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Cell therapy in periodontal regeneration. A double-blinded randomized parallel groups controlled clinical trial

Submission date
24/11/2014

Recruitment status
No longer recruiting

Registration date
16/12/2014

Overall study status
Completed

Last Edited
05/11/2020

Condition category
Oral Health

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Periodontal diseases are a group of inflammatory diseases affecting the tissues that surround and support the teeth: gingiva, alveolar bone (bone in the jaw that contains the tooth socket), periodontal ligament (tissue that connects the tooth to the tooth socket) and cementum (surface layer of tooth root which is attached to the tooth socket by the periodontal ligament). These diseases are a significant public health concern in a significant number of both developing and developed countries. Periodontitis, the most serious form of periodontal disease, involves the destruction of the supporting tissue and bone around the teeth. It's the most common cause of tooth loss in adults. According to recent research, severe periodontitis is the sixth-most common condition in the world. It is most likely to occur in people in their 30's and 40's. These data demonstrate how important is to treat this disease in order to avoid the destruction of the tooth supporting and, therefore, to improve patient's quality of life. Although non-surgical treatment of periodontitis does stop the disease from getting any worse, the reconstruction of tooth supporting tissues requires surgery and grafts using bone and other supportive tissues. However, the results of such reconstructive (periodontal regeneration) surgeries are unpredictable. The introduction of cell therapy opens a promising field in periodontal regeneration. Recent studies have confirmed the possibility of isolating non-differentiated mesenchymal stem cells from the periodontal ligament (periodontal ligament-derived stem cells "PDLSC") and improved regenerative results have been demonstrated when used in the treatment of severe periodontitis. Here, we want to test the safety and efficacy of cell-based therapy using autologous PDLSC embedded in a hydroxyapatite-collagen matrix (a component of bone) for periodontal regeneration in 1 and 2 wall- periodontal intrabony defects (destruction of alveolar and other supporting bone surrounding the teeth).

Who can participate?
Adults aged 25-70 years with moderate to severe periodontitis.

What does the study involve?
The participants are randomly allocated into one of two groups. Those in group 1 undergo periodontal regeneration surgery using autologous PDLSC embedded in a hydroxyapatite-

collagen matrix. Those in group 2 undergo periodontal regeneration surgery using the hydroxyapatite-collagen matrix scaffold only. The treatment is then assessed in both groups in terms of safety and efficacy.

What are the possible benefits and risks of participating?
If the study treatment is successful, the long term prognosis for teeth affected by periodontitis will improve and they will be less prone to falling out. The hydroxyapatite-collagen matrix scaffold has proven benefits for patient with periodontitis. The study covers all the costs, both in terms of the treatments and materials and therefore the treatment will be free for the participants. The main risks of participating in this study are those associated with any oral surgical procedure: swelling of the area, bleeding, pain, infection, local immune response, impaired healing, flap sloughing and bone loss. These risks are usually controlled with anti-inflammatory and antibiotic medication. Although not reported in the literature in principle there is the possibility of allergic reactions to collagen in the scaffold used.

Where is the study run from?
Faculty of Odontology, Complutense University of Madrid (Spain)

When is the study starting and how long is it expected to run for?
August 2014 to February 2019

Who is funding the study?
Department of Pharmacy and Health Products (Dirección General de Farmacia y Productos Sanitarios) Spanish Ministry of Health (Spain)

Who is the main contact?
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Clinical Trials Information System (CTIS)
2013-004035-77

Protocol serial number
EC10-095

Study information

Scientific Title
Comparison of periodontal ligament-derived mesenchymal stem cells embedded in hydroxyapatite-collagen scaffolds versus hydroxyapatite-collagen scaffolds alone in the regenerative treatment of 1 and 2 wall-intrabony defects in patients with chronic periodontitis in terms of clinical attachment level gains.

Acronym
PERIODONTAL-2013-01

Study objectives
Autologous periodontal ligament-derived mesenchymal stem cells (PDLSC) embedded in hydroxyapatite-collagen scaffolds will promote periodontal regeneration of 1 and 2 wall-intrabony defects with a greater clinical attachment level gains when compared to the control group (application of the scaffold alone).

Ethics approval required
Old ethics approval format

Ethics approval(s)
CEIC Area 7- Hospital Clínico San Carlos clinical trials ethics board (Madrid, Spain), 20/01/2011, ref. C.I 11/009.

Primary study design
Interventional

Study design
Single-centre double-blinded randomized parallel groups controlled clinical trial (pilot study).

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Periodontal regeneration after severe periodontitis using cell therapy.

Interventions
1. Experimental group (10 patients): 100mg hydroxyapatite-collagen scaffold (Bio-Oss-Collagen®, Geistlich Pharma AG, Suiza) with 10x106 autologous periodontal ligament- derived mesenchymal stem cells.
2. Control group (10 patients): 100mg hydroxyapatite-collagen scaffold (Bio-Oss-Collagen®, Geistlich Pharma AG, Suiza) plus saline solution (200µl).

