Stromal Vascular Fraction and Platelet-rich Plasma injectable to promote dermal wound healing.

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To quantify clinical and histological changes of the skin in promoting early wound healing when SVF + PRP injectable is used as treatment in comparison to SVF and PRP alone.

Ethical review	Not approved
Status	Will not start
Health condition type	Skin and subcutaneous tissue therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON45942

Source
ToetsingOnline

Brief title
SVF and PRP to promote dermal wound healing

Condition

- Skin and subcutaneous tissue therapeutic procedures

Synonym
mamma reduction, tissue healing

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Arthrex,arthrex.

Intervention

Keyword: PRP, SVF, wound

Outcome measures

Primary outcome

Postoperative clinical improvement is measured with the POSAS questionnaire containing the patient scar assessment and will focus on: vascularization, pigmentation, thickness, relief, pliability, pain, itchiness, stiffness and irregularity. Questionnaires will be given at predetermined time-points (2 weeks, 6 weeks, 12 weeks and 52 weeks postoperative). One questionnaire per patient is completed for each part of the scar of each breast every time.

Secondary outcome

Postoperative clinical improvement is measured with the POSAS questionnaire containing the observer scar assessment and will focus on: vascularization, pigmentation, thickness, relief, pliability, pain, itchiness, stiffness and irregularity. Questionnaires will be given at predetermined time-points (2 weeks, 6 weeks, 12 weeks and 52 weeks postoperative). One questionnaire is completed for each part of the scar of each breast every time.

Postoperative scar improvement is measured by histological observation of biopsies (into the dermal fat layer) at predetermined time-points (6 weeks and 12 weeks). Histological observation will focus on extracellular matrix remodelling, epidermis renewal, cell infiltration and new microvasculature formation. One biopsy is taken of each part of the scar of each breast every time.

Postoperative improvement analysed by a photographic panel assessment.

Photographic evaluation will focus on scar size reduction, change of colour and relief using a Visual Analogue Scale (VAS). Standardized photos will be taken at predetermined time-points (2 weeks, 6 weeks, 12 weeks and 52 weeks). One photograph is taken of the scar of each breast every time.

Study description

Background summary

Already 1980*s, the clinical observation has been made that adipose tissue transfer, also known as fat grafting, lipografting or lipofilling, can improve skin quality and reduce scarring. Since then, many case reports have described the seemingly beneficial effect of lipofilling on scar appearance. Also, in several retrospective and prospective clinical trials it has been investigated if scarring is reduced after lipofilling and/or if this is superior over placebo treatment.

In controlled and reproducible setting of different animal models, light has been shed on the mechanism behind the scar appearance improving and pain reducing properties of lipografting. In animal models, after radiation, radiation dermatitis can develop, which eventually can give rise to fibrotic skin, with epidermal thickening and irregular collagen deposition in the dermis. In clinical studies on lipofilling as an anti-scarring treatment, outcome is measured either by improvement of scar appearance, or in case of painful scars, by decrease in pain. The effectiveness of lipofilling for improvement of scar appearance has been investigated in fourteen case reports or clinical trials. Overall, all fourteen case reports or clinical trials report amelioration of scar appearance after lipofilling. Efficacy of lipofilling as means for pain reduction, was investigated in seven case reports or studies. Overall, all seven studies report a reduction of pain after treatment of painful scars with lipofilling.

We are particularly interested in the Stromal Vascular Fraction (SVF) injectables, which contains adipose tissue derived stem cells (ASCs). ASCs are mesenchymal stem cells from adipose tissue, which can be easily isolated from lipoaspirate, where they probably are adjacent as pericytes or periadventitial cells to little blood vessels. In animal wound healing models, where ASCs were used to speed up wound healing (25-28) it was observed that ASCs improved the wound healing rate and smaller fibrotic areas remained after wound healing. Furthermore, the quality of the epidermis increased, and the gene expression of the pro-fibrotic markers **-smooth muscle actin* and *transforming growth

factor-*1* decreased while the gene expression of anti-fibrotic fibroblast growth factor and pro-angiogenic vascular endothelial growth factor increased. (27) Together, this indicates that in vivo administered ASCs, suppress the formation of a dermal scar, through augmented wound healing.

Moreover, we believe that the addition of SVF to Platelet-rich Plasma (PRP) will ameliorate current results of PRP injection into dermal wounds. Thus far, positive effects of PRP in combination with fat grafts or ASCs on wound healing and tissue recovery have been shown in human trials (29-31), as well as the use of PRP as a treatment of chronic and soft tissue ulcerations. In all mentioned applications, PRP showed to have a positive influence on tissue recovery and regeneration. In vitro, Willemsen et al. showed that ASCs responded in a dose-dependent way to PRP addition. Addition of PRP resulted in a decrease of several paracrine genes, which is relevant to tissue repair and thus wound healing. (38)

To date, none of the published clinical trials regarding PRP and or SVF/lipografting for wound healing purposes have been performed in a proper randomized clinical setting. Therefore, we set up a randomized double blind clinical trial to prevent scar formation using a substance of adipose tissue: the stromal vascular fraction, after a mamma reduction (NL55651.000.16). In this trial, we and participating patients have witnessed improved wound healing rates in the wound of the breast which has been treated with the stromal vascular fraction as compared to the placebo group. Unfortunately, in this study, we only focus on the evaluation of scar formation after 6 months and 12 months postoperative. To objectify these results, we set up a new randomized double blind clinical trial to improve wound healing rates after a mamma reduction. In this trial, we focus on the early wound healing phase up to 52 weeks postoperative.

Study objective

To quantify clinical and histological changes of the skin in promoting early wound healing when SVF + PRP injectable is used as treatment in comparison to SVF and PRP alone.

Study design

Double blind randomized controlled multi-clinical trial

Intervention

All patients will randomly receive all treatments in one part of four predesigned equal parts of the two caudal scars of the mamma reduction wise pattern. Two equal parts per breast: 1) SVF + PRP (0.1 ml per 0.1 cm2 wound surface), 2) SVF (0.1 ml per 0.1 cm2 wound surface), 3) PRP (0.1 ml per 0.1 cm2

wound surface) and 4) 0.9% NaCl (0.1 ml per 0.1 cm2 wound surface). Each of the four different treatments will be applied in a surface area of 1cm by 5cm: part A is the lateral 5 cm2 starting from the most lateral part of the wound on the left side, part B is the medial 5 cm2 starting from the most medial part of the wound on the left side, part C is the medial 5 cm2 starting from the most medial part of the wound on the right side and part D is the lateral 5 cm2 starting from the most lateral part of the wound on the right side.

Study burden and risks

During the operation, two 0.2 cm biopsies (into the dermal fat layer) will be taken out of the resected (normal) skin. After every mamma reduction there will be some resected skin leftovers. Subjects will already be under full anaesthesia at the time of the first biopsies and preparation and injection of the SVF and PRP injectable and/or 0,9% NaCl injectable.
After a period of 2 weeks, 6 weeks, 12 weeks and 52 weeks postoperative each participant and observer will complete the POSAS Questionnaire for each part of the scar of each breast (i.e. four questionnaires per consult per patient) and scars will be photographs in a standardized fashion. Four biopsies (into the dermal fat layer) will be taken after 6 weeks and 12 weeks, 1 from each part of the scar of each breast. Each postoperative biopsy will be taken within the borderline between normal skin and scar, with a maximum size of 0.2 cm. Subjects will be under local anaesthesia at the time of the second and third biopsies. The duration of the follow-up moments is estimated at respectively 10, 30, 30 and 10 minutes. The duration of the operation is estimated at 2 hours (1.5 hours for the mamma reduction and half an hour for liposuction, concentrating the SVF and PRP, and injecting it into the wound edges). Blood will be drawn before the operation and concentrated during the surgical procedures. Potential risk of the included subject is low: PRP has been in use as an adjuvant since 1985. No health risks or (serious) adverse events have been reported(39) to this date. PRP is currently used for several applications in domestic and foreign hospitals.
Using SVF as treatment has not ever increased health risks nor has showed to increase adverse events of any kind to this date.

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

Females
Age 18-60
BMI equal to or below 30
Patients undergoing a mamma reduction

Exclusion criteria

Male
Aged below 18 or above 60 years
Aged between 18 and 60 and in the menopause or pre-menopause
BMI above 30
Surgical interventions of the mammae in the year prior to the date of surgery
Any oncological event in the patients* history
A known psychiatric condition
A known systemic disease that will impair wound healing (e.g. diabetes mellitus, known atherosclerosis with an event that required hospitalization, collagen diseases, diseases of the skin, HIV).
Prednisone or other immunotherapy
Smoking
Pregnancy or active child wish
Frequent exposure to known carcinogenic substances (e.g. work related).

Active or previous use of hormone replacement therapy.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	28
Type:	Anticipated

Ethics review

Not approved

Date:	21-02-2019
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

No registrations found.

In other registers

Register	ID
CCMO	NL67280.000.18