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REGENERATIVNA PARODONTALNA TERAPIJA – I DEO

REGENERATIVE PERIODONTAL THERAPY – I PART

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Sažetak

Uvod: *Pod konceptom regenerativne terapije parodontalnih tkiva, treba imati u vidu dva pristupa: prvi je koncept pasivne regeneracije, koji obuhvata upotrebu koštanih zamenika i vođenu regeneraciju parodontalnih tkiva primenom biomembrana,a drugi je koncept aktivne regeneracije, koji podrazumeva primenu faktora rasta. Pasivna regeneracija primenom koštanog matriksa (koštanih zamenika) ima za cilj stabilizaciju i popunjavanje defekta, sprečavanje urastanja epitelnog tkiva, kao i čuvanje prostora za stvaranje novog tkiva. Pod ovim konceptom podrazumeva se primena autogenih transplantanata, ksenograftova, alograftova, kao i aloplastičnih materijala. Nosioci aktivne regeneracije, faktori rasta (growth factors - GF) su prirodni biološki medijatori koji regulišu ćelijske procese krucijalne za regeneraciju tkiva.*
Cilj:*Prikazati savremene pristupeterapiji obolelog parodoncijuma koji su usmereni naregeneraciju i kompletnu rekonstrukciju parodontalnih tkiva.*
Zaključak:*U budućnosti, parodontalni regenerativni postupak progenitorskim ćelijama parodontalnog ligamenta trebalo bi da podstakne repopulaciju površina koje su bile zahvaćene parodontopatijom.*

Ključne reči:*parodontalna hirurgija, tkivna regeneracija*

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Abstract

Introduction: *Under the concept of regenerative periodontal therapy, there are two approaches: the first is the passive regeneration conceptthat includes bone substituents and guided periodontal regeneration by using of biomembranes and the second concept of active regeneration thatimpliesthe use ofgrowth factors. The aim of the passive regeneration, by using of bone matrix (bone substituens) has been stabilization and bone defects management, preventing epithelial tissue growth, as well as saving space for the new tissue regeneration. This concept implies the use of autogenous transplantats, xenografts, allografts, as well as alloplastic materials. The carriers for active tissue regeneration, growth factors – GF are biological mediators that regulate cellular processes and that is crucial for the tissue regeneration.*
Aim:*Presentation ofmodern approachesto periodontal therapy thatare focused on the attachment regeneration and complete reconstruction of periodontal tissue.*
Conclusion:*In the future, periodontal regenerative therapy with periodontalligament progenitor cells should encourage repopulation of the areas that have been affected by periodontal disease.*

Key words:*periodontal surgery, tissue regeneration*

Uvod

Oboljenja potpornog aparata zuba karakterišu se destrukcijom i gubitkom potpornih tkiva (gingive, cementa, alveolarne kosti i periodontalnih vlakana). Koncept regenerativne terapije parodontopatije baziran je na ideji kompletne regeneracije izgubljenih tkiva. "Prava" regeneracija parodoncijuma podrazumeva stvaranje novog cementa, nove gingive, alveolarne kosti i novog periodontalnog ligamenta na delu korena zuba, nakon hirurške intervencije[1].

Osnovni cilj parodontalne hirurgije je da obezbedi pristup za pravilno čišćenje površine korena zuba, ali, i pored toga, većina hirurških procedura rezultira redukcijom dubine parodontalnog džepa. Tradicionalno, eliminacija dubokih parodontalnih džepova postiže se gingivektomijom ili apikalnim pomeranjem mekotkivnog režnja, koje se izvodi udruženo sa oblikovanjem alveolarne kosti. U poslednje vreme, češće se koriste regenerativni tretmani, u cilju restauracije izgubljenog potpornog aparata zuba[2]. Veoma je bitno da parodontalna terapija da zadovoljavajuće rezultate, zbog toga što postoji dokazana veza između parodontalnih oboljenja i sistemskog zdravlja[3].

Indikacije

Parodontalni tretman, bez obzira da li se radi o hirurškom ili nehirurškom, dovodi do recesije gingive nakon oporavka[4]. Kod uznapredovalih slučajeva, ovo može dovesti do lošeg estetskog rezultata kod frontalnih zuba, naročito kod slučajeva gde hirurška procedura uključuje oblikovanje alveolarne kosti sa odstranjivanjem koštanih defekata. U slučajevima kod kojih nema oblikovanja alveolarne kosti u toku hirurškog tretmana, može doći do stvaranja rezidualnih parodontalnih džepova, koji su nedostupni za odgovarajuće održavanje oralne higijene. Ovi problemi mogu se izbeći ili redukovati pomoću regenerativnih hirurških procedura, kojima se obnavljaju izgubljeni potporni aparat zuba i koštani defekti. Indikacije za regenerativnu parodontalnu hirurgiju najčešće su bazirane na estetici, iako je pored toga važna činjenica da funkcija i dugoročna prognoza tretiranih zuba mogu biti poboljšane.

Lokalizovana gingivalna recesija može predstavljati estetski problem pacijentima i često je povezana sa hipersenzitivnim dentinom.

Introduction

Diseases of the tooth-supporting apparatus arecharacterized by destruction and loss of periodontal supporting tissues (gingiva, cement, alveolar bone and periodontal ligament). The concept of regenerative periodontal therapy is based on the idea of complete regeneration of periodontal tissues. "True" periodontal regeneration implies making of the new cementum, gingiva, alveolar bone and periodontal ligament on the part of tooth radix after surgical procedure[1].

The main goal of periodontal surgery is to achieve the space for regular cleaning of the tooth radix area, but the most common surgical procedures resulted only with reduction in depthof periodontal pocket. Traditionally, elimination of deep periodontal pockets is achieved by gingivectomy or apical movement of the soft tissue flap, which was performed in conjunction with alveolar bone remodeling. Recently, regenerative treatments have been used more often in order to restore the loss of the tooth-supporting apparatus[2].It is very important that periodontal therapy can provide satisfactory results because there has been found a proven link between periodontal disease and systemic health[3].

Indications

Periodontal treatment, whether surgical or non-surgical leads to gingival recession after recovery[4]. Advanced cases may lead to poor esthetical results in the front teeth, especially in patients wheresurgical procedure includes alveolar bone remodeling with the elimination ofosseous defects. In cases without alveolar bone remodeling through surgical treatment could lead to formation of residual periodontal pockets, which were unavailable for proper oral hygiene. These problems could be avoided or reduced by regenerative surgical procedures that resultin restoration of tooth-supporting apparatusand bone defects.The indications for regenerative periodontal surgery are most often based on aesthetics, although of importance is the fact that function and long-term prognosis of treated teeth could be improved.

Localized gingival recession may be an esthetic issue for patients and usually connected with the hypersensitive dentin. Situation like this is usually indication for regenerative periodontal surgery in order to achievetooth root coverage.

Ovakva situacija indikacija je za primenu regenerativne parodontalne hirurgije, kako bi se održala prekrivenost korena zuba. Na taj način, poboljšava se estetika i smanjuje hipersenzitivnost korena zuba. Uspešno prekrivanje korena zuba podrazumeva regeneraciju potpornog aparata na izloženoj površini korena, uključujući cement sa umetnutim kolagenim vlaknima i alveolarnu kost, kao i estetski prihvatljivu restauraciju anatomije mukogingivalnog kompleksa.

Još jedna indikacija za regenerativnu parodontalnu terapiju je zahvaćenost furkacija zuba. Predeo furkacije često je nepristupačan za adekvatnu obradu, što praktično dovodi do toga da adekvatno čišćenje, nakon resektivne hirurgije, nije moguće izvesti. Dugoročna prognoza za lečenje takvih zuba značajno je poboljšana uz pomoć regenerativne parodontalne terapije[5].

Regenerativne hiruške procedure

Regenerativna parodontalna terapija obuhvata specijalne procedure, osmišljene tako da restauriraju one delove potpornog aparata zuba koji je izgubljen tokom parodontopatije. Regeneracija je definisana kao reprodukcija ili rekonstrukcija izgubljenih ili oštećenih delova zuba i tkiva, na takav način da se kompletno restauriraju arhitektura i funkcija izgubljenog ili oštećanog tkiva[6]. Ovo znači da će se pripojni epitel zuba potpuno regenerisati kada se formira novi cement sa umetnutim kolagenim vlaknima na površini korena, dok regeneracija potpornog aparata zuba podrazumeva i obnavljanje alveolarne kosti. Procedure koje imaju za cilj restauraciju izgubljenog potpornog aparata zuba opisane su kao "reatečment" ili "novi atečment" procedure.

Periodontalna regeneracija podrazumeva sledeće hirurške procedure: biomodifikaciju površine korena zuba, kombinovanu sa koronarno pomerenim režnjem, primenu koštanih graftova / koštanih implanata ili upotrebu organskih/sintetskih biomembrana (vođena regneracija primenom bio-membrana). Iako postoji dokazana klinička uspešnost sa značajnim porastom nivoa alveolarne kosti, histološki je prisutan fibrozni sadržaj duž površine korena zuba, umesto depozita novog cementa[7]. Uspešna regene-racija procenjuje se na osnovu sondiranja, rendgenografskih analiza, direktnim merenjem nove kosti i histoškim metodama[8-11].

