

A Nonsurgical Treatment for Early Peri-Implantitis Using Mechanical, Antiseptic and Anti-Inflammatory Treatment

Viktoria Margaryan¹, Anna Khachatryan², Lazar Yessayan³ and Gagik Hakobyan^{4,5*}

¹Assistant Professor, Department of Oral and Maxillofacial Surgery, Yerevan State Medical University, Yerevan, Armenia.

²Associate Professor, Department of Oral and Maxillofacial Surgery, Yerevan State Medical University, Yerevan, Armenia.

³Professor, Head of Department of Therapeutic Stomatology, Yerevan State Medical University, Yerevan, Armenia.

⁴Professor, Head of Department of Oral and Maxillofacial Surgery, Yerevan State Medical University after M. Heratsi, Yerevan, Armenia,

⁵Adjunct Professor, Department of Dental Research Cell, Dr. D. Y. Patil Dental College and Hospital, Dr. D. Y. Patil Vidyapeeth (Pune), Pimpri, Pune, Maharashtra, India.

*Correspondence:

Professor. Gagik Hakobyan, Head of Department of Oral and Maxillofacial Surgery, Yerevan State Medical University, Yerevan, Armenia.

Received: 02 Jan 2025; **Accepted:** 04 Feb 2025; **Published:** 13 Feb 2025

Citation: Viktoria Margaryan, Anna Khachatryan, Lazar Yessayan, Gagik Hakobyan. A Nonsurgical Treatment for Early Peri-Implantitis Using Mechanical, Antiseptic and Anti-Inflammatory Treatment. Oral Health Dental Sci. 2025; 9(1); 1-8.

ABSTRACT

Purpose: The aim of our study is to evaluate the effectiveness of Armenicum paste in the conservative treatment of early peri-implantitis.

Methods: This is a blinded RCT clinical prospective study of 47 patients diagnosed with early peri-implantitis who were treated from 2023 to 2025.

Study population: The patients' age ranged from 32 to 64 years; 25 men and 22 women were included. The diagnosis of peri-implantitis was confirmed taking into account, indicators of bleeding on probing (BOP) > 20%, probing depth (PD) \geq 4 mm, radiological signs of bone loss (MBL) \geq 1 m. The study adheres to the CONSORT guidelines.

According to the selected treatment method, patients were randomly divided into two groups:

Group A (24 patients - 13 men and 11 women), 29 implant treatments included mechanical implant cleaning with titanium or plastic-curets, Air-Flow Perio Soft, irrigation of the circus-pocket with 0.12% chlorhexidine, additional use of local "Armenicum", past 10 days, and systemic antibiotics (amoxicillin 500mg and metronidazole) all the above antibiotics were administered per with duration of 7 days.

Group B (23 patients - 10 men and 13 women), 28 implant treatments included mechanical implant cleaning with titanium or plastic-curets, Air-Flow Perio Soft, irrigation of the circus-pocket with 0.12% chlorhexidine, and systemic antibiotics (amoxicillin 500mg and metronidazole) all the above antibiotics were administered per with duration of 7 days. The patient was under dynamic control, and professional hygiene was carried out.

To assess the effectiveness of treatment, the following clinical parameters were used:

1. Bleeding on probing (BOP);
2. Probing pocket depth (PPD) and both groups had comparable initial results before and after treatment.

Results: At each follow-up visit, biological and technical complications were assessed. There was a reduction in both PPD and BOP compared to baseline clinical measurements. Stable clinical scores of PPD and BOP were demonstrated after 6-month treatment

initiation and remained stable over the next three years. The average BOP value in patients Group A before treatment for peri-implantitis was 2.5 ± 0.31 . after 6 months, treatment month treatment 0.6 ± 0.24 . The mean PPD in patients before treatment of peri-implantitis was 4.2 ± 0.24 , after a 6-month treatment pocket was 3.1 ± 0.1 (table 2). The average BOP value in patients Group B before treatment for peri-implantitis was 2.6 ± 0.42 , after 6 months of treatment, 0.9 ± 0.29 . The mean PPD in patients before treatment of peri-implantitis was 4.1 ± 0.45 , after a 6-month treatment pocket was 3.8 ± 0.18 . The mean BOP and PPD showed a statistically significant difference from baseline to 6 months ($p \leq 0.05$) in both Group A and Group B. however, mean BOP, PPD, the duction gain was found to be greater in Group-A than in Group B ($p \leq 0.05$).

Conclusion: Effective therapy for early peri-implantitis is systemic treatment of peri-implantitis with antibiotics, antiseptic treatment of peri-implant pockets and local application of "Armenicum" paste has shown its effectiveness and can prevent further development of peri-implantitis.

Keywords

Combined therapy peri-implantitis, "Armenicum" paste.

Introduction

Currently, dental implants are the leading and predictable method of prosthetic treatment in patients with complete and partial edentulism, which improves chewing function and quality of life [1-3]. Despite the high effectiveness of implant treatment, various biological and prosthetic complications are recorded at various stages of the implantation process, that can occur from early failures to later stages [4-6]. According to various authors, in patients with implants, perimucositis and peri-implantitis is one of the most common late complications [7,8].

According to the European Federation of Periodontology, perimucositis is defined as an inflammatory lesion of the soft tissues surrounding the implant without involvement of the bone tissue [9]. Perimucositis manifested in the early stage by peri-implant mucosal lesions, which, if not treated in time, can develop into peri-implantitis. Peri-implantitis, is an inflammatory disease of the tissues surrounding osseointegrated dental implants with varying degrees of peri-implant bone loss, increased pocket formation, purulence and characterized by both inflammation and progressive bone loss. A consensus report identified the prevalence (5–10-year period) of peri-implantitis as 28% to 56% of patients and 12% to 40% of implants [10]. Peri-implantitis is caused by a variety of etiologies (Figure1) [11,12].

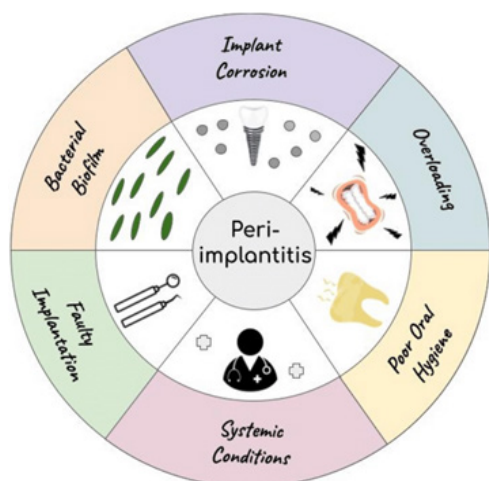


Figure 1: Etiologies of Peri-implantitis.

In most cases, plaque accumulation is the primary cause. It is believed that during implant placement, the oral microflora influences the formation of a biofilm on the implant surface. Scientific data confirm the important role of bacteria in inflammation of the tissues surrounding the implant. In the case of peri-implantitis, the most common microorganisms identified are: Include Staphylococcus epidermidis, Fusobacterium nucleatum, T. denticola, T. forsythia, P. intermedia, and P. gingivalis, but not Aggregatibacter actinomycetemcomitans, Staphylococcus aureus or Campylobacter rectus [13,14]. Pathogenic bacteria present in the periodontal pockets of natural teeth can migrate to the area of the placed implants, therefore the risk of peri-implantitis is particularly high in the case of periodontitis in the oral cavity.

Local Risk factors for peri-implantitis include; (Figure 2) [15-21].

- Poor oral hygiene
- Lack of regular supportive peri-implant care (SPIC).
- Lack of sufficient keratinized gingiva around the implants
- Retention of cement residues in the peri-implant gingival sulcus in case of cement fixation of prostheses to implants.
- Previous diagnosis of periodontitis,

Biomechanical factors include (Figure 2); [22-26].

- occlusal overload associated with irrational prosthetics,
- para-functional habits including bruxism

Smoking, systemic diseases, diabetes mellitus, osteoporosis, long-term treatment with corticosteroids and bisphosphonates, chemotherapy and diabetes are also important in the development of peri-implantitis (Figure 2) [27-30].

Perimucositis is manifested by the following clinical symptoms:

- hyperemia
- hyperplasia in peri-implantation mucosa.
- presence of calculus or stone in the cervical region of the implant.
- bleeding during probing.
- absence of bone resorption radiographically.

Peri-implantitis manifests as follows clinically with symptoms:

- swelling,
- hyperemia,
- hyperplasia in the peri-implant mucosa,
- presence of calculi or stones in the peri-implant area,

- bleeding during probing,
- increased probing depth,
- production of serous or pus from the gum pocket,
- destruction of peri-implant bone tissue,
- bone resorption radiographically.



Figure 2: Risk factors for peri-implantitis.

In the absence of appropriate treatment of peri-implantitis, ultimately leading to its disintegration and subsequent loss of the implant. There are various models for classifying peri-implantitis [31]. The most widely accepted is the Froum classification model (Froum and Rosen, 2012), where the assessment indicators include:

- bleeding on probing (BOP),
- peri-implant pocket depth (PD),
- degree of peri-implant bone loss (bone loss).

The classification of peri-implantitis into 3 categories according to Froum & Rosen (2012): [32]

- Early peri-implantitis - PD \geq 4 mm, BOP+, bone loss <25
- Moderate peri-implantitis - PD \geq 6 mm, BOP+, bone loss 25%-50%
- Advanced peri-implantitis - PD \geq 8 mm, BOP+, bone loss >50%

Treatment of peri-implantitis includes conservative or surgical methods (Figure 3).

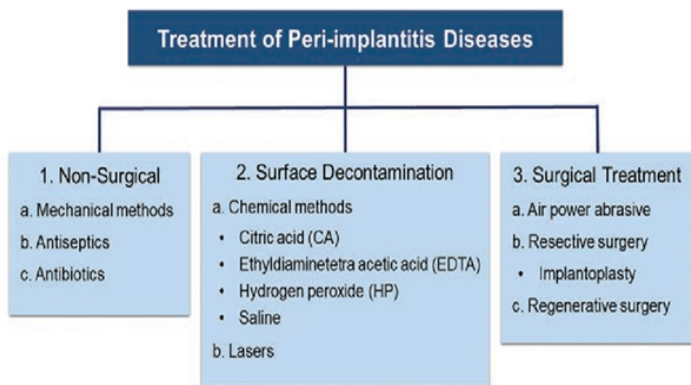


Figure 3: Treatment methods of peri-implantitis.

When developing a treatment strategy for peri-implantitis, the degree of peri-implantitis should be taken into account.

General clinical principles of peri-implantitis treatment;

- Elimination of infectious factors.
- Sanitation of the implant surface, removal of hard and soft deposits.
- Surgical or non-surgical methods of mechanical and chemical cleaning of the implant surface.
- Reduction of the depth of the gingival pockets in areas where they are not of aesthetic importance (resective method).
- Surgical interventions aimed at restoring lost tissues in the area of intraosseous defects (regenerative method).

Currently, there are various treatment protocols for peri-implantitis: conservative methods (chemotherapeutic disinfection, use of antibacterial agents, laser therapy) [33-39]. Conservative therapy for peri-implantitis includes mechanical debridement with plastic curettes, subgingival air-polishing devices, combined with antiseptic and/or antibiotic agents.

Recommended decontamination of the implant using a variety of mechanical and chemical methods (Citric Acid, Ethylenediaminetetraacetic Acid (EDTA), Hydrogen Peroxide (HP), Saline), 0.12% chlorhexidine, 3% hydrogen peroxide), local Atridox gel (doxycycline hyclate 10%), Elyzol gel (25% metronidazole), Periochip (chlorhexidine gluconate), then adjunctive systematic antibiotics, Simulated Radiation Emission (lasers), and oral hygiene instruction [40-46].

Some authors have also successfully used laser therapy, ozone therapy and platelet-rich plasma in the therapy of peri-implantitis [47-52]. Surgical treatment includes a variety of methods (resection and regenerative) treatment by filling the intraosseous peri-implant defect with bone graft material and absorbable membranes [53-55]. During restorative treatment, after removal of pathological tissues and antiseptic dressing, the peri-implant ossification defect is repaired with bone graft material and absorbable membranes [56,57].

Resective surgery, which removes bony ledges and flattens the bone irregularities around the implant [58,59]. Implantoplasty, where the threads on the screw of the implant are removed to leave a polished implant surface. However, no standard treatment protocol has yet been proposed that could lead to improved outcomes. All methods are effective to varying degrees, but so far no universal standard treatment method has been proposed that would be completely effective, which requires a search for new treatment methods. The strategy for choosing treatment measures for peri-implantitis and their effectiveness continues to be a subject of discussion, which makes scientific work in this direction relevant. In the conservative treatment of peri-implantitis, it is advisable to include antibacterial, local immunostimulating drugs which have anti-inflammatory and antimicrobial properties. According to the data of our previous study, taking into account the effectiveness of

local application of Armenicum paste in the complex treatment of patients with periodontitis, we considered it appropriate to include it in this study [60].

Preparation "Armenicum" pharmaceutical composition contains iodine, alpha-dextrin in concentration with organic compounds. "Armenicum" paste has antibacterial and antiviral activity, acts as an antioxidant at the site of infection and inflammation. "Armenicum" paste enhances tissue regeneration, wound healing, stimulates fibroblast migration and cell proliferation [61-64].

The mechanisms of this action of "Armenicum" are based on enhancing the intracellular death of bacteria in the body in the phagolysosomes of neutrophils and monocytes, stimulating the release of several endogenous antimicrobial substances, including intermediate products of the active form of oxygen, nitric oxide and the so-called halides [65-67].

The aim of our study is to evaluate the effectiveness of Armenicum paste in the conservative treatment of early peri-implantitis.

Methods

Study Design

This is a blinded RCT clinical prospective study of 47 patients diagnosed with early peri-implantitis according to the classification of Froum & Rosen (2012) who were treated from 2023 to 2025.

Study Population

The patients' age ranged from 32 to 64 years; 25 men and 22 women were included. The diagnosis of periimplantitis was confirmed taking into account, indicators of bleeding on probing (BOP) > 20%, probing depth (PD) \geq 4mm, radiological signs of bone loss (MBL) \geq 1m.

Assortment of Patients

All patients selected for study were examined under the inclusion and exclusion criteria and sign the written consent.

Inclusion criteria

Patients diagnosed with early peri-implantitis, non-smokers, systemically healthy, had not received any previous peri-implantitis treatment (within the previous year) no any antibiotic therapy or chemotherapeutic mouth-rinse or oral irrigation (within the last 6 months), were included. Patients who can perform oral hygiene selfcare and commitment to post-treatment follow-up visits were chosen.

Exclusion criteria

Patients with systemic diseases, smokers, pregnant females, previous peri-implantitis treatment (during the previous year) or antibiotic intake (during the past 3 months), were excluded.

Randomization, Blinding and Treatment Allocation

Patients are assigned randomization to the 2 intervention groups known only to the principal investigator, who is not involved in

the measurement. The study adheres to the CONSORT guidelines (Table 1).

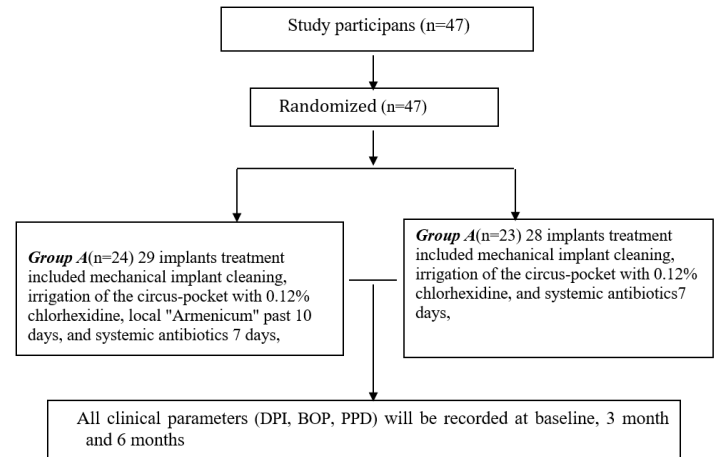


Table 1: CONSORT Study participants.

According to the selected treatment method, patients were randomly divided into two groups:

Group A (24 patients - 13 men and 11 women), 29 implants treatment included mechanical implant cleaning with titanium or plastic-curettes, Air-Flow Perio Soft, irrigation of the circus-pocket with 0.12% chlorhexidine, additional use of local "Armenicum" past 10 days, and systemic antibiotics (amoxicillin 500mg and metronidazole) all the above antibiotics were administered per with duration of 7 days.

"Armenicum" paste a commercially available product (manufacturing company ARMENIKUM, CJSC Armenia) in one syringe paste 25 g.

Group B (23 patients - 10 men and 13 women), 28 implants treatment included mechanical implant cleaning with titanium or plastic-curettes, Air-Flow Perio Soft, irrigation of the circus-pocket with 0.12% chlorhexidine, and systemic antibiotics (amoxicillin 500mg and metronidazole) all the above antibiotics were administered per with duration of 7 days. The patient was under dynamic control, and professional hygiene was carried out.

To assess the effectiveness of treatment, the following clinical parameters were assessed:

1. bleeding on probing (BOP);
2. probing pocket depth (PPD) and both groups had comparable initial results before and after treatment.

Statistical Analyzes

Performed using SPSS software for Windows, Version 29.0.0.0 (SPSS Inc, Chicago). The average values for the BOP, PPD, per implants were calculated. Significance level $P < 0.05$ was used to determine the significant differences between implants A, B groups.

Results

At each follow-up visit, biological and technical complications were assessed. There was a reduction in both PPD and BOP compared to baseline clinical measurements. Stable clinical scores of PPD and BOP were demonstrated after 6-month treatment initiation and remained stable over the next three years.

The average BOP value in patients Group A before treatment for peri-implantitis was 2.5 ± 0.31 of 6 months, treatment month treatment 0.6 ± 0.24 . The mean PPD in patients before treatment of peri-implantitis was 4.2 ± 0.24 , after a 6-month treatment pocket was 3.1 ± 0.1 . The average BOP value in patients Group B before treatment for peri-implantitis was 2.6 ± 0.42 of 6 months, treatment month treatment 0.9 ± 0.29 . The mean PPD in patients before treatment of peri-implantitis was 4.1 ± 0.45 , after a 6-month treatment pocket was 3.8 ± 0.18 . The mean BOP, PPD showed a statistically significant difference from baseline to 6 months ($p \leq 0.05$) in both Group A and Group B however, mean BOP, PPD, duction gain was found to be greater in Group-A than Group B ($p \leq 0.05$) (Table 2).

Table 2: Average Mean Clinical Indices at Baseline and After 6 months BOP, PPD in Patients Group-A, B.

Clinical indices	Baseline	6 months	p-value
Group A (n=24) 29 implants			
BOP	2.5 ± 0.31	0.6 ± 0.24	<0.05
PPD	4.2 ± 0.24	3.1 ± 0.1	<0.05
Group B (n=23), 28 implants			
BOP	2.6 ± 0.42	0.9 ± 0.29	<0.05
PPD	4.1 ± 0.45	3.8 ± 0.18	<0.05

*significant difference $p < 0.05$

Discussion

A number of protocols have been suggested for the treatment of peri-implantitis including various conservative (antibacterial pastes, emulsions) lasers for therapy and surgical treatments, but none of them is universal [68-70].

