ISRCTN17793055 https://doi.org/10.1186/ISRCTN17793055

A study of the benefit of fat transfer to the peri-oral area for scleroderma patients

Submission date
06/06/2019

Recruitment status
No longer recruiting

Registration date
10/09/2019

Overall study status
Completed

Last Edited
19/08/2020

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Scleroderma is an uncommon condition that results in hard, thickened areas of skin and sometimes problems with internal organs and blood vessels. Fibrosis is similar to scarring after injury but is excessive and leads to tightening and hardening of the skin. Fibrosis of the face inhibits facial movement and impairs mouth function. Facial fibrosis greatly impacts the quality of life of patients and most often leads to problems with eating, speaking and dental care. We are pioneering a new treatment option for facial fibrosis in SSc. The surgical technique utilizes the patients' own fat stores to reconstruct facial tissue. Facial volume is enhanced but most strikingly the effects of facial fibrosis are reversed. This has had profound effects on the patient's quality of life and has restored facial mobility and mouth function. These striking results need to be
confirmed in a controlled multi-centre clinical trial. The first step is a feasibility study to inform important aspects of the design, a single-site study that will take place in the Royal Free London NHS Foundation Trust.

Who can participate?
Patients with systemic sclerosis (scleroderma) affecting the face, aged >18 < 90 years

What does the study involve?
Participants will be allocated to receive surgery at the beginning or the end of the trial. The surgical procedure is called autologous lipotransfer and is a minimally invasive clinical procedure that is considered a standard of care procedure in reconstructive surgery. Participants will be asked to complete questionnaires and attend clinical appointments to discuss progress.

What are the possible benefits and risks of participating?
Benefits: Our previous retrospective study has demonstrated a significant benefit of the intervention to SSc patients. Mouth function is significantly improved, facial volume is restored, aesthetics improved and quality of life is significantly improved.
Risks: As with all surgical procedures there a is risk associated with anaesthesia. Participants will be carefully screened to ensure that they can safely undergo general anaesthetic as determined by heart and lung function. The intervention is low risk with very low risk of complications. Participants of Sys-Stem will have more follow up assessments than routine care, at 6 weeks, 3

months and 6 months compared to one follow up in this time. This may represent a burden to some patients although they will receive additional care, supervision and support which may offset any burden.

Where is the study run from?
Royal Free Hospital, UK

When is the study starting and how long is it expected to run for?
August 2019 to June 2021

Who is funding the study?
National Institute for Health Research (NIHR), UK

Who is the main contact?
Carole Frosdick
carole.frosdick1@nhs.net

Contact information

Type(s)
Public

Contact name
Ms Carole Frosdick

Contact details
Royal Free Hospital
Department of Plastic Surgery
Pond Street
London
United Kingdom
NW3 2QG
+442037582000 ex 36918
carole.frosdick1@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
42520

Study information

Scientific Title

Feasibility study of stem-cell enriched autologous lipotransfer to treat oro-facial fibrosis in systemic sclerosis

Acronym
Sys-stem

Study objectives
To understand the feasibility of using the Mouth Handicap in Systemic Sclerosis Scale MHISS to measure the outcome of autologous fat transfer for treating perioral fibrosis of systemic sclerosis

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/06/2019, London-Camden and Kings Cross Research Ethics Committee (HRA Skipton House, 80 London Road, London. SE1 6LH; 0207 972 2561; nrescommittee.london-camdenandkingscross@nhs.net), ref: 19/LO/0718

Study design
Single centre interventional open cohort study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Perioral fibrosis of systemic sclerosis (scleroderma)

Interventions
Sys-Stem is a single centre trial that will take place at the Royal Free London NHS Foundation Trust directly assessing feasibility for the main multi-centre trial.

Sys-Stem is an open-label design and will consist of 50 patients. 25 patients in the treatment arm and 25 patients in the control arm. A sample size of 50 was chosen for pragmatic reasons and is suitable for a feasibility study of this kind. We will attain information from a sample size of 50 that will allow a power calculation for the future multi-centre trial. SSc patients are high-risk surgical candidates and so it would be unethical and dangerous to perform a sham operation or placebo on a control group. For this reason, the control arm will be a no-treatment concurrent control receiving care-as-usual. However, we will not withhold treatment from the participants in the control arm. All
participants randomised to the control arm will be offered the intervention at the end of the assessment period/after 6 months. This ensures that our study is ethical and patient-focused.

Due to the study design, study participants cannot be blinded to the treatment they receive. To reduce bias, outcome assessors (researchers) will be blinded. To ensure this, participants will be assessed in a private clinic appointment by Prof. Butler who will have performed the surgeries and will be aware of the allocations. All clinical assessments and follow up related to the surgical

procedure will be performed by Prof. Butler. The participants will be asked not to disclose whether they have received the treatment or not to the other assessors. All other assessments and follow-up will be carried out by the blinded assessors in a separate clinic.

We will determine suitability for the trial based on inclusion and exclusion criteria. Suitable patients identified from the Royal Free SSc registry who match the inclusion criteria will be approached by the PI in clinic at their next scheduled visit or telephoned and invited to visit clinic to discuss the study. The study will be described to the patient by the PI and they will be provided with a detailed patient information sheet (PIS) detailing the specifics of the study and the risks and benefits involved. Potential participants will be given a full month to read the trial documentation and consider participation. The participants will then be asked to provide consent at their next clinic appointment. Informed consent will be taken by the trial nurse.

