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Hyaluronate [Viscoseal] injection after knee surgery; an evaluation

Submission date 10/02/2020	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 05/03/2020	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 22/11/2023	**Condition category** Surgery	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

Arthroscopic, or keyhole, surgery on the meniscus in the knee joint has benefits over open surgery. Nonetheless, there is scope to further improve outcomes for patients by reducing pain and discomfort and promoting enhanced recovery of knee joint functionality. The medical device Viscoseal contains hyaluronan and is designed to replenish levels of this compound in the knee joint following arthroscopic repair of the meniscus. Natrually, synovial fluid in the knee joint contains hyaluronan, but a lot of it is washed away when surgeons flush the knee joint during surgery to remove loose pieces of meniscus, cartilage, or bone. Previous studies, both in laboratory studies and patient trials, have demonstrated that Viscoseal can promote re-establishment of biological structure in the knee joint to allow it to return to a normal physiological state and protect cartilage.

Who can participate?

Patients aged 18 – 59 years due to undergo meniscal surgery of the knee for meniscal tear grade III (including repair, partial meniscectomy or complete meniscectomy).

What does the study involve?

This present prospective, randomised, controlled trial aims to build on this evidence by comparing standard care versus the injection of Viscoseal (26 vs 26 patients) at the end of arthroscopic meniscus repair surgery. The degree of pain, leg swelling and knee functionality experienced by patients after surgery will be measured using validated patient surveys focused on the meniscus. In addition, a detailed picture of what happens to the meniscus after surgery +/- administration of Viscoseal will be obtained through MRI radiologic imaging. The main objective is to determine if Viscoseal can achieve a minimal clinically important difference in pain relief after meniscal repair surgery when compared to standard care.

What are the possible benefits and risks of participating?

Benefits: For participants in the control group there is no direct benefit for taking part in this study. You will be cared for in exactly the same manner as you normally would, bar the introduction of a few questionnaires and a potential extra MRI scan. However, by taking part you will contribute to comparison of the effectiveness of adding hyaluronate to a meniscus operation, to optimise management of meniscus surgery in the future. For participants in the

Viscoseal® intervention group there may be benefits in terms of reduced pain and swelling after the procedure. However, this has not yet been proven and established beyond doubt, and this study is aimed to assess this further.
Risks: There is no significant personal safety risk anticipated regarding taking part in this study. Like with any invasive procedure, the meniscus surgery carries (post-operative) risks such as bleeding, blood clots and infection. However, the arhroscopic surgery itself is not classed as being part of this HIKE study; the injection of Viscoseal® at the end of the procedure is. Fifty percent of patients do not receive this and therefore for them there is no additional risk over and above that related to standard care.

Where is the study run from?
Cumbria Partnership NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2020 to July 2025

Who is funding the study?
TRB Chemedica (UK) Ltd.

Who is the main contact?
Dr Leon Jonker
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Integrated Research Application System (IRAS)
272362

Central Portfolio Management System (CPMS)
43835

Study information

Scientific Title
A single-centre, randomised, placebo-controlled single-blinded trial assessing patient and clinical outcomes of Viscoseal injection after meniscal surgery

Acronym
HIKE

Study objectives
To determine the level of index leg related pain experienced at day 7 post-operation and to compare the average pain scores of patients in the control and Viscoseal arm respectively, through administration of 100 mm visual descriptor scale (VDS) for pain at rest.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/01/2020, NHS HRA Wales REC 7 (c/o Public Health Wales, Building 1, Jobswell Road, St David's Park, SA31 3HB, UK; +44 (0)1267 611 164; sue.byng@wales.nhs.uk), ref: 19/EM /0363

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Elective orthopaedic surgery

Interventions
- Standard care (control) arm
All patients receive general anesthesia and a pneumatic tourniquet is used. Patients are already randomised prior to surgery to avoid delays with surgery and allow a vial of Viscoseal to be ready for the relevant patients. Joint irrigation is performed with the assistance of a manual arthroscopic pump using 0.9% NaCl solution at room temperature. Then, the remaining fluids are drained from the knee. At the end of the surgery, the knee is dressed while the tourniquet is still inflated. All surgeries are intended to be performed in a day-surgery facility with the patient being discharged the same day. Postoperatively, partial weight-bearing with crutches is allowed. Crutches are recommended for the first 48 hours, primarily for patient safety by minimising the risk of a fall.

- Viscoseal (intervention) arm
Apart from the difference in terms of Viscoseal administration to the intervention group, the surgical protocol for the Viscoseal arm is identical to that of the standard care group. At the end of the surgery, again all the remaining fluids are drained from the knee, but this is followed by injection of 10 mL of Viscoseal preparation. Used Viscoseal product and syringes will be disposed of in line with local guidelines on disposal of clinical waste.

Timeline and overview of different study visits
Visit 1# Pre-surgery (<0 weeks)
Written Informed Consent, Collection of baseline information (age, weight etc), Record use of any pain medication, Limb girth measurement, Validated patient-reported outcome measures (Lysholm scale; WOMET tool; Visual display scale for knee pain)

Visit 2# Day of surgery (day 0)
No research activity, apart from injection of Viscoseal if patient is randomised to this treatment arm (patient will not know if given Viscoseal or not)

Visit 3# , Day 2
Record use of any pain medication, Limb girth measurement, McGill pain questionnaire, Validated patient-reported outcome measures (Visual display scale for knee pain)

Visit 4# Day 7
Record use of any pain medication, Limb girth measurement, McGill pain , questionnaire, Validated patient-reported outcome measures (Visual display scale for knee pain)

Visit 5# Day 14
Record use of any pain medication, Limb girth measurement, McGill pain questionnaire, Validated patient-reported outcome measures (Visual display scale for knee pain)

Visit 6# Week 12
Record use of any pain medication, Validated patient-reported outcome measures (Lysholm scale; WOMET tool; Visual display scale for knee pain), Patient satisfaction questionnaire

Visit 7# Week 26
Record use of any pain medication, Validated patient-reported outcome measures (Lysholm scale; WOMET tool; Visual display scale for knee pain), Patient satisfaction questionnaire

MRI-substudy: one additional (optional) standard MRI scan of the knee at week 26

Intervention Type
Other

Primary outcome(s)
Level of index leg related pain experienced at day 7 post-operation measured using 100 mm visual descriptor scale (VDS) for pain at rest. The study is powered to detect the established minimal clinically important difference (MCID) of 15 mm on a 100 mm VDS pain.

Key secondary outcome(s)
1. Visual display score pain scale for knee (at rest) at baseline, and post-surgery at 48 hours, 7 days, 14 days, 12 weeks and 26 weeks
2. Visual display score pain scale for knee (walking) at baseline, and post-surgery at 12 weeks and 26 weeks
3. Pain description through McGill pain questionnaire at baseline, and post-surgery at 48 hours, 7 days, 14 days
4. Girth size of the affected leg at baseline, and post-surgery at 14 days and 12 weeks
5. Quality of life-related to meniscus function (Lysholme and WOMET surveys) at baseline, and post-surgery at 12 weeks and 26 weeks
6. Patient satisfaction with the surgical procedure through a survey at week 26
7. Optional MRI sub-study: radiological description of meniscal health at 26 weeks post-surgery

Completion date
31/07/2025

Eligibility

Key inclusion criteria
1. Meniscal surgery of the knee for meniscal tear grade III (including repair, partial meniscectomy or complete meniscectomy)
2. Aged 18 – 59 years
3. Proficient in English (reading and writing, due to surveys used)
4. Mental capacity to consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
59 Years

Sex
All

Key exclusion criteria
1. BMI > 35
2. Known hypersensitivity to hyaluronic acid, other constituents of Viscoseal, marcaine, codydramol
3. Any auto-immune disease that affects the limbs, such as rheumatoid arthritis, treated with immune-modulating drugs
4. Inflammatory arthropathy
5. Co-existing condition that significantly impacts on usual daily activities (including, but not limited to, lower limb amputation, cancer, neurodegenerative disease, or other condition that leaves patient invalid or to use a wheelchair) as assessed by recruiting clinician
6. Any other reason that would mean that compliance with the trial scheme would be challenging or impractical (eg extended travel abroad)
7. Contraindications for MRI diagnostics (see https://radiology.ucsf.edu/patient-care/patient-safety/mri/absolute-contraindications) since qualifying meniscal injury pre-surgery needs to be demonstrated by MRI

Date of first enrolment
01/01/2020

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Carleton Clinic
Cumbria Partnership NHS Foundation Trust
Cumwhinton Road
Carlisle
United Kingdom
CA1 3SX

Sponsor information

Organisation
North Cumbria University Hospitals NHS Trust

Funder(s)

Funder type
Industry

Funder Name
TRB Chemedica (UK) Ltd

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?
Protocol file	version v1.1	14/01/2020	05/03/2020	No	No
Protocol file	version 1.3	21/05/2021	17/08/2021	No	No
Protocol file	version 1.4	20/04/2022	05/07/2022	No	No