According to Schwartz et al., in the case of superficial peri-implant lesions, mechanical treatment and irrigation with an antiseptic solution (0.2% chlorhexidine solution) are recommended, leading to a statistically significant improvement in probing pocket bleeding around the implants [71]. Anca Silvia Dumitri et al. in their study documented the effectiveness of mechanical treatment and the use of chlorhexidine in reducing inflammation [72]. According to Yaniv Mayer et al., adjunctive treatment with local antiseptic and anti-inflammatory agents during the mechanical phase has a positive effect on reducing peri-implant inflammation [73]. Research results by André Büchter et al. have shown that the local use of Atridox gel (doxycycline hyclate 10%), in the treatment of peri-implantitis significantly improved clinical indices [74].

Research results E Stellani's have shown that metronidazole dental gel 25% topical antibiotic application is effective in the peri-implant treatment complex [75]. There are also works by many other authors who have presented various conservative treatment protocols for the treatment of periimplantitis [76-82]. Thus, for the

prevention and treatment of peri-implantitis, it is necessary to take an integrated approach and use drugs that can have a professional inflammatory effect, enhance tissue regeneration and increase local immunity. Taking into account the results obtained by the above-mentioned authors, we have included Armenicum paste in the peri-implantitis treatment complex in our work, taking into account the antioxidant, antibacterial and regenerative properties of this preparation and its demonstrated effectiveness in the treatment of periodontitis. "Armenicum" belongs to the group of physiologically active polymers (FAP) of the "grafting type", since it predominantly exhibits the properties of such a physiologically active substance as iodine [83].

This study describes clinical results of a non-surgical treatment of peri-implantitis. The success of the treatment method used in this study was assessed by objective clinical indices such as PPD and BOP; Significant clinical stabilization, statistically significant reductions in indices were recorded in the group of patients where the treatment protocol included mechanical cleaning of the implants, irrigation of the periapical pocket with 0.12% chlorhexidine, local "Armenicum" paste and additional use of systemic antibiotics. Hygienists play an important role in post-implant therapy, as they are the first responders. They must detect any signs of inflammation around the implant. But their role is primarily to educate patients that biofilm is a major risk factor for peri-implant disease. Long-term success of peri-implant treatment requires a maintenance program, including hygiene instructions. The limitation of this study is due to the number of implants and the lack of long-term clinical follow-up, which dictates that further work should be conducted with a larger number of patients and longer-term observation of treatment outcomes.

Conclusion

Conservative treatment with systemic antibiotics, pocket elimination and local use of "Armenicum" paste was an effective therapy in early periimplantitis.

References

- Duong HY, Rocuzzo A, Stähli A, et al. Oral health-related quality of life of patients rehabilitated with fixed and removable implant-supported dental prostheses. *Periodontol* 2000. 2022; 88: 201-237.
- Tzerbos F, Sykaras N, Tzoras V. Restoration-guided implant rehabilitation of the complex partial edentulism: a clinical report. *J Oral Maxillofac Res*. 2010; 1: 8.
- Velasco Ortega E, del Rocío Jiménez-Martin I, Moreno Muñoz J, et al. Long-Term Treatment Outcomes of Implant Prostheses in Partially and Totally Edentulous Patients. *Materials*. 2022; 15: 4910.
- Sakka S, Baroudi K, Nassani MZ. Factors associated with early and late failure of dental implants. *J Investig Clin Dent*. 2012; 3: 258-261.
- Kochar SP, Reche A, Paul P. The Etiology and Management of Dental Implant Failure: A Review. *Cureus*. 2022; 14: 30455.

