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DISTROFIA MUSCULAR DE DUCHENNE

DUCHENNE MUSCULAR DYSTROPHY

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Aureliano da Silva Guedes[1]

Aureliano da Silva Guedes II[2]

Catarynna Maciel Quaresma da Silva Guedes[3]

Rosana do S Maciel Quaresma[4]

ABSTRACT

Justification: Duchenne Muscular Dystrophy is characterised as a rare recessive disease, of a genetic nature, related to the X chromosome, generally due to the deletion of the Xp21 *locus*, which causes deficiency of the functional dystrophin protein, generally occurring in male individuals. **Objective:** disseminate initial information on the main signs and symptoms that may lead physiotherapy professionals and paediatric dentists to identify and refer patients for diagnosis and treatment of Duchenne Muscular Dystrophy. **Methodology:** exploratory-explanatory research, with search in the SciELO database and Virtual Health Library, through the descriptor “Duchenne Muscular Dystrophy”, in Portuguese, Spanish, French, Russian and English in an open period and, the team's experience in rare orofacial syndromes. **Conclusion:** There is still no cure for Duchenne Muscular Dystrophy. However, many therapies have emerged to improve the signs and symptoms, offering a better quality of life for patients and their caregivers. Physiotherapy has been fundamental in delaying some of the sequelae of Duchenne Muscular Dystrophy, whether in respiratory strength, muscle preservation, among other benefits to the patient. Aquatic physiotherapy stands out as an important resource due to the physical qualities of water. In paediatric dentistry, the prevention and correction of open bite, crossbite, treatment and prevention of caries, bruxism, malocclusion, periodontitis, masticatory dysfunction, dysphagia, among others, must be constant. Care at all stages of these patients' lives should have a humanised approach, including their caregivers and family members.

Keywords: Muscular dystrophy. Duchenne muscular dystrophy. Xp21 locus deletion. Rare diseases. Paediatric dentistry. Physiotherapy.

RESUMO

Justificativa: A distrofia muscular de Duchenne é caracterizada como uma doença rara, recessiva, de natureza genética, relacionada ao cromossomo X, geralmente devido à deleção do *locus* Xp21, que causa deficiência da proteína distrofina funcional, ocorrendo geralmente em indivíduos do sexo masculino. **Objetivo:** divulgar informações iniciais sobre os principais sinais e sintomas que podem levar fisioterapeutas e odontopediatras a identificar e encaminhar pacientes para diagnóstico e tratamento da Distrofia Muscular de Duchenne. **Metodologia:** pesquisa exploratória-explicativa, com busca na base de dados SciELO e na Biblioteca Virtual em Saúde, através do descritor "Distrofia Muscular de Duchenne", em português, espanhol, francês, russo e inglês, em período aberto, e com base na experiência da equipe em síndromes orofaciais raras. **Conclusão:** Ainda não existe cura para a Distrofia Muscular de Duchenne. No entanto, muitas terapias surgiram para melhorar os sinais e sintomas, oferecendo melhor qualidade de vida aos pacientes e seus cuidadores. A fisioterapia tem sido fundamental para retardar algumas das sequelas da Distrofia Muscular de Duchenne, seja na melhora da força respiratória, na preservação muscular, entre outros benefícios para o paciente. A fisioterapia aquática destaca-se como um importante recurso devido às propriedades físicas da água. Na odontopediatria, a prevenção e correção da mordida aberta, mordida cruzada, tratamento e prevenção de cáries, bruxismo, má oclusão, periodontite, disfunção mastigatória, disfagia, entre outras, devem ser constantes. O cuidado em todas as fases da vida desses pacientes deve ter uma abordagem humanizada, incluindo seus cuidadores e familiares.

Palavras-chave: Distrofia muscular. Distrofia muscular de Duchenne. Deleção do locus Xp21. Doenças raras. Odontopediatria. Fisioterapia.

1. INTRODUCTION

The first to identify and describe Duchenne Muscular Dystrophy (DMD) was the French physician Guillaume-Benjamin Armand Duchenne (1806-1875), also known as Duchenne de Boulogne. According to Pearce (1999), in 1849, Duchenne described a patient with progressive muscular atrophy that began in the hands and slowly spread to the arms and legs, without sensory signs, pain, or sphincter disturbance. Characteristically modest, he did not publish the case, but transmitted his observations to François Amilcar Aran, a physician at the Hôpital Saint Antoine. Aran did so[1].

The Duchenne Muscular Dystrophy affects 1 in every 3,500 to 5,000 live-born boys. It primarily affects boys, but can cause symptoms in girls or in mothers who carry the mutation[2].

Duchenne Muscular Dystrophy is characterised as a rare, recessive, X-linked genetic disease, usually caused by a deletion of the Xp21 *locus*, resulting in a deficiency of the functional dystrophin protein, generally occurring in male individuals.

There are cases of the disease among girls, which is associated with the XO karyotype, gonadotropic mosaicism, or the presence of abnormalities in chromosome structure. Approximately 70% of cases of the disease are caused by a defective dystrophin gene obtained from a mother carrying the pathological mutation. The remaining 30% are associated with the appearance of new mutations in the mother's ovule[3].

This article aims to identify the main signs and symptoms that may lead physiotherapists and paediatric dentists to identify and refer

patients to specialists for diagnosis and treatment of Duchenne Muscular Dystrophy.

The methodology is characterised as exploratory-explanatory research, with a search in the SciELO and Virtual Health Library (VHL) databases, using the descriptor "Duchenne Muscular Dystrophy", in Portuguese, Spanish, French, English and Russian, in an open period, and the team's experience in rare orofacial syndromes.

2. DIAGNOSIS

The main signs and symptoms, which appear in early childhood, include progressive musculoskeletal dystrophy, usually starting in the lower limbs and evolving into muscle atrophy, primarily in the gastrocnemius and soleus muscles, leading to equinus foot and compromising the patient's walking. Over time, the dystrophy affects other muscles, leading to kyphosis, lordosis, and/or scoliosis, delayed speech and motor development, difficulties with neck and head balance, and a wing-like scapular levator, among others, impairing muscle stability and strength, including in the face; postural instability; altered walking, frequently on tiptoes; Gowers' sign; as the condition worsens, there is cardiorespiratory compromise, which may lead to the patient's death.

Complications typically arise between the ages of 7 and 10, due to pronounced motor limitations. By age 12, patients typically lose the ability to walk, and by age 15, most patients completely lose the ability to move independently. The spread of the dystrophic process to the respiratory muscles leads to a progressive decline in lung vital capacity and, ultimately, to the inability to perform respiratory movements[3].

The differential diagnosis should take into account spinal muscular atrophy (SMA), Becker muscular dystrophy, Emery-Dreifuss muscular dystrophy, Erb-Roth muscular dystrophy, Pompe disease, Lambert-Eaton myasthenic syndrome (LEMS), amyotrophic lateral sclerosis (ALS), polymyositis, among others.

Laboratory tests are essential for evaluating markers of muscle injury and associated diseases. Creatine kinase (CK) dosage is one of the most useful tests, since elevated levels indicate active muscle damage[4]. Detecting elevated CK-MM levels in newborns may allow for early suspicion of Duchenne muscular dystrophy before the onset of symptoms[5]. Other markers include aldolase, lactate dehydrogenase (LDH), and myoglobin. Thyroid function tests, electrolyte levels, and vitamin D levels also help identify underlying endocrine and metabolic causes. Genetic testing is essential to confirm specific mutations[4].

Specific genetic testing for Duchenne Muscular Dystrophy is indicated to identify mutations in dystrophin genes and confirm the patient's diagnosis. In cases where there is any suspicion in the family, prenatal testing is recommended. Sample collection can be done simply, through blood, swab smear, among other methods, facilitating adherence by patients and their caregivers.

In cases where there is a clinical condition of muscular dystrophy and DNA analysis does not reveal the presence of a mutation, a muscle biopsy is indicated. The morphological examination of the biopsy determines the diversity and necrosis of the myocytes, and their replacement by connective tissue elements. Immunochemical analysis indicates the complete absence of dystrophin in the muscle fibres studied[3].