As part of the trial process, the clinical trials nurse will complete a clinical assessment of the face inclusive of qualitative and quantitative measurements. Mouth opening will be quantified using clinical measurement tools and participants will be asked to complete the Mouth Handicap in Systemic Sclerosis scale (MHISS) questionnaire which will assess the qualitative level of mouth dysfunction. All pre-intervention assessments will be recorded as screening notes in the participant's medical record and the CRF. Participants whose disease has a clinically relevant impact on facial function and appearance and with an MHISS score of ≥20 will be considered eligible for Sys-Stem. Randomisation of eligible participants to the control or treatment arm will then be performed by a computerised anonymous system called www.sealedenvelope.com. This computerised system ensures that none of the research team is aware of the treatment groups and there will be no researcher bias. Time from enrolment to participation in the study for each participant will be 2-3 months. All participants will then be scheduled for baseline assessments to be carried out by the research team. Baseline measurements will be conducted in clinic prior to the surgical procedure.

The surgical procedure will be carried out in theatre under general anaesthetic and will take less than one hour. The surgical procedure is called autologous lipotransfer and is a minimally invasive clinical procedure that is considered a standard of care procedure in reconstructive surgery. In brief, adipose/fat tissue is taken from the abdomen or thighs with a small liposuction cannula in the operating room. The adipose/fat tissue is then centrifuged to separate out the fraction that is rich in stem and progenitor cells and other fractions that contain blood and oils. Only the fraction containing the stem cells is used for the procedure. The stem cell rich fraction is then injected into the areas of the face to be treated using a minimally invasive technique. The entire surgical procedure will be performed by the lead investigator, Professor Peter Butler, in less than one hour. Volume injected and site of injections will be recorded in the participant's medical records/Case Report Form (CRF).

At the time of the lipotransfer under general anaesthesia, a 4mm skin biopsy of the participant's forearm will be taken. Following the biopsy, an aliquot of lipotransfer will be inserted into the area. This area will then be marked. At 6 months the same area will have another biopsy taken to assess the effect of the lipotransfer on the skin. The second forearm biopsy will be undertaken when the patient undergoes their second procedure for autologous lipotransfer for the peioral region to prevent any additional risks from underlying general anaesthesia.

Following baseline assessments and the intervention for those in the treatment arm, participants will be assessed in clinic at 6 weeks, 3 and 6 months after the procedure or 6 weeks, 3 and 6 months after baseline assessments for those in the control arm.

At each visit participants will have a clinical assessment with Prof. Butler, complete validated questionnaires and attend medical photography. The 2D and 3D images will assess volume augmentation in the face. The validated questionnaires will assess mouth function and psychological status pre- and post-treatment, quality of life and level of health care resource use. Mouth function will be assessed by the Mouth handicap in Systemic sclerosis scale (MHISS). Psychological status and quality of life will be assessed by the Derriford Appearance Scale (DAS24), Visual Analogue scale (VAS), Hospital Anxiety and Depression Scale (HADS) and Brief Fear of Negative Evaluation Scale
(BFNE), and the EuroQol EQ-5D-5L.

Sys-Stem will also determine the acceptability of a range of secondary objective outcome measures to assess fibrosis of the face. These will be carried out at baseline and 6 months. These will include mouth opening measurements, cutometry to measure skin elasticity, durometry to measure skin thickness and handheld visual capillary microscope (HVCS), thermography and ultrasound.

The duration of the trial for each participant will be 9 months from enrollment. All study participants will be contacted monthly initially for the first 3 months by telephone by a member of the study team and invited to attend clinic if they have any serious concerns or any side effects from treatment.

Treating patients with scleroderma with autologous fat transfer is apart of routine clinical practice. In addition, following the patients up using non-invasive methodology is also apart of normal clinical care. However, randomisation of the participants apart of the research protocol. Furthermore, the only intervention, which is not a part of the participant's normal standard of care, is the forearm biopsy. This study aims to ascertain the mechanism by which the autologous lipotransfer is reversing the skin fibrosis by conducting laboratory analysis on skin fibroblasts in participants with scleroderma.

Intervention Type
Procedure/Surgery

Primary outcome(s)
The Mouth Handicap in Systemic Sclerosis Scale (MHISS) to measure the outcome of autologous fat transfer for treating perioral fibrosis of systemic sclerosis, measured at each visit then post-intervention at 6 weeks, 3 months and 6 months

Key secondary outcome(s))
Feasibility of running a full trial:
1. Estimate recruitment rate required for the main trial.
2. Estimate attrition rate required for main trial.
3. Willingness of participants to be randomised
4. Feasibility of obtaining patient-reported outcomes via psychological and quality of life questionnaires; Visual Analogue Scale (VAS) Derriford Appearance Scale (DAS24), Brief Fear of Negative Evaluation Scale (BFNE), Hospital Anxiety and Depression Scale (HADS), EuroQol (EQ-5D-5L)
5. Feasibility of determining cost-effectiveness in main trial, by quality-adjusted life-years calculated from the EQ-5D-5L, and costs to the NHS according to health care service use questionnaires.

6. Acceptability of a range of qualitative and quantitative outcome measures (inter dental and mouth aperture measurements, cutometry, durometry, thermography, ultrasound, handheld visual capillary microscope (HVC).

Completion date
26/06/2021

Eligibility

Key inclusion criteria
1. Age >18 < 90 years
2. Limited or diffused forms of systemic sclerosis in the established phase of the disease
3. Clinically relevant impact on facial function
4. Willing and able to provide written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Body mass index <18.5
2. Pregnant
3. Not fit for a general anaesthetic as per heart and lung function.
4. Any active infection which precludes fat harvest or injection

Date of first enrolment
01/10/2019

Date of final enrolment
01/02/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Sponsor information

Organisation
UCL

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research; Grant Codes: PB-PG-1216-20042

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed 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?
Protocol article	protocol	18/07/2020	19/08/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes