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Neuromuscular electrical stimulation of the quadriceps muscle: a novel alternative to total knee replacement in the young patient

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Registration date 08/01/2009	**Overall study status** Completed	
Last Edited 08/01/2009	**Condition category** Musculoskeletal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Effect of pre-operative neuromuscular electrical stimulation on clinical outcomes and muscle function in delaying operative intervention of knee osteoarthritis: a single blinded, randomised, interventional/treatment, efficacy study

Study objectives
We propose that a neuromuscular electrical stimulation (NMES) program will induce quadriceps hypertrophy with resultant increased strength (isometric and isokinetic), decreased knee pain, and improved functional capacity compared to a control group. This change will be demonstrated at the macroscopic and biochemical levels. We believe this improved muscle strength will translate into improvement in disease symptoms and possible negation of early knee replacement.

We will examine the primary endpoint for an NMES program to improve symptoms of knee osteoarthritis utilising validated scoring instruments (Western Ontario McMaster University Arthritis index and the 36-item Short Form questionnaires).

Secondary endpoints:
1. Determine the effect of NMES in restoring quadriceps weakness and range of movement. Specific quadriceps strength testing will be determined using dynamometric isometric and isokinetic evaluation. Clinical assessments and functional testing will further evaluate improvements of subject performance.
2. Identify physiological and morphological basis for improvements in symptoms and quadriceps strength as a dose-response relationship to NMES. Increasing muscle strength should be preceded with up-regulation of target genes resulting in larger muscle volume. This can be quantified with magnetic resonance imaging (MRI) to calculate muscle cross-sectional area. At the molecular level, detect gene down-regulation of muscle atrophy pathways such as MuRF-1 and MARbx and up-regulation of IGF-1.
3. Patients with statistically significant improvement associated with NMES may be objectively quantified with several ways such as genotyping or SNP (single nucleotide polymorphism) discovery of candidate genes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Procedures, risks, benefits and safeguards have been approved by the Ethics Committee of Cappagh National Orthopaedic Hospital (affiliated with the Royal College of Surgeons in Ireland) in accordance with the Helsinki declaration. Approval received on 22nd February 2008 (ref: JO/10 /2007/013).

Study design
Single centre, interventional treatment, single-blind, randomised, active controlled, parallel assignment, prospective efficacy study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Knee osteoarthritis

Interventions

Intervention group:
Subjects assigned to the NMES group will receive specific instruction from a member of the study team on application and logbook recording of the stimulator. The device will be applied to the subject's affected thigh, with electrode placement depending on thigh length and girth according to the manufacturer's guidelines. We will ensure each subject is competent with garment application, stimulator controls, and completion of the log-diary before commencing training. They will also receive clear, written instruction on the device controls and the NMES training program schedule. All NMES sessions will be performed with the subject sitting with their knee flexed to 60 degrees. Wooden strips joined with a 60 degrees bend will be provided to all subjects to assist with positioning throughout the program. They will sit with their feet flat on the ground and their toes against a wall to prevent knee extension caused by the resulting quadriceps contractions and thus permit isometric training.

Subjects will then commence five sessions per week (Monday to Friday) for 6 weeks. Training sessions will last 20 minutes in duration and should be performed at the same time each day. Participants will be instructed to use the device early in the morning between 8 am and 10 am to minimise muscle fatigue that may occur after normal daily activities.

A log diary will be provided to all subjects to record session date, session duration and stimulation intensity during the training period. A student from DCU will attend the participants' home on day 8 to ensure the subject is using the device appropriately as well as adhering to the protocol. Telephone communication will occur weekly on Fridays with each subject in the intervention group to ensure they are adhering to the protocol. The stimulator has a built-in log that records the total number of completed sessions, total treatment time, and average intensities reached for each channel for the previous four sessions. Subjects will not be informed of this facility, so that we can later assess compliance with the diary log. Given that the device will not function unless attached to a subjects' thigh, this will provide reliable means to assess participant adherence to the program. We will document these readings at week 2, week 4, and week 6.

