Facet-joint injections for non-specific low back pain: a feasibility RCT

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Declared competing interests of authors: Rod S Taylor is the chairperson of the National Institute for Health Research (NIHR) Health Services and Delivery Research programme researcher-led panel and is a current member of the NIHR Priority Research Advisory Methodology Group (PRAMG). He was a member of the NIHR Health Technology Assessment General Board between 2014 and June 2017. Funding from BioQ Pharma has been awarded to the Swansea Centre for Health Economics to conduct a pilot study of the use of OneDose ReadyfusOR in the postoperative delivery of pain relief. Deborah Fitzsimmons is not involved in this study but is the Academic Director of the research centre that has received the grant. Stephanie Poulton reports personal fees from the Neuro Orthopaedic Institute (NOI) and personal fees from Pain and Performance, outside the submitted work. Pain and Performance is a private organisation that teaches and runs seminars about pain for professionals and treats people in pain (see www.painandperformance.com)

Published December 2017
DOI: 10.3310/hta21740

Scientific summary

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Health Technology Assessment 2017; Vol. 21: No. 74
DOI: 10.3310/hta21740

NIHR Journals Library www.journalslibrary.nihr.ac.uk

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Background

The Global Burden of Disease Study (GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016;**388**:1545–1602) has concluded that low back pain (LBP) causes more disability in the world than any other condition. LBP has a high lifetime prevalence, with significant economic and societal costs.

Common contributors to LBP in adults are thought to include lumbar facet-joints; treatment options for LBP with a likely facet-joint component include intra-articular facet-joint injections (FJIs), medial branch nerve blocks (which innervate the joints) or radiofrequency denervation of the medial branch nerves. Although the technique of lumbar FJI is not standardised, this typically involves injection of an active substance such as a corticosteroid into the joint.

The National Institute for Health and Care Excellence (NICE) guidelines for managing LBP were recently updated [NICE. *Low Back Pain and Sciatica in Over 16s: Assessment and Management*. NICE guideline (NG59). London: NICE; 2016] and do not recommend intra-articular FJIs on the grounds of there being insufficient high-quality evidence to support their use, recommending instead targeting the nerve supply of the facet-joints as the predominant pain generator source. Despite these recommendations, intra-articular FJIs remain in common use.

Review of the literature: a review of systematic reviews and meta-analyses

We undertook a literature search to identify systematic reviews and meta-analyses of randomised controlled trials of intra-articular lumbar FJIs for chronic LBP. Eleven systematic reviews met the inclusion criteria and their methodological quality was assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) checklist. Although 14 randomised controlled trials were identified across these reviews, no one review included all of these trials. The authors of these systematic reviews concluded that the level of clinical heterogeneity across included randomised controlled trials precluded any meta-analyses.

The conclusions drawn from the systematic reviews were generally equivocal. The limited to moderate quality of evidence to support the effectiveness of therapeutic lumbar FJIs in the management of chronic LBP indicates a need for further high-quality research in this area.

Rationale for a feasibility study

Because of the lack of high-quality, robust clinical evidence, the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme issued a commissioning brief in 2011 to answer the research question, 'Is a definitive study to assess the effectiveness and cost-effectiveness of facet-joint injections compared with best non-invasive care for people with persistent non-specific low back pain feasible?'.

Objectives

We aimed to assess the feasibility of conducting a definitive study to evaluate the clinical effectiveness and cost-effectiveness of FJIs compared with a sham procedure in patients with non-specific LBP of > 3 months' duration. Specific objectives were to:

- assess the eligibility criteria and recruitment and retention of patients in the two treatment arms (FJIs vs. sham procedure) by assessing the feasibility of recruitment to inform a potential definitive study

- assess the feasibility and acceptability of the two treatment arms from the point of view of patients and their pain teams
- assess the feasibility of the proposed definitive study design including testing of the randomisation and blinding procedures, development of an appropriate active and sham procedure for FJIs and assessment of the consistency of the trial sites in terms of delivering the combined physical and psychological (CPP) programme and their ability to collect the outcomes proposed for the main trial
- estimate outcome standard deviations (SDs) to inform the power calculation for a definitive study
- finalise the protocol design, statistical plan, number of centres required and study duration for the definitive study.

Methods

Study design

This feasibility study utilised a blinded parallel two-arm pilot randomised controlled trial design. A multicentre design was planned, with patients recruited from pain clinics at three participating NHS centres and their associated community-based pain clinics; however, recruitment took place at a single centre, Barts Health NHS Trust.

