ORIGINAL ARTICLE

EVALUATION OF EFFECTIVENESS OF TREATMENT-AND-PROPHYLACTIC COMPLEX IN TOBACCO-ADDICTED PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS ON THE BACKGROUND OF CHRONIC HYPERACID GASTRITIS

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ABSTRACT

The aim: To evaluate the clinical efficacy of treatment-and-prophylactic complex in patients addicted to tobacco with chronic generalized periodontitis with chronic hyperacid gastritis. **Materials and methods:** 68 patients (men and women) aged 25–44 years were examined. They were distributed into two groups: the main group — 48 patients addicted to tobacco with chronic generalized 1 degree periodontitis and chronic hyperacid gastritis, associated with *Helicobacter pylori*, the control group — 20 healthy individuals without bad habits. Patients of the main group were distributed at random into 2 subgroups (1.1, 1.2) depending on the chosen therapy. The patients of the subgroup 1.1 received the basic therapy and the developed treatment and prophylactic complex, the subgroup 1.2 received the basic therapy and the ultraphonophoresis procedures with placebo. Assessment of the effectiveness of therapy was carried out by determining hygienic index OHI-S and periodontal indices (PI, PMA index and MBI) at the immediate and late observation period.

Conclusions: Results of the study confirmed the effectiveness of the proposed treatment-and-prophylactic complex in therapy of chronic generalized 1 degree periodontitis in patients addicted to tobacco smoking with chronic hyperacid gastritis.

KEY WORDS: periodontitis, gastritis, smoking

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INTRODUCTION

Periodontal tissue pathology still remains an urgent problem of modern dentistry, taking into account its great incidence. Inflammatory and inflammatory-dystrophic diseases of periodontal tissues affect millions of people around the world [1]. It is known that periodontal pathology is characterized by polyetiological nature [2], and one of the most important factors in its development is smoking [3]. Its harmful effects are carried out directly through the primary contact of the oral mucosa of the smoker with toxic and carcinogenic substances in tobacco smoke and indirectly through systemic relationships [4]. The prevalence of periodontal disease among smokers is much higher than among non-smokers. The severity of clinical symptoms, the course and outcome of treatment directly depend on the number of cigarettes smoked and smoking history [5]. At the same time, based on the assessment of the levels of hygienic and periodontal indices, high incidence of periodontal disease among tobacco smokers is proved, which is manifested in significant accumulation of dental plaque, formation of deep pathological pockets, bone resorption of the alveolar process [6].

The modern dental science considers periodontitis as a comorbid pathology of periodontal tissues and internal organs [7]. The oral cavity and gastrointestinal tract (GIT) — the only morphofunctional system, the occurrence of changes in which is observed in violation of any of its links [8]. Chronic generalized periodontitis (CGP) is often combined with acid-dependent diseases of the stomach, such as chronic hyperacid gastritis (CHG), which is characterized by increased acidity of gastric juice [9]. Among the mechanisms of periodontal tissue pathology with gastrointestinal diseases are deterioration of oral hygienic condition, violation of salivation and rheological properties of saliva, pH changes, immunological changes and so on [10].

It is known that pathology of the stomach and duodenum develops more often in smokers than in non-smokers. This can be explained by the fact that smoking causes gastric secretion imbalance, disrupts pyloric activity, reduces bicarbonate secretion by the pancreas and prevents ulcers healing. Under conditions of risk factors and concomitant pathology combination, periodontal tissues are exposed to a more significant negative impact, which can manifest itself in a prolonged inflammatory process, recurrent nature, aggravation of the course, resistance to treatment [11].

So, the incidence rate of inflammatory periodontal diseases determines the need to find and develop new comprehensive methods for their treatment and prevention. Moreover, there is a growing interest in drugs of natural and herbal origin, which act gently, effectively and have fewer side effects, less risk of allergy. Increased attention to these drugs is explained to frequent cases of side effects and allergic reactions to antibiotics, synthetic, hormonal drugs and the development of resistance of pathogenic microflora to antibacterial agents [12]. It should be emphasized that bee products are an affordable natural material that has a wide range of biologically active substances. Currently, they are used in all fields of medicine, including dentistry. Bee products have antibiotic, anti-inflammatory, anesthetic, antimicrobial, antifungal, antitumor, antioxidant, angioprotective properties. They have regenerative and wound healing properties [13]. On the other hand, physiotherapeutic treatment in the complex therapy of periodontitis have a powerful sanogenic effect, stimulate the body's defenses, improve trophism and promote tissue regeneration [14].