Hiruške procedure, čija se primena zasniva na činjenici da sposobnost regeneracije imaju samo ćelije periodoncijuma, dok tu osobinu ne poseduju ćeliije epitela i vezivnog tkiva gingive.

This improves the aesthetics and reduces the hypersensitivity of the tooth root. Successful technique of the tooth root coverageinvolves the regeneration of the supporting apparatus on the exposed root surface including cement with inserted collagen fibers and alveolar bone, as well as an aesthetically acceptable restoration of the anatomy of the mucogingival complex.

One more indication for regenerative periodontal therapy is involvement of the tooth furcation. The furcation area is often inaccessible for adequate treatment, and it practically leads to the fact that adequate cleaning after resective surgery could not be done. The long-term prognosis for the treatment of such teeth has been significantly improved by regenerative periodontal techniques[5].

Regenerative surgical procedures

Regenerative periodontal therapy includes special procedures designed to restore those parts of the tooth-supporting apparatusthat was lost during periodontal disease. Regeneration is defined as the reproduction or reconstruction of lost or damaged parts in such a way that the architecture and function of the lost or damaged tissueshave been completely restored[6]. This means that the attached epithelium to the tooth will be completely regenerated, when a new cementumhas been formed with inserted collagen fibers on the root surface, while the regeneration of the tooth-supporting apparatusimplies and the alveolar bones regeneration. A procedure aimed at restoring lost the tooth-supporting apparatushas been described as a "re-attachment" or "new attachment" procedure.

Periodontal regeneration includes thefollowing surgical procedures: biomodi-fication of the tooth root surface combined with coronary displaced flap, using of bone grafts / bone implants or using of organic / synthetic biomembranes (guided regeneration using biomembranes). Although there is a proven clinical success rate with a significant increase in alveolar bone levels, histologically, there was fibrous content along the root surface of the tooth instead of the new cement deposits[7]. The successful regeneration was assessed on the basis of sounding, radiographic analysis, direct measurement of new bone levels and by histological methods[8-11].

Surgical procedures, which werebased on the fact that only periodontal cells have the ability to regenerate, while epithelial cells and connective tissue of the gingiva do not have that property.

Zbog toga se primenom terapije mora stvoriti barijera, koja sprečava urastanje ćelija epitela i krzna i omogućava repopulaciju parodontalnog džepa ćelijama periodoncijuma i ćelijama kosti, koje poseduju sposobnost regeneracije. U pokušaju da se stvori barijera, čiji je cilj sprečavanje prodora ćelija epitela i vezivnog tkiva u gingive i omogući naseljavanje ćelija periodoncijuma, koriste se dve metode[8]:

I metoda: čiji je cilj postizanje novog pripoja bez korišćenja transplantata, koja se odvija u tri faze:

1. Faza: uklanjanje pripojnog epitela i epitela parodontalnog džepa, koje se vrši ili kiretažom ili hirurškom procedurom. Nepotpuno uklanjanje patološki izmenjenih tkiva parodontalnog džepa sprečava pozitivan ishod svih terapijskih procedura;
2. Faza: onemogućavanje prodora vezivnog tkiva i epitela implantacijom određenih barijera (membrana), koje se klasifikuju kao resorptivne i neresorptivne. Neresorptivne membrane prave se od teflona, "Milipor filtera" politetrafluoretilena, silikonske gume, titanijuma i mnogih drugih materijala i uklanjaju se nakon 3 nedelje do 6 nedelja od trenutka hirurške intervencije, dok su resorptivne membrane napravljene od polilaktične kiseline, kolagena, smrznute dure mater, polikarbolaktana itd. Pored njih, aplikuju se i koštani i sintetički transplantati, koji treba da stimulišu stvaranje nove kosti;
3. Faza: obrada i priprema korena zuba za stvaranje novog epitelnog pripoja vrši se kiretažom (uklanjanjem pripojnog epitela i epitela parodontalnog džepa) i nekim medikamentima (kondicioniranje površine korena zuba). Cilj je da se iz parodontalnog džepa odstrane ostaci periodontalnih vlakana, mikroorganizmi i njihovi produkti, dok se sa korena zuba odstranjuje oštećeni cement. Za demineralizaciju cementa i dentina na korenu, koristi se limunska kiselina, kao i premazivanje korena zuba tetraciklinima, koji treba da olakšaju pripoj vezivnih vlakana za dentin. Može se umesto stavljanja membrane, površina korena premazati emdogainom (faktor rasta gleđi), koji sprečava apikalnu proliferaciju epitela.

