PRF vs EMD periodontal regenerative surgery : a double blind, randomized controlled trial on the treatment of furcation II involved molars

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Compare PRF and EMD regenerative potential in the surgical treatment of molar teeth with periodontal destruction in the furcation area.Evaluate induced Healing potential of the two materials. Correlate healing pattern with biomarkers in blood and...

Ethical review	Approved WMO
Status	Pending
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON46398

Source
ToetsingOnline

Brief title
PRF in periodontal regenerative surgery

Condition

- Bacterial infectious disorders
- Head and neck therapeutic procedures

Synonym
chronic adult periodontitis, periodontal disease, periodontitis

Research involving
Human

Sponsors and support

Primary sponsor: ACTA-Parodontologie afdeling
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: periodontal, PRF, regenerative, surgery

Outcome measures

Primary outcome

The primary aim is to evaluate if the adjunctive use of PRF during periodontal surgery (Open Flap Debridement + PRF) and the adjunctive use of EMD (Open Flap Debridement + EMD) improves the clinical outcomes (horizontal clinical attachment level, probing pocket depth, vertical clinical attachment level, bleeding on probing, bone fill) of furcation involved molars, compared to Open Flap Debridement alone (OFD).

Secondary outcome

The secondary aim is to clinically assess the wound healing process and to evaluate patient*s acceptance and morbidity of the different surgical procedures.

The tertiary aim is to investigate a possible correlation of systemic (peripheral blood) and local (gingival crevicular fluid) immunological responses with the quality of early wound healing evaluation and final clinical results.

Study description

Background summary

Periodontitis is an inflammatory disease of the supporting tissues of the teeth, namely connective tissue attachment and alveolar bone. Severe forms of periodontitis result in the loss of these tissues and eventually loss of the teeth. Active treatment of periodontitis includes the non-surgical and the surgical therapy. Ultimate aim of the periodontal therapy is to remove the infection and inflammation and, if possible, reconstruct or regenerate the lost periodontal tissues in order to retain the teeth as long as possible. In periodontitis, molar teeth run the highest risk of being lost in comparison to other teeth, because of their multi-rooted anatomy (furcation) which makes proper oral hygiene and professional maintenance difficult.

In molar teeth. the degree of furcation involvement, as a measure of inter-radicular bone loss, was demonstrated to be a prognostic indicator for the risk of future attachment and tooth loss.Several studies have demonstrated that, in multi-rooted teeth, sites presenting furcation defects respond less favourably to non-surgical therapy, compared to sites that do not have furcation involvement, and have higher risk for tooth-loss (Salvi 2014, HIrschfield and Wasserman 1978). Therefore, improving the furcation involvement of a molar could mean improving the prognosis of the tooth, and, as a consequence, improving the masticatory function and the quality of life of the patient.

Several surgical procedures have been proposed to treat molar teeth with furcation involvement. The most commonly used is the open flap debridement (OFD). In comparison to other surgical therapies, as respective of regenerative surgeries, molars treated with OFD showed a higher rate of re-treatment need (Dannewitz 2016).The periodontal resective surgery consists in bone resection and either tunnelling of the furcation area or root resection or root amputation. Drawbacks of these techniques are the need for endodontic treatment, the sacrifice of alveolar bone and tooth substance and, as a consequence, the high risk of complications.

In this perspective, the ultimate aim of the periodontal therapy is to re-establish the supporting tissues that have been lost due to the periodontal inflammation. To this aim, The Guided Tissue Regeneration (GTR) has been attempted during the past decades to recreate a new functional attachment apparatus in molar furcation areas. The need to focus future research on regeneration was underlined by a consensus report from the American Academy of Periodontology in 2014.

In the past 20 years, the use of enamel matrix derivate (EMD) in combination with periodontal surgery, demonstrated to increase the chance of achieving (partial) periodontal regeneration compared to OFD and Resection techniques (Casarin et al. 2010). From the study of Casarin, it can be concluded that EMD therapy promoted a reduction in the number of proximal furcations presenting a diagnosis of class II after 24 months of treatment, compared with OFD therapy. For these reasons, EMD is commonly used in periodontal regeneration.

Nevertheless, EMD is a xenogenic material of animal origin (porcine) and this aspect, together with the high cost of the product itself, still can bring problems in terms of patient acceptance (some religions don*t allow the use of animal material in human body; some patients prefers not having any animal derived material because of ethical reasons and/or beliefs).

More recently, an autologous material has been developed; Platelet Rich Fibrin (PRF). PRF has demonstrated to be beneficial in wound healing, due to the potential of slow Growth Factors release and the dense fibrin network. These characteristics seem to be favourable especially in the early phase of the wound healing process. In vitro studies and some clinical trials have reported promising results also in periodontal regeneration. Its advantage is the autologous origin and substantial reduced direct material cost for the patient (Dohan Ehrenfest 2006, 2009, 2010). Up to date, no studies have been published which compare PRF with EMD This is of importance to confirm PRF as a suitable alternative to EMD in the surgical treatment of molar teeth with periodontal destruction in the furcation area.

Study objective

Compare PRF and EMD regenerative potential in the surgical treatment of molar teeth with periodontal destruction in the furcation area.
Evaluate induced Healing potential of the two materials.
Correlate healing pattern with biomarkers in blood and gingival crevicular fluid.

Study design

In this double blind, randomized controlled trial, 3 different treatment modalities will be tested on the patient cohort.
The selected sites will be randomly allocated to receive A-PRF+ + OFD, EMD + OFD or OFD .

The screening will be carried out on the patient that received periodontal reevaluation at ACTA-Periodontology department e months after IPT . All the patients will already have full periodontal clinical measurements including Full Mouth Plaque Scores, Full Mouth Bleeding Scores, Pocket Depth, Attachment Level and full radiographic examination before IPT (initial periodontal treatment) since this is the standard protocol at the department of Periodontology.
After being screened and selected, patients will be contacted telephonically to ask for participation in this research. Patients will receive an information brochure about the content and the aim of the research. They will have 2 weeks time to think if they will agree to participate in this project. After agreement patients will be asked to sign an inform consent to bring back the

day of data collection.
Standardized (same conventional- film holder) Digital single solo Radiograph will be taken, using exposure of 0,1 s.
At the moment of the surgical intervention,GCF preoperative collections will be performed. Blood will be sampled preoperatively to start the PRF preparation protocol. Local anaesthesia is administered and bone sounding will be carried out. intraoperative measurements will be also made by the surgeon.
Postoperative GCF samples, together with Early Wound Healing Assessment, will also administer the postoperative Questionnaire to each patient.
Postoperative measurements and evaluations will be made at 6 months.

Intervention

PRF preparation

The A-PRF+ will be prepared according the recently introduced spinning protocol. Sterile plain glass-based vacuum tubes (A-PRF+ 10 mL tube) are used, and the centrifugation protocol includes 1300 rpm for 8 minutes (Ghanaati et al. 2014). After centrifugation, in the tubes is possible to retrieve 3 layers. From bottom to the top, these are red blood cells and plasma, fibrin clot, serum. In order to be removed, the PRF clot is gently taken from the tube and separated from the red element phase at the base with pliers. The PRF clot is then adapted in the proper PRF box (APRF, Nice, France), that allows a constant compression due to the lid (cover of the PRF box) on top of the clot. The compression lasts 5 minutes, after which it is possible to retrieve PRF membranes, equal in size and thickness. The test material from the OFD + EMD and OFD groups will be discarded according to the ACTA protocol for the disposal of biohazard materials. The tubes (only component non-sterile) are placed after centrifugation in a specific metal rack to keep them stable. At that point, the top of the tube is removed with not sterile gloves, and the fibrin clot is removed from the tube using sterile tweezers and sterile gloves. The all procedure is performed in the surgical room, with sterile instruments and in sterile setting. We highlight once more that PRF is an autologous material and each clot is obtained for immediate use and use in the same patient (only the OFD + PRF).

Surgical procedure

All surgical procedures are following standard principles and are performed by one experienced clinician who is blinded for the treatment allocation until the moment of placement of the material. Intraoral antisepsis will be performed with 0,12 % Chlorhexidin rinse for 1 minute, and perioral tissues will be disinfected with Chlorhexidin 0.12% as well. Local anesthesia on the buccal and lingual aspects will be performed with xylocaine 1:80.000.
A microsurgical approach will be performed with modified or simplified papilla

preservation technique depending on the width of the inter-dental space (Cortellini et al. 2001). If deep pockets are present in the distal side (retromolar area), the access will be performed with a trap technique, leaving as much tissue as possible in the middle of the ridge. This will allow a better coverage and stabilization of the gingival flap. Full-thickness flaps will be raised around the defects. The elevation of the flap will be performed in the most atraumatic way possible, leaving interdental tissues intact. In addition, the flaps will be extended apically to the defects and furcation entrances, to ensure that the barrier at placement will rest on bone along its entire peri-defect extension. Releasing incisions will be performed on the mid-buccal and mid-lingual side of the most mesial tooth involved in the flap.
Degranulation will be thoroughly made with curettes, including removal of granulation tissue from the furcation involved areas. After having access to the bone anatomy, ultrasonic debridement of roots will be performed with saline cooling, together with hand instruments. Clinical bone measurement will be at this moment performed, including horizontal and vertical bone in the furcation areas and, if present, measurements of infrabony defects (Tonetti et al. 2002). No bone corrections will be performed in any case. If enamel projections or enamel pearls are visible, they will be corrected and smoothened with diamond coated burs, until reaching the dentin below.
At this point, the person in charge for the randomization will open a randomized assigned envelope containing the treatment allocation and the surgeon will be informed. about which of the three approaches will be used (A-PRF or EMD or OFD only). If the patient is allocated to OFD alone group, the area will be rinsed with physiological solution (NaCl 0,9%), followed by a pause of 1 minute, and later copiously irrigated once again with the same solution. This will resemble the application of regenerative materials. At the end of the sham procedure, sutures are directly applied. In case of PRF allocation, sterile prepared PRF membranes will be minced by sterile scissors and compressed, as much as possible, into the furcation II defect of the molars involved in the surgery. In order to guarantee clot stabilization, an additional PRF membrane will be applied covering the graft material and protecting the furcation entrance around the tooth profile. The eventual application of the PRF will happen in less than 1 hour from the beginning of the surgery. In case of EMD, the manufacturer protocol will be applied, consisting of EDTA root conditioning for 1 min, rinsing with saline, and immediately after by EMD application for 1 min and suturing. The papilla at this point will be repositioned in the original buccal position. Horizontal 5-0 polypropylene tension-free sutures will be applied with the intention to achieve primary closure. An additional horizontal external mattress suture with a laurel loop is performed. This will allow the tissues to stay in a coronal position. The duration of surgical session will be recorded for each procedure, and it*s expected to be around 90 minutes.

Postoperative instructions

Every patient will be asked to avoid any form of brushing in the operated area and to rinse first with hydrogen peroxide for 2 mins and later with Chlorhexidine 0,12 % (PerioAid 0.12%, Dentaid, Barcelona, Spain) for 1 min twice per day. These instructions will be continued for 4 weeks.
Painkillers use (Paracetamol 500 mg, max 6g per day) will be advised if necessary and the patient will be requested to report the consumption of the medication in the provided diary/ questionnaires.
Sutures will be removed after 14 days. A prophylaxis protocol via gentle polishing with rubber cups and brushes will be performed on day 3, day 7, day 14, week 6 and month 3 after surgery.

Study burden and risks

This study also investigates whether there is a possible correlation between the general blood count (numbers of white blood cells), a number of biomarkers in the local gingival crevicular fluid (GCF) and early wound healing. The hypothesis here is that the application of PRF or EMD positively influences local wound healing.

Nature and extent of the burden and risks for patients due to their participation:
Benefits for patients: the surgical procedures are standard periodontal interventions to treat periodontal defects in molars with furcation problems. Degranulation, cleaning of the affected root surfaces etc are standard. The results of standard treatments for molars often result in deep recessions (withdrawn gums) and it is difficult for patients to clean between the roots in the new postoperative situation. So new methods to regenerate the affected bone between the roots (furcation defects) and reduce the furcation defects from class 2 to a class 1 are an important step forward. In addition, it is important to avoid artificial or animal materials by means of autologous regeneration.
The time for the procedure is standard 90 min, the application of the experimental approaches (PRF or EMD) does not give an extension of the estimated surgical time. Application of Enamel Matrix Proteins (EMD) is a procedure that has been used in periodontal surgery for more than 20 years and there are no reported risks. In the current study design, the application applies EMD as a "positive control" for regeneration of the furcation defect.
The blood collection (venipuncture in the antecubital fossa), is a very low risk for the patients; the sampling of the GCF is not invasive and does not pose a risk for the patient: this procedure is generally accepted and executed as a routine.
An extra effort is required from the patient by completing a questionnaire in the form of a VAS scale every day during the first week after the procedure. WIll be requested at day 14, 42 and 90. Filling out the questionnaire is estimated to require a 5 minutes time (total 10 x 5 min = 50 min).
The assessment of wound healing on day 3 is the only extra appointment that is

not included in the regular protocol of the periodontology section at ACTA for the surgical treatment of molars with furcation disorders. This extra visit takes 20 minutes, but is essential to assess the early wound healing. All other agreements are part of the regular clinical protocol for periodontal regenerative surgery.
The extra time per patient is in total 135 min, divided as follows:
Questionnaire completion: total 10 x 5 min = 50 min.
Evaluation of wound healing : total 5 x 5 min = 25 min
Sampling GCF: total baseline plus 5 x 10 min = 60 min

Contacts

Public
Selecteer

gustav mahlerlaan 3004
Amsterdam 1081 LA
NL
Scientific
Selecteer

gustav mahlerlaan 3004
Amsterdam 1081 LA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Age 18-80. Presence of at least one molar with furcation involvement 2 , with horizontal AL

>3 mm and residual pocket after non-surgical therapy of >5 mm.
< 20 % FMPS
< 30 % FMBS

Exclusion criteria

On a patient level: Uncontrolled diabetes, HIV, leukopenia, or any systemic diseases related to reduced healing potential. Allergy to any medication related with the study protocol (Paracetamol, Xilocaine). Pregnancy or lactation. Daily use of any medication suppressive for the immune system like corticosteroid or immunosuppressant. Antibiotics use before the study enrolment. ;On tooth level: Third molars. Terminal bone loss. Endodontically and non-Endodontically treated teeth with periapical radiolucency. Periapical radiolucency or vertical fracture. Mobility >1. Furcation involvement grade 0 or 1.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2018
Enrollment:	69
Type:	Anticipated

Medical products/devices used

Generic name:	Amelogenin
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	25-04-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL62656.029.17