THE AIM

The aim of the work is to evaluate the clinical effectiveness of the treatment-and-prophylactic complex in tobacco-addicted patients with chronic generalized periodontitis on the background of chronic hyperacid gastritis.

MATERIALS AND METHODS

68 patients (men and women) aged 25 to 44 years, divided into two groups, have been examined. The first group (main group) consisted of 48 patients with chronic generalized 1 degree periodontitis on the background of chronic hyperacid gastritis associated with *Helicobacter pylori* and chronic smoking. The smoking history was 5–7 years, the number of cigarettes smoked from 15 to 20 per day. The second group — control, consisted of 20 healthy individuals who had no history of oral pathology, comorbid somatic diseases and bad habits. All patients of the main group were diagnosed concomitant pathology (HCG) confirmed by a gastroenterologist.

The diagnosis of CGP was established on the basis of anamnesis, clinical examination, X-ray, determination of hygienic and periodontal indices according to the classification of periodontal diseases by N. F. Danilevsky (1994) [15].

The patients of the main group were also randomly divided into two subgroups (1.1, 1.2) depending on the selected method of treatment:

- subgroup 1.1. - application of the basic therapy of chronic generalized periodontitis (CGP) and developed treatment-and-prophylactic complex (TPC) — ultraphonophoresis procedures with the new developed gel based on bee products and other biologically active substances [16] and probiotic drug of local application for prevention

of dysbiosis [17], removal of inflammatory processes. On the injured areas of the gums with a spatula a thin layer of natural apigel was applied in amount of 0.05–0.2 g, followed by ultraphonophoresis (the ultrasound therapy device "UZT-3.01F", LLC "Med TeKo", Mytishchi, Russia) at an oscillation frequency of 830 kHz, with an intensity 0.4 W/cm² at a pulse sequence with exposure of 5 minutes, once a day, a total course of 10 procedures every other day [18]. The prophylactic course of application of the therapeutic-and-prophylactic gel was 3 times a year in the form of applications 2 times a day (morning and evening) until complete resorption. The probiotic drug was prescribed according to the instruction for medical use of the drug by 1 lozenge 2 times a day after meal and teeth-brushing during 15 days [19].

- subgroup 1.2 - the use of basic therapy of chronic generalized periodontitis and ultrasound phonophoresis with placebo.

Patients with CHG received general antihelicobacter therapy prescribed by a gastroenterologist.

The research was conducted in compliance with the basic provisions of the "Rules of ethical principles of scientific medical research with human participation", approved by the Declaration of Helsinki (1964–2013), ICH GCP (1996) and orders of the Ministry of Health of Ukraine № 690 dated 23.09.2009, № 944 dated 14.12.2009, № 616 dated 03.08.2012, with the voluntary informed consent of the patient both in the near and long-term follow-up.

The evaluation of the clinical effectiveness of the treatment and prophylactic complex was performed by determining the hygienic condition of the oral cavity according to the Green-Vermillion hygiene index (OHI-S — Oral Hygiene Index-Simlified, 1964), which allows to estimate the amount of plaque and tartar on tooth surfaces; the severity of inflammatory-destructive changes in periodontal tissues according to the periodontal index (PI) according to Russel A. (1956); inflammatory changes in the gingival mucosa according to the papillary-marginal-alveolar (PMA) index in the Parma modification (1960) and the degree of bleeding of the gingival sulcus and periodontal pocket when probing according to bleeding index Muhlemann H.P., Son S (1971), according to Cowell I. modification (1975).

Statistical processing of research data was performed using software packages Microsoft Excel XP, Statistica 6.0. In the tables, the data are presented as arithmetic mean values (M) and a mean error (\pm m). Differences in the data were considered statistically significant by p<0.05.

RESULTS

The results of the examination showed that in patients of subgroup 1.1, using basic therapy of CGP and developed TPC, the state of oral hygiene according to OHI-S on the 7th day of treatment decreased by 21.3%, on the 14th day — by 39.3% and already on the 21st day decreased by 54.8% according to the index before treatment, but throughout the course of treatment remained higher than the control group of patients (p<0.05). On the other hand, in patients

Indices	Control group, n=20	Main group, n=48								
		1.1 subgroup, n=24				1.2 subgroup, n=24				
		Before treatment	ln 7 days	in 14 days	in 21 days	Before treatment	in 7 days	in 14 days	in 21 days	
Green-Vermillion (OHI-S), score	1.00±0.09	3.05 ±0.06*	2.40 ±0.06*◊	1.85 ±0.04*◊	1.38 ±0.05*◊	3.08 ±0.07*	2.40 ±0.08*◊	2.23 ±0.08*◊	2.06 ±0.08*◊	
PI index (Russel A.), score	0.06±0.03	1.74 ±0.02*	1.44 ±0.02*◊	1.28 ±0.02*◊	1.10 ±0.03*◊	1.74 ±0.03*	1.67 ±0.03*	1.52 ±0.02*◊	1.47 ±0.02*◊	
PMA, %	1.25±0.56	35.36 ±0.66*	30.43 ±0.41*◊	25.92 ±0.30*◊	20.95 ±0.24*◊	35.89 ±0.67*	31.06 ±0.45*◊	29.27 ±0.47*◊	26.87 ±0.48*◊	
Mühllemanbleeding index, score	0.19±0.03	1.67 ±0.08*	1.45 ±0.08*	1.28 ±0.07*◊	1.02 ±0.07*◊	1.76 ±0.08*	1.59 ±0.08*	1.42 ±0.08*◊	1.23 ±0.07*◊	

Table I. Changes of measurements of hygienic state and periodontal tissues condition in patients of the main group during treatment (M±m)

Note: * – trustworthy as compared with the control group (p<0.05);

 \diamond – trustworthy as compared with the indicators before treatment (p<0.05).

Table II. Long-term results of indicators of oral hygiene and periodontal tissues condition in patients of the main group (M±m)

Indices	Control group, n=20	Main group, n=48								
		1.1 subgroup, n=24				1.2 subgroup, n=24				
		Before treatment	In 6 months	in12 months	in18 months	Before treatment	in6 months	in12 months	in18 months	
Green-Vermillion (OHI-S), score	1.00±0.09	3.05 ±0.06*	1.97 ±0.05*◊	2.26 ±0.06*◊	2.63± 0.07*◊	3.08± 0.07*	2.63 ±0.05*◊	2.91 ±0.07*	3.18 ±0.06*	
PI index (Russel A.), score	0.06±0.03	1.74 ±0.02*	1.20 ±0.02*◊	1.45 ±0.02*◊	1.61 ±0.03*◊	1.74 ±0.03*	1.55 ±0.02*◊	1.62 ±0.02*◊	1.70 ±0.03*	
PMA, %	1.25±0.56	35.36 ±0.66*	24.32 ±0.28*◊	27.35 ±0.35*◊	30.93 ±0.58*◊	35.89 ±0.67*	29.22 ±0.51*◊	31.49 ±0.54*◊	32.87 ±0.54*◊	
Mühllemanbleeding index, score	0.19±0.03	1.67 ±0.08*	1.20 ±0.07*◊	1.42 ±0.06*◊	1.51 ±0.05*	1.76 ±0.08*	1.47 ±0.07*◊	1.68 ±0.07*	1.81 ±0.06*	

Note: * — trustworthy as compared with the control group (p<0.05);

 \diamond — trustworthy as compared with the values before treatment (p<0.05).

of subgroup 1.2, who received basic therapy for CGP and ultrasound phonophoresis with placebo, there was a positive changes in oral hygiene according to OHI-S, but this process was less pronounced. So, on the 7th day of treatment, the OHI-S index decreased by 22.1%, on the 14th day — by 27.6% and on the 21st day — only by 33.1% according to the index before treatment (p<0.05). Despite the positive changes, during treatment this indicator in patients of subgroup 1.2 remained increased as compared to the patients of the control group and subgroup 1.1 (table I).