II metoda: rekonstruktivne mere korišćene za postizanje novog pripoja, upotrebom kalema (transplantata). Ovi zahvati vrše se u relativno malom operativnom polju – mikrohirurški zahvati, koji se obavljaju pod lupom ili sistemom lupa, koje se nose kao naočare. Nekada se intervencije vrše i pod posebno konstruisanim mikroskopom, za šta je neophodno korišćenje gracilnih instrumenata. Mikrohirurške zahvate pacijenti prihvataju lakše, zato što je prisutan manji postoperativni bol[8].

Therefore, the surgical therapy has to create a barrier, that prevents the ingrowth of epithelial and corium cells and enables repopulation of the periodontal pocket with periodontal and bone cells, that have the ability to regenerate themselves. In the attempt to create a barrier that plays arolein preventingpenetration of the epithelial cells and connective tissue of the gingiva and allows the repopulation of periodontal cells, these two methods were used[8]:

I method: the aim has been to achieve a new attachment without the using of the grafts,it has evolvedthrough three phases:

Phase 1. Removal of the epithelial attachment and periodontal pocket epithelium performed by either curettage or surgical procedure. Incomplete removal of pathologically altered periodontal pocket tissues prevents the positive outcome of all therapeutic procedures.

Phase 2. Preventing of the connective tissue and epithelium penetration by implanting certain barriers (membranes)that are classified as resorptive and non-resorptive. Non-resorptive membranes were made from Teflon, "Millipore filter" polytetra-fluoroethylene, silicone rubber, titanium and many other materials and have been removed after 3-6 weeks of surgery. While resorbable membranes were made from polylactic acid, collagen, frozen dura mater, polycarbolactan, etc. In addition, bone and synthetic transplants were applied, that should stimulated the formation of the new bone.

Phase 3. Processing and preparation of the tooth root for the creation of a new epithelial attachment have been performed by curettage (removal of the adnexal epithelium and periodontal pocket epithelium) and some medications (conditioning of the tooth root surface). The goal is to remove the remains of periodontal fibers, microorganisms and their products from the periodontal pocket, while the damaged cement has been removed from the root of the tooth. For demineralization of cementum and dentin of the tooth root, citric acid is used, as well as coating the tooth root with tetracyclines, which should facilitate the attachment of connective fibers to the dentin. Instead of applying a membrane, the tooth root surface can be coated with "Emdogain" (enamel growth factor), which prevents apical proliferation of the epithelium.

II method:reconstructive measure sused inrealization of new attachment by grafts (transplants). These procedures have been performed in a relatively small operative field - microsurgical procedures, performed underthe magnifying glass or under the system of

Postupci transplantiranja

U kliničkim studijama i eksperimentima na životinjama, režanj operacija kombinuje se sa ubacivanjem koštanih transplantanata ili materijala za implantaciju u kiretirani koštani defekt, sa ciljem da se stimuliše parodontalna regeneracija[12,13].

Različiti materijali za transplantante i implantate mogu se klasifikovati u četiri kategorije:

1. Autogeni transplantati uzeti su sa jednog mesta, a implantiraju se na drugo mesto kod iste osobe. To su: (a) kortikalna kost ili (b) spongiozna kost i koštana srž, bilo da su uzeti sa intraoralnog ili ekstraoralnog donorskog mesta;

2. Alotransplantati implantiraju se genetski različitim članovima iste vrste. To su: (a) zamrznuta spongiozna kost i koštana srž i (b) suvozamrznuta kost;

3. Ksenotransplantati ili hetero-transplantati uzeti su od donora, koji pripadaju drugoj vrsti;

4. Aloplastični materijali su sintetički ili neorganski materijali, koji se koriste kao zamena za koštane transplantate.

Razlog korišćenja koštanih transplantata ili aloplastičnih materijala je pretpostavka da utiču na rast alveolarne kosti i stvaranje novog pripojnog epitela, zbog toga što:

1. Sadrže ćelije koje utiču na formiranje alveolarne kosti (osteogeneza);

2. Služe kao matrica za koštanu formaciju (osteokondukcija);

3. Matriks koštanih graftova sadrži supstance koje indukuju formaciju kosti (osteoindukcija)[9,14]. Ovakva kompletna regeneracija pripojnog epitela pomoću transplantanata indukuje sposobnost koštanih ćelija da stvaraju novi cement sa kolagenim vlaknima na površini korena, koji je prethodno izmenjen parodontopatijom[15].

Autogeni transplantati

Autogeni transplantati mogu zadržati ćelijsku sposobnost da poboljšaju stvaranje kosti preko osteogeneze i/ili osteokondukcije. Oni se postepeno zamenjuju novom kosti. Osim toga, potencijalni problemi koji mogu nastati zbog histokompatibilnosti i potencijalnog prenošenja bolesti ovim putem su eliminisani. Autogeni transplantati mogu se uzeti sa intraoralnih i ekstraoralnih donorskih mesta.

magnifying glasses worn likeglasses. Sometimes interventions were performed under a specially constructed microscope, and the use of these graceful instruments was necessary. Patientsaccepted microsurgical procedures more easily, because they wereassociated with reduced postoperative pain[8].

