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Research Article

Regenerative Therapy for the Treatment of Peri-Implantitis

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Abstract

The purpose of this study is to evaluate the outcome of regenerative therapy of peri-implantitis. The 32 patients involved in this study with inflammatory-destructive processes in the field of peri-implant tissues of osseointegrated implants. The diagnostic parameters used for assessing peri-implantitis include clinical indices, Probing Pocket Depth (PPD), Bleeding On Probing (BOP), peri-implant radiography. 16 implants with peri-implant mucositis, 8 implants with early peri-implantitis and 5 implants with moderate peri-implantitis was treated only conservative treatments methods, 6 implants with early peri-implantitis, 7 implants with moderate peri-implantitis and 4 implants with severe peri-implantitis was treated surgically. PPD and BOP data at the re-examination were retrospectively compared to baseline data.

A statistical significant reduction in both PPD and BOP were seen at all-timepoints as compared with the baseline clinical measurements. Stable clinical measurements PPD and BOP were demonstrated after 1 year the initial treatment, remaining stable during the following three years. Surgical regenerative treatment combined with mechanical and chemical detoxification of the implants' surface, magneto-laser therapy and regenerative therapy using an autologous bone, xenograft, hyaluronic acid and a restorablemembrane a reliable method for stopping and treatment peri-implantitis.

Keywords: Peri-Implantitis; Dental Implant; Regenerative Therapy; Magneto-Laser Therapy; Hyaluronic Acid

Introduction

The use of dental implants has become a common method for treating partial and complete adentia. The recorded long-term results are quite successful, but the implantation process is also not immune from complications [1-3].

Complications after dental implantation can be divided into several groups: complications during implantation, in the early postoperative period, during implant engraftment and late complications of Osseo integrated implants during functional loading [4]. Of the late complications, the most common are peri-implantitis pathology and is represented in two forms: peri-mucositis and peri-implantitis [5, 6]. In the report of the Workshop in Periodontics held in 2008, peri-implant mucositis is defined as a reversible inflammatory response in the soft tissues surrounding the implant. Periimplantitis is an inflammatory and destructive bone disease surrounding the implant, radiologically characterized by a decrease in bone tissue around the implant neck, is clinically manifested by a complex of inflammatory symptoms: bleeding, swelling of the gum, pain sensations, serous purulent discharge and ultimately loss of the implant [7]. The incidence of peri-mucositis and peri-implantitis is a serious problem with regard to the prediction of long-term successful treatment outcomes, and the protocol for their treatment needs to be developed in detail, taking into account the principles of evidence-based medicine. The prevalence of peri-implant disease is still being discussed and varies in different studies. According to the results of world studies, 10-15 % of patients who had implants had a risk of peri-implantitis [8].

The etiopathogenesis of peri-implantitis is complex and includes 3 main factors: microbiological factors, biomechanical factors and factors associated with the patient [9,10].

The microbiological factor plays an important role in the implant installation process, and later, when the implant functions. The most commonly present microorganisms associated with failure of an implant are Gram-negative anaerobes, Prevotella intermedia, Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Bacterioides forsythus, Treponema denticola, Prevotella nigrescens, Peptostreptococcus micros, Fusobacterium nucleatum [11,12].

The formation of biofilms on the surface of the implant plays a significant role in the initiation and development of peri-implant diseases [13]. Periimplantitis as periodontitis occurs mainly as a result of changes in the microflora and immune response of the host. Markers are characteristic for both periodontal pathologies and for severe forms of peri-implantitis represented by a series of interleukins (IL-1, IL-6, IL-8, IL-12, tumor necrosis factor alpha-TNF-α) [14,15]. Biomechanical factors include excessive mechanical stress caused by occlusal overload due to improper bite, para-functional habit i.e. Bruxism. Prosthetic factors include excessive occlusal stress due to irrational prosthetics (resulting in cantilevers in the prosthesis) [16]. Cement left following restoration, mobility of the restorative component, fractured restorative component, can also play a significant role in the development of peri-implantitis [17].

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Factors associated with the patient include systemic diseases, for example, diabetes mellitus, osteoporosis, prolonged treatment of corticosteroids, chemotherapy, history of periodontitis, dental plaque, poor oral hygiene, smoking [18].

Peri-implantitis has been put under three categories depending on the pocket depth and bone loss: early peri-implantitis - bone loss <25% of the implant length, moderate- bone loss <25-50 % of the implant length, severe- bone loss >50% of the implant length [19].

Prevention and treatment of inflammatory processes affecting tissues around the implants is extremely significant, because they are the cause of disintegration and removal of implants.

According to published data, the effectiveness of therapy of peri-implantitis depends on the severity of the disease and the morphology of the lesion.

Peri-implant mucositis is usually treated by non-surgical therapy; it is aimed at eliminating local stimuli of the implant surface with or without surface decontamination.Various methods of influence are proposed, both systemic (antibacterial therapy) and local (use of various medicinal forms of antiseptics and antibiotics), abrasive technique with powder [20,21].

Laser therapy is another method of treatment for decontamination of implant surfaces and peri-implant tissues. The diode laser, carbon dioxide (CO_2) and ErbiumYttrium, Aluminum, Garnet (Er: YAG) lasers are suitable for irradiating the implant surface because of their bactericidal effects if they are used within the appropriate parameters [22,23].

Treatment of peri-implantitis may include non-surgical and surgical methods, either alone or together. The goals of peri-implantitis therapy are: a) cessation of inflammatory tissue phenomena around the implants to avoid the progression of tissue destruction, b) regeneration, when possible, of lost peri-implant tissues. What therapy will be applied depends on the level of destruction of the alveolar bone and the clinical characteristics of the per implant tissues.

The optimal result of the treatment of peri-implantitis is the restoration of the lost supporting soft and hard implant tissues. After eliminating the infection and reducing inflammation of the soft tissues, surgical intervention may be required. Regeneration of bone tissue in the area of the implant bed with peri-implantitis remains the most difficult task. If bone loss is at an incipient stage, treatment will be identical to that prescribed for peri-imlpant mucositis, with the addition of decontamination of the prosthetic abutments and antibiotics, prosthetic design also be modified if necessary. If bone loss is advanced or persists despite initial treatment, it will be necessary to surgical treatment. The surgical treatment can be divided into resection techniques and regenerative techniques [24]. The morphology of bone defects and the number of preserved bone walls determine the choice of the method of treatment and allow evaluation of the possibilities of bone repair.

Resection techniques are used when there are vestibular dehiscence's in a non-aesthetically compromised region. The objectives of respective surgery are to reduce pocket depth and secure adequate soft tissue morphology, in order to facilitate adequate hygiene and peri-implant health [25]. Regenerative procedures such as bone graft techniques with or without the use of barrier membranes resulted in various degrees of success [26]. However, as of today, no consensus exists regarding effective peri-implantitis treatment.

The abundance of methods for treating peri-implantitis illustrates an inadequate practical effectiveness of each of them, which dictates the need for the development of new approaches to this problem. The search for optimal methods for the treatment of peri-implantitis is ongoing.

Hyaluronic acid is a natural polysaccharide, which is part of the glycosaminoglycan group.

Hyaluronic acid has been successfully used in many branches of medicine for many years, in particular in orthopedics, aesthetic surgery and is used in dental practice. The precise chemical structure of HA contains repeating units of d-glucoronic acid and N-acetyl-d-glucosamine. Hyaluronic acid increases local immunity in the oral cavity, by strengthening the antibacterial function of cells, stimulates the migration of fibroblasts and cell proliferation, enhances tissue regeneration, which has a positive effect on the healing process.

The production of cytokines that stimulate the inflammatory process is blocked, and therefore, healing takes place with minimal complications. Antibacterial and wound healing properties of hyaluronic acid are widely described in the literature [27].

In the field of dentistry, Pagnacco and Vangelisti have conducted preliminary clinical trials in 1997 [28]. Hyaluronic acid has shown anti-inflammatory, antioedematous, and anti-bacterial effects for the treatment of periodontal disease, which ismainly caused by the microorganisms present in subgingival plaque. Ballini et al. Found that autologous bone combined with an esterified low-molecular hyaluronic acid preparation seems to have good capabilities in accelerating new bone formation in the infra-bone defects [29]. Due to the viscosity of hyaluronic acid, the penetration of bacteria and viruses slows down. The significant clinical advantages of hyaluronic acid are that it allows to optimize work with materials for bone regeneration. It effectively fixes the augmentation material, regardless of whether it is an autograft or an allogeneic graft, and acts as a biological membrane. Due to its specific properties, hyaluronic acid has great potential for application in implantology practice and could be a very valuable addition to those used to treat peri-implantitis. Viscous substance slows the penetration of bacteria, performing the function of a biological barrier, which has a positive effect on the healing process.

