0% of patients who received metronidazole alone; this indicates that the number of patients in group 2 who have hyperemia significantly decreased by 2.5 times ($p < 0.05$). Moreover, 28.6% of group 2 patients with moderate disease severity developed hyperemia versus 83.3% of group 1 patients, which indicates a decrease in the frequency of hyperemia by 2.9 times ($p < 0.01$).

Moreover, on day 6 of treatment, no significant differences were found in the frequency of edema, pain, pockets (mild periodontitis), and loose teeth in both groups ($p > 0.05$; Table 2).

After 6 days of treatment, co-trimoxazole + metronidazole was found to be more effective in reducing the incidence of hyperemia. The frequency of hyperemia in group 2 patients with mild and moderate CGP in comparison with group 1 decreased by 2.5 times ($p < 0.05$) and 2.9 times ($p < 0.01$), respectively.

A comparative analysis of the results obtained after 9 days of combined treatment revealed the dynamics of all clinical symptoms. All clinical symptoms in patients with mild CGP who received co-trimoxazole + metronidazole, have disappeared compared to patients who received metronidazole alone. The frequency of hyperemia, edema, presence of pockets, and loose teeth of patients with mild and moderate CGP decreased 3.5 times ($p < 0.01$) and 2.3 times ($p < 0.05$), respectively.

Immediately after treatment (Table 4) in group 2 patients with mild CGP compared with their counterparts in group 1, the PMA index decreased by 1.86 times ($p < 0.001$), with an average degree of 1.53 times ($p < 0.001$). The Mulleman–Cowell index decreased by 1.8 times ($p < 0.001$) for mild and 1.55 times ($p < 0.001$) for moderate CGP. The PI decreased by 1.66 times ($p < 0.001$) and 1.65 times ($p < 0.001$), respectively. The OHI-S immediately after treatment of patients with mild CGP in both groups did not differ significantly, but the OHI-S in group 2 patients with moderate CGP was 1.22 times lower than that in group 1 ($p < 0.05$).

At 6 months after combined therapy (Table 5), the average PMA index of group 2 patients with mild and moderate CGP was lower than that of group 1 by 1.67 times ($p < 0.001$) and 1.57 times ($p < 0.001$), the incidence of gum bleeding in patients with mild CGP was lower by 1.73 times ($p < 0.001$) and in moderate by 1.34 times ($p < 0.001$), and the PI was lower by 1.78 times ($p < 0.001$) and 1.72 times ($p < 0.001$) in mild and moderate CGP, respectively. The OHI-S of group 2 patients with mild and medium CGP at 6 months after treatment was lower by 1.44 times ($p < 0.001$) and 1.28 times than those in group 1 ($p < 0.01$), respectively.

Analysis of the PI and radiographs showed that the destructive process was stabilized, and this was more pronounced when using a combination

Table 3. Dynamics of objective clinical appearances of periodontitis before treatment and 9 days after treatment

Indicator	Time of monitoring	Group 1		Group 2	
		Mild (n=10)	Moderate (n=6)	Mild (n=10)	Moderate (n=7)
Hyperemia	Before treatment, n/%	7/70.0	6/100	8/80.0	6/85.7
	On day 9, n/%	2/20.0*	3/50.0*	—	1/14.3*.**
Edema	Before treatment,	9/90.0	6/100	9/90.0	6/85.7
	On day 6	2/20.0*	2/33.3*	—	1/14.3*.**
Pain	Before treatment,	7/70.0	5/83.3	7/70.0	5/71.4
	On day 9	1/10.0*	2/33.3*	—	—
Periodontal pockets	Before treatment,	6/60.0	6/100	6/60.0	6/85.7
	On day 9	2/20.0*	2/33.3*	—	1/14.3*.**
Tooth mobility	Before treatment,	—	6/100	—	7/100
	On day 9	—	2/33.3*	—	1/14.3*.**

Note: * statistical significance between indicators before and after treatment within the group; * * statistical significance of indicators between groups after treatment ($p < 0.05–0.001$).

Table 4. Values of indices after treatment of the examined groups

Indices	Group 1		Group 2	
	Mild	Moderate	Mild	Moderate
PMA	13.4±0.29%	17.6±0.28%	7.2±0.17% (p <0.001)	11.5±0.22% (p <0.001)
Muelleman–Cowell	0.43±0.019	0.65±0.027	0.24±0.019 (p <0.001)	0.42±0.023 (p <0.001)
PI	0.63±0.018	1.32±0.026	0.38±0.015 (p <0.001)	0.80±0.019 (p <0.001)
OHI-S	0.33±0.025	0.60±0.034	0.30±0.019	0.49±0.027 (p <0.05)

Note: p, statistical significance of differences between groups of patients according to the severity of periodontitis; PMA, papillary marginal alveolar index; PI, periodontal index; OHI-S, simplified oral hygiene index.

Table 5. Values of indices at 6 months after treatment between the examined groups

Indices	Group 1		Group 2	
	Mild CGP	Moderate CGP	Mild CGP	Moderate CGP
PMA	20.5±0.52%	28.6±0.61%	12.3±0.23% (p <0.001)	18.2±0.30% (p <0.001)
Mulleman–Cowell	0.78±0.031	0.98±0.089	0.45±0.024 (p <0.001)	0.73±0.028 (p <0.001)
PI	1.30±0.024	1.89±0.029	0.73±0.021 (p <0.001)	1.10±0.023 (p <0.001)
OHI-S	0.62±0.036	0.82±0.048	0.43±0.025 (p <0.001)	0.64±0.030 (p <0.01)

Note: p, statistical significance of differences between groups of patients according to the severity of periodontitis; PMA, papillary marginal alveolar index; PI, periodontal index; OHI-S, simplified oral hygiene index.

of antibacterial agents — metronidazole + co-trimoxazole.

As shown in Table 6, initially, this study included patients with both mild and moderate CGP. The pH level shifted to the acidic side, as reflected by the decrease in the ureolytic (average 33.8%, $p < 0.01$) and increase in glycolytic (average 50.2%, $p < 0.01$) activities for patients with mild and medium CGP and by 40.6% ($p < 0.01$) and 77.0% ($p < 0.001$), respectively, for patients with moderate CGP.

After the treatment, the ureolytic activity in group 1 patients with mild and moderate CGP increased by 16.5% ($p < 0.01$) and 23.1% ($p < 0.001$), respectively. In the same group, the glycolytic activity decreased during the treatment by 16.9%

Table 6. Changes in ureolytic and glycolytic activities in the oral fluid (min) of patients with CGP

Activity	Хронический генерализованный пародонтит							
	Group 1 (n = 16)				Group 2 (n = 17)			
	Before treatment		After treatment		Before treatment		After treatment	
	Mild	Moderate	Mild	Moderate	Mild	Moderate	Mild	Moderate
Ureolytic	14.5±0.35	13.0±0.31	16.9±0.56**	16.0±0.48*	14.7±0.41	13.4±0.38	18.1±0.86**	17.8±0.62*
Glycolytic	31.4±0.94	37.0±1.10	26.1±0.43*	26.9±0.48*	30.8±0.89	36.6±1.02	23.8±0.56**$^{\Delta\Delta}$	25.0±0.65*$^{\Delta}$

Note: * statistical significance between indicators before treatment $p < 0.001$; **$p < 0.01$; $\Delta p < 0.05$ relative to group 1 (after treatment); $\Delta\Delta p < 0.01$ relative to group (after treatment).

Table 7. Concentrations of malondialdehyde (MDA), diene conjugates (DC), and catalase in the oral fluids of patients before and after treatment

Indicators	Chronic generalized periodontitis							
	Group 1 (n = 16)				Group 2 (n = 17)			
	Before treatment		After treatment		Before treatment		After treatment	
	Mild	Moderate	Mild	Moderate	Mild	Moderate	Mild	Moderate
MDA, mmol/L	0.58±0.013	0.67±0.025	0.46±0.008*	0.50±0.015*	0.61±0.015	0.71±0.022	0.41±0.012*$^{\Delta\Delta}$	0.45±0.018*
DC, D233/mL	0.40±0.018	0.55±1.023	0.33±0.010**	0.38±0.014*	0.40±0.012	0.53±0.021	0.30±0.008*$^{\Delta}$	0.33±0.009*$^{\Delta}$
Catalase, μkat/L	1.45±0.09	0.90±0.11	3.0±0.07*	2.7±0.08*	1.43±0.10	1.1±0.12	3.8±0.04*$^{\Delta\Delta}$	3.2±0.05*$^{\Delta}$

Note: * statistical significance between indicators before treatment $p < 0.001$; **$p < 0.01$; $\Delta p < 0.05$ relative to group 1 (after treatment); $\Delta\Delta p < 0.01$ relative to group 1 (after treatment).