Transplant procedures

In clinical studies and animal experiments, flap surgery has been combined with the insertion of bone grafts or implant materials into a cured bone defect in order to stimulate periodontal regeneration[12,13].

Different materials for transplants and implants could be classified into four categories:

1. Autogenous transplants were taken from one partof the body and implanted in another partof the same person body. These were: (a) cortical bone or (b) spongy bone and bone marrow, whether taken from an intraoral or extraoral donor site.

2. Allografts have been implanted in the genetically different members of the same species. These were: (a) frozen spongy bone and bone marrow and (b) dry-frozen bone.

3. Xenografts or heterografts have been taken fromthe donor which belongs toanother species.

4. Alloplastic materials are synthetic or inorganic materials that were used as the substitute for bone grafts.

The reason why a bone graft or alloplastic material was used is the assumption that both affectthe growth of alveolar bones and the formation of a new adherent epithelium, because theyconsist of:

1. The cells that affect the formation of alveolar bone (osteogenesis), or

2.They are used as a matrix for bone formation (osteoconduction), or

3. The matrix of bone grafts, which contains substances that induce bone formation (osteoinduction)[9,14]. This complete regeneration of the adherent epithelium by usinggrafts have beeninducedby the ability of bone cells to create the new cementum with collagen fibers on the root surface, which waspreviouslyaltered by periodontal disease[15].

Autogenous transplants

Autogenous transplants may retain the cellular ability to improve bone formation through osteogenesis and / or osteoconduction. The transplants are gradually replaced by the new bone over time. In addition, potentialproblems due to histocompatibility and potential disease transmission in this way was eliminated.

Intraoralni autogeni transplantati

Intraoralni autogeni transplantati uzimaju se sa bezubih predela vilica, ekstrakcionih rana, tubera maksile ili retromolarnog predela mandibule, koji se često koriste u parodontalnoj regenerativnoj hirurgiji[16].

Spongiozna kost češće je u upotrebi kao materijal za transplantate, ali je i kortikalna kost u upotrebi, kada su u pitanju mali delovi[17]. Mešanje materijala sa krvlju, pre nego da se aplikuje u defekt[18,19], predstavlja napredak u regenerativnoj terapiji parodontalnih infrakoštanih defekata. Rezultati studija[20 – 23] prikazuju to da, kod infrakoštanih defekata, primena intraoralnog koštanog transplantata može dati bolje rezultate parodontalne regeneracije.

Ekstraoralni autogeni transplantati

Schallhorn[24,25]je uveo korišćenje autogenih transplantata od koštane srži sa kuka (srž uzeta sa criste iliacae za tretman infrakoštanih defekata i furkacija). Međutim, zbog invazivnog postupka više se ne koriste transpalantati srži ilijačne kosti.

Alogeni transplantati

Upotreba alotransplantanata uključuje izvestan rizik, s obzirom na antigenost, mada se oni prethodno zamrznu i izlože zračenju ili hemikalijama, kako bi se sprečile reakcije na strano telo.Dostupne vrste alotransplanata su: zamznuta spongiozna ilijačna kost i srž, mineralizovani transplantati suvo smrznute kosti (FDBA – freeze dried bone graft) i dekalcificirani suvo smrznuti koštani transplantat (DFDBA – decalcified freezed-dried bone allograft).

Ksenotransplantanti

Kod ksenotransplantanata primenjuju se nove metode, koje omogućuju odstranjivanje svih organskih sastojaka iz goveđe kosti, ostavljajući koštani matriks u nepromenjenom neorganskom obliku (npr. “Bio-Oss”, Geistlich AG, Wolhusen Switzerland; Endobone, Merck Biomaterialen, Darmstadt, Germany; Laddec®, Ost Development, Clermont-Ferrand, France; Bon-Apatite®, Bio- Interfaces Inc., San Diego, US). Ipak, postoje razlike u metodama prečišćavanja transplantata i manipulacije trasplantatom, što je dovelo do komercijalno dostupnih proizvoda sa različitim hemijskim osobinama. Ovi materijali dostupni su u različitim veličinama čestica ili kao blokovi.

Autogenous transplants could be taken from intraoral and extraoral donor sites.

Intraoral autogenous transplants

Intraoral autogenous transplants have beentaken from the edentulous areas of the jaws, from the extraction wounds, the maxillary tubers, or the retromolar area of the mandible has been often used in periodontal regenerative surgery[16].

The spongy bone has been more commonly used as a graft material, but cortical bone has been also used when small parts were involved[17]. Mixing the material with blood, beforeapplied for the defect[18, 19], represents an advance for the regenerative therapy of periodontal infraosseousdefects. The results of thesestudies[20-23]showed that in the case of infraosseous defects, using of an intraoral bone graft couldprovide better periodontal regeneration outcomes.

Extraoral autogenous transplants

The using of autogenous bone marrow transplants from the hip (marrow was taken from cristeiliacaefor the treatment of infraosseous defects and furcations) has been initiated by Schallhorn[24,25]. However, due to the invasive procedure, iliac bone marrow transplants wereno longer available in practice.

Allogeneic transplants

The using of allograftshas been associated with some riskregarding antigenicitymeasurment, although thesehave been pre-frozen and exposed to radiation or chemicals in order to prevent foreign body reactions.Available types of allografts are: frozen spongy iliac bone and marrow, mineralized freeze dried bone graft (FDBA) and decalcified dry frozen bone graft (DFDBA).

Xenotransplants

In xenotrasplants , the new methods thathave been applied, allow the removal of all organic constituents from bovine bone by leaving the bone matrix in unchanged inorganic form (e.g. Bio-Oss",Geistlich AG, Wolhusen Switzerland; Endobone", Merck Biomaterial, Darmstadt, Germany; Laddec®, Ost Development, Clermont-Ferrand, France;Bon-Apatite®, Bio-Interfaces Inc., San Diego, US).However, there are different methods of purification and manipulation of the graft, which led to commercially available

Aloplastični materijali

Aloplastični materijali su sintetski, neoorganski, biokompatibilni i/ili bioreaktivni zamenici kosti, koji imaju osteokonduktivne osobine. Postoje četiri vrste aloplastičnih materijala koje se koriste u regenerativnoj parodontalnoj hirurgiji: hidroksiapatit (HA), beta trikalcijum-fosfat (ß-TCF), polimeri i bioaktivna stakla (biostakla).

Hidroksiapatit (HA)

Hidroksiapatit (HA) upotrebljava se u parodontolnoj hirurgiji u dva oblika – u obliku čestica neresorptivne keramike (npr. Periograf®, Miter Inc., Warsaw, IN, US; Calcitite", Calcitek Inc., San Diego, US) i u obliku resorptivnih čestica (npr. OsteoGraf/LD®, CeraMed Dental, Lakewood, CO, US).

Betatrikalcijum-fosfat (ß-TCF)

Beta trikalcijum-fosfat (ß-TCP) je aloplastični materijal. To je sintetski, neorganski, biokompatibilni i/ili bioaktivni koštani zamenik, koji poseduje osteokonduktivni potencijal. Ovaj materijal karakteriše se izuzetno brzom resorptivnošću, pa je regeneracija parodontalnih tkiva bila nekompletna, u smislu formiranja novog acelularnog cementa i alveolarne kosti. Ipak, smatra se da ovaj materijal primarno deluje kao nosač za čuvanje prostora parodontalnih defekata[26].

Polimeri

Postoje dva polimerna materijala,koja se koriste kao zamena za kost u lečenju parodontalnih defekata: neresorptivni kopolimer od poli-meilmetakrilata (PMMA) i poli-hidroksiletilmetakrilat (PHEMA) prekriven kalcijum-hidroksidom, koji se naziva HTR (hard tissue replacement).

Bioaktivna stakla (biostakla)

Biostakla se sastoje od SiO_2, Na_2O, P_2O_5, tako da se resorbuju ili se ne resorbuju,u zavisnosti od odnosa njihovih sastojaka.

Kada se biostakla izlože tkivnim tečnostima, onda se na njihovoj površini stvori dvostruki sloj sicilijumskog gela i kalcijum-fosfata[27]. Komercijalno dostupna biostakla u obliku čestica, teoretski resorptivna, koriste se za parodontalno lečenje (PerioGlass'j, US Biomaterials Corp., Alachua, FL, US; BioGran®, Orthovita, Malvern, PA, US).

products with different chemical properties. These materials are available in different particle sizes or as blocks.

Alloplastic materials

Alloplastic materials are synthetic, inorganic, biocompatible and / or bioreactive bone substitutes that have properties of osteoconductive biomaterials. There are four types of alloplastic materials that are used in regenerative periodontal surgery: hydroxyapatite (HA), beta-tricalcium phosphate (ß-TCF), polymers, and bioactive glasses (bioglass).

Hydroxyapatite (HA)

HA is used in periodontal surgery in two forms, in the form of non-resorptive ceramic particles (e.g.Periograf®, Miter Inc., Warsaw, IN, US; Calcitite ", Calcitek Inc., San Diego, US) and in the form of resorptive particles (e.g.OsteoGraf / LD®, CeraMed Dental, Lakewood, CO, US).

Beta-tricalcium phosphate (ß-TCF)

Beta-tricalcium phosphate (β-TCP) is an alloplastic material. It is a synthetic, inorganic, biocompatible and / or bioactive bone substitute that has osteoconductive potential. This material is characterized by extremely fast resorption, so the regeneration of periodontal tissues was incomplete regarding the formation of new acellular cementum and alveolar bone. However, this material acts primarily as thecarrier in preserving periodontal defect space[26].

Polymers

There are two polymeric materials as a replacement for bone in the treatment of periodontal defects: a non-resorptive copolymer, made of polymethyl metha-crylate (PMMA) and polyhydroxyethyl methacrylate (PHEMA), coated with calcium hydroxide, called HTR (hard tissue replacement).

Bioactive glasses (bioglass)

Bioglasses are made of SiO_2, Na_2O, P_2O_5, so they are in a resorptive or a non-resorptiveform, depending on the ratio of their components.

When bioglass are exposed to tissue fluids, then a double layer of silica gel and calcium phosphate is formed on their surface[27].Commercially available bioglass in the form of particles, theoretically resorptive, isused for periodontal treatment (PerioGlass'j, US Biomaterials Corp., Alachua, FL, US; BioGran®, Orthovita, Malvern, PA, US).

Biomodifikacija površine korena

Ispituju se promene koje se javljaju na površini korena zuba, koji je zahvaćen parodontopatijom. Uklanjanje bakterijskih naslaga, kamenca i endoksina iz cementa smatra se osnovnim preduslovom za stvaranje novog vezivnog aparata[28]. Međutim, Stahl i sar.[29] upozorili su na to da bi deminerizacija površine korena, koja ima za posledicu izlaganje kolagena dentina, olakšala taloženje cementa podsticanjem mezenhimskih ćelija iz okolnog tkiva da se diferenciraju u cementoblaste. Biološka koncepcija postavljena je tako da se izlaganjem kolagenih vlakana dentalnog matriksa može omogućiti adhezija krvnog koaguluma za površinu korena zuba, a isto tako i migracija fibroblasta.

Faktori regulacije rasta parodontalne regeneracije

Faktor rasta opšti je pojam za označavanje grupe polipeptidnih hormona, koji stimulišu veliki broj različitih reakcija, kao što je proliferacija, hemotaksa, diferencijacija i produkcija ekstracelularnih matriksnih proteina[30]. Proliferacija i migracija ćelija periodoncijuma i sinteza ekstracelularnog matriksa, kao i diferencijacija cementoblasta i osteoblasta, preduslov su za regeneraciju parodonta. Samim tim, razumljivo je to što faktori rasta mogu predstavljati potencijalnu pomoć u pokušaju da se stimuliše regeneracija parodonta.

Faktori rasta (growth factors – GF) su prirodni biološki medijatori, koji regulišu ćelijske procese krucijalne za regeneraciju tkiva. Faktori rasta od značaja za parodontalnu regeneraciju su: trombocitni factor rasta – PDGF, transformišući faktor rasta, faktor rasta – EGF, osteogeni protein 1 – BMP-7, koštani morfogenetski protein – BMP-2, BMP-3 i angiogenetski faktori rasta TGFβ1 i TGFβ2, faktor rasta sličan insulinu – IGF i fibroblastni faktor rasta – FGF.

Trombocitni faktor rasta (PDGF) jedan je od glavnih humanih faktora rasta. Iako prvo primećen u alfa granulama trombocita, otkriveno je da ga sintetišu i ostale ćelije, kao što su makrofagi i ćelije endotelijuma[31]. Brojne studije, kako u medicini, tako i u stomatologiji, potvrdile su njegov pozitivni efekat na zarastanje rana. Smatra se da je on jedan od prvih faktora prisutnih u rani, koji započinje proces zarastanja okolnih tkiva[32]. Zabeleženo je da PDGF vrši mobilizaciju ćelija iz okolnog matriksa, kao i da utiče na hemotaksu i proliferaciju ćelija perio-dontalnog ligamenta i alveolarne kosti.

Root surface biomodification

The changes on the surface of the tooth root affected by periodontal disease are investigatedas well. Removal of bacterial deposits, tartar and endoxins from the cement is considered as a basic prerequisite for the formation of a new attachment apparatus28. However Stahl et al.[29] warned that demineralization of the root surfacehad as a consequence the exposure of dentin collagen, and that would facilitate cement deposition by encouraging mesenchymal cells from the surrounding tissue to stimulate its differentiation into cementoblasts. The biological concept was that ifthe collagen fibers ofdental matrixwereexposed, the adhesion to surface of tooth root of the blood coagulumcould be enabled, as well asthe fibroblasts migration.

