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Using functional magnetic resonance imaging to investigate the efficacy of menthol in chemotherapy induced peripheral neuropathy (CIPN)

Submission date
12/09/2013

Recruitment status
No longer recruiting

Registration date
23/09/2013

Overall study status
Completed

Last Edited
06/06/2018

Condition category
Cancer

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2013-003968-31

Protocol serial number
2013/MINT3 FMRI STUDY

Study information

Scientific Title
Using functional magnetic resonance imaging to investigate the efficacy of menthol in chemotherapy induced peripheral neuropathy (CIPN): a pilot exploratory study

Study objectives
Topical treatment with 3% menthol gel in patients with chemotherapy induced peripheral neuropathy (CIPN) will have central efficacy as demonstrated by alterations in pain network activation on fMRI.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland A REC, 02/12/2013, ref: 13/SS/0201

Study design
Pilot exploratory randomised double-blind placebo-controlled study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chemotherapy Induced Peripheral Neuropathy (CIPN)

Interventions
Menthol gel vs Placebo

Pilot exploratory fMRI study of menthol gel versus placebo (16 participants per group).

Participants will be randomised with equal probability to placebo or 3% menthol gel, using random permuted blocks of length 4. Randomisation will be carried out at the Edinburgh Clinical Trials Unit (ECTU), allowing researchers and participants to remain blinded to treatment allocation.

Treatment Allocation
Treatment will be allocated following randomisation at the ECTU. Participants will be given a standardised number of gel filled tubes. Both levomenthol and placebo will be in identical packaging labelled with the trial name and the patients trial number.

Dosing regimen
Patients will receive 6 weeks supply of gel (active or placebo) in a metered tube. If supply runs out, a resupply will be given and noted. Participants will be advised to apply the gel twice daily over the affected area and will be provided with instructions on how to do this. There is only one dose level throughout the study.

Participant compliance
Participants will be asked to return their empty tubes after six weeks. The tubes will be weighed. The patient will record start and end date of each tube in a diary.

Overdose
As the medication is a topical gel overdosing is not an issue.

Other medications
Non-Investigational Medicinal Products

Permitted Medications
All medications that the participant is taking will continue.

Prohibited Medications
No stable pre-existing medication or at least 30 days duration is prohibited during the study. If for any reason participants needed to use another topical application on the areas being used for the trial medication the patient would be withdrawn from the study.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Menthol

Primary outcome(s)
Delineation of analgesic effect of menthol as distinguished from placebo effects, by identifying diminished activation of established pain brain networks (BOLD signal activation on fMRI).

Age, sex, weight, height, co-morbidities, regular medication, chemotherapy type and dosing will be recorded by the researcher consenting the subject for the trial.

Primary outcome data:
Evidence of altered activity within the pain and placebo networks following standard pain provocation at baseline and after six weeks of treatment (menthol or placebo) will be identified using standardised MRI analysis. Second level analysis will adjust for CIPN20 scores as regressors of interest.

Key secondary outcome(s))
1. Thermal quantitative sensory testing (QST): to determine the cool temperature range causing discomfort to CIPN patients using a non invasive skin thermometer and standardized QST testing
2. Skin temperature after gel application: to assess the degree to which 3% menthol gel cools the patients skin on application
3. No worsening of pain after menthol gel application - assessment of cognitive / affective components of pain perception [(PAIN CAT and Hospital Anxiety and Depression Scale (HADS)]
4. Measures of side effects from treatment (SEQ).

Measured at baseline and after six weeks of treatment.

Completion date
03/11/2014

Eligibility

Key inclusion criteria
1. Patients have received any neurotoxic chemotherapy.
2. Patients have experienced post treatment chemotherapy induced peripheral neuropathy (CIPN) pain for a minimum of 3 months.
3. Patients reporting a distressing or uncomfortable neuropathic symptom (such as pain or tingling) with a score of ≥4 on a scale of 0-10 with 0 being none.
4. Male and female aged 18 years or over at study entry.
5. Patients Oncology team agrees to their taking part in the study.
6. Patients are able to provide written informed consent to participation in the study after explanation of the study protocol.
7. Patients have the ability to complete questionnaire assessments in English language.
8. In the opinion of the investigator, the patient is able to complete the various assessments.
9. Neuropathy must be confined to the distal extremities (distal to elbows and/or knees).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Preexisting or history of peripheral neuropathy due to any cause other than chemotherapy (diabetes, alcohol, toxin, hereditary, etc).
2. Patients with any contraindication to the use of topical therapy or menthol.
3. Neurological conditions which may influence findings (such as multiple sclerosis or residual signs/symptoms from a previous stroke).
4. Skin conditions which prevent assessment of the relevant areas affected by peripheral neuropathy.
5. Suffering from significant psychiatric illness, which would hinder their completion of the study.
6. General medical condition is unstable or rapidly deteriorating, such that they are unlikely to be able to contribute to the study.
7. In the opinion of the Research Team or their usual medical team, would be unable to complete the study protocol for any other reason.
8. Current treatment of ≤ 30 days duration with anticonvulsants, tricyclic antidepressants, monoamine oxidase (MAO) inhibitor, or other neuropathic pain medication agents such as carbamazepine, phenytoin, valproic acid, gabapentin, lamotrigine or amifostine. (If on a stable

dose of any of these medications for >31 days, patients will be asked to continue these for the duration of the study. Analgesic agents such as acetaminophen, nonsteroidal anti-inflammatory agents, or opioids, are allowed).
9. Application of topical lidocaine patch/gel or capsaicin cream or patch (to the limb extremities) currently or within the last 30 days (as this would interfere with application of the menthol cream and potentially study outcome).
10. Other medical conditions, which in the opinion of the treating physician/allied health professional would make this protocol unreasonably hazardous for the patient.
11. Contraindication to magnetic resonance imaging (MRI): e.g. aneurysm clips, other metal work in body, claustrophobia.

Date of first enrolment
04/11/2013

Date of final enrolment
03/11/2014

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Edinburgh Cancer Research UK Centre
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Sponsor information

Organisation
Academic and Clinical Centre Office for Research and Development (ACCORD) (UK)

ROR
https://ror.org/01x6s1m65

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust (UK) (099440/Z/12/Z)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes