The feasibility of a randomised controlled trial of physiotherapy for adults with joint hypermobility syndrome

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Scientific summary

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Scientific summary

Background

Joint hypermobility syndrome (JHS) is a heritable connective tissue condition, characterised by an increased range of motion and pain at multiple joints. JHS is associated with significant impairment in physical function, psychological function and quality of life. However, there is currently a lack of information about the experiences of living with, and managing, JHS. Physiotherapy, particularly exercise, is the mainstay of treatment, but there is also little existing robust research evidence regarding its effectiveness. Therefore, this research programme aimed to understand patient and health professional perspectives on the physiotherapy management of JHS; to use this information to develop, and then evaluate, a comprehensive physiotherapy intervention package; and to determine the feasibility of conducting a randomised controlled trial (RCT) in this area.

Objectives

The specific objectives of the research programme were to:

1. develop a comprehensive physiotherapy intervention for adults with JHS informed by patient and health professional focus groups (stage 1)
2. pilot implementation of the intervention in practice in two NHS trusts (stage 2)
3. conduct a pilot randomised controlled study of the intervention (stage 3) to determine:

    i. the number of potentially eligible patients with JHS
    ii. the feasibility of recruitment and retention
    iii. the acceptability of the research design and physiotherapy intervention to patients in terms of quality of life
    iv. the acceptability and feasibility of the physiotherapy intervention to physiotherapists in terms of training and implementation
    v. an estimate of the value of information (VOI) from a subsequent RCT.

Secondary outcomes from the pilot RCT (stage 3) were to pilot outcome measures planned for a definitive RCT. These included:

- physical function, pain, global status, fatigue and self-reported joint count [Multidimensional Health Assessment Questionnaire (MDHAQ)]
- pain at rest and on movement [visual analogue scales (VASs)]
- a new condition-specific physical function questionnaire developed by the research team [the Bristol Impact of Hypermobility (BIoH) questionnaire]
- a health-related quality-of-life preference score [European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L)]
- exercise self-efficacy [Exercise Self-Efficacy (ESE) scale]
- resource-use questionnaires
- adverse events.

Methods

During stage 1 focus groups were conducted across the UK with people with JHS and health professionals. The focus groups aimed to explore perspectives on physiotherapy for the management of JHS, but also collected information on patients' lived experiences. Also explored were thoughts about the design of a physiotherapy intervention and the design of a pilot RCT. This information was used by a working group of health professionals, researchers and patient research partners to design a comprehensive physiotherapy intervention package within a set of guiding principles that were agreed in advance. These guiding principles included the number of sessions (six), length of sessions (30 minutes) and duration of treatment (4 months); that treatment should be on a one-to-one patient–therapist basis; and that the package should be easily implemented across the UK (i.e. avoiding complex or resource-intensive interventions such as hydrotherapy). These principles aimed to maximise the likelihood of widespread adoption by reflecting current clinical delivery patterns and minimising resource requirements. The physiotherapy intervention was adapted from a pre-existing osteoarthritis programme with proven clinical effectiveness and cost-effectiveness. It aimed to enhance patients' ability to be more physically active through helping them to better understand and manage their condition.

Stage 2 of the research involved a pilot of the physiotherapy intervention in practice within the two NHS trusts taking part in the research. Four physiotherapists (two at each site) were trained in the delivery of the intervention. Participants were patients who were aged > 18 years, met the Brighton diagnostic criteria for JHS and had no other musculoskeletal conditions causing pain. Consenting patients then received the physiotherapy intervention package. Patients and therapists were interviewed to explore their perspectives on the intervention, including the training received by the physiotherapists. This information was used to refine the intervention and training packages.

Stage 3 was a pilot RCT of the intervention compared with an advice control. Participants were patients who were aged > 16 years (the minimum age was reduced slightly from stage 2), met the Brighton diagnostic criteria for JHS and had no other musculoskeletal conditions causing pain. All participants received a one-off advice intervention, supplemented by information booklets from the Hypermobility Syndromes Association and Arthritis Research UK. All participants had the opportunity to ask questions specific to their personal circumstances and to receive tailored advice from the physiotherapist. Following the advice intervention, all participants were randomly allocated to either receive physiotherapy (six 30-minute sessions over 4 months: advice and physiotherapy arm) or to usual care (no additional physiotherapy or advice: advice arm). Clinical outcome measures were taken at baseline and at 4 and 7 months, and included the MDHAQ, pain VASs, the BIoH questionnaire, EQ-5D-5L, ESE scale, resource use (only at 4 and 7 months) and adverse events (only at 4 and 7 months). Questionnaires were administered by post. Descriptive statistics were used to report recruitment and retention numbers and outcome measure data. Health economic data were also reported using descriptive statistics and the VOI of a future RCT was estimated. Patients and physiotherapists were interviewed to determine their perspectives on the advice and physiotherapy interventions, outcome measures and trial procedures.

Results

Stage 1

Stage 1 recruited 25 people with JHS (three men) and 16 health professionals (14 physiotherapists and two podiatrists; three men). Patients typically described living with a complex and unpredictable condition that impacted significantly on their well-being. It was common for a diagnosis to be much delayed, but once JHS was recognised it often led to appropriate onwards referral. There were a lot of commonalities between the perspectives of patients and health professionals with regards physiotherapy for the management of JHS. The need to treat the condition holistically, rather than treating single, acutely painful joints in isolation, was highlighted. The importance of education for health professionals, patients and, more widely, society was emphasised. The findings were used to design a physiotherapy intervention and

supporting patient handbook, with a flexible delivery model that could be tailored to individuals' needs. It focused on improving self-efficacy for exercise, physical activity and self-management; incorporating education on a number of key themes; and tools to support reflection and planning. Patient choice of general physical activity was encouraged, as opposed to therapist prescription, along with a 'menu' of joint-specific exercises that could be selected in partnership with patients.

Stage 2

Stage 2 recruited four physiotherapists (two at each of two clinical sites), who were trained to deliver the physiotherapy intervention. Eight people with JHS (all women) were recruited to receive the intervention. Interviews were conducted with all four physiotherapists and six of the patients to explore their experiences of the intervention, outcome measures and, for physiotherapists, the training received. The intervention package was generally very well received by patients and physiotherapists, and only minor changes were subsequently made to the patient handbook and the training package. Some patients and physiotherapists thought that the advice intervention would not be seen as comparable to the physiotherapy intervention and that this would adversely affect recruitment to the pilot RCT. Others understood why an advice control was being advocated. Information was gained on the rate of referrals and recruitment, and this was used to refine the eligibility criteria and to develop strategies to enhance referrals.

Stage 3

During stage 3 there were a total of 121 patient referrals received over the 8-month recruitment period. Ninety-two were excluded (35 not eligible, 25 no response, 23 declined and 9 did not attend). A total of 29 participants consented to take part in the pilot RCT (14 were randomised to advice and 15 to advice and physiotherapy). Three participants withdrew from the study (two from the advice arm and one from the advice and physiotherapy arm). Questionnaire return rates were 83%, 65% and 74% at baseline, 4- and 7-month follow-up, respectively. Return rates were higher for the advice and physiotherapy arm at all time points. When compared with the advice control, the advice and physiotherapy arm showed evidence of promise, as, although while confidence intervals were inevitably wide, the direction of differences between the groups was in favour of advice and physiotherapy for both primary and many secondary clinical outcomes. There was a higher incidence of adverse events (including withdrawal from the study) in the advice control, although we do not know the baseline adverse event rate in this population. The economic analysis estimated that the advice control was the most cost-effective intervention; however, uncertainty in the results meant that it was plausible that the advice and physiotherapy was the most cost-effective. The VOI analysis indicated the potential high value of new research if uncertainty was eliminated from the model. In summary, the exploratory results of this pilot trial seem to support a full evaluation of the physiotherapy intervention in a definitive trial.

Interviews were conducted with 18 patients and seven physiotherapists. In addition, six patients who declined to take part in the study were interviewed. The advice and physiotherapy interventions were both generally well received. However, a perceived lack of equipoise between the advice intervention and physiotherapy intervention seemed to be prevalent among patients and physiotherapists, and it is likely that this impacted on recruitment rates. There were some specific suggestions to improve the advice intervention. The training for physiotherapists was viewed positively, although it was suggested that training related to the trial procedures could be more explicitly separated from training related to delivery of the intervention.

Conclusions

This research is the first to describe in detail the lived experience of people with JHS. It is important that JHS is recognised as a complex and unpredictable long-term condition. Patients and health professionals agreed that physiotherapy for JHS should take a holistic, multijoint, long-term condition-management approach rather than treating individual acutely painful joints. Education for patients, health professionals and society more generally is required.

A comprehensive physiotherapy intervention package was developed which was generally very well received by both patients and physiotherapists, and shows evidence of promise in improving the impact of JHS. The perceived lack of equipoise between the physiotherapy intervention and the advice control was highlighted as the most significant challenge to conducting the pilot RCT.

Implications for practice and research

- A user-informed physiotherapy intervention for the management of JHS has been developed and evaluated positively by patients and physiotherapists.
- Although many patients valued the advice intervention, there was a perceived lack of equipoise between the physiotherapy and advice interventions in the pilot RCT. A future definitive RCT should use a more robust advice intervention as a comparator (to include telephone advice and face-to-face follow-up). Close attention should also be paid to training and monitoring of study personnel to ensure the use of consistent and effective messages regarding equipoise.
- A future RCT should be designed as a multicentre trial to ensure adequate recruitment. Study questionnaires should be completed face to face or over the telephone to improve data completeness. Adverse events should be recorded at baseline to more adequately determine changes in adverse event rates over time and between study arms.
- With the attrition rates and variability observed, a future RCT would require 122 patients per arm to detect a difference of 3.6 points on the Routine Assessment of Patient Index Data (RAPID3) subscale and 152 patients per arm to detect a 30-point change on the BIoH questionnaire (two-sided 5% alpha, 90% power, 35% attrition for both RAPID3 and BIoH).
- Based on the results of this research, a definitive RCT of physiotherapy for JHS seems feasible.

Trial registration

This trial is registered as ISRCTN29874209.

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