UDC 616.314.17-008.1-053.81-085.242-085.454.122-035
DOI https://doi.org/10.32782/2226-2008-2026-1-12

I. I. Sokolova[1] https://orcid.org/0000-0002-2339-4909
O. V. Garmash[1] https://orcid.org/0000-0001-7935-9371
Yu. O. Slynko[1] https://orcid.org/0000-0002-9718-5202
N. L. Khlystun[2] https://orcid.org/0000-0001-6943-1835

EFFICACY OF HYALURONIC ACID APPLICATION IN PATIENTS WITH PERIODONTITIS DURING THE HYGIENIC PHASE OF TREATMENT

[1] Kharkiv National Medical University, Kharkiv, Ukraine
[2] Dental clinic "Mriya", Kharkiv, Ukraine

UDC 616.314.17-008.1-053.81-085.242-085.454.122-035

I. I. Sokolova[1], O. V. Garmash[1], Yu. O. Slynko[1], N. L. Khlystun[2]

EFFICACY OF HYALURONIC ACID APPLICATION IN PATIENTS WITH PERIODONTITIS DURING THE HYGIENIC PHASE OF TREATMENT

[1] Kharkiv National Medical University, Kharkiv, Ukraine
[2] Dental clinic "Mriya", Kharkiv, Ukraine

Introduction. The problem of treating periodontal diseases, particularly generalized periodontitis, remains relevant worldwide. Therefore, there is still a need to continue the search for new therapeutic approaches for this pathology. In recent years, hyaluronic acid has gained popularity as a treatment modality for periodontal diseases, which supports the ongoing investigation of the efficacy of its various forms.

Objective of the study. To evaluate the clinical effectiveness of locally applied hyaluronic acid in combination with standard therapy during the hygienic phase of treatment for generalized periodontitis in young adults.

Materials and methods. The study included 68 patients aged 26 to 35 years, who were divided into two groups: a main group of 35 individuals and a control group of 33. The assessment of periodontal status in both groups was performed using periodontal tests and by calculating the following indices: the OHI-S index, the PBI bleeding index, the PMA index, the PI index, and the Schiller–Pisarev test. The condition of the periodontal tissues was evaluated before treatment and at 3 days, 2 weeks, and 1 month after treatment.

Results and discussion. The results of the study indicate that the use of hyaluronic acid contributes to a more rapid normalization of the periodontal tests and indices used for the objective assessment of periodontal tissue status during the hygienic phase of treatment of generalized periodontitis. The positive dynamics observed in the PMA and PBI indices, as well as the Schiller-Pisarev test, demonstrate a significant anti-inflammatory and anti-edematous effect of the hyaluronic acid hydrogel on the periodontal tissues, which is capable of stabilizing periodontal tissue condition after initial treatment of generalized periodontitis already within the earliest follow-up periods.

Conclusions. The local application of hyaluronic acid in the form of a hydrogel contributes to significant improvement of periodontal tissue status.

Keywords: periodontitis; topical therapy; hygienic phase; hyaluronic acid; periodontal indices.

УДК 616.314.17-008.1-053.81-085.242-085.454.122-035

І. І. Соколова[1], О. В. Гармаш[1], Ю. О. Слинько[1], Н. Л. Хлистун[2]

ЕФЕКТИВНІСТЬ ЗАСТОСУВАННЯ ГІАЛУРОНОВОЇ КИСЛОТИ У ХВОРИХ НА ПАРОДОНТИТ НА ЕТАПІ ГІГІЄНІЧНОЇ ФАЗИ ЛІКУВАННЯ

[1] Харківський національний медичний університет», Харків, Україна
[2] Стоматологічна клініка «Мрія», Харків, Україна

Статтю присвячено порівняльній оцінці клінічної ефективності місцевого використання гіалуронової кислоти та стандартної терапії на етапі гігієнічної фази лікування генералізованого пародонтиту в осіб молодого віку. До дослідження було залучено 68 пацієнтів у віці від 26 до 35 років, які увійшли до двох груп: основної з 35 осіб та контрольної – з 33. Після проведення маніпуляцій за сучасними протоколами пацієнтам контрольної групи призначено ротові ванночки з 0,12 % розчином хлоргексидину протягом 14 днів, а пацієнтам основної – з 0,025 % розчином гіалуронової кислоти в аналогічному режимі. Отримані результати свідчать, що гіалуронова кислота сприяє більш швидшій нормалізації пародонтальних проб та індексів, що використаних для об'єктивної оцінки стану тканин пародонта на етапі гігієнічної фази лікування генералізованого пародонтиту.

Ключові слова: пародонтит, місцеве лікування, гігієнічна фаза, гіалуронова кислота; пародонтальні індекси.

Introduction

Despite substantial advances in theoretical and clinical dentistry, periodontal diseases remain a significant problem worldwide due to several objective factors, including their high prevalence (about 11 % of the population; the sixth most prevalent disease worldwides) [1], progressive course, limited effectiveness of current therapies, and their marked negative impact on patients' psycho-emotional status and somatic health [2].

In Ukraine, the epidemiologic situation is discouraging. In recent years the number of adults, including young individuals, with generalized periodontitis (GP) has steadily increased [3]. Over the past decade, the prevalence of inflammatory and inflammatory-dystrophic periodontal

diseases among young adults has risen by 15 %. Although this increase is attributable to the initial gingivitis stage, gingivitis is a precursor of periodontitis.

Periodontal diseases are multifactorial, and their pathogenesis is extremely complex. Although the microbial factor is recognized as pivotal in GP etiopathogenesis, antimicrobial therapy combined with calculus removal alone does not prevent further inflammatory-destructive processes in periodontal tissues or achieve stable remission [4; 5].

A wide range of dental care is required for such patients – from various preventive programs and dispensary follow-up to comprehensive multidisciplinary rehabilitation. Nevertheless, dentists, therapists, and periodontists traditionally focus most on local pharmacotherapy of GP, as local treatment can deliver active agents directly to periodontal structures – from soft tissues (gingiva, periodontal ligament) to hard tissues (alveolar bone and cementum).

Accordingly, optimizing local treatment to enhance GP treatment effectiveness in young adults remains an urgent issue in contemporary dentistry.

A reduction in epithelial barrier and defensive functions owing to impaired tight intercellular contacts, facilitating penetration and spread of pathogens and their toxins, plays a certain role in GP pathogenesis [6; 7]. Hyaluronic acid (HA), a natural, non-sulfated glycosaminoglycan, is the principal component of the intercellular matrix and underlies numerous connective-tissue functions: structural integrity, trophic and transport activity, regulation of cellular differentiation, and maintenance of water and plasma protein homeostasis [8; 9]. Stabilizing the intercellular substance and preserving structural and homeostatic integrity may therefore reduce bacterial invasion and modulate the protective effects of HA on periodontal tissues.

In addition, HA supports tissue hydration, cellular resistance to mechanical damage, and bone regeneration, shows high biocompatibility with minimal adverse effects, and even exhibits antibacterial potential, which has attracted considerable interest across medical fields, including dentistry [9–14].

In recent years, HA has gained recognition as an adjuvant for treating chronic inflammatory diseases [15], warranting further evaluation of its various formulations.

Objective. To compare the clinical efficacy of local HA application with standard therapy during the hygienic phase of GP treatment in young adults.

Materials and Methods

Sixty-eight patients aged 26–35 years were enrolled and divided into a study group (n = 35) and a control group (n = 33). Groups were age- and gender-matched (Table 1).

Inclusion criteria were Stage I, Grade A GP (Figure 1) without any treatment in the preceding year; compliance with physicians' recommendations; and consent to attend follow-up visits. Exclusion criteria were decompensated systemic diseases, multiple dental defects and malocclusions, severe uncompensated occlusal anomalies, antibiotic or immunosuppressant use within the past 6 months, allergy to study medications, pregnancy or lactation, and non-compliance or missed visits.

Table 1

Characteristics of groups by age and gender, abs./%

Group	Women		Men		Total
	< 30 years	> 30 years	< 30 years	> 30 years	
Study					
n	8	10	8	9	35
%	22.9	28.5	22.9	25.7	100
Control					
n	8	9	8	8	33
%	24.2	27.4	24.2	24.2	100
Total					
n	16	19	16	17	68
%	23.5	27.9	23.5	25.1	100

The study design is presented in Figure 2.

Fig. 1. Panoramic radiograph of a 32-year-old patient (participant in the study group). Stage I, Grade A generalized periodontitis

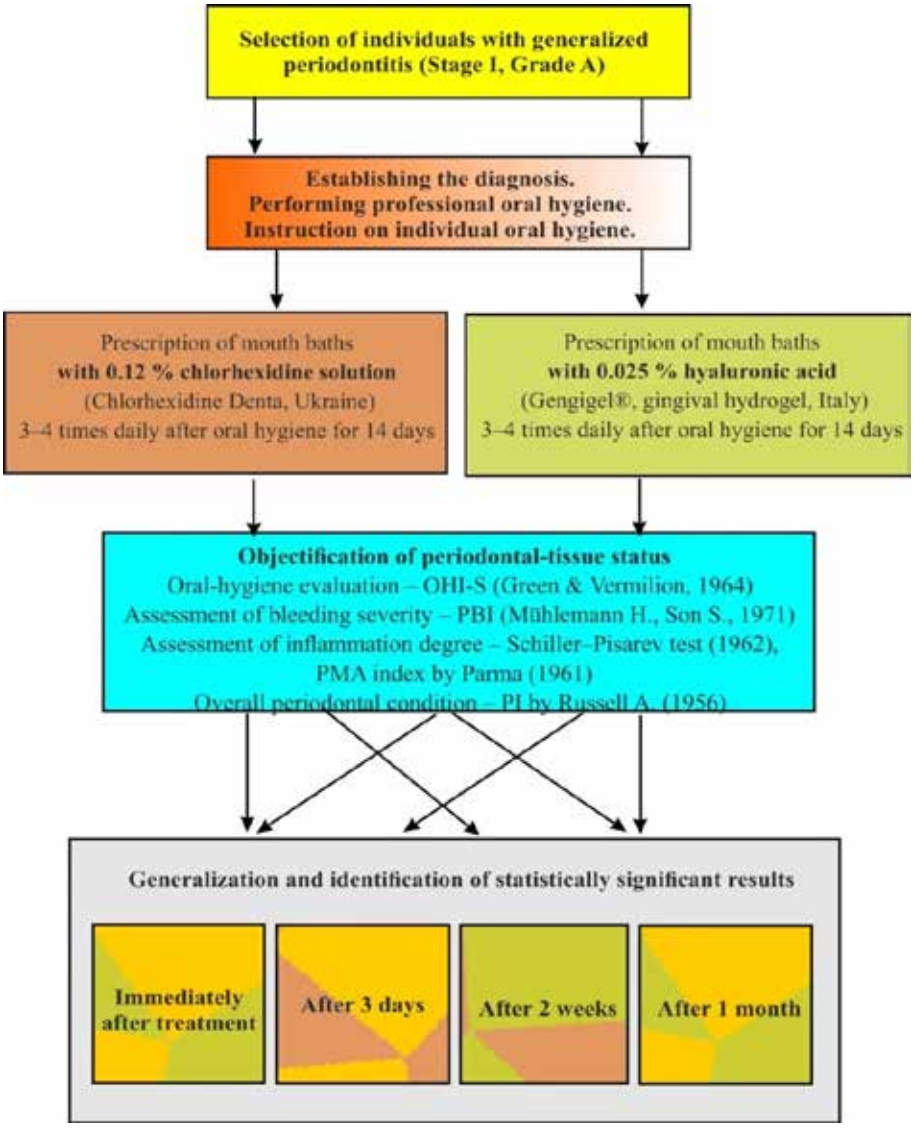

Fig. 2. Study design

All patients provided written informed consent in accordance with the Kharkiv National Medical University Bioethics Committee requirements (minutes No. 6 dated 04.06.2025). Dental Chart No. 043/o and a WHO-recommended individual card were used. The 2017 EFP/AAP periodontal disease classification [16] established the diagnosis.

After diagnosis, supra- and subgingival scaling and root planing (SRP) with biofilm removal via air-abrasive technique were performed. Patients then received individualized oral-hygiene instructions (toothpaste, brush selection, mouth-rinse regimen). The control group patients used 0.12 % chlorhexidine solution (Chlorhexidine Denta, Ukraine) as mouth baths 3–4 times daily for 14 days; the study group patients used 0.025 % HA oral gel (Gengigel®, Italy) on the same schedule. Both solutions were recommended to be held in the oral cavity for 1–2 min (10 mL) with no eating or drinking for 30 min thereafter.

Periodontal status in the control and study groups was assessed using a set of tests and indices: OHI-S (Green & Vermilion, 1964) for oral hygiene; PBI (Mühlemann & Son, 1971) for gingival bleeding; the Schiller–Pisarev iodine test (1962) and PMA index (Parma, 1961) for gingival inflammation; and the PI (Russell, 1956) as an overall periodontal index. Measurements were taken at baseline and after 3 days, 2 weeks, and 1 month. Data were processed using standard statistical methods [17].

Research results and their discussion

During the initial oral examination and evaluation of periodontal tests and indices in the selected cohort of patients with periodontitis, the correctness of group formation was confirmed. Specifically, the values of the OHI-S, PMA, PBI, and PI indices, as well as the Schiller–Pisarev test, showed no statistically significant differences either between the groups or between sexes ($p > 0.05$) (Table 2).

Regarding the dynamics of the analyzed indices, they evolved as follows (Table 2). The OHI-S index, which indicates the state of oral hygiene, had already improved markedly by Day 3 after treatment ($p < 0.01$), despite the presence of some signs of gingival trauma, in both the control group (1.9-fold in women and 1.7-fold in men) and the study group (1.9-fold in women and 1.8-fold in men),

Table 2

The condition of periodontal tissues in patients with GP at the stages of initial treatment (M ± m)

Index	Time point	Women		Men	
		Group			
		control	study	control	study
OHI-S (points)	Before treatment	1.57 ± 0.14	1.58 ± 0.13	1.66 ± 0.12	1.69 ± 0.15
	Day 3	0.81 ± 0.06[1]	0.83 ± 0.05[1]	0.98 ± 0.07[1]	0.93 ± 0.06[1]
	Week 2	0.78 ± 0.04[1]	0.69 ± 0.04[1.2]	0.88 ± 0.05[1]	0.74 ± 0.04[1.2.3]
	Month 1	0.72 ± 0.03[1]	0.58 ± 0.02[1.2.3]	0.84 ± 0.04[1]	0.68 ± 0.03[1.3]
PMA (%)	Before Treatment	54.3 ± 2.3	52.8 ± 2.1	58.7 ± 2.4	59.3 ± 2.5
	Day 3	48.3 ± 2.0[1]	47.2 ± 1.9[1]	51.2 ± 2.2[1]	49.4 ± 2.1[1]
	Week 2	31.4 ± 1.8[1.2]	24.3 ± 1.2[1.2.3]	36.8 ± 1.9[1.2]	28.5 ± 1.4[1.2.3]
	Month 1	25.3 ± 1.3[1.2]	15.4 ± 1.3[1.2.3]	28.7 ± 1.5[1.2]	18.7 ± 1.4[1.2.3]
Schiller –Pisarev test (points)	Before treatment	2.35 ± 0.21	2.41 ± 0.25	2.76 ± 0.28	2.77 ± 0.26
	Day 3	2.03 ± 0.19	1.55 ± 0.15[1.3]	2.28 ± 0.25	1.74 ± 0.15[1.3]
	Week 2	1.47 ± 0.10[1.2]	1.21 ± 0.08[1.2.3]	1.56 ± 0.11[1.2]	1.27 ± 0.09[1.2.3]
	Month 1	1.35 ± 0.07[1]	1.12 ± 0.05[1.3]	1.34 ± 0.08[1]	1.16 ± 0.05[1.3]
PBI (points)	Before treatment	2.45 ± 0.5	2.47 ± 0.16	2.57 ± 0.18	2.59 ± 0.19
	Day 3	2.36 ± 0.13	2.11 ± 0.09[1]	2.27 ± 0.11	2.05 ± 0.08[1]
	Week 2	2.03 ± 0.10[1.2]	1.75 ± 0.09[1.2.3]	1.95 ± 0.07[1.2]	1.76 ± 0.06[1.2.3]
	Month 1	1.53 ± 0.08[1.2]	0.67 ± 0.03[1.2.3]	1.59 ± 0.05[1.2]	0.81 ± 0.04[1.2.3]
PI (points)	Before treatment	1.97 ± 0.39	1.95 ± 0.39	2.09 ± 0.42	2.05 ± 0.41
	Day 3	1.73 ± 0.36	1.64 ± 0.31	1.81 ± 0.38	1.79 ± 0.35
	Week 2	1.52 ± 0.21	1.35 ± 0.16	1.68 ± 0.33	1.48 ± 0.21
	Month 1	1.17 ± 0.11[1]	0.82 ± 0.08[1.2.3]	1.23 ± 0.13[1]	0.91 ± 0.08[1.2.3]

Notes: [1] – $p < 0.05$ vs baseline; [2] – $p < 0.05$ vs previous time point; [3] – $p < 0.05$ vs control group.

which reflects the effectiveness of individualized hygiene instruction. Two weeks after the start of treatment, the trend toward improved oral hygiene persisted in all patients, although it was not as marked as at the previous observation point; nevertheless, statistically significant differences were still evident ($p < 0.05$), and certain distinctive features were noted. Specifically, in the control group the OHI-S index values for both sexes differed significantly from the corresponding pre-treatment values ($p < 0.05$). In the study group, significant differences were recorded both relative to baseline (women $p < 0.05$, men $p < 0.01$) and, for men, relative to the control group ($p < 0.01$). After one month of observation the earlier trends persisted, albeit with further deceleration. In women in the study group, the OHI-S index remained significantly different from its pre-treatment value, from the earlier observation points, 1 and from the control group ($p < 0.05$). In men the same index also showed statistically significant differences compared with the pre-treatment state and with the control group ($p < 0.05$).

The PMA index, which reflects the degree of gingival inflammation, showed a downward trend in all groups of patients with GP. In women of the control group, PMA values fell by 1.1-, 1.5-, and 1.2-fold on Day 3, at 2 weeks, and 1 month after the start of treatment, respectively, whereas in women of the study group the reductions were 1.1-, 1.9- ($p < 0.01$ vs control), and 1.6-fold ($p < 0.05$ vs control), respectively. It should be emphasized that although on Day 3 the dynamics and absolute PMA values were similar between groups ($p > 0.05$), by the 2-week mark a clearly greater decrease in gingival inflammation was evident in the study cohorts – 1.9-fold in women ($p < 0.01$) and 1.7-fold in men ($p < 0.01$) – relative to both sexes in the control group and the preceding observation point. This accelerated normalization of PMA in both sexes in the study group persisted after 1 month: a 1.6-fold reduction in women (versus 1.2-fold in the control group, $p < 0.01$) and a 1.5-fold reduction in men (versus 1.3-fold in the control group, $p < 0.01$).

The Schiller–Pisarev test, which provides information on the presence, intensity, and extent of inflammation, exhibited the following dynamics. Changes in the test values were recorded as early as Day 3 of observation. In the control group the test value decreased 1.2-fold in both women and men relative to baseline ($p > 0.05$), whereas in the study group it declined 1.6-fold in both sexes ($p < 0.05$). It should also be noted that by the first follow-up visit a statistically significant difference between the Schiller–Pisarev test values of the study and control subjects had already been established ($p < 0.01$). Two weeks after the start of treatment, a positive trend toward normalization of gingival status was observed in all patients of both groups, and the Schiller–Pisarev test values differed significantly both from the previous observation point and between groups of the same sex ($p < 0.05$). The decrease in the degree of inflammation persisted one month after initiation of treatment, with a significant difference between the study and the control groups ($p < 0.05$), although without statistical differences relative to the preceding observation time.

An objective indicator of inflammation is the degree of gingival bleeding, quantified by the PBI index. Its dynamics were favorable in all groups by Day 3 of observation, but only in the study group did the change reach statistical significance relative to the pre-treatment value ($p < 0.05$). Two weeks after the start of observation, the values for

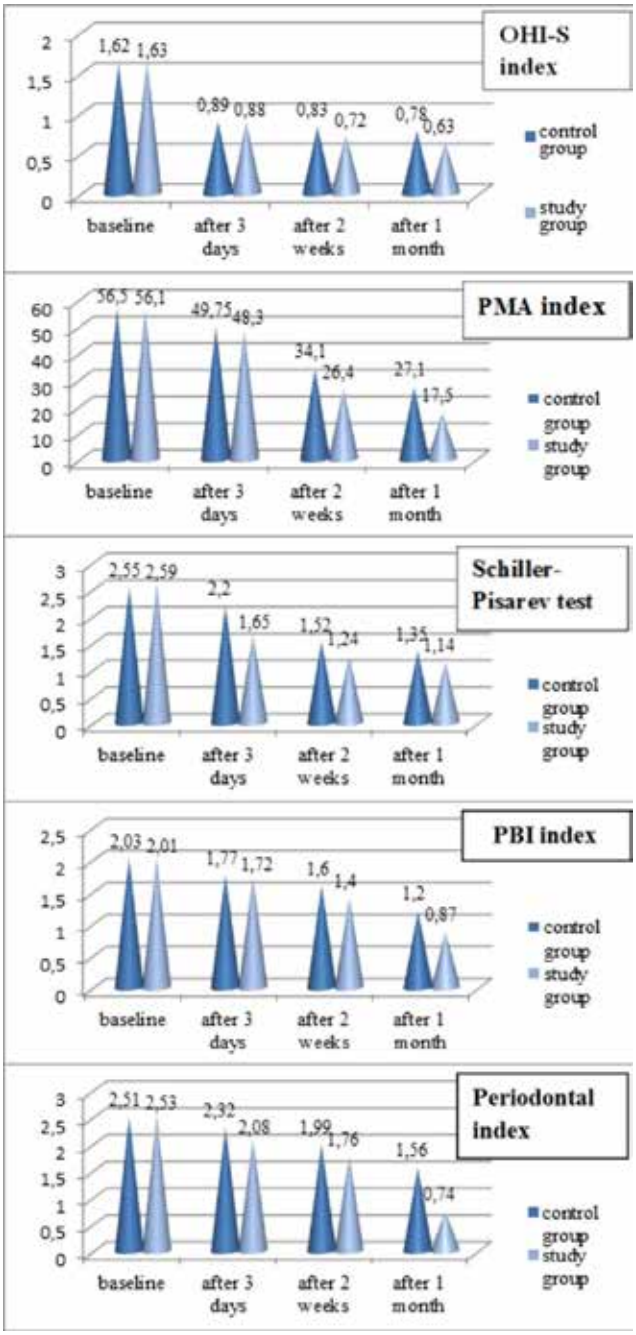

Fig. 3. Dynamics of periodontal tests and indices in individuals of the control and study groups

both sexes in the control group differed significantly from baseline and from the preceding data point, whereas in the study group the improving PBI dynamics were further accompanied by a significant difference from the control group ($p < 0.05$). The same trend was documented one month after treatment initiation: in the control group the PBI values differed significantly from those before treatment for both sexes, at Day 3, and at two weeks ($p < 0.05$), while in the study group, in addition to these differences, a significant disparity versus the control group persisted, with bleeding reduced 2.3-fold in women and 1.9-fold in men ($p < 0.01$).

The periodontal index (PI) provides a comprehensive evaluation of periodontal tissue status. PI values improved progressively at every observation point in the patient cohort, although its dynamics showed certain differences. In women in the control group, PI decreased 1.1-fold (on Day 3 and at 2 weeks) and 1.3-fold one month after the start of treatment. In men in the control group, the reductions were 1.2-fold (Day 3), 1.1-fold (Day 3 and 2 weeks), and 1.4-fold one month after the start of treatment. It should be noted that, in the control group, statistical significance between baseline and post-treatment PI values was recorded only at the final follow-up – 1 month ($p < 0.05$).

In the study group, normalization of periodontal tissues proceeded more rapidly: a 1.2-fold reduction at Day 3 and 2 weeks and a 1.6-fold reduction 1 month after the start of treatment in women, and likewise a 1.2-fold reduction at Day 3 and 2 weeks and a 1.6-fold reduction 1 month after the start of treatment in men. At the last follow-up visit, PI values differed significantly not only from baseline but also from the preceding observations and from the corresponding control-group data ($p < 0.05$–$p < 0.01$).

Visualization of the dynamics of periodontal tests and indices is presented in Figure 3.

Analyzing the obtained results, we can state that HA enabled a more rapid normalization of the periodontal tests and indices chosen for the objective evaluation of periodontal tissue condition during the hygienic phase of generalized periodontitis treatment. The favorable dynamics of the PMA and PBI indices and of the Schiller–Pisarev test indicate a pronounced anti-inflammatory and anti-edematous effect of the hyaluronic-acid hydrogel on periodontal tissues, stabilizing their status soon after the initial therapy. Improvement in the PI index is also indisputable; however, its complete normalization requires a longer follow-up – at least 6-8 weeks – to permit re-epithelial attachment to the root surface.

Participants also reported that the hyaluronic-acid gel was easy to apply and pleasant to use.

Consequently, periodontal diseases, and generalized periodontitis in particular, remain a focal point of active scientific investigation and of practical dental efforts both globally and in Ukraine. Unfortunately, they have not yet been fully brought under control; therefore, the search for optimized treatment protocols for generalized periodontitis is a pressing challenge today.

Over recent decades, considerable experience has been gained regarding the use of HA in the comprehensive treatment of generalized periodontitis. For example, Jentsch H. et al. (2003) and Johannsen A. et al. (2009) reported improvements in the PI index and the bleeding-on-probing index (BOP) after twice-daily topical application of 0.2 % HA for three weeks in patients with periodontitis. Subsequent studies [18; 19] demonstrated that subgingival administration of HA after SRP favorably affected periodontal tissues in generalized periodontitis, reducing the PI and BOP indices as well as periodontal pocket depth. Bertl K. et al. [20] further noted that local use of HA resulted in fewer sites requiring repeat SRP at three months and a higher frequency of pocket closure at 12 months.

Conclusions

1. Topical application of HA in hydrogel form improves periodontal tissue status, as confirmed by the favorable

dynamics of the OHI-S, PMA, PBI, and PI indices and the Schiller–Pisarev test.

2. Incorporating hyaluronic-acid hydrogel into comprehensive therapy for generalized periodontitis provides greater clinical efficacy than standard topical treatment alone.

3. Local use of hyaluronic-acid hydrogel may be recommended during the first, that is, the hygienic phase of generalized periodontitis management.

Future research should focus on studying the effects of HA on the condition of periodontal tissues during the maintenance phase of therapy.

BIBLIOGRAPHY

1. Kwon T, Lamster IB, Levin L. Current concepts in the management of periodontitis. *International Dental Journal*. 2021;71(6):462–476. DOI: 10.1111/idj.12630.
2. Fischer RG, Gomes Filho IS, Cruz SSD, et al. What is the future of periodontal medicine? *Braz Oral Res*. 2021;35(Supp 2):102. DOI: 10.1590/1807-3107bor-2021.vol35.0102.
3. Sluchevska OO, Pavlenko OV, Mochalov YO, Shupyatskyy IM. Deyaki aspekty poshyrenosti tyazhkykh form heneralizovanoho parodontytu sered naselennya Ukrayiny [Some aspects of the prevalence of severe forms of generalized periodontitis in the population of Ukraine]. *Visnyk sotsialnoyi hihiyeny ta orhanizatsiyi okhorony zdorovya Ukrayiny.* 2022;4:19–24. (In Ukrainian). https://doi.org/10.24144/2077-6594.4.1.2022.277066.
4. Elashiry M, Morandini AC, Cornelius Timothius CJ, Ghaly M, Cutler CW. Selective antimicrobial therapies for periodontitis: win the "battle and the war". *Int J Mol Sci*. 2021;22(12):59–64. DOI: 10.3390/ijms22126459.
5. Moshel T, Zaitsev A, Kotelevska N, Boychenko O, Ivanytskyi I. Assessment of the effect of oral hygiene on the course of inflammation in generalized periodontitis. *Eastern Ukrainian Medical Journal.* 2024;12(4):971–977. https://doi.org/10.21272/eumj.2024;12(4):971-977.
6. Sokolova II, Khlystun NL. Likuvalna diya oralnoho helyu z hialuronovoyu kyslotoyu ta kvertsetynom na rotovu porozhnynu u patsiyentiv z hinhivitom [Therapeutic action oral gel with hyaluronic acid and quercetin on the oral cavity for patients with gingivitis]. *Science & Healthcare*. 2015;4(1):441–450. (In Ukrainian). DOI: 10.34689/SH.2015.17.6.011.
7. Balitska OYu, Hasiuk PA, Piasetska LV, Dzetsiukh TI, Vorobets AB, Rosolovska SO. Functional state of the antioxidant defense system in the blood serum of patients with generalized periodontitis and type 2 diabetes mellitus. *Clinical and Preventive Medicine*. 2024;8(38):46–52. https://doi.org/10.31612/2616-4868.8.2024.05.
8. Salwowska NM, Bebenek KA, Żądło DA, Wcisło-Dziadecka DL. Physiochemical properties and application of hyaluronic acid: a systematic review. *J Cosmet Dermatol.* 2016 Dec;15(4):520–526. DOI: 10.1111/jocd.12237.
9. Yakout BK, Kamel FR, Khadr MAEA, Heikal LAH, El-Kimary GI. Efficacy of hyaluronic acid gel and photobiomodulation therapy on wound healing after surgical gingivectomy: a randomized controlled clinical trial. *BMC Oral Health*. 2023 Oct 27;23(1):805. DOI: 10.1186/s12903-023-03519-5.
10. Ostos-Aguilar BI, Pinheiro Furquim C, Muniz FWMG, Faveri M, Meza-Mauricio J. Clinical efficacy of hyaluronic acid in the treatment of periodontal intrabony defect: a systematic review and meta-analysis. *Clin Oral Investig.* 2023 May;27(5):1923–1935. DOI: 10.1007/s00784-022-04855-6.
11. Mansour A, Acharya AB, Alliot C, et al. Hyaluronic acid in Dentoalveolar regeneration: Biological rationale and clinical applications. *J Oral Biol Craniofac Res.* 2024 Mar-Apr;14(2):230–235. DOI: 10.1016/j.jobcr.2024.02.010.
12. Bhati A, Fageeh H, Ibraheem W, Fageeh H, Chopra H, Panda S. Role of hyaluronic acid in periodontal therapy (Review). *Biomed Rep.* 2022 Sep 28;17(5):91. DOI: 10.3892/br.2022.1574.
13. Alshehri FA, Alharbi MS. The Effect of Adjunctive Use of Hyaluronic Acid on Prevalence of Porphyromonas gingivalis in Subgingival Biofilm in Patients with Chronic Periodontitis: A Systematic Review. *Pharmaceutics*. 2023 Jul 4;15(7):1883. DOI: 10.3390/pharmaceutics15071883.
14. Olszewska-Czyz I, Kralik K, Prpic J. Biomolecules in Dental Applications: Randomized, Controlled Clinical Trial Evaluating the Influence of Hyaluronic Acid Adjunctive Therapy on Clinical Parameters of Moderate Periodontitis. *Biomolecules.* 2021 Oct 9;11(10):1491. DOI: 10.3390/biom11101491.
15. Casale M, Moffa A, Vella P, et al. Hyaluronic acid: Perspectives in dentistry. A systematic review. *Int J Immunopathol Pharmacol.* 2016 Dec;29(4):572–582. DOI: 10.1177/0394632016652906.
16. Papapanou PN, Sanz M, Buduneli N, et al. Periodontitis: Consensus report of Workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Clin Periodontol.* 2018;45(Suppl 20):162–170. https://doi.org/10.1111/jcpe.12946.
17. Rohach IM, Keretsman AO, Sitkar AD. Pravylno vybranyy metod statystychnoho analizu – shlyakh do yakisnoyi interpretatsiyi danykh medychnykh doslidzhen [Correct choice of statistical analysis method is the key way to high-quality interpretation of data of medical research]. *Naukovyy visnyk Uzhhorodskoho universytetu, seriya "Medytsyna".* 2017;2(56):124–128 (in Ukrainian). Available from: https://dspace.uzhnu.edu.ua/jspui/handle/lib/31008.
18. Polepalle T, Srinivas M, Swamy N, Aluru S, Chakrapani S, Chawdary BA. Local delivery of hyaluronan 0.8 % as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A clinical and microbiological study. *Journal of Indian Society of Periodontology*. 2015;19:37–42. DOI: 10.4103/0972-124X.145807.
19. Rajan P, Baramappa R, Rao NM, Pavaluri AK, Indeevar P, Rahaman SM. Hyaluronic acid as an adjunct to scaling and root planing in chronic periodontitis. A randomized clinical trial. *Journal of Clinical and Diagnostic Research*. 2014;8:11–14. DOI: 10.7860/JCDR/2014/8848.5237.
20. Bertl K, Vlachou S, Pandis N, Zampelis A, Stavropoulos A. Repeated local delivery of hyaluronic acid gel as adjunctive treatment of residual pockets in periodontitis patients undergoing supportive periodontal care. A randomized controlled clinical trial. *Clin Oral Investig*. 2024 Feb 20;28(2):158. DOI: 10.1007/s00784-024-05505-9.

Надійшла до редакції 10.07.2025.
Прийнята до друку 26.02.2026.
Електронна адреса для листування sdent_irina@ukr.net