At the same time, a digital decline in all indices of the periodontal tissues state in patients of both subgroups of the main group during treatment was determined. The use of the basic therapy of CGP and developed TPC provided an opportunity to obtain significantly better results in patients of subgroup 1.1: a clear decrease in the values of PI indices by 17.2%, PMA — by 13.9% and MBI — by 13.2% as compared to those before treatment on the 7th day of observations. On the 14th day, the levels of PI, PMA and MBI decreased by 26.4%, 26.7%, 23.4%, correspondingly (p<0.05). And on the 21st day, they reached the lowest values: PI decreased by 36.8%, PMA by 40.8% and MBI by 38.9% against those before treatment (p<0.05). A moderate

positive change of periodontal indices kept up in patients of this subgroup, but at a much lower level as compared with subgroup 1.1 indices. So, on the 7th day of observations, the values of the PI, PMA and MBI decreased by 4%, 13.5% and 9.7%, correspondingly. On th 14th day, PI decreased by 12.6%, PMA — by 18.4% and MBI — by 19.3% as for to pre-treatment values (p<0.05). However, on the 21st day they reached the lowest values: PI decreased by only 15.5%, PMA — by 25.1% and MBI — by 30.1% as compared to baseline at the beginning of treatment (p<0.05) (table I).

The results of long-term clinical observations indicate that patients in subgroup 1.1 who received a prophylactic course, oral hygiene and periodontal tissue condition during one and a half years of observation had significantly better results than at the beginning of treatment. At the same time, the results of clinical observations during 18 months in patients of subgroup 1.2 increased up to baseline at the beginning of treatment, which indicates the preservation of inflammatory and destructive processes in the periodontium (table II).

So, the OHI-S values of patients in subgroup 1.1 in 6, 12, 18 months after the start of treatment were significantly lower by 35.4%, 25.9% and 13.8% correspondingly, as

compared with the indicators before treatment, although there is a tendency to increasing over time (table II). The values of OHI-S patients of 1.2 subgroup only in 6 and 12 months were slightly lower than the value before treatment by 14.6% and 5.5% correspondingly, and in 18 months even exceeded the pre-treatment value by 3.2% (table II).

Periodontal indices of patients of subgroup 1.1 also remained reduced as compared to the beginning of treatment, gradually increasing over 18 months of the follow-up. So, the PI index in 6 months was significantly lower by 31% as compared to the initial data at the beginning of treatment, in 12 months — by 16.7% and in 18 months from the beginning of treatment — by 7.5%. The PMA index in 6 months from the beginning of treatment significantly decreased by 31.2%, in 12 and 18 months — by 22.7% and 12.5% correspondingly. A similar situation was observed with MBI indicators: after 6, 12 and 18 months there was a decrease by 28.1%, 15% and 9.6% correspondingly, as compared to data before treatment (table II).

The study of periodontal indices of the subgroup 1.2 patients showed a gradual increase in indicators to the level of baseline data before treatment. So, the PI index in 6 and 12 months was significantly lower than the initial data at the beginning of treatment by 10.9% and 6.9% correspondingly, and in 18 months almost reached the level of the pre-treatment indicator. The PMA index in 6 months from the beginning of treatment decreased by only 18.6%, in 12 and 18 months — by 12.3% and 8.4%, correspondingly. Determination of MBI showed a tendency to value increasing at the long term follow up period. So, in 6 and 12 months, the index was lower than before treatment by only 16.5% and 4.5% correspondingly, and in 18 months exceeded this value before treatment (table II).

DISCUSSION

The results of the study of oral hygiene and periodontal tissues condition before treatment revealed worsening of the studied indices in the presence of risk factors comorbidity — concomitant gastrointestinal pathology and bad habit smoking. Assessment of the dynamics of changes in the oral hygiene and periodontal tissues condition was performed during treatment on the 7th, 14th and 21st day and at the long term in 6, 12 and 18 months to determine the features of the treatment course and the time term of oral homeostasis improvement by indicators of OHI-S, PMA, PI and MBI.