The growth regulating factors of periodontal regeneration

The growth factor is a general term for a group of polypeptide hormones, and theystimulate a large number of different reactions such as proliferation, chemotaxis, differentiation and production of extracellular matrix proteins[30]. Therefore, it is understandable that growth factors could-potentiallymean help in trying tostimulate periodontal regeneration.

Growth factors (GF) are natural biological mediators which regulate cellular processes that are crucial for tissue regeneration. The important growth factorsfor periodontal regeneration are: platelet growth factor-PDGF, transforming growth factor-growth factor-EGF, osteogenic protein 1-BMP-7, bone morphogenetic protein-BMP-2, BMP-3 and angiogenic growth factors TGFβ1 and TGFβ2, insulin-like growth factor-IGF, fibroblast growth factor-FGF.

Platelet-derived growth factor (PDGF) isone of the main human growth factors. Although, it was first described as the part of platelet alpha granules, it was found to be synthesized in other cells, such as macrophages and endothelial cells[31]. Numerous studies, both in medicine and dentistry, have confirmed its positive effect on wound healing. It is considered to be one of the first factor presented in the wounds, andcould initiate the healing process of the surrounding tissues[32]. It was noticed that PDGF has mobilized cells from the surrounding matrix, as well as it hadinfluence on chemotaxis and proliferation of periodontal ligament and alveolar bone cells.

On takođe pospešuje regeneraciju alveolarne kosti, periodontalnog ligamenta i cementa, kao i delova potpornog aparata, koji su najkomplikovaniji za regeneraciju.

U jednoj od prvih studija na ovu temu, pokazano je to da aplikacija 0,15 mg/ml PDGF-a i 0,15 mg/ml IGF-a rezultira značajnim poboljšanjem ispunjenosti defekta novom kosti, u odnosu na konvencionalnu hirurško terapiju[33].

Zaključak

Može se zaključiti da postoje dokazi o tome da parodontalni ligament sadrži progenitorske ćelije, koje služe za obnavljanje izgubljenog epitelnog pripoja. U budućnosti, parodontalni regenerativni postupak ćelijama periodoncijuma trebalo bi da podstakne repopulaciju površina, koje su bile zahvaćene parodontopatijom.

Postavljanje koštanih transplantanata u infrakoštane parodontalne defekte može dovesti do boljih kliničkih rezultata, od onih koji se postižu klasičnom režanj operacijom, ali globalno gledano, koštani transpantati ili koštani zamenici primarno se smatraju materijalima izbora, koji služe za punjenje koštanih defekata.

Do sada je utvrđeno da potpuna regeneracija parodoncijuma nije moguća, uprkos primeni poznatih terapijskih procedura. U praksi, zadovoljavamo se sprečavanjem daljeg napredovanja patološkog procesa. Dobrim terapijskim rezultatom može se smatrati postizanje manjeg ili većeg stepena regeneracije parodoncijuma i stvaranje zdravih uslova, koji mogu omogućiti dobru funkciju potpornog zubnog aparata u dužem vremenskom periodu.

Izjava o sukobu interesa

Autori izjavljuju da nema sukoba interesa.

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It also promotes the regeneration of alveolar bone, periodontal ligament and cementum, as well as the parts of the supporting apparatus whichare the most challenging for regeneration.

One of the first studies about this topic showed that the application of 0.15 mg/ml PDGF and 0.15 mg/ml IGF resulted in a significant improvement of the new bone-defect-filing, compared to the conventional surgical therapy[33].

Conclusion

It could be concluded that there were evidencesofperiodontal ligament progenitor cells that served to restore the epithelial attachment loss. In the future, periodontal regenerative treatment with periodontal cells should encourage repopulation of the areas that have been affected by periodontal disease.

The placement of bone graftsin the infraosseous periodontal defects may lead to thebetter clinical outcomesfor patients thanclassical flap surgery, but globally, bone grafts or bone substitutes were primarily considered as material choiceforfillingthe bone defects.

So far, it has been noticed that complete periodontal regeneration has not been possible despite application of known therapeutic procedures. In practice, we are satisfied with the goal of preventing further progression of the pathological process. A successful therapeutic outcome can be considered as the achievement of therapeutic goals described like a greater or lesser percent of periodontal regeneration and the creation of health condition that can enable a good function of the supporting dental apparatus in a long period of time.

Conflicts of Interest statement

The authors declare no conflicts of interest.

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