Systemic Sclerosis: The Challenge for Rehabilitation Remains

Esclerose Sistémica: O Desafio da Reabilitação Mantém-se

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Abstract

Systemic sclerosis is a rare, multi-system disease that is difficult to control. Thus, functional deficits can be varied, making rehabilitation an essential pillar. However, literature lacks a holistic approach addressing all facets of systemic sclerosis, as well as the various therapies available.

A literature review was conducted on existing rehabilitation programmes applied to patients with systemic sclerosis. We included 28 higher quality articles which contained keywords and results associated with the objective of this work.

With this narrative review, we intend to summarise the existing evidence on the various rehabilitation programmes proposed and applied in patients with systemic sclerosis.

In fact, the evidence on rehabilitation programmes for the manifestations of systemic sclerosis is limited. This paper integrates and summarises narrative reviews and clinical cases, allowing a comprehensive approach.

Nevertheless, more randomized clinical trials are needed to evaluate the validity and evidence of rehabilitation in the treatment of systemic sclerosis.

Keywords: *Scleroderma, Systemic/complications; Scleroderma, Systemic/diagnosis; Scleroderma, Systemic /rehabilitation*

Resumo

A esclerose sistémica é uma doença rara, multissistémica e de difícil controlo. Assim, os défices funcionais podem ser variados, tornando a reabilitação um pilar essencial. No entanto, a literatura carece de uma abordagem holística que aborde todas as facetas da esclerose sistémica, bem como as várias terapêuticas disponíveis.

Foi realizada uma revisão da literatura sobre os programas de reabilitação existentes aplicados a doentes com esclerose sistémica. Foram incluídos 28 artigos de qualidade superior que continham palavras-chave e resultados associados ao objetivo deste trabalho.

Com esta revisão narrativa, pretendemos resumir a evidência existente sobre os vários programas de reabilitação propostos e aplicados em doentes com esclerose sistémica.

De facto, a evidência sobre programas de reabilitação para as manifestações da esclerose sistémica é limitada. Este artigo integra e resume revisões narrativas e casos clínicos, permitindo uma abordagem abrangente.

No entanto, são necessários mais ensaios clínicos randomizados para avaliar a validade e a evidência da reabilitação no tratamento da esclerose sistémica.

Palavras-chave: Esclerose Sistémica/complicações; Esclerose Sistémica/diagnóstico; Esclerose Sistémica/reabilitação

Introduction

Systemic sclerosis (SS) is a rare disease of autoimmune nature and unknown etiology, characterized by vascular dysfunction and progressive fibrosis of skin and internal organs. Classically classified based on the extent of cutaneous involvement, more frequent in women, it can

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occur at any age, but with a peak of higher incidence between 20 and 50 years.[1]

Given the various subtypes of systemic sclerosis, there are several classification methods, the most sensitive and specific being the ACR/EULAR classification criteria (2013). Thus, it is possible to identify 6 subtypes of SS namely limited cutaneous SS, diffuse SS, scleroderma sine, SS induced by environmental/toxic factors and overlap with other rheumatic diseases.[1,2]

In recent years there have been several advances in the treatment of the various complications of SS, allowing greater control of exacerbations of the disease, as well as a greater quality of life of these patients. However, given the multi-systemic reach of this disease, Physical and Rehabilitation Medicine plays an essential role, with all its valences having an important contribution in the therapeutic approach of SS.[3]

Our objective is to identify and organize the evidence in the literature on rehabilitation in systemic sclerosis in all its clinical components.

Methods

We reviewed the literature in the following databases: PubMed, Clarivate WEB OF SCIENCE, CENTRAL and PEDro (Physiotherapy Evidence Database). The following terms were used: 'systemic sclerosis', 'rehabilitation', 'kinesiotherapy', 'aerobic exercise', 'hydrotherapy', 'thermotherapy' and 'massotherapy'. Only papers written in English and Portuguese were included. Papers dated between 1950 and 1985 were assessed, but with less relevance in the course of this review. Book chapters are also cited.

We included 40 clinical cases and narrative reviews conducted in the last 25 years.

Clinical Manifestations:

The disease often affects the skin, but also joints, muscles and vital organs such as heart and lungs.

Despite the 6 forms described and listed above, traditionally systemic sclerosis is divided into two main types: diffuse cutaneous SS (DCSS) and the most common form, limited cutaneous SS (LCSS). DCSS is associated with proximal cutaneous stiffness, interstitial lung disease, cardiac fibrosis and, consequently, a worse prognosis. Patients with LCSS usually have distal skin stiffness and a better prognosis, despite a higher risk of developing pulmonary hypertension.[4]

Most organ involvement occurs in the early stages of the disease and some manifestations, like Raynaud phenomenon and gastroesophageal reflux, are relatively common in the general population.[5]

In addition to organic involvement, pain and fatigue are cardinal manifestations and the presence of fatigue is associated with worse functional outcome.[6]

After the suspicion of systemic sclerosis is confirmed, patients must be evaluated to make a definitive diagnosis. This usually involves fulfilling the criteria of the 2013 European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR).[1,6]

There are no disease-modifying drugs for systemic sclerosis. However, early screening and management of patients appear to improve mortality. For example, regular pulmonary function testing is recommended during the first 3–5 years after diagnosis, since interstitial lung disease is an early complication of systemic sclerosis.[7]

The following paragraphs are a more detailed description of the main clinical manifestations of the disease.

1. Skin

Cutaneous manifestations are the most studied and recognized. Skin involvement can cause substantial morbidity, but it is not associated with increased mortality *per se*.[8] However, severe or rapid progressive skin involvement in an early stage of the disease is associated with increased mortality and prevalence of internal organ implication.[1,3,9]

The cutaneous thickening presents with varying extent and severity, reaching fingers, hands and face earlier. Edema and erythema may precede thickening and progressive fibrosis associated with worse pulmonary outcome. Puffy fingers are a manifestation of early onset.[11] Many patients will have aggressive functional limitations, with repercussions on activities of daily living (ADL).[9-11]

Additionally, digital vasculopathy is characterized by a reversible vasospasm with vascular structural alterations, with risk of events such as ischemic pain and digital ulceration.[10]

2. Musculoskeletal

Articular involvement is common in SS, affecting 46% to 95% of patients, with arthralgias and stiffness being among the most common manifestations. Joint pain is the result of fibrosis in periarticular structures, joint destruction, ankylosis and fibrotic changes, resulting in multiple functional deficits. Although the involvement is normally polyarticular, the most involved joints are the extensor/flexor compartment of the wrist and fingers, the extensor elbow, the patellar compartment of the knee and the ankle compartment.[1,12]

Fixed flexion contractures of the proximal interphalangeal (PIP) joints are the most common, which can be associated with fixed extension deformities of metacarpophalangeal (MCP) joints.[12]

Distal interphalangeal (DIP) joints can also be affected by contractures in flexion and the thumb in adduction.[11,12]

Additionally, it is also common to find tenosynovitis, tendon rupture, and tendon friction rubs (TFR). TFR can be defined as the sensation of frictional and rubbing movement while moving a particular tendon.[12]

Several studies have aimed TFR as predictors of prognosis, which may be associated with the presence of muscle weakness, pulmonary fibrosis and proteinuria.[12]

Bone involvement occurs in 20%-25% of cases and is characterized by partial resorption of the distal phalanx (acro-osteolysis), being more frequent in the hands.[12,13]

3. Gastrointestinal

Gastrointestinal manifestations of systemic sclerosis are present in 50%-90% of patients, although half of patients have no symptoms. The esophagus is the most affected portion. The main symptoms are dysphagia, heartburn, diarrhea, constipation and fecal incontinence, greatly contributing to the loss of quality of life in these patients and an associated mortality rate of about 6%-12%.[14,15]

Dysphagia can have several causes, namely reduced peristalsis, esophageal candidiasis, gastroesophageal reflux, or an esophageal stricture when the luminal diameter is less than 13 mm. Oropharyngeal deglutition abnormalities can occur in up to 25% of patients and may lead to aspiration.[15]

4. Pulmonary

Some degree of pulmonary involvement occurs in 80% of cases, being the main cause of mortality in these patients. However, only 30% develop progressive interstitial lung disease.[10] Pulmonary disease in SS may include involvement of the interstitium and/or pulmonary arterial hypertension (PAH). The main clinical manifestations are fatigue, exertion dyspnea and/or ineffective cough.[1,14] PAH affects about 15% of patients with systemic sclerosis.[5]

When vascular involvement occurs, with PAH, the patient can remain asymptomatic until reaching more advanced stages. The early diagnosis depends on a regular monitoring (semiannual to annual) with respiratory-function tests (RFT), diffusing capacity of the lungs for carbon monoxide (DLCO) and echocardiogram with serial Doppler.[1] The gold standard for diagnosis is right heart catheterization, which can differentiate PAH from other causes of PH.[16]

5. Cardiac

Cardiac involvement occurs in 10%-30% of these patients and is often diagnosed in an advanced state of the disease. All aspects of the heart can be affected, including the myocardium, pericardium, and conduction system.[1] Cardiac manifestations can be either due to the fibrotic and vascular process or secondary to pulmonary arterial hypertension (PAH), interstitial lung disease, or scleroderma renal crisis. Some medications used in the treatment of systemic sclerosis such as cyclophosphamide may cause some degree of cardiac toxicity.[17]

Some studies report that patients with systemic sclerosis with clinically evident cardiac involvement may have a 5-year mortality rate of 70%. Indeed, earlier detection and treatment are both feasible and advisable.[18]

6. Renal

Renal involvement in systemic sclerosis occurs in 60%-80% of patients. However, severe presentation occurs in only 15%.[19]

7. Neuromuscular

There are no classification criteria to characterize myopathy associated with systemic sclerosis. The clinical picture can range from weakness and generalized atrophy to the slight elevation of muscle enzymes. This manifestation should be suspected when proximal symmetrical muscle weakness is objectified, with or without elevation of muscle enzymes.[20]

In patients with severe myopathy, the presence of dysphagia should always be screened. Such diagnosis should be made by a specialized doctor.[20]

Neuropathy is an uncommon manifestation and peripheral polyneuropathy is much rarer than myopathy. Possible manifestations include carpal tunnel syndrome or sensory-motor peripheral neuropathy. Autonomic dysfunction has also been described in patients with systemic sclerosis, with possible changes in vascular tone, esophageal contractility and cardiac frequency.[21]

Functional Evaluation:

The initial assessment corresponds to the cross-sectional appreciation of patients with functional deficits, who need adaptations to their social context. It is necessary to assess the living conditions and accessibility in the patient's home, namely whether they live in an apartment or in an individual house, the access is by elevator or stairs, and the presence of a bathtub or shower base. In addition, it is important to assess if the patient has eventual caregivers, if needed, the current autonomy, employment status, as well as which is the dominant side.[22-24]

After socio-family assessment, it will be important to ask the

patient about functional deficits and implications for ADL. In fact, it is important to characterize pain, presence of stiffness and joint contractures, to evaluate active and passive joint range of motion (ROM) using a goniometer, the presence of edema, muscle strength according to the Medical Research Council (MRC) scale, fatigue, gait and transfers capacity and autonomy.[23,24]

This functional assessment can be quantified with the use of appropriate scales. Among the several existing scales, the Functional Independence Measure (FIM), Barthel index, Short Form Health Survey (SF-36), the Abilhand Questionnaire or the Hand Mobility in Scleroderma (HAMIS) stand out. The HAMIS test has significant correlation between hands skin involvement and ADL, and it is sensitive to functional changes and useful as an outcome measure. This last scale allows to assess deficits in hand movements in patients with SS and evaluates a set of items related to various movements and grips, associated with patient's ADL.[24,25]

The Role of Rehabilitation:

The literature has described several hypotheses of rehabilitation treatments that may be applied according to the main manifestations of systemic sclerosis. In this work we focused on the following manifestations: skin, musculoskeletal, pulmonary, cardiac, neurological and renal alterations.

Pain control must start with the use of medication, physical agents and analgesic techniques, as also through an exercise program that must be done progressively.

1. Skin

The main objective of rehabilitation treatments with physical agents in the cutaneous manifestations is to delay progression at an early stage of the disease.

1.1. Thermotherapy:
Superficial moist heat applied for 3 minutes increases soft tissue temperature about 3°C down to a depth of 1cm, producing a beneficial sensation of warm skin and increasing skin flexibility.[26] It allows the increase of surface temperature with ROM gain and arterial vasodilation. There's also solid evidence in the use of paraffin immersion[27] as well as continuous-mode ultrasound.[28]

1.2. Kinesiotherapy:
Kinesiotherapy is a central component in the treatment of these patients. In fact, exercises for ROM gain allow to prevent skin retractions and increase skin vascularization.

Additionally, passive and active-assisted mobilization of affected limbs, in the edematous or atrophic phase, and massage-assisted mobilization allow to reduce edema and have analgesic effect, as well as enable myotendinous adhesions reduction.[29]

1.3. Massotherapy:
The connective tissue massage increases local blood flow and allows the connective tissue adhesions to be reduced through stretching.[30]

The use of manual lymph drainage (MLD) for treatment of SS patients with edematous hands improves hand edema, hand function and perceived quality of life.[30] This technique uses manual adapted pressure with stimulation of the musculature of lymphatic vessels, allowing a greater dynamization of the lymphatic fluid, reducing pain and relaxing muscle tension.[30]

The McMennell joint manipulation is a technique developed specifically for systemic sclerosis and is based on joint manipulation of the metacarpophalangeal joints and proximal and distal interphalangeal joints, allowing to increase ROM, analgesia and stretching of articular and ligament capsules.[31]

2. Myotendinous Manifestations

During periods of greater exacerbation of the disease, these patients may spend a long time in bed. In fact, muscle can lose about 30% of its size in a week and 5% of its strength in a day when held in immobilization.[32]

Other contributors to the loss of strength are myositis, myopathy secondary to steroids and the direct muscle effects of the disease.

The objective of rehabilitation of musculoskeletal manifestations in systemic sclerosis involves the recovery of any deficits in passive and active joint ROM, gain in muscle strength and recovery of physical and functional capacity to perform ADL.[32]

2.1. Transcutaneous Electrical Nerve Stimulation (TENS):
The use of TENS in systemic sclerosis has been previously outlined in existing literature reviews. It is suggested that incorporating TENS into treatment regimens could serve as a valuable adjunct to pharmacological interventions. Various modes of TENS application have been suggested, including high-intensity, low-frequency, and acupuncture mode (type A). TENS type A is more effective in activating the endorphinic analgesic system for acute polyarticular pain; high frequency and low intensity TENS is used in arthralgia caused by passive and active movements of a certain limb.[3]

2.2. Thermotherapy and Diathermy:
Increasing the skin surface temperature to values from 40°C to 45°C can reduce the stiffness of the metacarpophalangeal joints and an increase from 5°C to 7°C enhances the extensibility of collagen, permitting a greater ability to gain joint amplitude during kinesiotherapy. The use of deep heat (diathermy), through short-wave and microwave, allows an increase in temperature in deeper structures.[3]

The use of heat has a myorelaxant effect, allowing analgesic effects and facilitating kinesiological techniques.[3]

2.3. Kinesiotherapy:
The main components of kinesiotherapy in these patients are passive and active-assisted mobilization (especially if myotendinous retractions), dynamic muscle strengthening exercises, the use of neuromuscular facilitation techniques (proprioceptive neuromuscular facilitation (PNF), Bobath, Brunnstrom, Kabat), proprioceptive training, and effective manual dexterity practice.[33]

In fact, Kabat's method is a well-known neurorehabilitation facilitation technique that uses spiral and diagonal movement patterns in conjunction with stretch, resistance and other proprioceptive facilitation techniques to improve neuromuscular recruitment.[33]

The association of hand connective massage and Mc Mennell joint manipulation[31] or the association of Kabat's technique and a specific kinesiotherapy program seem to be more effective than a non-specific passive mobilization protocol or a simple home-based exercise program.[30]

The initial approach should start with isometric exercise, evolving to dynamic exercise programs. Additionally, exercises and recreational activities that allow greater adaptation to ADL should be prescribed.[30]

2.4. Orthosis:
It was thought that the use of wrist-to-finger orthoses could delay the development of contractures, but studies argue that these support products are not very useful in systemic sclerosis.[34]

2.5. Hydrotherapy:
Exercising in water has several advantages, including reduction in gravity with a reduction in joint compressive forces and pain. This allows greater muscle relaxation, which facilitates the passive and active kinesiological treatment program, as well as greater tolerance to aerobic exercise.[35]

Hydrotherapy can be performed in patients without ulcers or skin infections in a 30° pool (1 hour session, once a week). Each session can begin with an initial 10 minutes warm up (walking front ways, sideways, back ways, swimming), followed by 20 minutes of stretching and pulmonary rehabilitation. Additionally, aquatic therapy can focus on local and global pain by individualized exercises increasing mobility, muscle strength, body awareness, coordination and balance.[36]

3. Gastrointestinal

Dysphagia should always be suspected in patients with systemic sclerosis. Therefore, early and periodic screening should be carried out, given the high risk of aspiration and development of aspiration pneumonia. If patients have criteria to start a treatment program, the Speech Therapist will play an important role in this phase. The progression of dysphagia severity can also be quantified using the Functional Oral Intake Scale (FOIS).[37]

4. Pulmonary Rehabilitation

Pulmonary rehabilitation is described as an adjunct to traditional therapeutics in diseases with arterial and pulmonary interstitium involvement. In fact, the American Thoracic Society supports the use of respiratory rehabilitation in any chronic lung disease, regardless of its cause.[38]

Patients with respiratory manifestations should be followed up and examined to assess whether they have criteria for entering a respiratory rehabilitation program.[38]

Some absolute contraindications to a respiratory rehabilitation program are: angina pectoris, recent myocardial infarction, myocarditis or active pericarditis, severe pulmonary hypertension, congestive heart failure, unstable diabetes, inability to exercise due to orthopedic or other reasons, severe exercise-induced hypoxemia not correctable with O_2 supplementation, and active smoking is considered a contraindication in some countries.[38]

If there is no lung involvement, patients can be recommended to be as physically active as the general population. If there is mild lung involvement, these patients should be advised to exercise at moderate intensity.[38]

Before the beginning of any program, an evaluation of the initial respiratory function should be made, through the performance of arterial gasometry, 6-minute walk test (6MWT), Health-related quality of life (HRQoL), SF-36 and the use of the Borg scale to quantify dyspnea.[39] However, evidence is still scarce in interstitial diseases.

Among the various strategies that can be used in the respiratory rehabilitation of these patients, we highlight respiratory exercises: glossopharyngeal breathing, abdominodiaphragmatic breathing, techniques of ventilation to the bases and effective cough. Additionally, we also highlight aerobic training (treadmill, cycle ergometer...), anaerobic resistance training (light weights, resistance bands), energy-saving techniques and O_2 supplementation to maintain $SatO_2$ above 90%.[4]

A clinical trial evaluated the outcome of an individualized rehabilitation program in patients with lung fibrosis. The patients performed breathing exercises, aerobic exercise on a treadmill or outdoor walks, and 10 individual rehabilitation sessions during a two-week period. After four months, the exercise group had improved in self-reported quality of life and hand functions, and had reduced exercise heart rates and lowered perceived exertions during the 6 MWT, while the non-randomized control group remained unchanged.[40]

5. Cardiac Rehabilitation

About 25% of deaths associated with SS are due to cardiac causes.[41] Although all aspects of the heart may be involved, the main changes are typically myocardial fibrosis and myocarditis.[17]

Even though cardiac rehabilitation has Level A evidence in the treatment of various pathologies, evidence in systemic sclerosis is scarce. In this way, it follows the general patterns of cardiac rehabilitation, with no specificity regarding this disease.

Among the various indications proposed for beginning a cardiac rehabilitation program, we highlight compensated heart failure of various etiologies or ischemic heart disease. These are also possible manifestations of systemic sclerosis.[18]

On the other hand, there are several contraindications to this program, with emphasis on the presence of myocarditis or active pericarditis, which are also possible manifestations of systemic sclerosis.[42]

Thus, patients with manifestations of cardiac involvement should be followed and screened to assess whether they have criteria to enter a cardiac rehabilitation program.

An evaluation of physiological responses to an increase in metabolic needs should be made through an objective medical evaluation, cardiorespiratory stress test or conventional stress test, other submaximal tests: 6 MWT, shuttle-test, talk-test...), an analytic study with lipid profile, glucose, glycated hemoglobin, lipoproteins, electrocardiogram (ECG), Holter, transthoracic echocardiogram, among other tests.[42]

Discussion

Physical and rehabilitation medicine has the ability to help patients with systemic sclerosis. However, the multisystemic manifestation of this disease is a challenge. Therefore, a dynamic and multidisciplinary approach is essential to improve the quality of life of these patients, allowing a better social and labor adaptation.

There are several papers published where various rehabilitation treatment options for the manifestations of systemic sclerosis are exposed. On the other hand, there are few papers that cover all the most common manifestations of this disease and list the various treatment options that physical and rehabilitation medicine has to offer.

Although this work reviews the existing protocols for each manifestation and organizes them in a more practical way, randomized clinical trials will be necessary to allow a greater validation of these protocols.

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