An examination of the musculoskeletal and cardiovascular systems should also be performed – including orthopaedic consultations, spinal x-ray, chest x-ray, consultation with a cardiologist, ECG, and echocardiography. If indicated, it is recommended to consult an endocrinologist, pulmonologist, and other specialists[3].

3. THERAPIES

Most patients with Duchenne Muscular Dystrophy die from respiratory failure or cardiomyopathy. There are significant unmet needs for treatments for Duchenne Muscular Dystrophy, as the standard of care is primarily limited to symptom relief through treatments[6]. Currently, Duchenne Muscular Dystrophy is treated with a combination of physiotherapy and pharmacological interventions that limit the progression of the disease[7]. Of all treatments, the only drugs still considered capable of modifying the course of the disease are corticosteroids (prednisone/prednisolone/deflazacort). Other drugs (coenzyme Q10 and creatine) have some effect on certain functions, without adverse reactions. Idebenone appears to improve respiratory function in the long term[8].

Some medications, such as Ataluren (Many medicines regulatory agencies in various countries have not yet approved it for stop codon mutations), are not yet approved for this purpose. Casimersen, Deramiocel, Eteplirsen, Givinostat (non-steroidal and available in oral form, which facilitates patient adherence), Golodirsen, Viltolarsen, among others, have been used to treat Duchenne Muscular Dystrophy. However, many medicines regulatory agencies in various countries have not yet approved their use. Professionals should consult their country's regulatory agency and consider the type of

use, side effects, contraindications, interactions with other drugs administered to the patient, expected costs and benefits, among other factors.

Improvements in patient care and disease management have slowed the progression of the disease, but current treatments cannot prevent the relentless loss of muscle tissue and function, which leads to premature death[9].

Research is ongoing to develop effective therapies for Duchenne Muscular Dystrophy, for example: gene addition therapies, exon skipping, stop codon reading, and genome editing can restore the expression of the partially functional dystrophin protein, while other therapeutic approaches aim to improve muscle function and quality by targeting the pathways involved in the pathogenesis of Duchenne Muscular Dystrophy[9].

Adeno-associated virus-vectored gene therapies to restore dystrophin protein expression using gene replacement or modulation of pre-mRNA splicing mediated by antisense oligonucleotides have emerged, making significant advances in overcoming barriers to gene therapies for Duchenne Muscular Dystrophy[10]. Assays involving mRNA transcription, using nonsense mutations or exon 51 suppression, show some beneficial results in certain functional tests, but are limited to a small group of patients with Duchenne Muscular Dystrophy[8].

Physiotherapy should intervene giving guidance for daily life activities, protect joints and promote range of motion, mitigate the stage of inflammation by promoting analgesia and maintaining and / or strengthening muscles, among others[11,12,13,14].

Physiotherapy should be tailored to all age groups of patients, taking into account their individual condition and the signs and symptoms presented, aiming to improve quality of life through balance training, gait correction, postural positioning, exercises, active stretching, passive stretching, proprioceptive exercises, and more[14]. fundamental to the patient's quality of life

Physiotherapy consists of passive stretching, joint mobilisation, trunk exercises using adapted toys, stimulation of cervical control and midline alignment, sitting training, and functional stimulation (encouraging rolling, stimulating the ability to grasp objects)[15]. Other postural training and walking exercises should be evaluated to maintain and/or strengthen the patient's musculature, such as active/assisted kinesiotherapy, proprioceptive, isotonic, isometric and/or isokinetic, plyometric exercises, among others, should be considered according to the patient's assessment. Orthotics can greatly contribute to treatment, but they must be very well evaluated and chosen appropriately for the patient, considering both physiological adaptation and economic factors.

It is important to emphasise the need to advise patients and caregivers about the dangers of excessive exercise at home, as it can lead to problems due to strain on muscles, tendons, etc., often compromising the treatment plan established by the physiotherapy team and, in some cases, resulting in musculoskeletal complications for the patient[11].

Regarding the role of respiratory physiotherapy, bronchial hygiene techniques should be used, such as: percussion, compression/decompression, vibrocompression, and postural drainage, in order to displace secretions. The therapeutic approach,

in this case, aims to implement improvements in thoraco-pulmonary expansion and oxygenation[15].

It is important to encourage voluntary control of breathing through proprioceptive diaphragmatic stimulation, chest expansion exercises with active inspirations, sustained inspiration, and fractionated inspirations[16]. Deep breathing exercises, assisted coughing, and spirometry should be performed to strengthen the muscles[17]. Vibrocompression, postural drainage, respiratory kinesiology, and respiratory incentive devices are some of the recommended resources.

As the respiratory muscle groups become increasingly weak, the patient may require mechanical ventilation and, in some cases, a tracheostomy. In these cases, the physiotherapist must monitor the patient's blood gas analysis periodically, adjusting the equipment controls to the patient's needs, performing aspiration, evaluating and adjusting equipment parameters, positioning the patient in bed, and elevating the head of the bed are fundamental, among other care measures.

In the case of tracheostomy, in addition to these recommendations, care must be taken with the tracheal prosthesis to prevent displacement, hygiene must be maintained, among other things, and the necessary recommendations must be given to the patient, if possible, and to relatives and caregivers.

It is important to note that the removal of pulmonary secretions in patients on mechanical ventilation or with ineffective cough is achieved through tracheal and oropharyngeal aspiration, allowing

for adequate ventilation and oxygenation and preventing respiratory complications[18].

It is also important to stretch and strengthen the muscles responsible for supporting the head. Stretching these muscles can be done with hydrotherapy, for example Watsu, because it has some movements that facilitate the patient's adaptation in a passive way[12].

In facial kinesitherapy, the goal is to strengthen the muscles involved in jaw movements, such as protrusion, retraction, lateral movements, and elevation and lowering of the jaw, thus improving chewing, swallowing, speech, yawning, facial expression, and other functions[12].

Hydrotherapy has been used in the treatment of Duchenne Muscular Dystrophy and has demonstrated effectiveness in improving mobility and daily activities. The physical properties of heated water promote pain relief and facilitate movement, in addition to providing a favourable and playful environment for children's activities[19]. Due to its buoyancy, it reduces stress on muscles and joints, and improves circulation[17].

It is worth noting that while altered gravity and the drag effect of water are positive, respiratory. heart rates and, blood pressure, as well as any signs of fatigue in the patient, should always be monitored. It is worth noting that there are several methods that can be chosen by the physiotherapist, such as: Bad Ragaz, Halliwick, Watsu, among others.

Aquatic therapy is very well applied by multidisciplinary treatment teams when individuals with Duchenne Muscular Dystrophy need to

delay disease progression, as it can help with gait, quality of life, interpersonal interaction, among many other things[20].

Other resources can be used by the physiotherapist, such as a therapy manual, Low-Level Laser Therapy (LLT) and/or phototherapy, equine therapy, among others. However, the professional must master the techniques, consider the patient's limitations and stage of dystrophy, age, comorbidities, use of prostheses or orthoses, acceptance of therapy, etc. Dance therapy, low-impact sports, and recreational games may also be recommended by physiotherapists at certain phases of Duchenne Muscular Dystrophy to complement other therapies, given their easy acceptance by the patient.

Low-impact physical and sporting exercises can be applied if we consider: the patient's interest, the phase of the dystrophy, physical and cardiorespiratory condition, the team's opinion, risks, among others.

Since patients with Duchenne Muscular Dystrophy suffer from a decrease in respiratory muscle fibres, exercises that stimulate the muscle groups responsible for respiration appear to be useful in treatment[21].

Proper nutrition for the patient, tailored to the degree of dystrophy, is essential to reduce the myasthenia gravis characteristic of Duchenne Muscular Dystrophy. One of the problems that hinders patient nutrition is dysphagia, leading at a certain point to soft diet or even liquid diets; in more complex cases, enteral nutrition (through feeding tubes) may be necessary, and in the last resort, parenteral nutrition (bloodstream). The nutritionist must consider

the micro and macronutrients necessary to meet the patient's nutritional needs.

Patients with Duchenne Muscular Dystrophy exhibit alterations in body composition, including increased body fat and loss of lean mass, due to decreased ambulation and basal energy expenditure (BEE)[22]. Nutritional interventions are fundamental for maintaining the nutritional status of patients with Duchenne Muscular Dystrophy and can significantly contribute to improving quality of life and controlling the progression of the disease[22].

In dentistry, due to dystrophy, some muscles of orofacial importance may be compromised, causing dysarthria, masticatory dysfunction, and dysphagia, requiring intervention by the dental surgeon. Another factor is the intubations that occur in the patient, requiring the hospital dentist to perform some interventions related to the patient's oral health.

Duchenne Muscular Dystrophy is a condition that changes over time, so it is necessary to identify the type of therapeutic intervention that should be carried out at each particular moment by the paediatric dentist, who should be part of the multidisciplinary team, and should actively work in programs and protocols that guarantee effective dental care. These patients are vulnerable during treatment because they may experience respiratory system impairment, communication difficulties, or other types of disabilities[23].

The increase in cases of malocclusion with age may be an indicator of disease progression, because changes in the function of the masticatory muscles are time-dependent and increase the

transverse width of the mandible, causing more prevalent malocclusions such as crossbite and open bite[24].

In addition to treatment for caries prevention, prevention and correction of open bite, crossbite, bruxism, malocclusion, dental crowding, periodontitis, masticatory dysfunction, among others, the paediatric dentist should guide the patient, family and caregivers on rigorous oral hygiene, a non-cariogenic diet, and a diet appropriate to the condition of dysarthria, masticatory dysfunction, and dysphagia, which the patient may present with the progression of Duchenne Muscular Dystrophy.

From a psychological perspective, the behavioural characteristics associated with Duchenne muscular dystrophy reveal particularities related to intelligence profile and the progression of motor impairment[25]. For example, children with Duchenne Muscular Dystrophy showed poor performance in reading tasks and in some memory functions, such as story recall and verbal recognition[26]. Attention deficit (hyperactivity) disorder (ADHD) is a common feature in Duchenne Muscular Dystrophy. The risk of ADHD appears to be higher in patients carrying mutations that are predicted to affect dystrophin isoforms expressed in the brain and are known to be associated with a higher risk of cognitive impairment[27]. However, social inclusion, especially in the school context, is important for the patient's quality of life.

Providing compassionate care to patients at all stages of Duchenne Muscular Dystrophy should be considered and extended to family members and caregivers, who also require support. Family members and caregivers who perform mechanical handling also need physiotherapy; daily stress means that relatives and caregivers

need psychological care to prevent the progression of depression; among other things, the therapeutic care team also needs quality of life and personal guidance.

4. CONCLUSION

It should be noted that the therapies discussed here are merely suggestions, reflecting the current state of scientific knowledge regarding Duchenne Muscular Dystrophy. Professionals should keep abreast of new studies and dynamic scientific advancements on this topic.

At the time of publication of this article, no cure has yet been discovered for Duchenne Muscular Dystrophy. However, many therapies have emerged to improve the signs and symptoms, offering a better quality of life for the patient and their caregivers, and genetic studies have advanced.

Physiotherapy has been fundamental in delaying some of the sequelae of Duchenne Muscular Dystrophy, whether in respiratory strength, muscle preservation, among other benefits to the patient. Aquatic physiotherapy is highlighted as an important resource in treatment due to the physical qualities of water. In addition to recommendations and advice for caregivers and patients.

In paediatric dentistry, the prevention and correction of open bite, crossbite, treatment and prevention of caries, bruxism, malocclusion, dental crowding, periodontitis, masticatory dysfunction, dysphagia, among others, must be constant. Care for these patients, at all stages of their lives, must be humane, including for caregivers and family members.

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[1] Paediatric dentist, Bachelor's degree in Chemistry, Professor at the Federal University of Pará/Director of the Faculty of Chemistry at the Ananindeua Campus, PhD and Postdoc in ICPD by FLUP/University of Porto (Portugal). E-mail: aurelian@ufpa.br; epidemiologist_aureliano@hotmail.com

[2] Dental surgeon, Bachelor's degree in Chemistry. Specialisation in Paediatric dentistry and Environmental Chemistry, MSc in Risk Management and Disasters. PhD student in Environmental Sciences

[3] Dental surgeon, Specialisation in sports medicine

[4] Social Worker. Specialisation in Public Policies. MSc in Social Work