Regenerative surgical treatment of peri-implantosseous defects - a multicenter randomized prospective clinical study

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Project description:A controlled randomized multicentre prospective clinical trial of 12 months duration at 5 centres. To evaluate and compare appliance of porous titanium granules (PTG) during surgical treatment of peri-implant osseous defects of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Dental and gingival conditions
Study type	Interventional

Summary

ID

NL-OMON36465

Source
ToetsingOnline

Brief title
Peri-implantitis/Tigran study

Condition

- Dental and gingival conditions
- Hepatobiliary neoplasms malignant and unspecified
- Bone and joint therapeutic procedures

Synonym
infection of toothimplant surrounding tissues, Peri-implantitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Centrum voor Tandheelkunde Amsterdam (ACTA)

Source(s) of monetary or material Support: Ministerie van OC&W,Tigran AB

Intervention

Keyword: bone regeneration, implant, infection, titanium granules

Outcome measures

Primary outcome

The main aim is to show a mean difference in change in FILL (bone regeneration of peri-implant osseous defects) in patients treated with titanium granules compared with patients treated with sham at 12 months.

Secondary outcome

Analysis of secondary endpoints

The secondary parameters to be analysed are:

1) change in clinical parameters (PPD, BoP, PUS)

2) change in subclinical parameters (radiographic defect resolution)

3) change in microbial composion of the peri-implant sulcus before and after treatment

4) in vitro cytokine production of fibroblasts of peri-implant origin (discarded during the operation) in response to pathogens (especially P. gingivalis). Response of the fibroblasts from patient colonozed with P. gingivalis will be compared with the response of the cells from the patients not colonized with P. gingivalis.

5) To evaluate soft parameters such as patients subjective satisfaction.

6) Aesthetics

Study description

Background summary

Peri-implantitis is an infection of peri-implant tissues with subsequent bone loss around an implant. If the condition is left untreated it often leads to further loss of bone tissue, and eventually there is an imminent risk that the entire implant is lost. In such cases, the jawbone must be regenerated before it is possible to anchor a new implant. This takes a long time and is both demanding and costly for the patient. If peri-implantitis is not treated properly, there is also a risk that adjacent teeth and implants may be affected. Peri-implantitis develops as a result of several factors such as oral pathogens colonizing peri-implant pocket and tissues, host*s genetic susceptibility and lifestyle factors. The microbial pathogens elicit an inflammatory response that may progresses into a chronic situation.
The traditional method of treating peri-implantitis is cleaning around the implant to attempt to remove the infection. However, experience shows that peri-implantitis attacks usually continue despite this cleaning. There is currently no established scientifically documented treatment strategy with a certain outcome. A number of surgical techniques have been tested, but the results have rarely produced lasting and predictable effects.
Nowadays, bone granules of a bovine origin are widely used within dentistry. Yet, there is growing hesitation to use this xenotransplantation material. Inert titanium granules may be a good alternative for alveolar bone regeneration.
Tigran* porous titanium granules are irregularly shaped and porous granules manufactured using commercially pure titanium. The granules are between 0.7 mm and 1.0 mm. When they are mixed with the patient*s blood or with a saline solution the granules attach to each other due to the capillary force. The granules that have a porosity of about 80% and an osteoconductive surface structure, imitate properties of human bone and create a scaffolding for bone generation that stimulates osteoblast colonization and osseointegration. The granules are non-resorbable and keep their volume during the operation and the entire healing period which ensures mechanical stability and a desired aesthetic result. This novel bone regeneration material has retained the mechanical strength, permanent volume fill and the osteoconductivity of titanium, while at the same time offer a porous architecture for optimal cellular ingrowth, revascularization and bone in-growth.

Tigran Technologies has its origins in orthopedics. The first use of Tigran*s porous titanium granules was in 1987*88, when they were used for the fixation of hip prostheses (1, 2). The titanium granules were found to provide initial mechanical stability, a scaffold for bone regeneration and ingrowth and excellent long-term clinical results.
Animal experiments using a hemiarthroplasty model demonstrated bone ingrowth

through the porous granules and suggest the possibility of obtaining the permanent prosthetic fixation by direct contact (osseointegration) between bone and prosthesis (3, 4).
In a pilot study on depression fractures of the lateral tibial plateau, where titanium granules were used to support the elevated articular surface, the clinical and radiological results were excellent (5). The titanium granules were found to offer several advantages compared with autograft bone and commercially available bone substitutes. The most important: The granules are not resorbed.

The first dental application with Tigran*s porous titanium granules was performed in 1995, when the titanium granules were successfully used to enhance bone regeneration following a ridge splitting in a case of a severely resorbed maxillary dento-alveolar ridge and this allowed a cross arch bridge installation (6). The titanium granules were also used successfully in cases with large cystic cavities, which were removed, whereupon the bone voids were filled with titanium granules * all patients recovered quickly with very good results (7).
Many implant treatments today begin with bone regeneration treatment for both functional and aesthetic reasons. Tigran porous titanium granules can be used for bone regeneration in a number of application areas, such as peri-implantitis, sinus lift and extraction cavities.

SINUS FLOOR AUGMENTATION
The first sinus floor augmentation with titanium granules was performed in 2003 with excellent clinical and radiological results (8). Later, sinus floor augmentation with titanium granules was performed in sixteen patients, comprising of 23 tooth implants that were followed for 1*3 years (9).
FURCATION DEFECTS
A randomized animal experiment has indicated that titanium granules can be safely used as bone graft substitute in degree II molar furcation defects (10, 11)).
PERI-IMPLANTITIS
With Tigran titanium granules the affected implants (peri-implantitis) can often be saved by bone regeneration around the implant and in this way unnecessary intervention and major costs related to replacing the implant are avoided.
The results of the pilot study were presented during the fall of 2008 and clearly show that bone can be regenerated using porous titanium granules. Tigran is first to through biopsies show that new bone grows in and around the titanium granules and recreates bone tissue around the implant. Following bone loss caused by peri-implantitis, parts of the implant surface becomes exposed to inflammatory cells, microbes and organic contaminants. A human biopsy taken 12 months after treatment of a peri-implant osseous defect with titanium granules showed well-integrated granules with bone ingrowth through the porosities of the granules and re-osseointegration of the implant (12).
Improved osseous regeneration was seen in a series of animal experiments (13)

and improved osseous defect fill in a prospective randomized case control study of 30 patients with peri-implant osseous defects (14). The present study is similar to the previous study but has a multicentre approach. The titanium granules are commercially available in the Netherlands (Solid Benelux BV, Vreeland), and are used by dentists and oral surgeons.

We hypothesize that the patients treated with the titanium granules will regenerate new bone around dental implants resulting in enhanced support of the implants and therefore better implant endurance.

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Study objective

Project description:
A controlled randomized multicentre prospective clinical trial of 12 months duration at 5 centres. To evaluate and compare appliance of porous titanium granules (PTG) during surgical treatment of peri-implant osseous defects of implants with sham (flap operation without appliance of PTG).

Primary Objective
To evaluate if appliance of porous titanium granules (PTG Tigran Technologies AB) during surgical treatment of peri-implant osseous defects:
a) gives significantly enhanced defect fill and
b) limit the progression of the decease after 12 months in comparison to sham.

Secondary Objectives
* To evaluate clinical parameters (Pocket probing depth (PPD), BoP, PUS)
* To evaluate subclinical parameters (radiographic defect resolution)
* To evaluate microbial composion of the peri-implant sulcus before and after treatment
* To evaluate interaction between the host (fibroblasts) and pathogens (especially P. gingivalis) in peri-implantitis, and further to study susceptibility to peri-implantitis on cellular level. Fibroblasts will be stimulated with P. gingivalis, but also with other commensal oral microorganisms (defined later), and cytokine-response to these cells will be defined.
* To evaluate soft parameters such as patients subjective satisfaction.
* Aesthetics

Study design

Controlled randomized multicentre prospective clinical trial of 12 months duration at 5 centres. To evaluate and compare appliance of porous titanium granules (PTG) during surgical treatment of peri-implant osseous defects of non submerged implants with sham (treatment without appliance of PTG).

Intervention

In each centre 6 test patients will be treated during the flap operation with debridement and porous titanium granules, and 6 control patients will be treated during the flap operation only with debridement (sham).

Study burden and risks

Each patient will be treated with a ordinary flap operation for peri-implantitis but the test patients will be treated during the flap operation also with porous titanium granules.
During flap surgery tissue material will removed (waste) and otherwise throuwn away. Now we would like keep this material and grow fibroblasts in vitro from this material.
Using a sterile paper point, additional subgingival bacterial samples (standard protocol, non-invasive) for microbiological diagnostics will be taken 6 and 12 months after surgery.
The risks associated with taking part in this clinical study are no greater than with ordinary flap surgery. As with ordinary flap operation, there may be some bleeding, pain and swelling for the first few days after the procedure.
There is a risk that the implant anyhow will come loose as may happen after ordinary flap operation as well. If this happens the loose implant and the granules will be removed through further surgery.
There is also a risk that the titanium granules will not anchor sufficiently.
If this happens the granules will be removed and ordinary flap operation will take place.

Contacts

Public
Academisch Centrum voor Tandheelkunde Amsterdam (ACTA)

Gustav Mahlerlaan 3004
1081 LA Amsterdam
NL
Scientific
Academisch Centrum voor Tandheelkunde Amsterdam (ACTA)

Gustav Mahlerlaan 3004
1081 LA Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

The patient should have;
* A peri-implant intraosseous defect with at least 3 mm defect depth as seen on an intraoral radiograph.
* Clinically a probing depth * 5 mm combined with bleeding and/or pus should be present at the site.
* During surgical exploration an intraosseous component of at least 3 mm at the deepest point must be present.
* The defect should have a minimum of 3 osseous walls (a circumference of the osseous defect of at least 270 degrees). Only 3 and 4 wall intraosseous defects will be included.
* The defect must not be wider than 4 mm and the defect angle must be less than 35 degrees (from axis of implant).
Implants included in the study must have been in function for more than 12 months.
Note: If the same patient has more than one defect meeting the inclusion criteria only one such defects will be included in the study. Other defects will be treated according the standard protocol.

Exclusion criteria

Main exclusion criteria:
* Subjects with diabetes mellitus (HbA1c >6.5)
* Subjects taking corticosteroids or other anti-inflammatory prescription drugs
* Subjects taking medications known to induce gingival hyperplasia
* Subjects must not be allergic to penicillin
* Subjects with a history of taking systemic antibiotics in the preceding month
* Subjects must not be pregnant or lactating
* Implants placed in grafted bone or previously augmented with bone /bone substitute or other type of regenerative material

* Implants previously treated for peri-implantitis
* If stability of the titanium granules cannot be accomplished in the defect
* Failure of obtaining soft tissue closure
* Mobile implants

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-12-2010
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	Tigran (TM) Porous Titanium Granules
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	07-10-2011
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	NL34816.029.11