Greater Trochanteric Pain Syndrome: A comparison of image guided steroid injection and focused shockwave therapy

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Compliance

The trial will be conducted in compliance with the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent Amendment Regulations[1], the protocol, GCP, Data protection Act, NHS research governance and other regulatory requirements, as appropriate.

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ABSTRACT

Greater trochanteric pain syndrome (GTPS) is a common problem affecting 10-25% of the population It encompasses a number of diagnoses including partial tears or avulsions of the gluteal tendons, snapping hip syndrome (coxa saltans) or inflammation of the bursae around the lateral hip or ilio-tibial tract. GTPS is characterised by lateral hip pain, tenderness over the greater trochanter and pain when lying on the ipsilateral side. It is more common in women (4:1) and primarily found in 40-60 year olds. Any condition which causes altered biomechanics around the hip can predispose to the development of GTPS including, leg length discrepancy, osteoarthritis, total hip or knee replacement and obesity[1].

Many treatments have been described in the management of GTPS including physiotherapy, anti-inflammatories, corticosteroid injections and surgery. Extracorporeal shockwave therapy (ESWT) has been used to good effect in other forms of tendonopathy. There are minimal studies describing the use of shockwave therapy in GTPS, however results appear favourable.

This study is an un-blinded randomised control trial to establish whether ESWT with physiotherapy is a better treatment than a corticosteroid injection with physiotherapy in the management of recalcitrant GTPS. 140 patients will be recruited to the study and randomised into two arms. Group 1 will have 3 doses of ESWT followed by physiotherapy. Group 2 will have a single corticosteroid injection performed by the same consultant hip surgeon using ultrasound guidance, followed by physiotherapy. The same physiotherapist will deliver therapy to all patients in both groups at every stage of the study. Both groups will be followed up at 3 and 12 months.

Our primary outcome measures are a visual analogue score to assess pain and a Harris hip Score to assess function.

Secondary outcomes will include a Trendelenburg test to assess abductor function, patient subjective improvement on a Likert scale, and an SF-36 patient health questionnaire to assess overall well-being. Patient diary will be used to assess complications and compliance with physiotherapy regimen.

Currently, there is limited evidence for the use of ESWT in GTPS . NICE have reviewed the evidence of this treatment and have recommended further research into this area. If found to be a successful, it is hoped that we will be able to perform further research in this field to ascertain if Clinical Commissioning Groups (CCGs) should make this treatment more widely available to patients.

1. BACKGROUND

Greater trochanteric pain syndrome (GTPS) is a common problem affecting 10-25% of the population[1,2] and has an incidence of 1.8 per 1000 population[2]. Previously known as trochanteric bursitis, it was recognised that inflammation of the bursae does not need to be present and that a number of other conditions can reproduce the same symptoms. GTPS encompasses a number of diagnoses including partial tears or avulsions of the gluteal tendons, snapping hip syndrome (coxa saltans) or inflammation of the bursae around the lateral hip or ilio-tibial tract[1-3,26]. It is characterised by lateral hip pain, tenderness over the greater trochanter and pain when lying on the ipsilateral side[2]. It is more common in women (4:1) and primarily found in 40-60 year olds. It is most commonly unilateral, but can be bilateral. If bilateral, mobility is more likely to be affected.

Any condition which causes altered biomechanics around the hip can predispose to the development of GTPS including, leg length discrepancy, osteoarthritis, total hip or knee replacement and obesity[1,2]. Athletes can also suffer with GTPS especially road-runners with similar difficulties in treatment success[4].

GTPS doesn't usually cause significant mobility problems,[1] however, it still has a significant impact on the patients quality of life[5]. No gold standard treatment exists; rest, non-steroidal anti- inflammatories, physiotherapy, corticosteroid injections, shock wave therapy, iliotibial band lengthening and surgical debridement have all been described in the management with variable results[13-15,25].

In our unit, lateral hip pain constitutes approximately 10% of all referrals. Most patients will have exhausted conservative measures available in primary care (NSAIDs, physio and corticosteroid injections) prior to secondary care referral for consideration of further treatment modalities including surgery which remain unproven in their efficacy.