Control group:
Subjects assigned to the control group will receive standard care. They will attend DCU at baseline, week 3, week 6, and week 12 for quadriceps strength assessments. All functional and clinical evaluations, as well as magnetic resonance imaging (MRI) scanning, self-report questionnaires and muscle biopsies will be performed as in the intervention (NMES) group. They will also receive weekly telecommunication to answer any questions they may have in relation to the study.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. The Western Ontario McMaster University Arthritis index (WOMAC) is a disease-specific questionnaire that assesses the patient's perception of their own level of mobility. It has been designed for hip or knee osteoarthritis with well-established reliability and validity and consists of 24 questions categorised into pain, stiffness, and physical function and scores range from 1 to 96 (best to worst respectively). WOMAC subscales scores will be transformed to a 0 - 100 scale: 100 - [actual raw score x 100/possible raw score range]. A WOMAC score of 100 indicates that

the patient has no problems and a score of 0 indicates that the patient has extreme difficulty. In between, a score of 25 indicates that a patient has severe difficulty, 50 indicates moderate difficulty, and 75 mild difficulty. Differences in WOMAC functional scores of more than 10 points on the transformed 0 - 100 WOMAC scale are generally perceptible to patients.
2. The Medical Outcomes Study 36-item Short Form Health Survey (SF-36) was formed as a culmination of several scales in the Medical Outcomes Study (MOS). It evaluates general health using a 36-item questionnaire under eight parameters: physical and social functioning, role limitations because of emotional problems or physical problems, mental health, bodily pain, vitality, and general health perceptions. Reliability and validity have been established.

Key secondary outcome(s))

1. Functional and clinical evaluation: performed at baseline and repeated at week 1, week 3, week 6 and week 12; providing four sets of comparable data (weeks 1, 3, 6, 12):
1.1. Specific measurements of extension lag, flexion deformity, axial alignment (varus/valgus) and thigh girth
1.2. Documented range of motion, including flexion and extension limits both active and passive
1.3. Height and weight measurements, to determine the body mass index (BMI - kg/m^2)
1.4. Physical activity level of each subject, classified into light, moderate or heavy based on the number of hours per day and days per week as follows:
1.4.1. Community active: light exercise x 2 per week
1.4.2. Moderate exercise: greater than or equal to 30 minutes x 3 per week
1.4.3. Heavy exercise: greater than or equal to 30 minutes greater than x 3 per week
2. Performance outcome measures: performed three times with the fastest recorded and used for statistical analysis. Assessments are performed in the same order for each participant at each assessment point. Pain was assessed during each test using a 10-point numeric rating scale (NRS) where 0 represented no pain, and 10 represented the worst pain imaginable.
2.1. 25-metre timed walk test
2.2. Timed Stair-climb Test (TST)
2.3. Up/down Seated Test (Timed Chair Rise)
3. Radiological evaluation
4. Magnetic resonance imaging (MRI): performed to determine quadriceps and hamstring cross-sectional area (CSA) of both thighs using a Gyroscan Intera 1.5T MRI scanner (Philips Medical Systems, Holland, Europe). Scanning to determine CSA will be performed at baseline (week 0) and repeated again after intervention on week 6, and finally at the end of the de-training period (week 12).
5. Quadriceps muscle strength (Torque): a Biodex Multi-joint System 3 dynamometer (Biodex Medical Instruments, Shirley, NY) will be used to determine torque achieved by the quadriceps femoris (QF) muscle of both the involved knee and uninvolved knee. Subjects will attend DCU for bilateral QF torque assessments both isometrically and isokinetically at baseline, week 1 (end of familiarisation period), week 3 (midway through training period), week 6 (end of the training period), and week 12 (end of de-training period).
6. Complications of muscle biopsy
7. Muscle sample analysis
8. Fibre type distribution
9. Percent fibre type area
10. Regulatory protein analysis
11. RNA isolation

Completion date

31/10/2009

Eligibility

Key inclusion criteria
1. Male and female patients aged 45 - 55 years old
2. Grade 3 - 4 knee arthritis diagnosed arthroscopically
3. Conservatively managed
4. Ambulatory patients

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Morbid obesity (body mass index [BMI] greater than 40)
2. Uncontrolled hypertension
3. Anticoagulant therapy
4. Neurological disorder
5. Other lower limb impairment affecting function including amputation
6. Malignancy
7. Inflammatory arthritis
8. Implanted pacemaker or defibrillator
9. Dermatological conditions affecting the thigh
10. Recent participation in an exercise or strength training program
11. Inability to walk unassisted

Date of first enrolment
01/10/2007

Date of final enrolment
31/10/2009

Locations

Countries of recruitment
Ireland

Study participating centre

13 Lock-keepers Walk
Dublin
Ireland
D15

Sponsor information

Organisation
Cappagh National Orthopaedic Hospital (Ireland)

ROR
https://ror.org/03vc5bf16

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Cappagh National Orthopaedic Hospital (Ireland) - facilities used to perform clinical assessments, muscle biopsies and MRI scans

Funder Name
Dublin City University (DCU) (Ireland) - laboratories used for the analysis of the muscle samples and strength testing

Funder Name
Bio-medical Research (Ireland) - providing neuromuscular stimulators (KNEEHAB®) at no cost. No financial benefit or agreement for same has been made.

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes