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**What are the most effective physical therapy interventions for managing the symptoms of Ehlers-Danlos Syndrome, Hypermobility type? A Critically Appraised Topic.**

**Clinical Scenario:**

 A 40-year-old female with a diagnosis of Ehlers-Danlos Hypermobility type (EDS-HT) presents to an outpatient physical therapy clinic with complaints of chronic pain, fatigue, and general disability. She has a past medical history of multiple orthopedic surgeries, including bilateral rotator cuff repairs (both failed, underwent revision on left side) and left anterior cruciate ligament repair. She scored a 7/9 on the Beighton scale and demonstrates marked skin extensibility. She complains of constant, diffuse pain rated at 6/10. This patient leads an active lifestyle and does yoga, Pilates, and cycle regularly. She is interested in receiving physical therapy services to manage the symptoms of EDS-HT, specifically chronic pain, in order to maintain her quality of life as she ages.

**Background:**

 Ehlers-Danlos Syndrome Hypermobility type (EDS-HT) is a rare but potentially debilitating disease if not managed properly. To date, there does not exist high-quality evidence supporting optimal interventions to manage the symptoms of this disease, including chronic pain, fatigue, and decreased health-related quality of life. The literature that does exist, mostly case reports and narrative reviews, lacks generalizability and convincing evidence in support of physical therapy interventions. There is a pressing need to determine the most effective physical therapy interventions to treat this population.

**Clinical Question:**

What are the most effective physical therapy interventions for managing the symptoms of Ehlers-Danlos Syndrome, Hypermobility type?

**Search Strategy:**

 The first step in the search strategy was to identify the terms to be used. “Ehlers Danlos” AND “Hypermobility” AND “Physical Therapy” were used as terms in the Advanced Search feature of PubMed. This search produced 52 articles. Of these titles, six were deemed appropriate and relevant to the case and clinical question. The next database searched was PEDro and a simple search of “Ehlers Danlos Hypermobility” was conducted. Two articles were found: one that had already been identified through the PubMed search and another RCT that was appropriate for review. Cochrane Library was then searched using the advanced search feature and the terms “Ehlers Danlos Syndrome” AND “Hypermobility” AND “Physical Therapy” and produced three results. One was promising but is still in the recruiting phase of the clinical trial and thus excluded from review. Finally, CINAHL online database was searched using the terms “Ehlers Danlos Syndrome” AND “Exercise” and one more title out of 21 results was deemed appropriate and relevant to include in this CAT. Due to the paucity of literature on EDS-HT, the inclusion and exclusion criteria were limited to including trials that had already been conducted and published after the year 2000 and excluding articles written in a language other than English.

**Table 1: Results of Search:** Arranged by level of evidence.

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| Author (Year) | Level of Evidence\* | Relevance to Clinical Scenario\*\* | Study Design |
| Peterson (2018)1 | 1a | Low | Systematic Review |
| Reychler (2019)2 | 1b | Medium  | RCT |
| Scheper (2016)3 | 2a | High | Meta-Analysis |
| Palmer (2014)4 | 2a | High | Systematic Review |
| Pennetti (2018)5 | 4 | Medium  | Case Report  |
| Rombaut (2011)6 | 4 | High | Cross Sectional Study |
| Engelbert (2017)7 | 5 | High | Narrative Review |
| Bathen (2013)8 | 5 | High | Pilot Study |

\*Portney & Watkins Table 16.1 (2009)

\*\*Relevance based on comparison of demographics, disease course, presentation and subjective complaints of patient in clinical scenario

**Summary of Best Evidence:**

**The effectiveness of therapeutic exercise for joint hypermobility syndrome: a systematic review by Palmer et al. 2014.**

**Objective:** To establish the effectiveness of therapeutic exercise in managing Joint Hypermobility Syndrome (JHS).

**Study design:**

Search strategy: Nine online databases were searched: AMED, BNI, CINAHL, Cochrane Library, Embase, HMIC, Medline, PEDro, and SportDiscus. The primary search terms used were “joint hypermobility syndrome” and “therapeutic exercise.” Alternative terms were identified through an online thesaurus and team discussion. Identical search strategies were used for EBSCO, OVID, ProQuest and the Cochrane Library but the PEDro search required an adapted search where the individual search terms for “joint hypermobility syndrome” were required to perform the search.

Selection criteria: The inclusion criteria were as follows: people with JHS (as opposed to asymptomatic generalized joint laxity), therapeutic exercise used as an intervention, human participants, primary data reported, English language and published research.

Methods: The search was conducted as described above and the inclusion criteria were applied to abstracts and then again to full texts. All decisions were discussed and agreed upon by the team. Key data was extracted from the final texts and risk of bias was assessed using the CASP checklists. The checklists were individually applied to the final articles by each team member and any disagreements were resolved by group consensus. From 2,001 potential articles, 4 were identified as meeting the criteria and were included in this systematic review.

Included titles: Kemp et al. 2010, Sahin et al. 2008, Ferrell et al. 2004 and Barton and Bird 1996

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| --- | --- | --- | --- | --- |
|  | Kemp (2010) | Sahin (2008) | Ferrell (2004) | Barton and Bird 1996 |
| Study Design | RCT | RCT | Cohort Study | Cohort Study |
| Participants (range of ages, males vs. females, sample size) | 7-16 38M, 19Fn=57 | 20-456M, 29Fn=40 | 16 to 492M, 16Fn=18 | Age not reported2M, 23Fn=25 |
| Interventions | Whole body exercisesGeneral vs. targeted | Knee proprioception exercises vs. no exercise control | Knee proprioception exercises, balance exercises, knee strengthening (no control) | Whole body exercises- mobility, specific joint, propr-ioception (no control) |
| Outcome measures (primary) | Pain (VAS) | Knee pain (VAS) | Knee pain (VAS) | Pain at rest and with movement (VAS) |
|  Main Findings | No difference between groups; combined group results showed improvement | Exercise reduced pain and improved knee joint proprioception | TherEx improved proprioceptive acuity, balance, strength, reduced pain and improved physical functioning on SF-36 | Significant improvement in pain w/ movement |
| Standardized Effect Size for pain | Child’s pain (VAS)= 1.37 | VAS at rest=0.75, w/ movement=1.72 | VAS= 1.12 | Not calculated |

Table 2. Articles included in systematic review.

**Original Authors’ Conclusions:** Patients who received an exercise intervention improved and no adverse events occurred. There was no convincing evidence that generalized exercise is better than joint-specific exercise. Thus, a clear cause and effect relationship for exercise and management of JHS cannot be determined. There is a need for further studies with higher methodological quality, including studies with longer follow up, complete description of exercise intervention, and adequate statistical power and control conditions.

**Critical Appraisal:**

Validity: The strengths of this systematic review are that nine online databases were searched thoroughly, the search was supplemented with a hand search and snowballing, and methodological quality of included studies was assessed individually and discussed as a group for consensus. The weaknesses were that the included studies were of low methodological quality, there was no pooling of results, one included study was published in 1996 and is this potentially outdated, and only one true controlled trial was included. As for generalizability, this review included both genders and wide range of ages (7-49), however two studies were specific to knee joint and thus results may not be generalizable to other joints.

Interpretation of results: There is some evidence that symptoms of joint hypermobility can improve with exercise, but there is no definitive conclusion supporting one specific type of exercise over another. However, no adverse events were reported, and therefore exercise (strengthening, proprioceptive exercises, balance, and specific joint exercises) may be safely incorporated into a PT plan of care. Due to the low methodological quality of the studies, the results should be considered with caution.

Applicability of results: Though this systematic review included populations outside of my clinical scenario, the objective of the study was relevant to my case. Proprioceptive-based exercises, strengthening exercises, balance exercises and functional stability exercises are appropriate to include as part of a PT intervention for this patient.

**Disability in Adolescents and Adults Diagnosed with Hypermobility-Related Disorders: A Meta-Analysis by Scheper et al. 2016.**

**Objective:** To establish the association of the most commonly reported symptoms of hypermobility-related disorders on disability. To study the effectiveness of treatment on disability in patients with Ehlers-Danlos Syndrome and hypermobility syndromes (HMS).

**Study design:**

Search strategy: Electronic searches were conducted separately for each of the objectives. The databases searched were CENTRAL and MEDLINE. The search terms were classified according to the ICF model (population, symptoms, disability, and treatment). MeSH terms and free-text terms were used in the primary search. The search was conducted independently by 3 researchers.

Selection criteria: For this meta-analysis, the inclusion criteria are studies that have clearly defined disease status by objective clinical criteria, subjects older than 16 years of age, include outcome measures at each ICF domains, and are published in English. The exclusion criteria included letters, dissertations, editorials and abstracts, case studies and case series in which treatment was main topic, and interventions of surgery, medical intervention, or assistive devices.

Methods: After the search and selection criteria were applied to identified articles, the included studies were assessed for risk of bias independently by 2 assessors. Key data was extracted and a meta-analysis was performed. From the 714 publications identified after the primary search, 16 were included in analysis of symptoms (objective #1), including 14 comparative cohort and 2 cross-sectional studies. Regarding treatment (objective #2), 19 publications were identified and 5 were included for analysis.

Treatment effectiveness: 5 publications were included in the analysis (1 RCT, 4 clinical controlled trial) with a total of 200 subjects, all with a diagnosis of with HMS. The mean age of subjects was 35.7 years and the median Beighton score was 6/9. All studies reported outcomes on the level of activity and participation according to the ICF model and pain intensity.

Interventions: The interventions included in this review were multidisciplinary approaches and included medical treatment, OT, PT and social work. Interventions focused on enhancing physical fitness through proprioceptive-based exercises, strengthening exercises, balance exercises and joint-stabilizing exercises, both open- and closed-chain. Cognitive intervention for pain management and lifestyle was also included through education regarding illness beliefs, pain management, relaxation techniques and lifestyle advice. A home exercise program was monitored by telephone.

Main findings: Pain, fatigue and psychological distress have a significant impact on disability. Significant pain reduction can be achieved through a variety of physical and cognitive approaches. However, treatment effectiveness on disability was inconclusive. The role of pain intensity on disability may not be as important as pain sensitization, vigilance and coping. Fatigue, psychological distress, environmental factors greatly influence disability in patients with EDS-HT.

Original Authors’ Conclusions: Though disability is known to commonly occur in patients with HMS and EDS-HT, effective interventions to reduce disability lack scientific evidence. Clinical characteristics of HSM and EDS-HT show significant variability. Clinicians should conduct comprehensive assessments, including all aspects of the ICF model with these patients.

**Critical Appraisal:**

Validity: The strengths of this meta-analysis include its high level of evidence, use of the ICF Model as the framework to guide assessment and treatment, and assessment of risk of bias of included studies. The weaknesses are that the studies did not have a long-term follow up and were of low methodological quality. Due to the wide variability within the phenotype and the inconsistent and insufficient current classification system for hypermobility syndromes, generalizability is difficult. Additionally, disability is subjective and the perception of disability may differ between individual perspectives.

Interpretation of results: Disability is multifactorial and pain is only one of the factors; therefore, an intervention plan must be multidisciplinary and incorporate treatment of fatigue and psychosocial factors (such as social isolation, anxiety and depression) to be effective.

Applicability of results: The objective of this meta-analysis is highly relevant to the clinical scenario of my CAT as I am interested in determining effective interventions for patients with EDS-HT. The demographics of the included studies also closely aligned with my case.

**Clinical Bottom Line:**

The treatment of EDS-HT should be tailored to specific phenotypes and individual patient presentation and needs. There is no conclusive evidence supporting one type of intervention over another; treatment of EDS-HT should be multidisciplinary and patient-centered. There is a need to establish universal clinical outcomes, standard diagnostic criteria and identify pathways of development of disability in EDS-HT. Future research should include high-quality RCT designs comparing specific, defined interventions to a no-exercise control to establish cause and effect relationships.

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