The use of Extracorporeal Shockwave Therapy (ESWT) has been described in the treatment of tendonopathies such as plantar fasciitis and Achilles tendonitis[6-9]. A shock wave is a high amplitude sound wave. There are two broad types of ESWT; focused and radial. Critics say that radial ESWT is not true ESWT as the shockwave is not focused on a particular target and that the wave effects are too greatly dispersed in the superficial tisses[10]. The radial unit does not produce waves with the characteristic of shockwaves i.e. lower peak pressure and energy density. Focused ESWT can be generated using electrohydraulic, electromagnetic or piezoelectric principles. The use of piezoelectric crystals in the device ensures that the shockwave generated is very precisely targeted without causing any significant effects to the skin surface itself.[6,11] The waves are focused on a specific target and have both a direct and indirect effect on the targeted tissues causing an increase in the release of analgesic substances (substance P), increased neovasularity (new blood vessel formation), inhibition of COX-II thereby decreasing inflammation and causing hyperstimulation of nerve fibres thereby blocking true pain signals (gate-control theory of pain).[11]

Evidence for the use of ESWT in managing GTPS is limited with only 2 studies found in the literature. Furia et al[12] performed a case-control study involving 66 patients looking at ESWT versus conservative management (33 patients in each arm). Significant improvement was seen in pain and functional scores in the ESWT groups versus the conservative treatment group at 1, 3 and 12 months. Rompe et al[13] performed an RCT comparing physiotherapy, corticosteroid injection and ESWT in a total of 229 patients. At 1 month, pain score was significantly better in patients who had the corticosteroid injection versus ESWT or physiotherapy alone. At 4 months, ESWT showed significantly better results than corticosteroid injection or physiotherapy and at 12 months, ESWT and physiotherapy where better than corticosteroid injection.

The use of corticosteroid injection is well documented for the treatment of GPTS[13-17]. Brinks et al[14] in 2011 performed an RCT in 120 patients of corticosteroid versus expectant treatment. There was an early reported improvement in the corticosteroid group versus the expectant care group with 55% of patients stating they had improved versus 34%. However, by 12 months, there was no significant difference between the groups reporting a 61% and 60% improvement respectively. The outcomes from Rompe's[13] study also showed that there was early improvement in the corticosteroid group at 1 month compared to physiotherapy and ESWT however, that effect was not sustained long-term where they showed that ESWT and physiotherapy had a better outcome. It also makes no difference whether the corticosteroid injection is given "blind" (aiming for the clinical tender spot) or whether the injection is fluoroscopically guided.[15]

NICE issued guidelines on the use of ESWT in the management of GTPS in January 2011[18-20] stating that "Evidence on the efficacy and safety of extracorporeal shockwave therapy (ESWT) for refractory greater trochanteric pain syndrome is limited in quality and quantity. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research." They also offered guidance on future research: "NICE encourages further research into ESWT for refractory greater trochanteric pain syndrome. Research studies should clearly describe patient selection, imaging, and treatment protocols. Outcomes should include functional and quality-of-life scores with at least 1 year of follow-up."

The aim of this study is to discover whether focused ESWT is a more effective treatment for GTPS than the standard treatment of a corticosteroid injection. This is the first study to use focused ESWT in this context. If found to be beneficial, ESWT could be made more widely available to patients thus relieving unnecessary pain in this patient population and allow for further research in this field.

2. TRIAL OBJECTIVE

The following null hypotheses will be tested:

There is no difference in patients' outcome when comparing Extracorporeal Shockwave Therapy (ESWT) with physiotherapy to an ultrasound guided corticosteroid injection with physiotherapy in the treatment of Greater Trochanteric Pain Syndrome.

3. TRIAL DESIGN

3.1. Randomisation

Participants will be randomised in to one of two groups:

Group 1 will undergo a course of 3 ESWT treatments followed by a course of physiotherapy.

Group 2 will have an ultrasound guided corticosteroid injection followed by a course of physiotherapy.

Central Randomisation

Randomisation of participants into either Group 1 or Group 2 of the study will be performed using the '**Stratos'** application based at RJAH. Patients will be randomised during a specialist consultant led research clinic. There will be no cover over weekends or bank holidays.

Patient stratification

Patients will be stratified by age, sex, and baseline visual analogue pain score and Harris Hip Score to achieve balanced groups with respect to these four variables.

