Bone augmentation with autologous adipose tissue-derived mesenchymal stem cells and calcium phosphate carriers in the human maxillary sinus floor elevation model

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> Primary Objective:This is a pilot study, aiming at the clinical evaluation with respect to safety and feasibility of a one-step surgical procedure for maxillary sinus floor augmentation for the placement of dental implants, using a ceramic bone...

Ethical review	Approved WMO
Status	Pending
Health condition type	Bone disorders (excl congenital and fractures)
Study type	Interventional

Summary

ID

NL-OMON35169

Source
ToetsingOnline

Brief title
Adipose stem cells in the sinus floor elevation model (STEM CELL LIFT)

Condition

- Bone disorders (excl congenital and fractures)

Synonym
jaw bone athrophy, jaw bone loss

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: NWO-ZonMw

Intervention

Keyword: adipose tissue, bone regeneration, mesenchymal stem cells, sinus floor elevation model

Outcome measures

Primary outcome

Occurrence of any AE or SAE related to the product and/or procedure (in order

to determine the follow-up regime for dose-response studies)

Secondary outcome

1) Radiological/clinical assessment of bone formation

2) Histological/histomorphometrical evaluation of biopsies taken 6 months after

sinus floor elevation

Study description

Background summary

Previous in vitro and large animal studies within our laboratory have shown feasibility and safety of a novel concept employing bone substitutes in combination with freshly isolated adipose tissue stem cells, which can be harvested in a short time frame yielding clinically relevant numbers of mesenchymal stem cell-like regenerative cells. The whole one-step surgical procedure could be performed in 2 hours within the surgical theatre, thus avoiding costly GMP stem cell expansions and second intervention. Clinical studies are now needed to evaluate this concept for safety and efficacy within the human sinus floor elevation model, combining clinical outcome with histology. If successful, this offers broad potential for other bone tissue engineering applications.

Study objective

> Primary Objective:
This is a pilot study, aiming at the clinical evaluation with respect to safety and feasibility of a one-step surgical procedure for maxillary sinus floor augmentation for the placement of dental implants, using a ceramic bone substitute seeded with freshly isolated autologous mesenchymal stem cells derived from adipose tissue
> Secondary Objective(s):
Histological evaluation from biopsies obtained with hollow drills, routinely collected during the insertion of the dental implants, six months after sinus floor elevation

Study design

This pilot study will be an exploratory, randomized, open, placebo-controlled phase I intervention study.

Intervention

There will be three surgical interventions:
1. Sinus floor elevation procedure: This intervention will consist of two arms: In the first arm, the acquisition of abdominal adipose tissue, its automated processing using a CE-marked device to obtain the stem cell preparation, and its subsequent seeding on a calcium phosphate (CaP) scaffold to generate the bioactive implant. In a parallel arm, a routine sinus floor elevation procedure is performed by the Oral maxillofacial surgeon. These two arms are combined, as the surgeon inserts the bioactive scaffold material in the patient*s sinus cavity. The comparator group will receive CaP which is *seeded* with vehicle (ringers lactate solution) only. The remainder of the cells will be used for in vitro characterizations.
2. The 2nd intervention (6 months later) consists of the placement of dental implants by using hollow trephine drills. These drillings produce bone biopsies, which will be evaluated histologically / histomorphometrically.
3. The 3rd intervention encompasses the placement of the final fixed prostheses (crowns or bridges) on the dental implants

Study burden and risks

The procurement of the SVF and seeding on the scaffold has been the subject of extensive pre-clinical research. Re-implantation of the seeded scaffolds does not differ from the normal sinus floor elevation procedure, with which there is vast experience. In our preclinical studies and in recent reports on the use of mesenchymal stem cells from bone marrow and caP scaffolds in sinus floor elevation procedures no adverse effects were documented. Thus, post-implantation complications other than those associated with the standard sinus elevation procedure (infections [<10% of cases], massive loss of graft [< 1% of cases] and occurrence of voids or graft fragmentation [seldom]) are not

expected.
All previous and current human studies of transplanted cells, have involved the use of autologous or allogenic cells that required ex vivo expansion of the cells, which is costly, time-consuming and strictly regulated, making it an intricate procedure. By utilizing the Celution® 800 technology of Cytori Therapeutics, Inc., freshly isolated autologous adipose stem cell preparations (stromal vascular fraction, SVF) will be generated through minimal manipulation of the tissue and cells. Clinical costs may also be reduced, as the number and duration of hospital admissions may be diminished, and the need for expensive stem cell culture facilities is eliminated.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- minimal bone height of 4 mm at planned implant site(s)
- no local need for horizontal bone augmentation
- healthy appearance sinus maxillaris
- smoking below 10 sigarettes a day
- Age 18 years or older

Exclusion criteria

- History of malignancy or chronic infectious disease (i.e. HIV, Hepatitis)
- irradiation history in jaw area
- destructive sinus surgery indicated during anamnesis
- endocarditis or heart valve abnormalities, or heart valve prostheses
- abnormalities in the immune system, or use of immune suppressants
- severe bone metabolic disorders (e.g. severe osteoporosis treated with bisphosphonates)
- Chronic use (>7 consecutive days) of anticoagulants (such as aspirin) or Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) within 15 days prior to lipoaspriation
- Signs or symptoms of infection at the time of the surgical procedure
- pregnant or nursing, or intention to become pregnant

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2010
Enrollment:	20

Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	31-05-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-12-2011
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 24484
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2009-015562-62-NL
CCMO	NL29581.000.09
OMON	NL-OMON24484