($p < 0.01$) and 27.4% ($p < 0.01$) for patients with mild and moderate CGP, respectively. In group 2, on the background of a complex therapy with the inclusion of co-trimoxazole + metronidazole, the ureolytic activity in patients with mild CGP increased by 23.1% ($p < 0.01$) and the glycolytic activity decreased by 22.7% ($p < 0.01$). In the same group, the ureolytic and glycolytic activities in those with moderate CGP increased and decreased by 32.8% ($p < 0.001$) and 31.7% ($p < 0.001$), respectively.

The inclusion of the proposed combination of co-trimoxazole and metronidazole in the treatment of both severities of CGP in group 2 provided a significant decrease in glycolytic activity ($p < 0.01$ in mild CGP and $p < 0.05$ in moderate CGP) in contrast to group 1. In short, co-trimoxazole + metronidazole more effectively reduced the glycolytic activity.

During the study, the concentrations of MDA, DC, and catalase were determined according to the treatment regimen. As shown in Table 7, when comparing the initial level of MDA in the oral fluid of the representatives of the control group with that of patients with mild and moderate CGP, the latter revealed relatively high MDA level, with an average of 1.7 and 2.0 times ($p < 0.05$), respectively.

After treatment in group 1 patients with mild and moderate CGP, the concentration of MDA in the oral fluid decreased by 20.7% ($p < 0.01$) and 25.4%, respectively ($p < 0.01$) in comparison with the indicators before treatment. After treatment, the concentration of MDA in group 2 patients with mild and moderate CGP also decreased by 32.8% ($p < 0.01$) and 36.6% ($p < 0.01$), respectively. Notably, after treatment, the level of MDA in group 2 was closer to the control level.

The concentration of DC increased with the severity of periodontitis (Table 7). Before treatment, the DC level of patients with mild and moderate CGP exceeded the control level by 1.6 times ($p < 0.05$) and 2.2 times ($p < 0.05$) on average, respectively. After treatment in group 1, the concentration of DC in patients with mild and moderate CGP decreased by 17.5% ($p < 0.01$) and 30.9% ($p < 0.001$), respectively. In group 2, compared with the indicators before treatment, the level of DC in patients with mild and moderate CGP decreased by 25.0% ($p < 0.001$) and 37.7% ($p < 0.001$), respectively.

The concentration of catalase in the oral fluid of patients with CGP tended to decrease with an increase in pathological activity. The level of catalase in the oral fluid of patients with CGP is lower than the control level. Thus, in patients with mild CGP before treatment, the catalase level exceeded 3.1 times ($p < 0.01$) and in those with moderate CGP by 5.0 times ($p < 0.001$). The treatment resulted in an increase in the concentration of catalase in the oral

Table 8. Concentrations of lysozyme and secretory immunoglobulin A (sIgA) before and after treatment in the oral fluids of patients with chronic generalized periodontitis

Indicators	Chronic generalized periodontitis							
	Group 1 (n = 16)				Group 2 (n = 17)			
	Before treatment		After treatment		Before treatment		After treatment	
	Mild	Moderate	Mild	Moderate	Mild	Moderate	Mild	Moderate
Lysozyme, μg/mL	47.3±0.33	44.0±0.41	52.6±0.40*	51.1±0.32*	49.2±0.68	45.5±0.90	54.8±0.51*$^{\Delta\Delta}$	53.5±0.37*$^{\Delta}$
sIgA, г/л	0.366±0.007	0.331±0.004	0.497±0.004*	0.482±0.004*	0.388±0.006	0.340±0.007	0.533±0.003*$^{\Delta}$	0.521±0.004*$^{\Delta}$

Note: * statistical significance between indicators before treatment $p < 0.001$; **$p < 0.01$; $^{\Delta}p < 0.001$ relative to group 1 (after treatment); $^{\Delta\Delta}p < 0.01$ relative to group 1 (after treatment).

fluid of patients with mild and moderate CGP, i.e., by 2.1 and 3.0 times in group 1 ($p < 0.001$) and by 2.6 and 2.9 times in group 2 ($p < 0.001$), respectively.

The results showed an increase in the concentration of catalase after treatment, and for patients with mild and moderate CGP who received co-trimoxazole + metronidazole (group 2), the amount of enzymes in the oral fluid was 1.2 and 1.4 times lower than the control parameters, while after local infiltration of metronidazole (group 1), the difference was 1.5 and 1.7 times, respectively. Consequently, co-trimoxazole + metronidazole demonstrated a more effective antioxidant property.

After treatment in both groups, co-trimoxazole + metronidazole showed a more effective effect on mild and moderate CGP. After the combined use of co-trimoxazole + metronidazole, the catalase activity in the oral fluids of patients with mild CGP was 26.7% ($p < 0.01$) higher than that in group 1, where only metronidazole was used, and those with moderate CGP, it was 18.5% ($p < 0.05$). A similar pattern was observed in MDA and DC. The treatment resulted in a 10.9% ($p < 0.01$) and 9.1% ($p < 0.05$) decrease in the concentrations of MDA and DC in the oral fluids of patients with mild CGP in group 2 compared with the same indicators in group 1, and those with a moderate CGP degree decreased by 10.0% ($p > 0.05$) and 13.2% ($p < 0.05$), respectively.

As regards the level of sIgA in the oral fluid, it was reduced by an average of 1.7 times ($p < 0.05$) compared with the control level of patients with mild CGP, and it was 1.9 times ($p < 0.05$) in patients with moderate CGP. After treatment, a tendency to increase was observed. In average, the level of sIgA in the oral fluid increases by 35.8% ($p < 0.001$) for group 1 patients with mild CGP and by 45.6% ($p < 0.001$) for patients with moderate CGP compared with the value before treatment. In group 1, the sIgA level in mild CGP increased by 37.4% ($p < 0.001$) and by 53.2% ($p < 0.001$) in moderate CGP.

A comparative analysis showed that the increase in lysozyme level after treatment with co-trimoxazole and metronidazole in patients with mild and moderate CGP was 4.2% and 4.7% higher, respectively, than after treatment with metronidazole alone. A similar pattern is recorded relative to the concentration of sIgA in the oral fluids. After treatment of group 2 patients with mild and medium CGP, this indicator was higher by 7.2 and 8.1%, respectively.

Discussion

The final results of the indicators and laboratory studies successfully abolished inflammation in the periodontium when traditional measures for the treatment of CGP were supplemented with a combination of co-trimoxazole and metronidazole. Although patients in both groups showed significant differences in the hygiene index and periodontal indices with the initial parameters as well as a steady decrease in bleeding, inflammation signs, and intensity of inflammatory and destructive changes, a marked anti-inflammatory effect was observed in group 2. At the same time, according to the visual clinical changes in the oral cavity, the aforementioned combination of agents had a more positive effect on the normalization of the pH of the oral fluid, restoration of the antioxidant protection, and activation of immunological indicators. Therefore, both clinical and laboratory data showed a statistically significant decrease in the inflammatory process, thanks to the procedures performed.

In the treatment, where metronidazole + co-trimoxazole was used as the active component of therapy, and not metronidazole alone, the selected timing for evaluating the results on days 6 and 9, with an overall treatment duration of 12 days, allowed us to determine the dynamics of the regression of the pathological process in the periodontium of the studied groups, which was confirmed first by clinical and later by laboratory indicators. The results of treatment of periodontal diseases are eva-

luated by different parameters, and often, digital index values are taken as criteria sufficient to confirm the effectiveness of the measures taken. Indeed, the accepted criteria, in particular the index values, are sufficiently informative, and reliable for evaluating the results of clinical or scientific research. At the same time, in our opinion, the importance of evaluating the quality and effectiveness of treatment by both the doctor and the patient is not given due consideration. This consideration of the effectiveness of the treatment allows the assessment to cover a larger range of possible changes in the oral cavity before and after treatment [13].

During the treatment of patients with mild and medium CGP, a combination of co-trimoxazole + metronidazole can be applied in the following sequence: irrigation with antiseptic agents, application of appropriate anesthesia, removal of dental pockets with antiseptics, introduction of powder containing co-trimoxazole and metronidazole into the periodontal pocket (at a dose of 960 + 250 mg, accordingly, per 1–2 quadrants), application of insulating dressing after the procedure for 1.5–2 h, followed by its self-removal by patients and antiseptic irrigation of the oral cavity, and curettage of periodontal pockets.

Conclusions

1. Combined treatment with co-trimoxazole and metronidazole contributes to the positive dynamics of the OHI-S, PMA, PI, and Mullemann–Cowell index and concentrations of MA, DC, catalase, lysozyme, and sIgA in the oral fluids and causes rapid resolution of the characteristic symptoms of CGP.

2. Combined treatment with co-trimoxazole + + metronidazole positively affects the level of ureolytic and glycolytic activities, has an antioxidant effect, and increases the immune response.

3. Combination of co-trimoxazole and metronidazole can be included in the treatment of inflammatory periodontal diseases.

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