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The role of an over-the-counter green tea extract in scarring: Priming the skin prior to injury

Submission date
28/05/2020

Recruitment status
No longer recruiting

Registration date
04/06/2020

Overall study status
Completed

Last Edited
05/05/2021

Condition category
Skin and Connective Tissue Diseases

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

Plain English summary of protocol

Background and study aims
A scar is a natural part of healing. Most people produce fine, thin scars but this can depend on a number of factors. It is thought that a long time for wound healing and skin closure can cause thicker, more raised scars. These unsatisfactory scars are often itchy, painful and cause distress to the sufferers.
The antioxidant properties and health benefits of green tea, Camellia sinensis, a popular beverage, have been known for centuries and used in traditional Chinese medicine. A component of green tea, has been shown to influence a range of areas including cancer, inflammation, photo protection, anti-aging and wound healing.
In the first stage of this trial we have shown that a topical cream known as EGCG (green tea) had beneficial effects in improving scars.
Therefore, we postulated that priming of the zone of injury prior to performing the experimental tissue damage could further maximise these effects by targeting the source of inflammation earlier. The aim is to further understand the role of EGCG in priming the wound site.

Who can participate?
Healthy volunteers aged at least 18 years

What does the study involve?
Participants will be given two punch biopsies to create controlled scars in a concealed place on the inner upper arm. Participants are split into four groups, each group will receive skin treatment application at different times. In each group participants will be randomly given either the active treatment (green tea extract) or a placebo to apply to the scars twice a day. Biopsies are performed again at week 4 and week 8. Measurements of skin condition are taken weekly for the duration of the trial.

What are the possible benefits and risks of participating?
There were no direct benefits to participants in this study. Participants are carefully screened so that risks to them taking part (i.e. allergies to any of the topicals or local anaesthetic/dressings) are minimised. They are however left with a scar, which may take time to fade.

Where is the study run from?
Wythenshawe Hospital (UK)

When is the study starting and how long is it expected to run for?
December 2015 until September 2019

Who is funding the study?
Funded by a gift donation

Who is the main contact?
Sara Ud-din, sara.ud-din@manchester.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
The role of an over-the-counter topical containing Camellia sinensis in the cosmetic management of skin scars in priming the skin prior to injury

Study objectives
To evaluate the role of topical application of Camellia sinensis in scar cosmetic appearance against a placebo and the effects of priming the zone of injury

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/10/2014, University of Manchester Ethics Committee 4 (University Research Ethics Committee, Research Governance, Ethics and Integrity, 2nd Floor Christie Building, The University of Manchester, Oxford Road, Manchester, M13 9PL, UK; +44 (0)161 275 2206/2674; research.ethics@manchester.ac.uk), ref: 14333

Study design
Interventional randomized controlled blinded single-centre design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Skin scarring

Interventions
40 participants were screened and split equally into 4 groups. Each group represents a mode of topical application.
Group 1: Pre-emptive Priming 7 days – Application of topicals 7 days prior to initial biopsies on day 0
Group 2: Pre-emptive Priming 3 days – Application of topicals 3 days prior to initial biopsies on

day 0
Group 3: Immediate delivery – Immediate application of topicals on day 0 (initial biopsies)
Group 4: Delayed delivery – Delayed application of topicals 2 weeks post-initial biopsies

On day 0, participants received two 5 mm punch biopsies to both upper inner arms to create the scars. They are independently randomised as to which arm should receive either treatment or placebo topicals.
Treatment: Camellia Sinensis (Green Tea extract)
Placebo: Same base as treatment topical but no active ingredient
Participants apply both topicals according to instructions, (one to each scar, with arms independently randomised by a medical statistician at the University of Manchester).
6mm re-biopsies were performed at weeks 4 and week 8.

Topicals are applied twice daily, massaged into the scar for a period of 2 minutes.
Non-invasive measurements are taken on a weekly basis for each participants' duration of the trial.
Final scar biopsies are used for histological, gene and protein analysis.

This is the second stage of ISRCTN18643079.

Intervention Type
Other

Primary outcome measure
1. Elasticity is measured using Dermalab combo elastin probe (Cortex technologies, Denmark) validated by IHC stains for elastin
2. Blood flow is measured using FLPI-2 (Moor Instruments, UK), and OCT (Michelson Diagnostics, UK) validated by IHC stains for multiple immune cells including mast cells, and angiogenic markers including CD31 and VEGF-A
3. High frequency ultrasound (Cortex Technologies, Denmark) measures skin thickness
4. RNA sequencing and QRT-PCR performed to validate IHC analyses.

All clinical devices (Elasticity probe, FLPI, OCT and Ultrasound) are measured at weekly time points (Day 0, Week 1, Week 2, Week 3, Week 4, Week 5, Week 6, Week 7, Week 8).
All IHC, PCR and mRNA sequencing were used on Day 0, Week 4 and Week 8.

Secondary outcome measures
Symptom scoring including pain, itching and redness are evaluated by the patient using a numerical value out of 10 in a daily diary

Overall study start date
23/08/2013

Completion date
12/09/2019

Eligibility

Key inclusion criteria
1. Aged 18 years and older
2. Able to fully understand the study requirements and attend all follow-up visits.

3. Provide written informed consent to participate in the study.
4. Appropriate size and weight - between 40 and 150kg, with a body mass index 20-35 kg/m² (as described in the Quetelet's index – weight (kg)/height² (m))

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
40

Total final enrolment
40

Key exclusion criteria
1. Known allergy to any components of the topical formulation
2. History or evidence of keloid scarring or fibrotic disorders (self-reported or determined by physical examination)
3. Pregnant or are planning to conceive in the next 3 months
4. Chronic or active skin disorder considered to adversely affect the scar healing by the investigator
5. Any likely healing impairment due to a significant medical condition such as renal, hepatic, haematological, neurological or immune disease, including:
5.1. Rheumatoid arthritis
5.2. Chronic renal impairment
5.3. Diabetes Mellitus
5.4. Significant hepatic impairment
5.5. Inadequately or uncontrolled congestive heart failure
6. Malignancy – diagnosed or treated within the past 5 years
7. Immunosuppressive, radiation or chemotherapy within the last three month
8. Receiving anticoagulant therapy, systemic steroids, hormone replacement therapy or any investigational drugs, or have taken any in the previous month prior to Day 0
9. Evidence of drug abuse
10. Have had or are known to have serum hepatitis or are carriers of hepatitis B surface antigen, hepatitis B core antibodies or hepatitis C antibodies. Previous vaccination against hepatitis B and C is not excluded.
11. Previously had a positive result to the HIV antibody test, or admit to belonging to a high-risk group.
12. Have been involved in other studies in the past two months prior to Day 0 must discuss the exact details of the previous studies prior to a decision being made of eligibility for inclusion in this trial
13. Allergic to other amide local anaesthetics

Date of first enrolment
22/12/2015

Date of final enrolment
12/09/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Wythenshawe Hospital
Clinical Research Facility
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Sponsor type
University/education

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ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Other

Funder Name
A gift donation

Results and Publications

Publication and dissemination plan
Planned publication in high-impact peer reviewed journal.

Intention to publish date
30/07/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Sara Ud-Din, sara.ud-din@manchester.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		08/04/2021	05/05/2021	Yes	No