According to the analysis of the obtained results we assume that application of the proposed set of treatment measures significantly improved oral and periodontal hygiene, reduced inflammation and reduce periodontal indices in tobacco-addicted patients of subgroup 1.1 at the near and long-term follow up period. There was a significant positive change in all dental indices in subgroup 1.1: improvement of the hygienic condition of the oral cavity by preventing microbial contamination of mucous membranes; reduction of PI and PMA indices as indicators of the degree of inflammatory and destructive processes in the periodontium and prevalence of inflammation in the gum tissue; reduction of bleeding, which is associated with improved microcirculation of periodontal tissues and angioprotective effect of TPC. Sanogenic, anti-inflammatory, angioprotective, keratoplastic and regenerative therapeutic effect was achieved due to the synergism of the active components of TPC and physiotherapy of apigel and antidisbiotic drug. The tendency of increasing indicators of the studied indices in patients of subgroup 1.1 at the long-term follow-up can be explained by continuation of the negative impact of smoking on the periodontal tissues, which underlines the importance of smoking cessation in this category of patients.

At the same time, the patients of subgroup 1.2 had lower clinical effect. The results of the indicators of oral hygiene and periodontal tissues condition in these patients during 18 months increased up to the initial data at the beginning of treatment, which is evidence of inflammatory and destructive processes in the periodontium. The obtained negative changes of hygienic and periodontal indices is explained by the continuation of the irritating effect of smoking, a decrease in the body's defense mechanisms and the lack of preventive measures in this category of patients.

CONCLUSIONS

The obtained data testify to the effectiveness of the proposed TPC for treatment and prevention of inflammatory and destructive periodontal diseases in tobacco-addicted patients with CHG, proved by the results of periodontal and hygienic indices in dynamics of short-term and longterm follow-up.

REFERENCES

- 1. Dzampaeva Zh.V. Osobennosti etiologii i patogeneza vospalitel`nykh zabolevanij parodonta [Features of the etiology and pathogenesis of inflammatory periodontal diseases]. Kubanskij nauchny`j mediczinskij vestnik. 2017; 5: 103-110 (In Russian).
- Czepov L.M., Nikolaev A.I., Nesterova M.M. et al. Patogeneticheskie osobennosti formirovaniya khronicheskoj vospalitel`noj patologii parodonta (obzor) [Pathogenetic features of the formation of chronic inflammatory periodontal pathology (review)]. Vestnik Smolenskoj gosudarstvennoj mediczinskoj akademii. 2018; 17(3): 206-214 (In Russian).
- 3. Winn D.M. Tobacco use and oral disease. J. Dent. Educ. 2001; 65(4): 306-312.
- Apatzidou D.A., Riggio M.P., Kinane D.F. Impact of smoking on the clinical, microbiological and immunological parameters of adult patients with periodontitis. J. Clin. Periodontol. 2005; 32 (9): 973-983.
- Ilchyshyn M.P., Furdychko A.I., Barylyak A.Ya. Poshyrenist zakhvoryuvan parodontu sered tyutyunozalezhnykh osib [Prevalence of periodontal diseases among tobacco addicts]. Novyny stomatologiyi. 2018; 4 (97): 86–8 (In Ukranian).
- 6. Al'-Tabib M.M., Gerasimova L.P., Kabirova M.F. et al. Osobennosti stomatologicheskogo statusa u kuryashchih pacientov molodogo vozrasta [Features of dental status in young patients smoking]. Med. vestnik Bashk. 2014; 9 (1): 57-60 (In Russian).
- Goncharuk L.V., Kosenko K.N., Goncharuk S.F. Vzaimosvyaz vospalitelnykh zabolevaniy parodonta i somaticheskoy patolohii [Relationship between inflammatory periodontal disease and somatic pathology]. Sovremennaya stomatolohiya. 2011; 1:37–40 (In Russian).

- Manashchuk N.V., Chorniy N.V., Shmanko V.V. Vzayemozv'yazok patologiyi parodonta ta patologiyi shlunkovo kyshkovogo traktu [Relationship between periodontal pathology and gastrointestinal pathology]. Klinichna stomatologiya. 2011; 1 (2): 23-27 (In Ukranian).
- Matviychuk Kh.B. Parodontalnyi status u khvorykh na vyrazkovu khvorobu shlunka i dvanadtsyatypaloyi kyshky [Periodontal status in patients with peptic ulcer of the stomach and duodenum]. Aktualni pytannya stomatologiyi sogodennya. 2010; 1: 11-12 (In Ukranian).
- Osipova YU.L., Bulkina N.V., Tokmakova E.V. et al. Patogeneticheskaya vzaimosvyaz'vospalitel'nyh zabolevanij parodonta s gastroehzofageal'noj reflyuksnoj bolezn'yu [Pathogenetic relationship of inflammatory periodontal diseases with gastroesophageal reflux disease]. Fundamental'nye issledovaniya. 2015;1(7):1397–1400 (In Russian).
- 11. Golub`, A.A., Chemikosova T.S., Gulyaeva O.A. Vliyanie kureniya i nalichiya somaticheskoj patologii na sostoyanie slizistoj obolochki polosti rta [The effect of smoking and the presence of somatic pathology on the condition of the oral mucosa]. Parodontologiya. 2011; 16(3): 66-69 (In Russian).
- Dvulit I.P. Aktualnist zastosuvannia fitopreparativ yak likuvalnoprofilaktychnykh zasobiv u parodontolohichnykh khvorykh [The relevance of the use of phytopreparations as therapeutic and prophylactic agents in periodontal patients]. Klinichna stomatolohiia. 2016; 2: 8-13 (In Ukranian).
- 13. Bruschi M., Lara E., Martins C. et al. Preparation and antimicrobial activity of gelatin microparticles containing propolis against oral pathogens. Drug. Dev. Ind. Pharm. 2006; 32 (2): 229-238.
- 14. Haybullina R.R., Gilmutdinova L.T., Gerasimova L.P. et al. Primenenie fonoforeza s propolisom na etapah reabilitatsii patsientov s hronicheskim generalizovannyim parodontitom [The use of phonophoresis with propolisom at the stages of rehabilitation of patients with chronic generalized periodontitis]. Sovremennyie naukoemkie tehnologii. 2012; 9: 72-75 (In Russian).
- Danilevskiy N.F., Borisenko A.V. Zabolevaniya parodonta [Periodontal Disease]. Kyyiv: Zdorov'ya. 2000: 462. (In Russian).
- 16. Kravchenko L.S., vynakhidnyk; Odeskyy natsionalnyy medychnyy universytet, patentovlasnyk. Gel «Apisan» dlya mistsevoho likuvannya ta profilaktyky travmatychnykh urazhen slyzovoi obolonky porozhnyny rota. Patent Ukrainy №119715. 2017: 10. (In Ukrainian).
- 17. Ostrovskij A.V. Algoritm professional`noj gigieny` polosti rta u licz s vospalitel`ny`mi zabolevaniyami parodonta [The algorithm of professional oral hygiene in individuals with inflammatory periodontal diseases]. Vi`snik stomatologi`yi'. 2013; 4: 135-137 (In Russian).

- Kravchenko L.S., Zolotukhina O.L., Romanova lu.H. vynakhidnyk; Odeskyy natsionalnyy medychnyy universytet, patentovlasnyk. Sposib mistsevokho likuvannia zapalnykh zakhvoriuvan slyzovoi obolonky porozhnyny rota i tkanyn parodontu. Patent Ukrainy №130112. 2018: 26. (In Ukrainian).
- 19. Kravchenko L.S., Romanova Iu.H., Zolotukhina O.L. vynakhidnyk; Odeskyy natsionalnyy medychnyy universytet, patentovlasnyk. Sposib likuvannia zapalnykh zakhvoriuvan tkanyn parodontu ta slyzovoi obolonky porozhnyny rota z elementamy hiperkeratozu v kurtsiv tiutiunu. Patent Ukrainy №121919. 2017:26. (In Ukrainian).

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Conflict of interest:

The Authors declare no conflict of interest.

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