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| **CRITICALLY APPRAISED TOPIC** |

**FOCUSED CLINICAL QUESTION**

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| For an adult female with Ehlers Danlos hypermobility type, is physical therapy intervention more effective than non-care in managing chronic pain? |

**AUTHOR**

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**CLINICAL SCENARIO**

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| The patient is a 60-year-old female who was diagnosed with Ehlers Danlos Syndrome (EDS) hypermobility type when she was 7 years old. Since her diagnosis, she has suffered many torn ligaments and injuries due to her disease, including three rotator cuff tears and an ACL/MCL/meniscus tear in her knee most recently. She underwent surgery to fix these injuries but the surgeries often failed due to the compromised integrity of her tissues, requiring additional revision surgeries. She has consistently been attending physical therapy for 4 years to help manage her symptoms of EDS and chronic pain. She presents with consistent, global pain rated at 7/10 and a Beighton score of 7/9. Her goal is to manage her symptoms of EDS, specifically her chronic pain, and to maintain her health-related quality of life as she ages.  Hypermobile patients have a decrease in joint position sense and postural stability, leading to chronic musculoskeletal pain and injuries.1 While physical therapy and exercise programs are understood to be beneficial for patients with joint hypermobility, there is a significant knowledge gap when it comes to the most advantageous exercise intervention for these patients, including type, frequency, dosage, duration, and delivery method.2 There exist few reports of high-quality, prospective studies evaluating specific exercises for hypermobile patients, further indicating the need for an evidence-based physical therapy intervention for this population.1 I am interested in finding a safe and effective treatment so this patient can successfully manage her chronic pain and improve her health-related quality of life. Due to the limited evidence available and for the purpose of this assignment, “Ehlers-Danlos,” “joint hypermobility syndrome” and “hypermobility syndrome” are used synonymously. |

**SUMMARY OF SEARCH**

[Best evidence appraised and key findings]

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| Eight studies that met the inclusion/exclusion criteria were identified; including two systematic reviews, two RCTs, two case reports, a cross-sectional study and a narrative review.   * A multimodal intervention consisting of postural re-education exercises, myofascial trigger point release, spinal mobilization, core, cervical and spinal stabilization exercises, self-treatment strategies and a home exercise program can restore pain-free AROM, improve muscular endurance and reduce pain in patients with joint hypermobility syndrome.1–3 * Closed kinetic chain exercises and proprioception exercises can reduce pain, improve knee proprioception and increase quality of life.4 * There is no convincing evidence for specific types of exercise or even that exercise is better than non-care.5 |

**CLINICAL BOTTOM LINE**

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| The limited evidence available provides support that a multimodal exercise program including postural re-education, closed-chain, graded exercises, stabilization exercises and proprioceptive exercises can reduce pain and improve quality of life in patients with joint hypermobility syndrome. There is a gap in the literature as to what type of exercise intervention, if any, is the most effective in managing chronic pain and maintaining quality of life in adult hypermobile females. For the exercise interventions that are supported in the literature, suggested parameters are lacking as well as a long-term follow-up period. |

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| ***This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor*** |

*The above information should fit onto the first page of your CAT*

**SEARCH STRATEGY**

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| **Terms used to guide the search strategy** | | | |
| **P**atient/Client Group | **I**ntervention (or Assessment) | **C**omparison | **O**utcome(s) |
| “Ehlers Danlos Syndrome”  “EDS”  “hypermobility” | Strength training  Resistance training  Physical therapy | Kinesio tape  Orthotic  Brace | Pain  Chronic pain  Patient-reported  Numeric Pain Rating Scale |

**Final search strategy (history):**

*Show your final search strategy (full history) from PubMed. Indicate which “line” you chose as the final search strategy.*

1. “Ehlers-Danlos Syndrome” [MeSH]
2. Hypermob\*
3. “Joint hypermobilities” [MeSH]
4. “Joint hypermobility” [MeSH]
5. Strength training
6. Resistance training
7. Physiotherap\* or physical therap\*
8. “Orthotic devices” [MeSH]
9. “Brace” [MeSH]
10. “Chronic pain” [MeSH]

Search Strategy: (final search strategy is in bold)

((((ehlers danlos syndrome[MeSH Terms]) OR hypermob\*)) AND (((((strength training) OR resistance training) OR ((physiotherap\*) OR physical therap\*)) OR device, orthotic[MeSH Terms]) OR brace[MeSH Terms])) AND chronic pain[MeSH Terms] Sort by: Best Match

((hypermobilities, joint[MeSH Terms]) AND (((((strength training) OR resistance training) OR ((physiotherap\*) OR physical therap\*)) OR device, orthotic[MeSH Terms]) OR brace[MeSH Terms])) AND chronic pain[MeSH Terms]

((joint hypermobility) AND (((((strength training) OR resistance training)) OR ((physiotherap\*) OR physical therap\*)) OR ((device, orthotic[MeSH Terms]) OR brace[MeSH Terms]))) AND chronic pain[MeSH Terms]

**((joint hypermobility[MeSH Terms]) AND ((physiotherap\*) OR physical therap\*)) AND chronic pain[MeSH Terms]**

*In the table below, show how many results you got from your search from each database you searched.*

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| **Databases and Sites Searched** | **Number of results** | **Limits applied, revised number of results (if applicable)** |
| PubMed | 13  7  10  6 | Revisions: changed “orthotic” to “orthotic device [MeSH]” and “brace” to “brace [MeSH].” Eliminated “kinesio\* tape.” Eliminated “self-report” and “numeric pain rating scale” and only used “chronic pain [MeSH].”  Changed “ehlers-danlos syndrome [MeSH]” to just “joint hypermobilities [MeSH].”  Changed “joint hypermobility [MeSH]” to “joint hypermobility” in all fields  Only used physiotherap\* and physical therap\* as interventions |
| PEDro | 24 | Simple search “hypermobility” |
| CINAHL | 11 | (joint hypermobility) AND (physical therapy or physiotherapy or rehabilitation) AND (chronic pain) |
| Cochrane Library | 41 trials | “Ehlers Danlos syndrome” |
| Web of Science | 25 | **TOPIC:** (joint hypermobility) *AND* **TOPIC:** (physical therapy) *AND* **TOPIC:** (chronic pain) |

## INCLUSION and EXCLUSION CRITERIA

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| **Inclusion Criteria** |
| * Patient population of adults (>18 years old) * Patient population with diagnosis of hypermobility * Studies published since 1995 |
| **Exclusion Criteria** |
| * Studies including surgical interventions * Not published in English |

**RESULTS OF SEARCH**

**Summary of articles retrieved that met inclusion and exclusion criteria**

*For each article being considered for inclusion in the CAT, score for methodological quality on an appropriate scale, categorize the level of evidence, indicate whether the relevance of the study PICO to your PICO is high/mod/low, and note the study design (e.g., RCT, systematic review, case study).*

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| **Author (Year)** | **Risk of bias (quality score)\*** | **Level of Evidence\*\*** | **Relevance** | **Study design** |
| Palmer (2013)5 | AMSTAR- 6/11 | 2a | High | **Systematic Review** (one controlled trial, one comparative trial, two cohort studies) |
| Smith (2014)6 | AMSTAR- 8/11 | 2a | Low | **Systematic Review** (one RCT, a single system design study, quasi-experimental) |
| Celenay (2016)1 | PEDro Scale- 5/10 | 2b | Moderate | RCT |
| Daman (2017)4 | PEDro Scale- 5/10 | 2b | Moderate | RCT |
| Zhou (2018)3 | JBI Critical Appraisal Checklist for Case Reports- 3/8 | 5 | Moderate | Case Report |
| Pennetti (2018)2 | JBI Critical Appraisal Checklist for Case Reports- 7/8 | 5 | Moderate | Case Report |
| Arthur (2015)7 | JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies- 5/8 | 5 | High | Cross-Sectional Study |
| Castori (2012)8 | AMSTAR- 2/11 | 5 | High | Narrative Review |

\*Indicate tool name and score

\*\*Use Portney & Watkins Table 16.1 (2009); if downgraded, indicate reason why

**BEST EVIDENCE**

The following 2 studies were identified as the ‘best’ evidence and selected for critical appraisal. Rationale for selecting these studies were:

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| * Palmer et al (2013): I chose this study because it is a systematic review and thus has the highest level of evidence out of the articles I identified in my literature search. Additionally, it is also the most relevant study to my PICO as the objective of this study is to establish the effectiveness of therapeutic exercise for hypermobile patients. * Daman et al (2017): I chose this study because it is an RCT and thus has a high level of evidence. The objective is also relevant to my PICO as it aimed to evaluate the effectiveness of exercise therapy (closed kinetic chain exercise and proprioception exercises) on pain intensity in patients with hypermobility syndrome, specifically for the knee joint. Furthermore, this study clearly identified the intervention and the exact exercises that were used. |

**SUMMARY OF BEST EVIDENCE**

**(1) Description and appraisal of (The effectiveness of therapeutic exercise for joint hypermobility syndrome: a systematic review) by (Palmer et al, 2013)**

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| **Aim/Objective of the Study/Systematic Review:** |
| To review published literature in order to determine the effectiveness of therapeutic exercise for patients with joint hypermobility syndrome. |
| **Study Design**  [e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]  Note: For systematic review, use headings ‘search strategy’, ‘selection criteria’, ‘methods’ etc. For qualitative studies, identify data collection/analyses methods. |
| * **Systematic review** * **Search strategy:** 9 online databases were searched (AMED, BNI, CINAHL, Cochrane Library, Embase, HMIC, Medline, PEDro, and SportDiscus). A manual search of relevant journals was also conducted and included the Australian Journal of Physiotherapy (1988-2009), British Journal of Sports Medicine (1992-2010), Clinical Rehabilitation (1995-2004), Physical Therapy (1984-2010), Physical Therapy Reviews (1997-2010), Physiotherapy (1985-1994), Physiotherapy Canada (1987-2010), Physiotherapy in Sport (1987-2006), Physiotherapy Practice (1985-1988), Physiotherapy Research International (1996-2006), Physiotherapy Theory and Practice (1986-1998) and The Physician and Sports Medicine (1990-2005). Key search terms were joint hypermob\*, benign joint hypermobility syndrome, JHM\*, JHS, HMS, BJH\*, therapeutic exercis\*, exercise therap\*, physical exercis\*, physical therap\*, aerobic\*, balanc\*, hydrotherap\*, activit\*, strength training, and physical intervention\*. * **Selection criteria:** Inclusion criteria included participants with joint hypermobility syndrome, therapeutic exercise of any kind used as the intervention, human participants, primary data reported, English language, and published research. There were no restrictions on publication date or study designs. * **Methods:** After all studies were identified, duplicates were removed and inclusion criteria were applied to the abstracts and then to full texts. The decisions were discussed and agreed upon by a group of researchers. From 2,001 potentially relevant articles, 4 titles were included in the qualitative synthesis and key data was extracted from these articles. Risk of bias was assessed using the Critical Appraisal Skills Program (CASP) checklists and any disagreements were resolved through a group consensus. Due to the heterogeneity of the selected articles, no attempt was made to synthesize results across studies. * **Included titles:** Kemp et al (2010), Sahin et al (2008), Ferrell et al (2004), Barton and Bird (1996) |
| **Setting**  [e.g., locations such as hospital, community; rural; metropolitan; country] |
| * The systematic review was conducted by researchers in the United Kingdom. The locations of the four included articles were the Children’s Rheumatology Department in the UK (Kemp et al), the Physical Medicine and Rehabilitation Department Outpatient clinic in Turkey (Sahin et al), a Hypermobility clinic in the UK (Ferrel et al) and hospital referral or patient support group in the UK (Barton and Bird). |
| **Participants**  [N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]  Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article. |
| * N=57 (Kemp et al); n=40 (Sahin et al); n=18 (Ferrell et al); n=25 (Barton and Bird) * Barton and Bird did not disclose their diagnostic criteria; the others used the Brighton 1998 criteria * Kemp et al had a pediatric population (mean age=10.9 years); others had adult samples: mean age 26.9 years (Sahin et al) and 27.3 years (Ferrell et al); Barton and Bird did not disclose * Sahin et al and Ferrell et al were specific to the knee joint; others were whole body exercise * The interventions lasted 6-8 weeks * CASP tool for RCTs was used to asses Kemp et al and Sahin et al; CASP tool for cohort studies was used to asses Ferrell et al and Barton and Bird * All four studies used convenience sampling * Kemp et al and Ferrell et al lost participants to drop out; others were not reported |
| **Intervention Investigated**  [Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| * Kemp et al had a general exercise (not targeted) intervention consisting of shuttle-runs, bunny hops, squat-thrusts, sitting-to-standing, step-ups, and star-jumps. These were performed at the clinic once per week for 30 minutes and was supervised by a PT. The exercises were progressed from starting at 30 seconds or 10 repetitions and adding 15 seconds or 5-10 repetitions at a time. * Sahin et al had a no exercise control group * Ferrell et al and Barton and Bird did not have a comparison group |
| *Experimental* |
| * Kemp et al: Targeted exercise program focusing on controlling a neutral joint position, retraining dynamic control, motion control, and specific tissue lengthening. The exercises were progressed by reducing support and increasing repetitions, speed and duration. These exercises were performed at the clinic once per week for a total of 6 weeks. These 30-minute sessions were supervised by a PT. * Sahin et al: The intervention included knee exercises performed at the clinic 3 times per week for 8 weeks. Participants were supervised by a doctor. The exercises included walking backwards, heel walking, toe walking, walking with eyes closed, single leg stance, forward-backward bends on one leg, sit-to-stands, plyometric exercises, walking exercises, and exercises using a biomechanical ankle platform system balance board. Exercises were progressed by increasing duration and difficulty (i.e. sit to stands from lower surface). * Ferrell et al: Knee exercises performed at home four times a week for 8 weeks with no supervision. Exercises included squats, pliés, bridges, front lunges, static hamstring exercises, balance board exercises and side lunges. Exercises were progressed by increasing repetitions. * Barton and Bird: Whole body exercise intervention performed at home for 6 weeks with no supervision. Exercises included warm up/mobility exercises, specific joint exercises (hamstring curls, hip extensions, pelvic tilts, sit-ups, chest press in supine, arm elevations, heel raises, toe-heel walking, and bicep curls. The intervention also included proprioceptive exercises consisting of single leg ball-rolling and single leg balance. Assessments were taken every 2 weeks. |
| **Outcome Measures**  [Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| Kempt et al assessed patients at follow-up periods of 2 months and 5 months; Sahin et al and Ferrell et al took measurements at baseline and after the 8-week intervention; Barton and Bird took measurements at baseline, after the 6-week intervention and again 6 weeks later (12 weeks).  The following outcome measures were included among the four studies:   * Visual Analog Scale (VAS): To assess pain at rest and with movement (0mm-10mm); Kemp et al had parents assess their child’s pain and impact of pain using the VAS. This was the primary outcome measure used in all four studies. * Knee joint proprioception: Assessed using the active-active method with the Biodex system 3pro multi-joint system isokinetic dynamometer * Childhood Health Assessment Questionnaire (CHAQ): To assess functional impairment (higher score= more functional impairment) * Short-Form Health Survey 36 (SF-36): To assess quality of life (0 being the worst possible score and 100 being the best possible score). Physical functioning and mental health scales were used. * Balance: Assessed using instrumented balance board * Knee strength: Assessed using Kin-Com isokinetic dynamometer * Joint ROM: Assessed using Loebl hydrogoniometer * Six-minute shuttle run |
| **Main Findings**  [Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. You may summarize results in a table but you must explain the results with some narrative.] |
| |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | Kemp et al | Sahin et al | Ferrell et al | Barton and Bird | | Statistically Significant findings after treatment | **Targeted Exercise group:** reduced parents’ global assessment on VAS (p=0.017) and reduced CHAQ (p=0.045)  **Combined groups:** reduced pain (p<0.001), reduced parents’ assessment of pain (p<0.001), reduced parents’ global assessment of pain (p=0.005), reduced CHAQ (p=0.024) | **Exercise group:** reduced pain (p<0.05) and increased knee proprioception (p<0.001) | Reduced pain (p=0.003), increased proprioceptive acuity (p<0.001), increased balance (p<0.001), increased quadriceps and hamstring muscle strength (p<0.05), and improved quality of life (physical functioning scale p=0.029 and mental health scale p=0.008) | Reduced pain with movement (p<0.001), increased maximum distance walked (p<0.006), reduced knee ROM (left knee p=0.003, right knee p=0.022) | | Effect size | VAS= 1.37 | VAS at rest=0.75  VAS w/ movement= 1.72 | VAS= 1.12 | Unable to calculate |   Kemp et al found no differences between exercise groups (targeted and generalized) regarding child’s pain, parents’ assessment of child’s pain, CHAQ scores, or the six-minute shuttle test. The only difference between the two groups was an improved parents’ global assessment of pain in the targeted exercise group at 5 months but not at 2 months.  Sahin et al found that both pain and knee proprioception significantly improved in the experimental group compared to the no-exercise control group. However, a between-group statistical analysis was not reported and therefore conclusions cannot be drawn about the true effectiveness of the exercise program.  Ferrell et al found that therapeutic exercise significantly improved pain, proprioceptive acuity, balance, strength, and quality of life.  Barton and Bird et al found that whole-body exercise significantly improved maximum distance walked and pain with movement. |
| **Original Authors’ Conclusions**  [Paraphrase as required. If providing a direct quote, add page number] |
| The evidence from the four studies included in this systematic review suggests that patients who received an exercise intervention improved over time. No adverse effects were reported. However, there was no strong evidence that generalized exercise was superior than joint-specific exercise or that the knee exercises were superior than the control. Thus, no clear cause-and-effect relationships can be determined. The studies included in this review were of moderate to poor methodological quality, lacking statistical power and adequate control conditions. There still remains a gap in the literature regarding the effectiveness of therapeutic exercise for the management of patients with joint hypermobility syndrome. |
| **Critical Appraisal** |
| **Validity**  [Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.] |
| **AMSTAR score:** 6/11  Strengths: The researchers performed a thorough search of nine online databases, in addition to a hand search and snowballing to gather all potential titles. All decisions regarding article selection were discussed and agreed upon by a group of researchers, therefore ensuring the inclusion criteria was applied adequately. Risk of bias was assessed using the Critical Appraisal Skills Program (CASP) and each group member independently applied the checklist to each article; any disagreements were resolved by group consensus. The results from the CASP tools were used appropriately in determining their conclusion.  Weaknesses: The researchers limited their search to only published literature in the English language, therefore increasing the possibility of publication bias. There was no restriction on study design and therefore the studies included are of moderate to poor quality. The included studies demonstrated problems with sampling, diagnostic criteria and sample sizes, which can increase the likelihood of a type II error. All studies used a convenience sampling. The studies that did report a randomization and blinding protocol were not clear, increasing possibility of bias. Intention-to-treat analyses were not used in the studies who lost participants, leading to possible attrition bias. Only one study had a substantial follow-up period.  External Validity: This systematic review included studies with a variety of patient ages (pediatric to adult) and genders (male and female) and therefore these results may generalize to a wider population. However, two of the studies focused exclusively on the knee joint, which may not be generalizable to the presentation of the entire joint hypermobility syndrome population. There is the possibility for a type II error due to issues with sampling, which would decrease the external validity. Some of the interventions were employed with no supervision and another met three times a week, both may not be realistic for a healthcare setting.  Overall this study provides support that a therapeutic exercise intervention can improve symptoms of joint hypermobility syndrome, including pain intensity. While the evidence from this systematic review is limited due to the poor quality of the included studies, the authors’ assessment using the CASP tool was considered and appropriately applied when formulating their conclusion. |
| **Interpretation of Results**  [This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.] |
| The results from this systematic review report a large effect size for pain at the end of treatment in every study except Barton and Bird, in which the effect size was unable to be calculated. Therefore, this provides support for a strong relationship between therapeutic exercise and improved pain in this patient population. However, due to the poor methodological quality of the included studies, the conclusions drawn from this systematic review should be guarded. The included studies have high possibility for bias. The exercise interventions are varied and include proprioceptive, balance, and strength exercises, meaning improvements cannot be attributed to one type of exercise. Furthermore, some of the interventions were not supervised, meaning adherence to correct protocol is unknown. There is also a lack of a follow-up period which would be beneficial to make conclusions about long-term improvements since hypermobility is a chronic condition. |
| **Applicability of Study Results**  [Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.] |
| This systematic review has moderate relevance to my clinical scenario. The populations of the studies included in the review differ from my patient in age and gender (much younger and include males). My patient’s goal is consistent with the objective of this review: to determine if therapeutic exercise can reduce chronic pain in patients with hypermobility syndrome. The interventions detailed in the review are feasible in an outpatient physical therapy clinic, similar to the one my patient attends, and do not require additional equipment or resources. With no adverse events reported, it appears the potential benefits would outweigh the potential harms of incorporating these types of therapeutic exercise into a physical therapy plan of care. While perhaps not the singular intervention used, therapeutic exercise can contribute to a multimodal physical therapy intervention for my patient. |

**(2) Description and appraisal of (The effect of combined exercise therapy on knee proprioception, pain intensity and quality of life in patients with hypermobility syndrome: a randomized clinical trial) by (Daman et al, 2017)**

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| **Aim/Objective of the Study/Systematic Review:** |
| To determine the effect of a combined exercise therapy program consisting of closed kinetic chain exercises and proprioception exercises on knee proprioception, pain intensity and quality of life in patients with hypermobility syndrome. |
| **Study Design**  [e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]  Note: For systematic review, use headings ‘search strategy’, ‘selection criteria’, ‘methods’ etc. For qualitative studies, identify data collection/analyses methods. |
| * Single-blind randomized clinical trial * Participants were randomly allocated into intervention or control group using a computer-generated random number table * A physical therapist supervised all patients in the intervention group while a second physical therapist blinded to the group allocation evaluated the participants before and after the intervention * Measurements were taken before intervention and immediately following the 4-week intervention |
| **Setting**  [e.g., locations such as hospital, community; rural; metropolitan; country] |
| * Shiraz School of Rehabilitation Sciences, Iran |
| **Participants**  [N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]  Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article. |
| * N= 24 * Participants were women aged 18-30 years old with diagnosis of hypermobility syndrome according to Brighton 1998 diagnostic criteria * Participants were recruited through announcements posted on bulletin boards * All participants were patients at physical therapy, orthopaedic knee and rheumatology clinics affiliated with Shiraz University * Mean age= 22.25 (intervention) and 21.66 (control) * Participants were excluded if they were athletes, exercised regularly (at least 3 times a week), had a history of knee trauma, history of rheumatoid disease or knee osteoarthritis, knee ligament injury, knee arthroplasty, or neuromuscular or musculoskeletal disorder * Intervention and control groups were comparable at baseline regarding age, height and weight |
| **Intervention Investigated**  [Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| * The control group received no intervention (n=12) |
| *Experimental* |
| * N=12 * The intervention was a combined exercise therapy program that met 3 times per week for 4 weeks * The intervention was supervised by an expert physical therapist * The exercises consisted of closed chain and proprioceptive exercises and were progressed throughout the four weeks as detailed below: * **First week:** squats, bridges, pliés (1 set of 5 reps), backward walking (30 seconds), heel walking (30 seconds), toe walking (30 seconds), walking with eyes closed (30 seconds), single leg stance (30 seconds), and bending forward and backward on one leg with eyes closed (30 seconds), and with eyes opened (30 seconds) * **Second week:** squats, bridges, pliés (1 set of 10 reps), front lunge and side lunge (1 set of 5 reps), backward walking (30 seconds), heel walking (30 seconds), toe walking (30 seconds), walking with eyes closed (30 seconds), single leg stance (30 seconds), and bending forward and backward on one leg with eyes closed (30 seconds), and with eyes opened (30 seconds), slow sit to stands (1 set of 10 reps) * **Third week:** squats, bridges, pliés (2 sets of 10 reps), front lunge and side lunge (1 set of 10 reps), backward walking (30 seconds), heel walking (30 seconds), toe walking (30 seconds), walking with eyes closed (30 seconds), single leg stance (30 seconds), and bending forward and backward on one leg with eyes closed (30 seconds), and with eyes opened (30 seconds), slow sit to stands (1 set of 10 reps), and dynamic gait exercises at fast and slow speeds, in narrow and broad circles (1 set of 5 reps) * **Fourth week:** squats, bridges, pliés (2 sets of 15 reps), front lunge and side lunge (2 sets of 10 reps), backward walking (30 seconds), heel walking (30 seconds), toe walking (30 seconds), walking with eyes closed (30 seconds), single leg stance (30 seconds), and bending forward and backward on one leg with eyes closed (30 seconds), and with eyes opened (30 seconds), slow sit to stands (1 set of 10 reps), and dynamic gait exercises at fast and slow speeds, in narrow and broad circles (1 set of 5 reps) |
| **Outcome Measures**  [Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| * All outcome measures were taken by a physical therapist who was blinded to the group allocation * Measurements were taken immediately before and after the 4-week intervention, following the exact same protocol * The measurements were taken when the participants were not at the beginning of their menstrual cycle so the increased levels of sex hormones (estrogen and progesterone) did not affect joint laxity * Pain intensity was measured with the Visual Analog Scale (VAS) (range= 0 mm- 10 mm) * Quality of life was measured with the Short Form 36 Health Survey (SF-36) with 0 being the worst possible score and 100 being the best possible score. The physical functioning and mental health scale were assessed. * Knee joint proprioceptive acuity was measured with a goniometer by measuring the error rate in joint angle repositioning. The axis of the goniometer was positioned at the lateral femoral epicondyle, with one arm along the long axis of the femur and the other arm aligned with the leg. The measurements were taken in both a weight-bearing and a non-weight bearing position. In the weight-bearing position (standing), the patient was asked to actively bend her lower extremity to 30 degrees of knee flexion and then to reproduce this angle actively (active-active method). In the non-weight bearing position, (sitting at edge of bed with eyes closed), a 30-degree angle of knee flexion was produced passively, then the knee was extended. The patient was then asked to reproduce that angle actively (passive-active method). The angle error was recorded after each assessment and each measurement was taken 5 times with the average of the 5 trials used for analyses. |
| **Main Findings**  [Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. Use a table to summarize results if possible.] |
| Angle error from the joint angle repositioning measurement was significantly reduced in the intervention compared to the control group in both the weight-bearing and non-weight-bearing positions. Pain intensity was significantly reduced in the intervention compared to the control group. Quality of life improved significantly in the intervention group compared to the control.  Angle error (degrees) in the weight-bearing position before and after intervention: \*indicates significance   |  |  |  |  | | --- | --- | --- | --- | |  | Before | After | P value | | Intervention (mean±SD) | 6.24±5.39 | 2.53±2.71 | 0.005\* | | Control(mean±SD) | 5.62±4.43 | 5.69±4.69 | 0.92 |   Statistical significance was achieved for the reduction of the angle error in the intervention compared to the control in the weight-bearing position after the 4-week intervention.  Angle error (degrees) in the non-weight-bearing position before and after intervention: \*indicates significance   |  |  |  |  | | --- | --- | --- | --- | |  | Before | After | P value | | Intervention (mean±SD) | 3.84±3.68 | 2.07±1.81 | 0.01\* | | Control (mean±SD) | 4.90±3.41 | 5.02±3.05 | 0.70 |   Statistical significance was achieved for the reduction of the angle error in the intervention compared to the control in the non-weight-bearing position after the 4-week intervention.  Visual Analog Scale scores before and after intervention: \*indicates significance   |  |  |  |  | | --- | --- | --- | --- | |  | Before | After | P value | | Intervention (mean±SD) | 4.98±1.32 | 2.25±1.48 | 0.001\* | | Control (mean±SD) | 4.87±1.86 | 5.37±2.07 | 0.20 |   Statistical significance was achieved for the reduction of pain intensity as measured by VAS in the intervention compared to the control after the 4-week intervention.  Short Form 36 Health Survey scores before and after intervention: \*indicates significance   |  |  |  |  |  | | --- | --- | --- | --- | --- | | Domain |  | Before | After | P value | | Physical Functioning | Intervention (mean±SD) | 59.90±6.28 | 71.89±9.39 | P<0.001\* | |  | Control (mean±SD) | 60.50±9.70 | 60.55±9.55 | 0.94 | | Mental Health | Intervention (mean±SD) | 57.39±16.75 | 58.05±17.06 | 0.31 | |  | Control (mean±SD) | 51.80±17.49 | 52.56±13.63 | 0.69 |   Statistical significance was achieved for improved quality of life scores on the physical functioning domain on the SF-36. |
| **Original Authors’ Conclusions**  [Paraphrase as required. If providing a direct quote, add page number] |
| “In the present sample of patients with joint hypermobility syndrome, combined exercise therapy reduced pain intensity and improved joint proprioception and quality of life immediately after the intervention.” (p.204) |
| **Critical Appraisal** |
| **Validity**  [Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.] |
| PEDro Scale= 5/10 (internal validity)  Strengths: Though the sample size seemed small (n=24), a power analysis was performed prior to the study to determine the necessary number of participants per group. To achieve 80% power, 12 women were needed per group. There were no dropouts and all 24 women completed the intervention. The participants were randomized to groups, reducing bias by ensuring the groups were similar on certain demographics (age, height, weight). The PT taking the measurements was blinded, reducing potential bias. The same PT supervised each session and a second PT took all the measurements, increasing reliability. The angle error measurement was taken five times and the average of these numbers was used for analysis, minimizing human error in goniometric measurements.  Weaknesses: There were no follow-up measurements taken after the 4-week post intervention assessment, therefore the longevity of the results is unknown. There was no concealed allocation, which increases bias. The control group was not blinded to their group as they received no intervention. The intervention period was short, only 4-weeks and does not represent a true physical therapy plan of care.  External Validity: This study has a relatively homogeneous sample: women, young adult (18-30 years old), all recruited from the same University-affiliated clinics. Information regarding diagnosis, age of diagnosis, and disease process is absent and would contribute to the generalizability of the results.  Overall this study provides good evidence that a combined exercise therapy intervention consisting of closed-chain exercises and proprioceptive exercises reduces pain, increases quality of life and improves joint proprioception in patients with hypermobility syndrome. The single-blind RCT design with a detailed intervention program provides strong evidence that can easily be reproduced in another setting. The study had sufficient power and did not lose anyone to follow-up. |
| **Interpretation of Results**  [This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.] |
| This study provides support that a multimodal exercise intervention consisting of closed-chain exercises and proprioceptive exercises can reduce pain and improve quality of life and joint proprioception in patients with hypermobility syndrome. While the results were significant after the 4-week intervention period, there was no long-term follow-up, which is important in understanding if these improvements are maintained over time. Furthermore, there is still a lack of consensus regarding which specific exercises, if any, are superior in treating patients with hypermobility syndrome. Therefore, an additional intervention group who received a different exercise program would have provided additional support for this specific type of intervention. I conclude there is sufficient evidence to incorporate these exercises into a physical therapy exercise program for a patient with joint hypermobility syndrome. |
| **Applicability of Study Results**  [Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.] |
| This study has moderate applicability to my clinical question. The participants in this study, while female, are much younger than my patient. The objective of the study is relevant to my clinical scenario as my patient’s goals are to decrease pain and improve quality of life. These types of exercises are feasible in the outpatient physical therapy setting. The exercises do not require additional equipment or resources and could easily be incorporated into a physical therapy plan of care. There does not seem to be any potential harm for my patient as the exercises are body-weight exercises and balance/gait activities. While it is difficult to conclude if this is the most effective intervention for my patient, there is enough support to incorporate these exercises into a multifaceted intervention plan. |

**SYNTHESIS AND CLINICAL IMPLICATIONS**

[Synthesize the results, quality/validity, and applicability of the two studies reviewed for the CAT. Future implications for research should be addressed briefly. Limit: 1 page.]

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| **Synthesis of evidence:** Overall, there remains a gap in the literature as to what therapeutic exercise, including specific type and parameters, is most effective for patients with hypermobility syndrome. Based on the two studies review for this CAT, there is moderate evidence that a combined exercise therapy program consisting of closed-chain exercises, proprioceptive exercises, balance and strength exercises can reduce pain, increase joint proprioception and improve quality of life in adult patients with joint hypermobility syndrome. These types of exercises are feasible and applicable in an outpatient physical therapy clinic setting. Until further research as to specific parameters is published, there is moderate evidence for the efficacy of a multimodal exercise intervention for hypermobile patients. Therefore, it can be concluded that physical therapy intervention may be more effective than non-care in managing the chronic pain that is commonly experienced in patients with Ehlers-Danlos hypermobility type.  **Implications for clinical practice:** These studies include a variety of interventions that fall under the scope of physical therapy practice, including therapeutic exercise. These exercises, including strength, balance, and proprioceptive exercises, are commonly performed in outpatient physical therapy clinics and are used to treat a variety of conditions, including pain and musculoskeletal impairments. These studies also commonly used the Visual Analog Scale and Short Form Health Survey 36 as outcome measures to assess change and these are widely used and validated tools that are appropriate for use in the clinic. It should be noted that evidence-based practice includes the application of the clinician’s expertise and clinical judgement to each patient case and scenario and the patient’s unique needs should be considered when formulating a plan of care.  **Implications for future research:** There is a significant need for future high-quality evidence to determine the most effective type, frequency, and duration of physical therapy intervention to improve symptoms of hypermobility syndrome. A prospective RCT with a multi-center sampling population and long follow-up period is necessary to elucidate the optimal treatment for these patients. Diagnostic criteria should be standardized and a complete description of the exercise interventions should be detailed in order to replicate these findings in the clinical setting. Future studies should directly compare types of exercise interventions to determine which intervention is most effective and safe for this population. |

**REFERENCES**

[List all references cited in the CAT]

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| Bibliography  1. Toprak Celenay S, Ozer Kaya D. Effects of spinal stabilization exercises in women with benign joint hypermobility syndrome: a randomized controlled trial. *Rheumatol Int*. 2017;37(9):1461-1468. doi:10.1007/s00296-017-3713-6  2. Pennetti A. A multimodal physical therapy approach utilizing the Maitland concept in the management of a patient with cervical and lumbar radiculitis and Ehlers-Danlos syndrome-hypermobility type: A case report. *Physiother Theory Pract*. 2018;34(7):559-568. doi:10.1080/09593985.2017.1422207  3. Zhou Z, Rewari A, Shanthanna H. Management of chronic pain in Ehlers-Danlos syndrome: Two case reports and a review of literature. *Medicine*. 2018;97(45):e13115. doi:10.1097/MD.0000000000013115  4. Daman M, Shiravani F, Hemmati L, Taghizadeh S. The effect of combined exercise therapy on knee proprioception, pain intensity and quality of life in patients with hypermobility syndrome: A randomized clinical trial. *J Bodyw Mov Ther*. 2019;23(1):202-205. doi:10.1016/j.jbmt.2017.12.012  5. Palmer S, Bailey S, Barker L, Barney L, Elliott A. The effectiveness of therapeutic exercise for joint hypermobility syndrome: a systematic review. *Physiotherapy*. 2014;100(3):220-227. doi:10.1016/j.physio.2013.09.002  6. Smith TO, Bacon H, Jerman E, et al. Physiotherapy and occupational therapy interventions for people with benign joint hypermobility syndrome: a systematic review of clinical trials. *Disabil Rehabil*. 2014;36(10):797-803. doi:10.3109/09638288.2013.819388  7. Arthur K, Caldwell K, Forehand S, Davis K. Pain control methods in use and perceived effectiveness by patients with Ehlers-Danlos syndrome: a descriptive study. *Disabil Rehabil*. 2016;38(11):1063-1074. doi:10.3109/09638288.2015.1092175  8. Castori M, Morlino S, Celletti C, et al. Management of pain and fatigue in the joint hypermobility syndrome (a.k.a. Ehlers-Danlos syndrome, hypermobility type): principles and proposal for a multidisciplinary approach. *Am J Med Genet A*. 2012;158A(8):2055-2070. doi:10.1002/ajmg.a.35483 |