Experimental or control treatment will be surgically introduced within the periodontal defects. In both groups, a surgical technique combining a coronal advanced buccal flap and a simplified papilla preservation approach at the level of the defect (as described by Zucchelli and De Sanctis 2008) will be used. After this intervention, patient's follow up will be 1 year for evaluating efficacy outcome variables and 5 years for assessing safety parameters.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Safety parameters: presence/absence of adverse reactions/events 1, 2, 4, 12, 24 and 36 weeks and 12, 24, 36, 48 and 60 months after the intervention. (Presence=1; Absence=0)
2. Efficacy parameters: clinical attachment level gains measured at 12 months, (in mm.) with a computerized pressure-controlled periodontal probe (Florida Probe®, Florida Probe Corporation, FL, USA). Clinical attachment level measurements will be performed at baseline, 24 and 36 weeks and 12 months after the intervention by a trained and calibrated examiner.

Key secondary outcome(s)
1. Probing Pocket Depth reduction (in mm.) measured with a computerized pressure-controlled periodontal probe (Florida Probe®, Florida Probe Corporation, FL, USA). Measurements will be performed at baseline, 24 and 36 weeks and 12 months after the intervention by a trained and calibrated examiner
2. Changes in gingival recession (in mm.) measured with a computerized pressure-controlled periodontal probe (Florida Probe®, Florida Probe Corporation, FL, USA). Measurements will be performed at baseline, 6, 9 and 12 months after the intervention by a trained and calibrated examiner
3. Radiographic bone fill measured in standardized periapical x-rays performed with long cone technique and bite blocks at baseline, immediately after surgery and at 3, 6, 9 and 12 months by a trained and calibrated examiner. Measurements (in mm.) done in DBSWIN imaging software (DentaScan): radiographic bone fill= (Alveolar bone crest-cementoenamel junction)-(base of the defect-cementoenamel junction)
4. Patient-based quality of life assessment by using a patient-self reported questionnaire (OHIP)

at baseline and 12 months
5. Tooth loss at 12 months
6. Patient-based aesthetic outcomes by using a VAS scale (1-10) at 12 months
7. Postoperative morbidity: wound healing assessment at 1, 2 and 4 weeks after intervention (1. Complete closure; 2. Thin fibrin line; 3. Fibrin; 4. Incomplete closure; 5. Necrosis)

Completion date
28/02/2019

Eligibility

Key inclusion criteria
1. Patients from 25 to 70 years old (women in fertile age will need a negative urine pregnancy test and will be willing to use contraception with a failure rate <1% (oral contraceptives, double barrier method, intrauterine devices)
2. Absence of relevant medical condition
3. Non-smoker patients
4. Patients with moderate-severe chronic Periodontitis, treated with non-surgical periodontal therapy in the School of Dentistry of Complutense University (Madrid).
5. Patients with at least one tooth with clinical attachment level loss greater than 5mm and a 1-2 wall intrabony defect deeper than 4mm
6. Patients with at least one tooth with a hopeless prognosis or third molars, planned to be extracted
7. Band of keratinized gingiva of at least 2mm at the level of the tooth with the intrabony defect
8. Patients with good oral hygiene (Plaque Index lower than 25%)
9. Patients with optimal compliance

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
20

Key exclusion criteria
1. Patients in which the teeth intended to regenerate have type III mobility, type III furcation involvement, periapical pathology and vertical root fracture
2. Patients with aggressive periodontitis
3. Pregnant and lactating woman
4. Patients with diseases that affect connective tissue metabolism
5. Patients with history of rapidly progressive dementia/ neurological illness of unknown etiology
6. Patients with previous treatment with pituitary-derived hormone

7. Patients with uncontrolled infection (systemic/ local in the tissue of interest)
8. Patients with history, risk factors, clinical evidence or positive tests for HIV, HBV, HCV and HTLV I/II.
9. Patients with history of chronic autoimmune disease that can have caused injury of the tissues of interest
10. Patients with disease-transmission risk factors related to travelling history and local prevalence of local infections
11. Patients with Diseases that affect connective tissue metabolism
12. Patients with Risk of invalidation of diagnostic tests due to hemodilution or immunosuppressive-treatment.
13. Patients with Presence of physical signs that may entail a risk for disease transmission
14. Patients with history of recent vaccination with attenuated virus that may entail a source of infection
15. Patients who have participated in an intervention clinical trial in the same quadrant in the last 2 months

Date of first enrolment
01/08/2014

Date of final enrolment
28/02/2018

Locations

Countries of recruitment
Spain

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Sponsor information

Organisation
Department of Pharmacy and Health Products (Dirección General de Farmacia y Productos Sanitarios) Spanish Ministry of Health.

Funder(s)

Funder type

Government

Funder Name
Ministerio de Sanidad, Servicios Sociales e Igualdad

Alternative Name(s)
Ministry of Health, Social Services and Equality

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2020	03/11/2020	Yes	No