3.2. Patient Entry Criteria

A patient is **eligible** for the trial if the patient:

1. Is aged 18+ years
2. Has symptoms consistent with GTPS (lateral hip pain with focal tenderness) for at least 6 months
3. Failed conservative management in any other care setting

A patient is **ineligible** for the trial if the patient:

1. Has hip joint osteoarthritis requiring treatment (conservative or surgical) on a plain radiograph
2. Had surgical treatment specifically targeted at GTPS within last 6 months e.g. bursectomy/ITB lengthening
3. Has ipsilateral Total Hip Replacement. (patient will not be able to undergo corticosteroid injection in clinic setting)
4. Has contraindictions to ESWT treatment; pregnancy, anticoagulant therapy, advanced peripheral neuropathy, local infection, malignancy, unresolved fractures
5. Has a previous history of complications with ESWT
6. Has a recent history of acute hip trauma

7. Has a recent history of acute sciatica
8. Is not able to attend or comply with treatment or follow-up scheduling
9. Participates in any other clinical trial

Non-English speaking patients may be entered if there is a translator present at the time of consent and they have someone to help them fill in the questionnaires.

Patients who are not eligible for the study will be fed back into the NHS system and treated as per normal clinical practice.

4. TRIAL PROCEDURE

Patients will be recruited from NHS Consultant hip surgeon clinics once the diagnosis of GTPS has been confirmed through a thorough history and examination. A plain radiograph will be taken of the hips to exclude osteoarthritis as the cause and any further imaging will be performed on a case-by-case basis. Participants will be given information on the study and if interested will then attend a Consultant led, specialist research clinic to be consented and recruited to the trial. Once a patient is recruited to the study, baseline outcome scores will be obtained and the patient will be randomised to one of two groups.

Group 1 will receive 3 ESWT treatments by a fully trained member of the team (as per manufacturer's guidelines). The most clinically tender area will be identified on examination. Using the Piezowave 2 (Impact Medical Ltd, Liverpool UK) a F10G6 transducer probe will be used to deliver 2500 shocks (power level will be set between 0.15 - 0.35mJ/mm2 depending on patient tolerance). The same settings are the same for each treatment occasion. Each treatment will take approximately 5 minutes and be repeated as weekly intervals.

Group 2 will receive an ultrasound guided corticosteroid injection. This will be given in a clinic setting on the same day as consent is taken if the patient is happy. All injections will be performed by the same Consultant surgeon. Under aseptic conditions, 80mg of depo-medrone (methylprednisolone) with 5ml 0.5% bupivicaine and 5ml 1% lignocaine will be combined in a single syringe and injected using a long 21G (green) needle under ultrasound guidance to target burase and tendon insertions whilst avoiding wholly intramuscular injections. Patients will be monitored for 15 minutes following the procedure before being allowed to resume all normal activities

Directly following the treatment, both groups will be seen by a physiotherapist, assessed and given an exercise program comprised of progressive slow repetitive exercises, strengthening the gluteal and core muscles as well as generic stretching, advice and education (see Appendix for full programme). They will be reviewed 2 weeks after their initial assessment by the same physiotherapist then reviewed further as felt appropriate by the physiotherapist depending on clinical presentation and any difficulties with the programme up to a total of 6 sessions. All patients will be assessed and followed up by the same blinded physiotherapist to reduce bias.

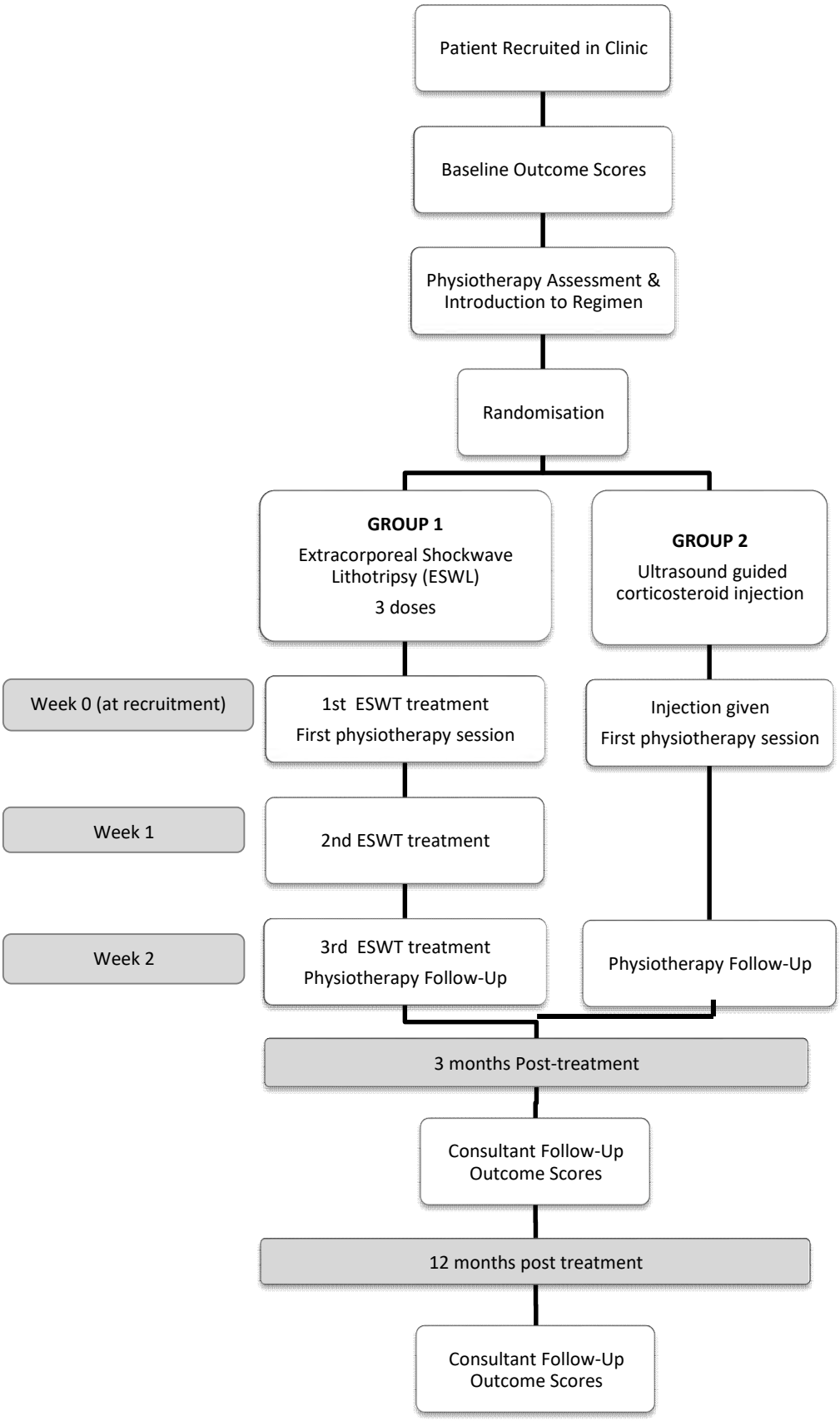
Patients will then be reviewed in the consultant led research clinic at 3 and 12 months for assessment and collection of outcome data.

Following their initial treatment, patients will be given a diary in which they will be asked to document any complications that arise, any thoughts or concerns about the treatment as well as their physiotherapy regimen. Diaries will be collected for qualitative analysis.

Blinding

Participants cannot be blinded in this study as they will fully aware of the treatment they receive.

The physiotherapist who will assess and review every patient will be blinded to the treatment group.


Patient Recruited in Clinic
Baseline Outcome Scores
Physiotherapy Assessment & Introduction to Regimen
Randomisation
GROUP 1
Extracorporeal Shockwave Lithotripsy (ESWL)
3 doses
GROUP 2
Ultrasound guided corticosteroid injection
Week 0 (at recruitment)
1st ESWT treatment
First physiotherapy session
Injection given
First physiotherapy session
Week 1
2nd ESWT treatment
Week 2
3rd ESWT treatment
Physiotherapy Follow-Up
Physiotherapy Follow-Up
3 months Post-treatment
Consultant Follow-Up Outcome Scores
12 months post treatment
Consultant Follow-Up Outcome Scores

5. OUTCOME MEASURES

Assessment	Outcome measure	Collected from	At entry	3 mth	12 mths
Functional status	Trendelenburg test (Clinical Examination)	Patient	✓	✓	✓
	HHS	Patient	✓	✓	✓
	Likert scale	Patient		✓	✓
Pain score	VAS	Patient	✓	✓	✓
Quality of life	SF-36	Patient	✓	✓	✓
Physiotherapy	Diary	Patient/ Parent/carer	✓	✓	✓
Complications	Diary/Research dept contact	Patient/ Parent/carer	✓	✓	✓

5.1. Primary outcome measures

Visual Analogue Pain Score (VAS)[21]

This is a ranked pain score where 0 is no pain and 10 being worst pain imaginable. It is a widely used, accepted and validated way of documenting pain although it is subjective. The primary outcome will be the improvement in VAS (by at least 2 points),

Harris Hip Score (HHS)[22]

Is a validated widely used functional scoring system. An improvement in HSS of 10 points will be deemed significant.

5.2 Secondary outcome measures

Trendelenburg Test[23]

A clinical test assessing hip abductor function which has been shown to be the most sensitive test in GTPS. Will be assessed at baseline, 3 and 12 months by one of the consultant hip surgeons to see if it is negative or positive to assess if there has been any improvement from the baseline test at the outset of the study.

Likert Scale

Patients will be asked to score their subjective improvement; completely recovered, much improved, same, worse or much worse.

SF-36[24]

Patient health survey looking at all aspects of their health including emotional, mental and social and has been shown to be useful is establishing whether a treatment is cost-effective.

Diaries

Patient diaries will be issued following their treatment to document any complications, concerns or thoughts on the procedure as well as their physiotherapy activity.

5.3. Qualitative data and analysis

Patient diaries will be issued at the time of the initial intervention operation with instructions and examples of the type of information they might write about (e.g. how well the intervention is tolerated, any complications/side-effects from the intervention and what effect they think about their treatment and recovery. Diaries will continue for the full 12 months but most will focus on the first 3 months post-intervention.

Content analysis will be applied to the diary comments to identify common themes and unique patient experiences which will be represented through selected quotations reported anonymously in articles and presentations. This will be carried out independently by a researcher without knowing the identity or group allocation of the patient.

5.4. Serious Adverse Events (SAEs)

The study is a non-CTIMP study thus only Suspected Unexpected Serious Adverse Reactions (SUSARS) need be reported. These are events which are not expected but considered by the PI to be related to the study procedure(s). Such events should be reported immediately to the study co-ordinator.

6. STATISTICAL ANALYSIS

A power study was undertaken prior to commencing this study. Based on data extracted from studies by Rompe et al and Furia et al, as well as the data from Mahomed et al, the study should be powered to detect a minimum difference of 0.5 times the within-group standard deviation. Assuming a confidence level of p=0.05 and assuming 80% power, the study will require a total sample size of 128 patients in this study (64 in each arm). Allowing for a drop-out rate of 10%, we aim to recruit at least 70 patients to each arm of the study.

Statistical analysis will be done using R/Deducer-statistical analysis software. The primary outcome measures (follow-up VAS for pain and HHS) will be analysed using Analysis of Covariance (ANCOVA). The stratifying variables (age, sex and baseline VAS and HHS) will be used as covariates in this analysis. The frequencies of adverse events will be compared using a chi-squared or Fisher exact test, depending on whether the assumptions for the chi-squared test will be met. Secondary outcome measures will be analysed using appropriate statistical tests (ANCOVA for continuous and chi-squared/Fisher's exact for nominal data).

7. ORGANISATION

The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust (RJAH) will act as the Sponsor and lead co-ordinating centre for the trial.

8. PUBLICATION POLICY

The results of this research will be of benefit to orthopaedic surgeons and other clinicians who refer patients for treatment of GTPS, managers and healthcare economists. The results will be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT statement)[27] and submitted for presentation at the British Hip Society annual conference and publication in peer-reviewed journals such as the Bone and Joint Journal. To reach the wider health and management community the results may also be submitted for presentation at the NICE annual conference and as an article in the Health Service Journal.

It is essential that the trial protocol is followed and that no additional investigations conflict with either the treatments or the outcome measures as far as possible. For this reason it is requested that any proposals for additional studies related to the trial be referred to the Trial Steering Committee for consideration.

Trial results will be provided to **all** patients.

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