6. Sakka S, Baroudi K, Nassani MZ. Factors associated with early and late failure of dental implants. *J Investig Clin Dent*. 2012; 3: 258-261.
7. Schwarz F, Derks J, Monje A, et al. Peri-implantitis. *J Clin Periodontol*. 2018; 89: 246-266.
8. Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. *J Clin Periodontol*. 2015; 42: 158-171.
9. Heitz Mayfield LJA, Salvi GE. Peri-implant mucositis. *J Clin Periodontol*. 2018; 45: 237-245.
10. Berglundh T, Armitage G, Araujo MG, et al. Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Clin Periodontol*. 2018; 20: 286-291.
11. Khammissa RA, Feller L, Meyerov R, et al. Peri-implant mucositis and peri-implantitis: clinical and histopathological characteristics and treatment. *SADJ*. 2012; 67: 124-126.
12. Fragkioudakis I, Tseleki G, Doufexi AE, et al. Current Concepts on the Pathogenesis of Peri-implantitis: A Narrative Review. *Eur J Dent*. 2021; 15: 379-387.
13. Carvalho ÉBS, Romandini M, Sadilina S, et al. Microbiota associated with peri-implantitis-A systematic review with meta-analyses. *Clin Oral Implants Res*. 2023; 34: 1176-1187.
14. Săndulescu M, Sîrbu VD, Popovici IA. Bacterial species associated with peri-implant disease – a literature review. *Germes*. 2023; 13: 352-361.
15. Rokaya D, Srimaneepong V, Wisitrasameewon W, et al. Peri-implantitis Update: Risk Indicators, Diagnosis, and Treatment. *Eur J Dent*. 2020; 14: 672-682.
16. Monje A, Aranda L, Diaz KT, et al. Impact of maintenance therapy for the prevention of peri-implant diseases: a systematic review and meta-analysis. *J Dent Res*. 2016; 95: 372-379.
17. Hashim D, Cionca N. A Comprehensive Review of Peri-implantitis Risk Factors. *Curr Oral Health Rep*. 2020; 7: 262-273.
18. Frisch E, Ziebolz D, Vach K, et al. The effect of keratinized mucosa width on peri-implant outcome under supportive postimplant therapy. *Clin Implant Dent Relat Res*. 2015; 17: 236-244.
19. Pimentel SP, Shiota R, Cirano FR, et al. Occurrence of peri-implant diseases and risk indicators at the patient and implant levels: a multilevel cross-sectional study. *J Periodontol*. 2018; 89: 1091-1100.
20. Quaranta A, Lim ZW, Tang J, et al. The impact of residual subgingival cement on biological complications around dental implants: a systematic review. *Implant Dent*. 2017; 26: 465-474.
21. Staubli N, Walter C, Schmidt JC, et al. Excess cement and the risk of peri-implant disease-a systematic review. *Clin Oral Implants Res*. 2017; 28: 1278-1290.
22. Miyata T, Kobayashi Y, Araki H, et al. The influence of controlled occlusal overload on peri-implant tissue: a histologic study in monkeys. *Int J Oral Maxillofac Implants*. 1998; 13: 677-683.
23. Heitz Mayfield LJ, Schmid B, Weigel C, et al. Does excessive occlusal load affect osseointegration? An experimental study in the dog. *Clin Oral Implants Res*. 2004; 15: 259-268.
24. Lee SJ, Alamri O, Cao H, et al. Occlusion as a predisposing factor for peri-implant disease: A review article. *Clin Implant Dent Relat Res*. 2023; 25: 734-742.
25. Rokaya D, Srimaneepong V, Wisitrasameewon W, et al. Peri-implantitis Update: Risk Indicators, Diagnosis, and Treatment. *Eur J Dent*. 2020; 14: 672-682.
26. Ceresuela P, Montero J. Biomechanical Factors in the Prognosis of Implants: A Clinical Study. *Prosthesis*. 2024; 6: 896-912.
27. Dutta SR, Passi D, Singh P, et al. Risks and complications associated with dental implant failure: Critical update. *Natl J Maxillofac Surg*. 2020; 11: 14-19.
28. Farronato Davide, Lorenzo Azzi, Luca Giboli, et al. Impact of Smoking Habit on Peri-Implant Indicators following Different Therapies: A Systematic Review. *Bioengineering*. 2022; 9: 569.
29. Sachelarie L, Scrobota I, Cioara F, et al. The Influence of Osteoporosis and Diabetes on Dental Implant Stability: A Pilot Study. *Medicina*. 2025; 61: 74.
30. Dioguardi M, Cantore S, Quarta C, et al. Correlation between Diabetes Mellitus and Peri-implantitis: A Systematic Review. *Endocr Metab Immune Disord Drug Targets*. 2023; 23: 596-608.
31. Tallarico M, Canullo L, Wang HL, et al. Classification Systems for peri-implantitis: a narrative review with a proposal of a new evidence-based etiology codification. *Int J Oral Maxillofac Implants*. 2018; 33: 871-879.
32. Froum SJ, Rosen PS. A proposed classification for peri-implantitis. *Int J Periodontics Restorative Dent*. 2012; 32: 533-540.
33. Monje A, Aranda L, Diaz KT, et al. Impact of maintenance therapy for the prevention of peri-implant diseases: a systematic review and meta-analysis. *J Dent Res*. 2016; 95: 372-379.
34. Frisch E, Ratka Krüger P. A new technique for peri-implant recession treatment: Partially epithelialized connective tissue grafts. Description of the technique and preliminary results of a case series. *Clin Implant Dent Relat Res*. 2020; 22: 403-408.
35. Prathapachandran J, Suresh N. Management of peri-implantitis. *Dent Res J (Isfahan)*. 2012; 9: 516-521.
36. Nguyen Hieu T, Borghetti A, Aboudharam G. Peri-implantitis: from diagnosis to therapeutics. *J Investig Clin Dent*. 2012; 3: 79-94.
37. Hakobyan G. Comparative assessment of conservative and surgical treatment methods of peri-implantitis. *SciTz Dentistry: Research amp Therapy*. 2017; 2: 1-10.

38. Hakobyan G. Comparative assessment of conservative and surgical treatment methods of peri-implantitis. *SciTz Dentistry: Research amp Therapy*. 2017; 2: 1-10.
39. Hakobyan G. Regenerative therapy for the treatment of periimplantitis. *Modern dentistry*. 2021.
40. Sivaramakrishnan G, Sridharan K. Photodynamic therapy for the treatment of peri-implant diseases: a network meta-analysis of randomized controlled trials. *Photodiagnosis Photodyn Ther*. 2018; 21: 1-9.
41. Frizzera F, Oliveira GJPL, Shibli JA, et al. Treatment of peri-implant soft tissue defects: a narrative review. *Braz Oral Res*. 2019; 33: 73.
42. Fickl S. Peri-implant mucosal recession: Clinical significance and therapeutic opportunities. *Quintessence Int*. 2015; 46: 671-676.
43. Cheng J, Chen L, Tao X, et al. Efficacy of surgical methods for peri-implantitis: a systematic review and network meta-analysis. *BMC Oral Health*. 2023; 23: 227.
44. Daugela P, Cicciù M, Saulacic N. Surgical Regenerative Treatments for Peri-Implantitis: Meta-analysis of Recent Findings in a Systematic Literature Review. *J Oral Maxillofac Res*. 2016; 7: 15.
45. Ting M, Alluri LSC, Sulewski JG, et al. Laser Treatment of Peri-Implantitis: A Systematic Review of Radiographic Outcomes. *Dent J (Basel)*. 2022; 10: 20.
46. Butera A, Gallo S, Pascadopoli M, et al. Ozonized Water Administration in Peri-Implant Mucositis Sites: A Randomized Clinical Trial. *Applied Sciences*. 2021; 11: 7812.
47. Sila Cagri Isler, Berrin Unsal, Fatma Soysal, et al. The effects of ozone therapy as an adjunct to the surgical treatment of peri-implantitis. *J Periodontal Implant Sci*. 2018; 48: 136-151.
48. Deppe H, Horch HH, Neff A. Conventional versus CO2 laser-assisted treatment of peri-implant defects with the concomitant use of pure-phase beta-tricalcium phosphate: a 5-year clinical report. *Int J Oral Maxillofac Implants*. 2007; 22: 79-86.
49. Isler SC, Unsal B, Soysal F, et al. The effects of ozone therapy as an adjunct to the surgical treatment of peri-implantitis. *J Periodontal Implant Sci*. 2018; 48: 136-151.
50. Karaca IR, Ergun G, Ozturk DN. Is Low-level laser therapy and gaseous ozone application effective on osseointegration of immediately loaded implants? *Niger J Clin Pract*. 2018; 21: 703-710.
51. Özalp Ö, Göksu O, Toru HS, et al. Comparing the effects of low-level laser therapy and gaseous ozone as a preventive measure on medication-related osteonecrosis of the jaws following tooth extraction: a rat model. *Eur J Med Res*. 2024; 29: 359.
52. Pisano M, Amato A, Sammartino P, et al. Laser Therapy in the Treatment of Peri-Implantitis: State-of-the-Art, Literature Review and Meta-Analysis. *Applied Sciences*. 2021; 11: 5290.
53. Matys J, Jaszczak E, Fliieger R, et al. Effect of ozone and diode laser (635 nm) in reducing orthodontic pain in the maxillary arch—a randomized clinical controlled trial. *Lasers Med Sci*. 2020; 35: 487-496.
54. Roos Jansåker AM, Persson GR, Lindahl C, et al. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a 5-year follow-up. *J Clin Periodontol*. 2014; 41: 1108-1114.
55. Daugela P, Cicciù M, Saulacic N. Surgical regenerative treatments for peri-implantitis: Meta-analysis of recent findings in a systematic literature review. *J Oral Maxillofac Res*. 2016; 7: 15.
56. Schwarz F, Sahn N, Bieling K, et al. Surgical regenerative treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane: a four-year clinical follow-up report. *J Clin Periodontol*. 2009; 36: 807-814.
57. Renvert S, Polyzois I, Claffey N. Surgical therapy for the control of peri-implantitis. *Clin Oral Implants Res*. 2012; 23: 84-94.
58. Daugela P, Cicciù M, Saulacic N. Surgical Regenerative Treatments for Peri-Implantitis: Meta-analysis of Recent Findings in a Systematic Literature Review. *J Oral Maxillofac Res*. 2016; 7: 15.
59. Roos Jansåker AM, Renvert H, Lindahl C, et al. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a prospective cohort study. *J Clin Periodontol*. 2007; 34: 625-632.
60. Romanos GE, Nentwig GH. Regenerative therapy of deep peri-implant infrabony defects after CO2 laser implant surface decontamination. *Int J Periodontics Restorative Dent*. 2008; 28: 245-255.
61. Margaryan V, Aghasyan E, Yessayan L, et al. Adjunctive therapea - a promising method in the treatment of periodontal disease. *Clin Oral Investig*. 2025; 29: 78.
62. Davtyan TK, Mkrtychyan NR, Manukyan HM, et al. Dexamethasone, colchicine and iodine-lithium-a-dextrin act differentially on the oxidative burst and endotoxin tolerance induction in vitro in patients with Behçet's disease. *Int Immunopharmacol*. 2006; 6: 396-407.
63. Davtyan TK, Hakobyan IS, Muradyan RE, et al. Evaluation of amino acids as mediators for the antibacterial activity of iodine-lithium-a-dextrin in vitro and in vivo. *J Antimicrob Chemother*. 2007; 59: 1114-1122.
64. Ghazaryan A, Avagyan S, Topchyan H, et al. Shifts in the content of samatostatin in blood serum of intact rats under experimentally induced wound process with the application of Armenicum drug and paste. *N Armenian Med J*. 2016; 10: 53-56.
65. Zilfyan A, Avagyan S, Ghazaryan A. The Effect of Armenicum Paste on the Course of Wound Process. *Monograf LAB LAMBERT Academic Published*. 2016.
66. Oganyan TG, Galstyan AM, Aleksanyan AZ, et al. The use of the drug «Armenicum» (paste) in the treatment of patients

- with infected wounds and wound surfaces. *Med Sci Armenia NAS RA LVI*. 2016.
67. Kazaryan AV, Akopyan IS, Topchyan AV, Oganessian AS. Comparative analysis of antibacterial action of preparations for external use containing iodine complexes. *Med Sci Armenia NAS RA Yerevan*. 2010; 3: 90-95.
68. Ghazarayan AV. Fibronectin-dependent mechanisms involved in fibroplastic process activation in aerobic purulent wound under armenicum paste topical treatment. *N Armenian Med J*. 2015; 9: 90-94.
69. Chrcanovic BR, Albrektsson T, Wennerberg A. Diabetes and oral implant failure: a systematic review. *J Dent Res*. 2014; 93: 859-867.
70. Rothwell BR, Richard EL. Diabetes mellitus: medical and dental considerations. *Spec Care Dentist*. 1984; 4: 58-65.
71. Chrcanovic BR, Albrektsson T, Wennerberg A. Diabetes and oral implant failure: a systematic review. *J Dent Res*. 2014; 93: 859-867.
72. Schwarz F, Sculean A, Bieling K, et al. Two year clinical results following treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane. *J Clin Periodontol*. 2008; 35: 80-87.
73. Dumitriu AS, Păunică S, Nicolae XA, et al. The Effectiveness of the Association of Chlorhexidine with Mechanical Treatment of Peri-Implant Mucositis. *Healthcare*. 2023; 11: 1918.
74. Mayer Y, Ginesin O, Horwitz J. A nonsurgical treatment of peri-implantitis using mechanic, antiseptic and anti-inflammatory treatment: 1 year follow-up. *Clin Exp Dent Res*. 2020; 6: 478-485.
75. André Büchter, Ulrich Meyer, Birgit Kruse Lösler, et al. Sustained release of doxycycline for the treatment of peri-implantitis: Randomised controlled trial. *Br J Oral Maxillofac Surg*. 2004; 42: 439-444.
76. Stellini E, Migliorato A, Mazzoleni S, et al. [Topical treatment of peri-implantitis with metronidazole dental gel 25%. Clinical analysis and microbiological control]. *Minerva Stomatol*. 2000; 49: 59-67.
77. Polyzois I. Treatment planning of peri-implant mucositis and peri-implantitis. *Implant Dent*. 2019; 28: 150-154.
78. Wang CW, Renvert S, Wang HL. Nonsurgical treatment of peri-implantitis. *Implant Dent*. 2019; 28: 155-160.
79. Butera A, Maiorani C, Gallo S, et al. Evaluation of Adjuvant Systems in Non-Surgical Peri-Implant Treatment: A Literature Review. *Healthcare*. 2022; 10: 886.
80. Selimović A, Bunæs DF, Lie SA, et al. Non-surgical treatment of peri-implantitis with and without erythritol air-polishing a 12-month randomized controlled trial. *BMC Oral Health*. 2023; 23: 240.
81. Prathapachandran J, Suresh N. Management of peri-implantitis. *Dent Res J (Isfahan)*. 2012; 9: 516-521.
82. Nguyen Hieu T, Borghetti A, Aboudharam G. Peri-implantitis: from diagnosis to therapeutics. *J Investig Clin Dent*. 2012; 3: 79-94.
83. David Herrera, Tord Berglundh, Frank Schwarz, et al. Prevention and treatment of peri-implant diseases-The EFP S3 level clinical practice guideline. *J Clin Periodontol*. 2023; 26: 4-76.
84. Davtyan TK, Hakobyan IS, Muradyan RE, et al. Evaluation of amino acids as mediators for the antibacterial activity of iodine-lithium-a-dextrin in vitro and in vivo. *J Antimicrob Chemother*. 2007; 59: 1114-1122.