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An investigation of the effect of radiofrequency electric field stimulation of spinal nerves on the contents of spinal fluid in patients with chronic radicular pain

Submission date
21/10/2019

Recruitment status
No longer recruiting

Registration date
22/10/2019

Overall study status
Completed

Last Edited
08/11/2019

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Pulsed radiofrequency treatment (PRF) is commonly used to treat chronic nerve pain that has not responded to tablets prescribed by the GP and physiotherapy. Nerve pain originating from the spinal cord is one of the most common nerve pains, and is associated with changes in the immune cells and proteins around the spinal nerves. Preliminary results from an ongoing study from the Department of Pain Medicine at St James Hospital demonstrates a change in the levels of these proteins and cellular function after PRF treatment in patient with chronic never pain. These patients also report a significant improvement in their pain. This randomised blinded control study aims to define the effect PRF has on the neuroimmune cells and associated proteins. This study will improve our understanding of the mechanism of action of PRF allowing us to optimise the use of this techniques with improved pain relief for patients.

Who can participate?
Patients aged 18-60 with chronic radicular pain

What does the study involve?
Participants will be randomised to receive PRF or placebo for 120 seconds. Measurements will be taken at follow-up visits over the next six months

What are the possible benefits and risks of participating?
Benefits: Participants will receive more frequent reviews from medical and nursing staff (compared to patients not in the study) during the 6 months of the study. This study will also help to clarify the role and usefulness of pulsed radiofrequency in patients.
Risks: Performing PRF before a standard diagnostic nerve block does not pose any additional risks. The procedure will be prolonged by 2 minutes because of the PRF treatment, but participants will not experience additional pain. The 2 lumbar punctures are rarely associated with infection, bleeding, nerve damage and headache. The risk of serious complications is < 1 in 1,000 cases, and we have not reported any of these complications in our previous studies

Where is the study run from?
St James Hospital, Dublin, Ireland

When is the study starting and how long is it expected to run for?
June 2016 to October 2018

Who is funding the study?
St. James Chronic Pain Reserach and Education Fund, UK

Who is the main contact?
Prof. Connail McCrory
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title

An investigation of the effect of pulsed radiofrequency treatment (PRF) of the dorsal root ganglion (DRG) on cerebrospinal fluid cellular and neuropeptide concentrations with clinical outcome correlation in patients with chronic cervical and lumbosacral radicular pain

Study objectives
In a patient who responds to PRF treatment an effect on CSF neuropeptide and T cell populations will be identified

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/09/2015, The Adelaide and Meath Hospital, Dublin, SJH/AMNCH Research Ethics Committee Secretariat (Tallaght, Dublin 24, Ireland; +353 3 4142199; claire.hartin@amnch.ie), ref: 2015-09

Study design
Interventional single centre randomised triple blinded control study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic radicular pain

Interventions
Chronic radicular pain is a central neuroimmune phenomenon. Pulsed radio frequency treatment (PRF) to the appropriate level dorsal root ganglion is an effective treatment however its mechanism of action is unknown. It is hypothesised that PRF must have an effect on neuropeptide concentration implicated in pain chronicity in the cerebrospinal fluid and on T cell populations. Once a patient is recruited to the study clinical pain parameters are recorded and a sample of cerebrospinal fluid (CSF) is taken for analysis of neuropeptides and T cell populations.

Randomisation will be performed by an independent Clinical Nurse Specialist (CNS). They will use a computerised, random number generator and use block allocations (block sizes of 2 and 4). Patients will be randomised on the morning of treatment, and the RF machine operator (theatre nurse) will be given a sealed envelope to open with the treatment direction when the RF needle is sited. The machine operator will return the form with patient ID and treatment details in a sealed envelope to the randomisation centre. If the DRG block procedure fails, regardless of whether the patient receives PRF or not, details of the failed block will be included on the randomisation sheet and the patient will be excluded from the study, and another patient will be re-allocated by the CNS to this group. Patients will be assessed in the pain clinic, and if they meet the inclusion criteria (listed below) they will be given an opportunity to take part in the trial. They will be reassured that the management of their condition will not be influenced by their decision in any way, and they may withdraw consent at any stage during the trial. Potential candidates will also receive a patient information sheet on the trial. Their GP will be informed that they have been invited to participate in the study. They will be contacted no sooner than 2

weeks following their clinic appointment to ask if they wish to consent or not. Once the needle tip is appropriately positioned, the stylet is replaced with the RF probe. A small volume (0.5-1ml) of radio-opaque dye is injected to demonstrate spread along the nerve root to the epidural space, and to rule out vascular injection. The final position of the needle tip depends on appropriate stimulation of the DRG. Sensory stimulation (50 Hz) is sought at an output of less than 0.4 Volts. The needle is manipulated until the patient reports paraesthesia in a distribution concordant with the usual painful distribution. If the paraesthesia is not elicited in the correct dermatome, another needle will be placed at a neighbouring DRG to map the paraesthesia to the usual pain distribution. Once this is achieved, motor stimulation (2 Hz) greater than 1.5 times the sensory stimulation is checked. Impedence less than 450 Ohms is required. One ml of lidocaine 1% is applied to the DRG.

Following this, the theatre nurse operating the RF machine will open the randomisation envelope (see randomisation section) and follow the directions - all other personnel in the theatre including the patient and pain specialist will be blinded to the treatment delivered. The treatment group (LA + PRF) receive one pulsed radiofrequency treatment to the DRG - at less than 42 degrees Celsius for 120 seconds with pulses (20 milliseconds at 500,000 Hz) at 2 Hz and a voltage output of 45 Volts. The patients in the control group (LA) receives 120 seconds free of stimulation.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Number of neuroimmune cells (CD4+ T Cell, CD8+ T Cells, and Natural Killer cells) in the cerebrospinal fluid following PRF to the DRG
2. Neuropeptides and cytokines commonly associated with chronic pain conditions following PRF (BDNF, Substance P, NGF, MCP-1, VEGF, IFN-gamma, IL-1, IL-6, TNF)

Key secondary outcome(s))
Assessments will be made at the following time points:
Immediately before the procedure (T0)
1 hour after the procedure (GPE and NRS only) (T1)
1 month post procedure (T2)
3 months post procedure (T3)
6 months post procedure (T4)

1. CSF related:
1.1. NK cell and CD8+ T cell numbers at T3
1.2. CD4+/CD8+ ratio at T3
1.3. CSF neuropeptide and cytokine concentrations at T3

2. Clinical:
2.1. Success of PRF treatment at T3. Clinical success is defined as at least a 50% improvement in symptoms (score of 6 or 7 on the Likert Scale), and a reduction of at least 2-points on the NRS score
2.2. Global Perceived Effect (GPE) on Likert Scale and pain score (NRS) at one hour (T1), one month (T2), and 6 months (T4) post PRF
2.3. Changes in Quality of Life (RAND-36) at T2, T3, and T4
2.4. Functional ability (Oswestry Disability Index) at T2, T3, and T4
2.5. Medication usage (Medication Quantification Scale III) at T2, T3, and T4

2.6. Adverse events at T1, T2, T3, and T4
2.7. Further interventions required at T2, T3, and T4

Completion date
01/07/2017

Eligibility

Key inclusion criteria
1. Age range 18-60 years
2. Unilateral monosegmental radicular pain in the cervical or lumbosacral nerve roots
3. Symptoms consistent with MRI findings of a contained herniated disc
4. Chronic pain lasting more than 3 months
5. Failed conservative medical management for over one month (medication and physical therapy)
6. Radicular pain is the primary complaint with minimal axial pain.
7. NRS of > 3 (on 11-point NRS)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Key exclusion criteria
1. Patient refusal
2. Atypical or bilateral radicular pain patterns
3. Axial pain
4. Cognitive impairment or language barriers that could impair the patients understanding and reporting of outcomes
5. Malignancy
6. Vertebral fractures
7. Multiple sclerosis
9. Connective tissue diseases
10. Infection
11. Pregnancy or breast feeding
12. Prior spinal surgery
13. Lumbar spine interventions in the last 6 months (epidural injections or PRF)

14. Coagulation disorder or anti-coagulant treatment
15. Psychiatric disorder
16. Allergy to local anesthetics or contrast medium
17. Pre-operative NSAID, corticosteroid, methotrexate, or opioid therapy
18. Patients will be excluded from the study if appropriate nerve stimulation during the PRF procedure or pain relief (more than 50%) post DRG block are not achieved

Date of first enrolment
01/12/2015

Date of final enrolment
21/12/2016

Locations

Countries of recruitment
Ireland

Study participating centre
St. James Hospital
James Street
Dublin
Ireland
D8

Sponsor information

Organisation
Haughton Institute

ROR
https://ror.org/04c6bry31

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
St. James Chronic Pain Reserach and Education Fund

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?
Participant information sheet		22/10/2019	08/11/2019	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes