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Review Article

# Pediatric physiotherapeutic intervention in Classical Ehlers-Danlos

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## ABSTRACT

Ehlers-Danlos Syndrome (EDS) is a group of genetic connective tissue disorders characterized by mutations in the genes encoding collagen, collagen-modifying enzymes and other extracellular matrix proteins. These alterations result in clinical manifestations such as joint hypermobility, skin fragility and musculoskeletal complications, which have a significant impact on patients' quality of life. Although scientific evidence on the physiotherapeutic management of EDS is limited, it has been observed that specific interventions can improve joint stability, muscle strength and functionality, especially in pediatric patients. The aim of this article is to provide an updated review of EDS in the pediatric population and to propose a comprehensive and multidisciplinary physiotherapeutic approach focusing on the prevention of complications, management of symptoms and promotion of active participation in activities of daily living.

**Key words:** ehlers-danlos syndrome (eds); classical ehlers-danlos syndrome (ceds); pediatrics; physical therapy; treatment; collagen.

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## RESUMEN

El Síndrome de Ehlers-Danlos (SED) es un grupo de trastornos genéticos del tejido conjuntivo caracterizados por mutaciones en los genes que codifican el colágeno, las enzimas modificadoras de colágeno y otras proteínas de la matriz extracelular. Estas alteraciones generan manifestaciones clínicas como hiperlaxitud articular, fragilidad cutánea y complicaciones musculoesqueléticas, que impactan significativamente en la calidad de vida de los pacientes. Aunque la evidencia científica sobre el manejo fisioterapéutico del SED es limitada, se ha observado que intervenciones especializadas pueden mejorar la estabilidad articular, la fuerza muscular y la funcionalidad, especialmente en pacientes pediátricos. Este artículo tiene como objetivo proporcionar una revisión actualizada sobre el SED en población pediátrica y proponer un abordaje fisioterapéutico integral y multidisciplinario, centrado en la prevención de complicaciones, el manejo de síntomas y la promoción de la participación activa en las actividades de la vida diaria.


**Palabras clave:** síndrome de ehlers-danlos (sed); síndrome de ehlers danlos clásico (cSED); pediatría; fisioterapia; tratamiento; colágeno.

## INTRODUCTION

Ehlers-Danlos Syndrome (EDS) is a group of inherited connective tissue disorders characterized by defects in collagen synthesis leading to widespread structural weakness of the skin, joints, blood vessels and other tissues. The term was first introduced in 1934 by Pommeau Delille and Soussie, referring to the Danish dermatologist Edvard Laurits Ehlers, who described dermal hyperelasticity and joint hypermobility in 1901, and the French physician Henri-Alexandre Danlos, who identified molluscoid pseudotumours in 1908.[1]

The 2017 International Classification of EDS defines 13 different types, including classical (cEDS), vascular (vEDS) and hypermobile (hEDS), each with unique genetic and clinical characteristics. These conditions often result in musculoskeletal instability, chronic pain, frequent dislocations, proprioceptive deficits and fatigue, which significantly impair daily function and quality of life. Given these challenges, physiotherapy plays a key role in optimizing joint stability, preventing injury and promoting functional independence.[2]

An essential component of physiotherapeutic management in cEDS is progressive strength training, which targets muscle groups to compensate for joint laxity and improve dynamic stability. Strengthening exercises, particularly those focusing on core stability and postural control, help reduce the incidence of joint subluxations and improve biomechanical efficiency. Additionally, neuromuscular re-education and proprioceptive training enhance joint awareness, reducing the risk of falls and injuries.

The Physiotherapeutic Intervention Model (PIM) provides a structured framework for patient care, encompassing examination, evaluation, diagnosis, prognosis, intervention, and re-evaluation. By integrating the International Classification of Functioning, Disability, and Health (ICF), physiotherapists can tailor interventions to address both physical impairments and activity limitations, ensuring a holistic and patient-centered approach.

Ultimately, a well-designed physiotherapy program that includes strength training, joint stabilization exercises, proprioceptive retraining and pain management strategies can significantly improve the functional outcomes and quality of life of people with EDS. Through a combination of targeted interventions and patient education, physiotherapists empower individuals to manage their condition effectively, promoting long-term musculoskeletal health and improved daily function.[3]

## MATERIALS AND METHODS

A comprehensive literature search was conducted in the PubMed database using Medical Subject Headings (MeSH) terms, guided by the PICO (population, intervention, comparison, outcome) framework to ensure a focused research question. The PICO question was formulated as follows: In pediatric patients with Classical Ehlers-Danlos Syndrome (cEDS), does the use of physiotherapy interventions (such as strengthening exercises, hydrotherapy and early mobilization) improve joint stability, reduce pain, increase muscle strength and improve quality of life compared with standard care without specialized physiotherapy? The search strategy included the following MeSH terms: ("Ehlers-Danlos Syndrome"[Mesh]) AND "Physical Therapy Modalities"[Mesh]) OR "Exercise"[Mesh]) OR "Hydrotherapy"[Majr]) AND "Muscle Strength"[Mesh]) OR "Quality of Life"[Majr]) OR "Joint Instability"[Majr].


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The selection of articles was carried out in three stages. First, duplicates were removed using reference management software. Second, titles and abstracts were screened to identify studies that met the inclusion criteria, which required explicit mention of Ehlers-Danlos syndrome and a focus on physiotherapy interventions in pediatric populations. Finally, full-text articles were reviewed to confirm their relevance. Initially, 754 articles were retrieved. After applying the inclusion criteria, the selection was narrowed down to 28 articles that specifically addressed physiotherapy management in pediatric patients with CEDS.

The search was limited to articles published between 2013 and 2023 and available in English and Spanish. Only studies conducted on human subjects, specifically paediatric patients diagnosed with CEDS, were included. Only open access articles were included to ensure accessibility and reproducibility of results. Systematic reviews with meta-analyses and clinical trials were prioritised due to their high level of evidence; however, observational studies and case reports were also included to provide a broader understanding of the topic.

Data extraction included study design, sample characteristics, intervention details, outcomes measured and key findings. This methodology ensured a structured and transparent approach to identifying, appraising and synthesising the available evidence on physiotherapy interventions for paediatric patients with classic Ehlers-Danlos syndrome.

## Classical Ehlers-Danlos

Ehlers-Danlos syndrome is an autosomal dominant connective tissue disorder characterised by atrophic scarring, hypertensive skin and joint hypermobility. Patients with classical Ehlers-Danlos syndrome also have frequent rapid bruising, fragile skin that feels "velvety" to the touch, and frequent wounds that leave atrophic scars. Patients with classic Ehlers-Danlos often have scoliosis and mitral valve prolapse[4,5.]

## Molecular and genetic mechanisms

Collagen and protein defects are found in all types of Ehlers-Danlos, with an abnormal nucleation of collagen fibrils so there is an alteration in the organization of cell fibrils. Due to the mutation in the COL5A1 and COL5A2 genes in patients with Classical Ehlers-Danlos, it synthesizes approximately half of the type V collagen compared to people without the mutation or structural involvement.[6-8]

The collagen fibers in Classical EDS have a variable fiber diameter with an irregular border.[6]

## Epidemiology

According to the Ehlers Danlos Society, the prevalence of Ehlers-Danlos syndrome varies depending on the type. Specifically speaking of Classical Ehlers-Danlos, the prevalence is 1 in 20,000-40,000 people worldwide, however, information on the epidemiology in Mexico is limited.[9]

## Natural history of the disease

Classical Ehlers-Danlos syndrome involves several clinical features and changes over time. The progression of the manifestations of EDS depends on different factors.

The first clinical manifestation that patients encounter is easy bruising in early childhood when they are learning to crawl and appear with the slightest trauma.[10] Likewise, skin hyperextensibility and joint hypermobility can lead to an increased propensity for joint dislocation become visible in early stages.[11] Other visible signs are "cigarette paper" scars and slow tissue repair as patients are easily injured and must be sutured.[4] Patients may experience pain throughout their lives; however, it is not disabling.

Voermans mentions that patients may have minimal, moderate or severe muscle weakness, delaying developmental milestones.[12] It is common for patients with a proper diagnosis to be monitored with cardiac workup.

A study in the American Journal of Medical Genetics states that 33% of patients with cEDS have osteopenia.[10] In the ocular aspect, patients may have thin, transparent and steep corneas.[13] Another characteristic is gastrointestinal problems with nausea being the main symptom.[4]

Patients have a normal life expectancy compared to someone without the disease,[11] however they may have cardiovascular problems such as aneurysms, ruptured arteries, and ruptured mitral and tricuspid valves.[10]

## Diagnosis

To make a proper diagnosis it is important to first identify that the patient does have the disease and then specify the type.

For the screening of Ehlers-Danlos, the Beighton test (1998) must be performed.[15] The specifications of this test can be found in (Table 1). It is also necessary to complement family history to find where the inheritance comes from, and which are the signs that the relative presented. To determine the type, it is necessary to consult the criteria shown in the International Classification of Ehlers-Danlos Syndrome (2017).[16]

**Table 1.** Specific tests

| Test | Description |
|---|---|
| Observation and palpation | Observation can provide an overview of the patient's development.[19] To complement the evaluation, palpation of the tissues is necessary to perceive joint motion, muscle weakness or tension, edema/fibrosis, and areas of reflex activity.[20] |
| Beighton (1998) | It requires 4 points or more out of a total of 9. The subjects are evaluated on a 9-point scale, considering 1 point for each hypermobile site, performed on both hemispheres and measuring the following:[15]<br>– Hyperextension of the elbows (more than 10º), with the subject seated on a stool and with the arm explored by the examiner in extension.<br>– Passive touching of the forearm with the thumb, with the wrist in flexion, with the subject in the same position as before.<br>– Passive extension of the index finger to more than 90°, with the subject seated and with the palm of the hand fully resting on the examination table.<br>– Hyperextension of the knees (10° or more), with the subject in the supine position. The examiner explores the joint, determining its degree of extension. |
| Canadian Occupational Performance Measure (COPM) | It is a tool used to measure patients' improvement in daily activities.[21] |
| Faces Pain Scale-Revised (FPS-R) | The Faces Pain Scale-Revised (FPS-R), is used to assess pain in pediatric patients by means of 6 faces, ranging from 0 to 10 in multiples of 2 (0, 2, 4, 6, 8, 10).[22] |
| Functional tests | The pediatric balance scale and the Functional Strength Measurement to assess balance and strength actively with different movements.[23] |
| Maximum repetition | To measure the force, it is recommended to evaluate the patient's Maximum Repetition,[23] "defined as the capacity of a defined muscle or muscle group to exert force against a resistance in a single maximal effort".[24] |
| Maximum heart rate | Patients with Ehlers-Danlos may present cardiovascular manifestations such as mitral valve prolapse; tricuspid valve prolapse or aortic dilation.[7] |
| Gait examination | A gait examination can prevent, and correct sequelae caused by different pathologies.[25] |
| Neurological evaluation | Patients with Ehlers Danlos may have alterations in the nervous system; therefore, it is recommended to test for myotomes, dermatomes and osteotendinous reflexes.[26] |


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If the diagnosis is unclear, it can be confirmed by genetic testing to determine which gene or enzyme is affected.[16]

## Multidisciplinary approach

It is crucial to note that EDS involves several factors, and a comprehensive approach is essential for this intervention, which will require transdisciplinary collaboration.

Since there is no cure for the disease, the treatment should be focused on preventing the progression and complications of the disease by a multidisciplinary team where the health-care specialists can assess the affections that patients have in their respective fields.[11] This team commonly includes a geneticist, physical therapist, rheumatologist, orthopedist, cardiologist or vascular surgeon, pain specialist, neurologist, nutritionist, psychologist, and psychiatrist to manage all the symptoms that these patients may have throughout their lives.[17,18] Also the patient's family members can be referred to a psychologist for support if required.[8]

## Physiotherapeutic assessment

In order to provide personalized treatment and meet the needs of pediatric patients, it is necessary to carry out a series of specific tests on an ongoing basis. (Table 1) These help to get to know the patient better and to define short- and long-term goals more precisely, in a measurable and observable way.

## Physiotherapeutic intervention

The physiotherapeutic intervention approach for Ehlers-Danlos syndrome in pediatric patients must be adapted to a preventive model. Since the diagnosis is part of the prevention and risk reduction associated with the syndrome, the intervention will be directed towards the creation of new physical practices with the purpose of maintaining the patient's well-being (Table 2).

**Table 2.** Example of a Pediatric Physiotherapeutic Intervention in Classical Ehlers Danlos

| Type | Description |
|---|---|
| Workout games | It has been shown that workout games are an effective way to include daily activities as part of the treatment. They make the rehabilitation plan and physical therapy activities more entertaining and interactive.[29] |
| Strength | A circuit combining stability and strength exercises will be performed in which different muscle groups will be worked by strengthening the closed kinetic chain (CKC) and open kinetic chain (OKC) in the most didactic way and integrating their daily life activities.[30] Exercise will be used to prevent pain, to improve proprioception, balance and strength.[31] To carry out the strengthening plan, it is recommended for it to be done through games that involve weight load in several muscle groups using 40% of the maximum repetitions (MR) for each of the muscle to begin with, and each week it should be increased by 5% until they reach 60% of the MR.[24,32] |
| Hydrotherapy | It is recommended to assist swimming lessons in a 28-32°C pool, since exercise without load is useful to promote muscle development and coordination. For sessions of 30 minutes to tolerance. When working in an aquatic environment, the goal is to provide a setting where the patient feels safe and faces a reduced risk of injury. Heart rate must be monitored and kept between 40-60% of their maxHR.[30,33] |
| Protection for injury prevention | Patients should be encouraged to wear joint protection during physical activity, free play or walks to school. Bandages, knee, elbow and shin pads can be used to prevent dermal injuries due to skin fragility.[34] |
| Home plan | Develop personalized work plans by giving families the necessary guidance to continue therapy at home. This approach aims to actively involve the family in the rehabilitation process while integrating therapeutic exercises into their daily routines.[35] |

| | |
|---|---|
| Family education | Education is essential to positively influence the relationship between patients and family members in matters related to their health. When there is no information and education about pathologies, there are different problems such as the wrong use of medications, ineffective treatments and lack of treatment attachment.[36] The exercises that are performed in the therapy so that the family members can learn and support the treatment for better results. |
| Notes for the therapist<br>- While performing the exercises, take care of the patient's posture and the correct performance of the exercises.<br>- If the patient experiences pain or discomfort, reduce the time or end the exercise.<br>- If the patient cannot do the exercise, it must be modified. | |
| CKC = *Closed Kinetic Chain*, OKC = *Open Kinetic Chain*<br>MR = *Maximum Repetitions*, maxHR = *Maximum Heart Rate* | |

The approach will be "Top-Down"; these interventions are also called "activity interventions." because it "focuses on the functional goals of the client, rather than those client factors or skill deficits that impede function".[27] Since EDS has no known cure, the approach seeks to manage symptoms and promote quality of life from a global perspective (Table 2). According to the WHO, meaningful participation can also improve quality of life by increasing acceptance and support from family members, caregivers, peers and the community.[28]

## DISCUSSION

An in-depth review was conducted to analyze the population, interventions, comparisons and outcomes of pediatric physiotherapy interventions in Classical Ehlers-Danlos Syndrome (cEDS). Despite efforts to gather relevant information, a significant gap in scientific evidence regarding the physiotherapeutic management of cEDS has been identified. This lack of research and awareness often results in inadequate treatment for patients.

For this reason, it is of utmost importance to make an informative and formative program to educate the general population, as well as health professionals, so that patients with Ehlers-Danlos are treated in the best way in all the health fields they require, depending on the signs and symptoms they present. Despite the limitation in the lack of information about the disease, in physiotherapy, we work on the different body functions and structures through exercises, mobilizations and different techniques that provide patients with stability and strength, among other things. It is of utmost importance that in a patient with pediatric EDS there are interventions based on the patient's participation and activities of daily living to improve the affected structures. This syndrome is a heterogeneous disease, therefore, the goals and treatment of patients should be specialized and individualized for each one of them, always focusing on improving their quality of life and achieving their personal goals. Understanding the disease is essential, both by the patient and family members, so that patients can have a follow-up treatment and a home plan and can work with the prevention of complications and sequels.

## CONCLUSION

Although there is still no cure, treatment should focus on preserving function and preventing complications of the disease to give these patients a better quality of life.

Exercise games are a great tool for rehabilitation plans and the implementation of physical activity, as they make the experience more didactic and entertaining for children. For an optimal outcome, the family should be educated about the disease and the importance of physiotherapy intervention. It is also important to involve other health professionals to cover the areas outside the scope of physiotherapy.

As a suggestion for future studies, it is recommended to test the proposed intervention in a child who has Classical Ehlers Danlos, adapting it to the child's needs and characteristics, to obtain the results and improvements of the proposed intervention.


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## CONFLICTS OF INTEREST

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