Participants

The study sought patients referred by their general practitioner (GP) to the pain and spinal orthopaedic clinics who had non-specific LBP of at least 3 months' duration and clinical indicators for pain of facet-joint origin, despite receiving at least two components of NICE-recommended best non-invasive care, including education and one of a physical exercise programme, acupuncture or manual therapy. Patients who had already received lumbar FJIs or who had had previous spinal surgery were excluded.

Following a positive diagnostic medial branch nerve block with lidocaine (> 50% pain relief on a numerical rating scale lasting for > 30 minutes), eligible participants were individually randomised in a 1 : 1 ratio to receive either the FJI (intervention group) or a sham (placebo injection) procedure (control group). The intervention group received intra-articular lumbar FJIs with local anaesthetic and steroid, whereas the sham group received periarticular injections with normal saline.

Both the intervention group and the control group received a CPP programme after their active or sham injections. At the time of establishing this study, NICE clinical guideline CG88 (2009) had recommended a CPP programme as part of best usual care.

Sample size calculation

At the outset of the study it was expected that a total of 60 patients would be recruited, to be able to estimate the precision of an assumed 20% attrition rate with an error of ±5% at the 95% confidence level. Assuming that 24 full data sets per arm were completed at the end of the study, this would give a reasonable estimate of the variance of outcomes.

Outcomes

The outcome questionnaire visits took place in research nurse-led clinics at baseline (pre randomisation) and at 6 weeks, 3 months and 6 months post randomisation. The outcome questionnaires covered a range of pain- and disability-related issues including pain intensity and characteristics, use of co-analgesics in the previous week, lack of efficacy or side effects of pain relief, expectation of benefit, health-related quality of life, functional impairment, satisfaction with treatment, complications and adverse events, co-psychological well-being, health-care utilisation and costs and impact on productivity.

Statistical analysis

As this was a feasibility study, it was not planned to formally inferentially test differences in outcomes or costs between or within the groups. Mean recruitment and attrition rates were calculated with 95% confidence intervals. Means and SDs for all outcomes for the two groups at baseline and at all follow-up visits were reported. A detailed statistical analysis plan was prepared by the study statistician prior to any data analysis. Analyses were performed blinded to group allocation.

Health economics analysis

A health economics analysis plan was developed in collaboration with the study's health economist and statistician. A formal economic analysis was not proposed (as this was a feasibility study). Any outcomes from this feasibility study would be used in the design of the definitive study. In particular, the analysis looked at the ability to collect the outcomes proposed for the main trial.

Results

Although recruitment was planned across three centres, given the delays in study set-up the funder directed that this take place at only one centre, Barts Health NHS Trust. Recruitment took place over 9 months, with the first participant recruited in January 2016 and the last participant recruited in September 2016.

During the recruitment period, 628 patients referred to the recruiting clinics by their GP with non-specific LBP were screened for eligibility to enter the study. Of the 50 patients who met the inclusion criteria, 16 agreed to take part in the study and 11 received the diagnostic test for facet-joint disease. Nine participants had a positive response and were randomised to receive either lumbar FJIs with steroid or a sham procedure. Eight participants completed the study; one randomised participant was lost to follow-up.

The participant screening-to-recruitment ratio was 70 : 1 (628 : 9), which contrasts with an expected prestudy ratio of 17 : 1 (1000 : 60). The recruitment rate varied between zero and four patients per month. The main reasons for screening failure included that patients had received previous lumbar FJIs ($n = 192$), had other dominant or widespread pain ($n = 92$) or had radicular pain ($n = 64$).

Each pain consultant visit was associated with a cost of £148.03 and the delivery of the intervention or sham procedure incurred a cost of £691 per patient. The CPP programme had a mean cost of £2500 per patient. The intervention group was observed to have higher resource use costs than the sham group, with a cost of £193 (SD £219) per participant in the intervention group and a cost of £75 (SD £73) per participant in the sham group. Although there are limitations of the analysis associated with the highly skewed costs and small sample size, this suggests that a potential downstream effect of FJI is a subsequent increase in medication use and associated costs within primary care.

Discussion

The small number of participants recruited to the study and the feasibility design preclude us from drawing any conclusions on the clinical effectiveness or cost-effectiveness of intra-articular lumbar FJIs in the management of non-specific LBP. However, the clinical procedures used appeared to be safe and well tolerated, with no significant adverse events related to the steroid injection. Furthermore, we were able to successfully collect clinical and economic outcomes from the majority of patients over the duration of the study.

Cost differences were identified between the intervention group and the sham group in the feasibility study, which may be a reflection of the inherent skewness in the data and the very small sample size.

The main weakness of the study was the failure to achieve our expected recruitment target and the consequent early closure of the study by the funder. There were substantial system-level barriers that the study team were unable to control, which led to long delays in obtaining research governance.

It became clear early in the recruitment phase that many patients presenting to the pain clinics with LBP of > 3 months' duration were not suitable for the study and that patients screened in the spinal orthopaedic clinics also did not meet the eligibility criteria. Despite employing additional strategies in the final stages of recruitment, we conclude that patients presenting to these hospital-based specialist clinics were generally not suitable because of the complexity of their pain problems and that we may have had better success in recruiting from primary care-based services.

We were unable to meet our feasibility objective of a recruitment target of 60 randomised LBP patients across three investigative sites. Instead, we were able to randomise only nine patients at one investigative site. However, we believe that we met our other pre-stated feasibility objectives, as detailed in the following sections.

Assess the eligibility criteria and recruitment and retention of patients in the two treatment arms

Recruitment took place at a single centre only, largely because of delays in study set-up and a decision by the funder to terminate the study early because of the lack of time available to open the other two sites. A number of reasons for the delays have been identified, including regulatory issues, staffing problems, specific recruitment challenges, factors affecting clinician and patient participation and the study population itself.

Assess the feasibility and acceptability of the two treatment arms from the point of view of patients and their pain teams

A Delphi exercise was undertaken by 42 interventional pain physicians in the UK to agree on the methods for the FJI and sham procedures; the two treatment arms can therefore be considered to be feasible and acceptable by pain clinicians.

Of the 34 patients who met the eligibility criteria but who declined to take part in the study, none cited the lack of acceptability of the two treatment arms as the reason for not wishing to take part.

Assess the feasibility of the proposed definitive study design

We believe that this feasibility study did allow us to demonstrate the feasibility of the study design to inform a definitive study. We were able to develop an appropriate active injection technique and sham procedure. No patients refused participation on the grounds of randomisation to an active or a sham procedure. We were able to maintain the blinding of patients and clinicians. The CPP programme was consistently delivered to small groups of participants and was well aligned to the latest NICE guidelines (NICE, 2106).

Estimate outcome standard deviations to inform the power calculation for a definitive study

We reported the SDs for all proposed clinical and economic outcomes at baseline and follow-up but would express caution in using these SDs to inform the sample calculation for a future definitive study because of the small sample size. Probably the only parameter for a future definitive study that this study was able to estimate with precision was the screening/recruitment rate.

Finalise the protocol design, statistical plan, number of centres required and study duration of the definitive study

Given the failure to meet the study recruitment target and the small number of patients recruited from one centre, the study team deemed it inappropriate to present a finalised protocol for a definitive study on the basis of this feasibility study.

Conclusions

A successful trial can be defined as one that achieves success in recruitment and is able to answer the research questions. Although we have successfully demonstrated our ability to develop a robust study protocol and deliver the intended interventions, and address many of the feasibility objectives, failure to achieve the target recruitment rate remains a key finding of this study. However, there are lessons learned here that can be used to inform and improve patient recruitment for a future definitive study.

Two research teams were funded by the NIHR to answer the research questions: (1) the Facet Feasibility study (the addition of intra-articular FJIs to best usual non-invasive care) (reference number HTA 11/31/01) led by Professor Martin Underwood, University of Warwick, and (2) this project, the FACET (Feasibility of Assessing the Clinical- and cost-Effectiveness of Therapeutic lumbar facet-joint injections) feasibility study, led by Professor Richard Langford, Barts Health NHS Trust. Neither research team met the target recruitment rate and Professor Underwood's team concluded that a definitive study is indeed feasible but that recruitment from pain clinics alone was insufficient. Both teams experienced significant delays in study set-up.

Based on our findings, we would agree with the Underwood team that a definitive study is potentially feasible, with adjustments made to the target population and increased primary care involvement to enable patients to be screened earlier in their pain trajectory. To optimise recruitment for a definitive study, we would contend that any future studies in this area should involve stronger collaborations with primary care physicians and musculoskeletal physiotherapists with the aim of making these procedures more accessible to these patients who would not otherwise have been referred on for specialist services.

Trial registration

This trial is registered as EudraCT 2014-003187-20 and Current Controlled Trials ISRCTN12191542.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.236

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

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HTA programme

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The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: http://www.nets.nihr.ac.uk/programmes/hta

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 11/31/02. The contractual start date was in July 2015. The draft report began editorial review in May 2017 and was accepted for publication in September 2017. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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