Thus, the use of hyaluronic acid in oral implantology is advisable, but the effectiveness of this drug for the treatment of peri-implantitis requires further study. Based on the foregoing, it was reasonable to study the effectiveness of the therapeutic effect of hyaluronic acid preparations in the treatment of inflammatory processes affecting the tissues around the implants, which determined the purpose of this study.The high prevalence of peri-implantitis reflects insufficient effectiveness of methods of their prevention and treatment, which makes it important to search for new therapeutic and prophylactic approaches.

The aim of this study was to evaluate the outcome of combined surgical regenerative therapy of peri-implantitis using autologous

bone, a xenograft in combined with a hyaluronic acid gel and collagen membrane.

Materials and Methods

The 32 patients involved in this study (14 females, 18 males, at a mean age 48, 3years) with inflammatory-destructive processes in the field of peri-implant tissues of osseointegrated implants. A total of 46 implants were treated. (16 implants diagnosed with peri-implant mucositis, 14 implants-early peri-implantitis, 12 implants-moderate peri-implantitis and 4 implants severe peri-implantitis).

In 24% of patients peri-implantitis was developed early, already after having implants in function for 1 years. In 37% of the cases periimplantitis was developed after 2 years and in 39% between 3 and 5 years of implants in function.

Peri-implantitis was observed: In 14 patients with unsatisfactory hygiene; in 12 patients with non-observance of the periodicity of dispensary examination and occupational hygiene; 6 in patients with the initial presence of periodontitis.

The patients were examined clinically and radiographically. The diagnostic parameters used for assessing peri-implantitis include clinical indices, Probing Pocket Depth (PPD), Bleeding On Probing (BOP), suppuration, mobility, periimplant radiography. The criteria were the presence of ≥2mm of peri-implant marginal bone loss based on baseline periapical radiographs after delivery of the final restoration and BOP and/or suppuration with or without concomitant deepening of peri-implant pockets.

Bleeding On Probing (BOP), evaluated as present if bleeding was evident within 30s after probing or absent if no bleeding was observed within 30s after probing.

BOP indices was evaluated according to the following criteria

0-there is no bleeding

1-bleeding occurs not earlier than 30 seconds

2-bleeding occurs less than 30 seconds

3-bleeding occurs when eating or brushing your teeth

The degree of bleeding was judged by the evaluation criteria

0,1-1,0 - mild inflammation

1,1-2,0 - the average inflammation

2,1-3,0 - severe inflammation

Probing Pocket Depth (PPD) was measured full millimeter with a manual periodontal probe from the mucosal margin to the bottom of the examined pocket.

Marginal bone loss readings from periapical radiographs (taken at the baseline diagnostic appointment). Clinical and radiographical parameters were recorded before treatment (baseline) and at 3, 6 and 12 months after treatment.

16implants with peri-implant mucositis, 8 implants with early peri-implantitis and 5 implants with moderate peri-implantitis was treated only conservative treatments methods, 6 implants with early peri-implantitis, 7 implants with moderate peri-implantitis and 4 implants with severe peri-implantitis was treated surgically. Patients were given a detailed description of the treatment procedures and the signature of the form of informed consent.

Table 1: Bleeding On Probing (BOP) Conservative treatments methods.

	Patients (n)	M±σ	m
Before treatment	8	2,3± 0,33*	0,11
1 months after the treatment	8	0,9±0,15*	0,05
3 months after the treatment	8	0,6±0,11*	0,04

Table 2: Bleeding On Probing (BOP) Surgical treatments methods.

	Patients (n)	M±σ	m
Before treatment	17	2,5± 0,31*	0,08
1 months after the treatment	17	0,6±0,14*	0,03
3 months after the treatment	17	0,4±0,12*	0,03

Table 3: Probing Pocket Depth (PPD) Conservative treatments methods.

	Patients (n)	M±σ	m
Before treatment	8	5,3± 0,4*	0,15
1 months after the treatment	8	4,5±0,31*	0,11
3 months after the treatment	8	3,9±0,28*	0,1

Table 4: Probing Pocket Depth (PPD) Surgical treatments methods.

	Patients (n)	M±σ	m
Before treatment	17	5,4± 0,24*	0,06
1 months after the treatment	17	3,7±0,17*	0,04
3 months after the treatment	17	3,2±0,17*	0,04

Treatment Protocols

Conservation treatment

Including systemic antibiotics (amoxicillin 500mg and metronidazole 200mg or augmentin 875mg or ciprofloxacin 250mg) all the above antibiotics were administered per with duration of 7-10 days. Microbial testing allows choosing the most effective antibiotic for every case. Mechanical implant cleaning with titanium or plastic-curettes, Air-Flow Perio Soft, local antiseptic medication (irrigation of the circus-pocket with 0.12% chlorhexidine, hydrogen peroxide), magneto-laser therapy with a wavelength of 810nm power density of 100mW during 60 seconds(Laser therapy apparatus MILTA-F-8-01,CJSC" Space Instrument Engineering" Moscow, RF), local applications 25% metronidazole dental gel (Elzylol dental gel). Patients received 10 days magneto-laser therapy with a wavelength of 810 nm power density of 100mW during 2 min.

Surgical treatment can be subdivided into two phases

1. The anti-infective phase (to reduce clinical signs of inflammation before surgery);

2. The regenerative phase.

Professional hygiene was conducted 7 days before surgery, the patients rinsed twice a day for 1 min. with chlorhexidine 0.12%. The patients were prescribed systemic antibiotics(amoxicillin 500mg and metronidazole 200mg or augmentin 875mg or ciprofloxacin 250mg)

all the above antibiotics were administered per os with duration of 7-10 days. The antibiotic therapy was initiated the day before surgery. Microbial testing would allow them to choose the most effective antibiotic for every case. Local anesthesia was accomplished by articain 4% (Ubistesin forte, 3M ESPE AG, Seefeld, Germany). Following local anesthesia, the supra-structure was removed, a sulcular incision was made around the neck of the implant abutments and a full-thickness flap was elevated to allow access to the periimplant defect and the exposed implant surface. The abutment was removed and cover plugs were inserted in the implant. Granulation tissue was carefully removed in the bone defect with titanium instruments. The implant surface is decontaminated with Air-Flow Perio Soft, successive topical applications of citric acid, 0.12% chlorhexidine, sterile physiological saline and adjunctive magneto-laser therapy with a wavelength of 810nm power density of 100mW during 30 seconds. After degranulatin and antiseptic preparation the bone loss was evaluated intrasurgically. A autologous bone and Bio-Oss had mixed with Gengigel outside the mouth and the periimplant bone defect was filled. A bioresorbable collagen membrane Bio-Gide was placed over the filled defect. After bone grafting full thickness buccal and lingual flaps were repositioned and sutured, postoperative instructions were provided. The wound healing was performed in a submerged mode. Following surgery, the patients rinsed twice a day for 1min. with chlorhexidine 0.12% for a period of 2-3 weeks. After surgery the patients received 7 days magneto-laser therapy with a wavelength of 810nm power density of 100mW during 2min. The sutures were removed 7 days to 10 days after the surgery.

Patients observed the first 4 weeks to monitor healing, and then with a three-month interval.

After 3 months of submerged healing the cover plugs of the implants were replaced with prosthetic abutments. After 1 weeks of soft-tissue healing, prosthetic components were inserted. Patients were recalled every three months for data collection and maintenance therapy. Professional hygiene was conducted every six months. In four cases (severe peri-implantitis) with bone resorption at>50% implant length the implants were removed.

Statistical analysis

Statistical processing of the data was performed in the environment of the SPSS 11.5 package

Comparisons of quantitative traits were carried out using Student's t-test. The paper presents the arithmetic mean and its error (M ± m). All differences were of statystical significance ($p< 0.01$).

Results

Treatment was considered successful if the following criteria were met: (1) absence of progressive bone loss, (2) absence of suppuration, (3) bleeding on probing at ≤ 50% of sites and

(4) Probing pocket depth <5mm. Radio graphically, increased or stable marginal bone levels compared with the baseline periapical x-rays were synonymous with treatment success.

Clinical evaluation of the results of treatment after 1, 3 months showed reduction in both PPD and BOP were as compared with the baseline clinical measurements, more pronounced changes in the surgical method of treatment (Table 1,2,3,4). After 6 months x-ray examination demonstrated newly formed hard tissue was observed filling the defects around the implants. Stable clinical measurements PPD and BOP were demonstrated after after 6 months, 1 year the initial treatment, remaining stable during the following three years, only two patients showed signs of perimucositis in area of 3 implants without formation of pathological pockets, after the conduct of professional hygiene phenomenon of mucositis disappeared. Longer periods of observations continued to show positive dynamics clinical dental status. A prerequisite for the long-term stability of treatment results obtained is the ability of the patient to maintain good oral hygiene.

Discusion

A number of protocols have been suggested in the treatment of peri-implantitis. There have been proposals various methods of treating peri-implantitis, however, until now, no methodology has been used as a gold standard [30].

A consensus report from the 8th European Workshop on Periodontology emphasized the need for identifying a standard mode of therapy for the treatment of peri-implantitis [31]. The insufficient effectiveness of the proposed methods of treatment of perimplantitis requires the improvement of surgical techniques, as well use innovative biomaterials for the treatment of peri-implantitis.

This study describes clinical results of a treatment of peri-implantitis. The evaluation of outcomes in the present study was confined to treatment success criteria that included the combination of findings from clinical and radiological assessments. Significant reductions in both PPD and BOP were shown in the group with less pronounced bone loss pre-surgery. Treatment led to positive effects on clinical and radiologic parameters over the long-term subsequent period of time. Based upon in our clinical experience conservative treatment methods are effective in the treatment of peri-implant microsites and early peri-implantitis. When peri-implantitis category moderate and severe effective surgical treatment combined conservative therapy. Implants with less bone loss before surgery presented better treatment result than more severe cases.

Laser treatment may serve as an alternative or adjunctive treatment to conventional therapy peri-implantitis. Magneto-laser therapy unites in themselves widely spread in modern medicine therapeutic factors: magnetic field, low laser radiation and light-diodes infra-red radiation (magnet-light-laser therapy). Curative effect of magneto-laser therapy is determined by the biostimulation and mobilization of the existing energetic potential and is manifested as immune-modulating, anti-inflammatory, antispastic, regenerative, normalizing blood rheology and hemodynamics. The use of magneto-laser therapy in our study for decontamination of the affected surface of the implant has demonstrated promising results treating peri-implantitis. Magneto-laser therapy is not only beneficial because of its bactericidal effect but it can accelerates regeneration processes in periimplant area. Magneto-laser therapy has advantages in comparison to traditional therapy, with faster healing of the wound. This combination of surgical and therapeutic treatment aims at improvement of the quality of regenerated bone structures.

Our results suggest that hyaluronic acid Gengigel represents a reliable adjunctive treatment to conventional therapy. Protective

action and slow absorption of hyaluronic acid provide reliable and predictable regeneration of augmentate. This barrier function of hyaluronic acid is very important in the healing process of the wound, it as a highly promising material for improving outcomes treatment of peri-implantitis.

The surgical protocol described in this article gives positive results, therefore it is recommended as a simple and effective method therapy peri-implantitis.

The long-term success of peri-implant treatment requires a program of maintenance, including instructions in hygiene. The concept of prevention based on early detection and regular examination plays a major role in reducing the number of peri-implantitis.

Conclusion

The results of this study indicated that surgical regenerative treatment combined with mechanical and chemical detoxification of the implants' surface, magneto-laser therapy and bone graft techniques using a autologous bone, Bio-Oss, hyaluronic acid Gengigel with barrier membranes a reliable method for stopping and treatment peri-implantitis.

Ethical Approval

The study was reviewed and approved by the Ethics Committee of the Yerevan State Medical University after M. Heratsi (protocol N6 15.10.16) and in accordance with those of the World Medical Association and the Helsinki Declaration.

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