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Physical therapy for the management of motor symptoms in amyotrophic lateral sclerosis: protocol for a systematic review

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ABSTRACT

Introduction The prescription of an intervention plan can be challenging for the physical therapist, considering clinical phenotypes, individual prognosis and the rapid, progressive and deteriorating nature of amyotrophic lateral sclerosis (ALS). In this context, therapeutic exercises (eg, resistance and aerobic exercises) for patients with ALS remain controversial and may influence the treatment plan. Therefore, this review aims to critically assess whether physical therapy interventions are effective for improving functional capacity, quality of life and fatigue of individuals with ALS.

Methods and analysis Studies will be selected according to eligibility criteria, and language, geographical area or publication date will not be restricted. Four databases will be used: MEDLINE, EMBASE, Cochrane Library (CENTRAL) and Physiotherapy Evidence Database (PEDro). Searches will also be conducted on ClinicalTrials.gov and references from included studies. We plan to conduct the searches between October and December 2022. Two independent authors will examine titles and abstracts and exclude irrelevant studies and duplicates. We will assess the quality of studies and quality of evidence, and disagreements will be resolved with a third researcher. The findings will be presented in the text and tables; if possible, we will perform meta-analyses.

Ethics and dissemination No ethical approval is required because this study does not involve human beings. We will publish our findings in peer-reviewed journals.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We will critically assess whether motor physical therapy techniques are effective for treating patients with amyotrophic lateral sclerosis (ALS).
⇒ We intend to analyse different types of physical therapy interventions.
⇒ Diversified characteristics related to ALS may lead to heterogeneity of results.
⇒ Despite a comprehensive literature search, only limited clinical trials of adequate quality may be available.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a degenerative and disabling disease of the nervous system that involves the loss of motor neurons in the cortex, brainstem and spinal cord.[1] It is characterised by muscle weakness leading to loss of ambulation and functionality, swallowing difficulties, respiratory muscle dysfunction and death due to ventilator insufficiency.[2 3] ALS may be clinically classified according to symptom onset: spinal, which initially affects upper or lower limbs or both; and bulbar, which initially affects head and neck regions.[4–6] The prevalence of spinal ALS worldwide may be higher than bulbar ALS (58%–82%).[7]

Progressive muscle weakness may occur in the early stages of the disease and be asymmetric between upper and lower limbs, leading to reduced functional performance and interfering negatively with quality of life.[8] Although this progression varies substantially between individuals, it usually begins with the involvement of limbs, followed by other body regions. Individuals with ALS also report fatigue, which is experienced as a generalised feeling of tiredness and difficulty performing maximal muscle contraction.[9] Spasticity is another disabling symptom that is present in most individuals with ALS.[10]

Considering the prognosis and lethal characteristics of ALS, the treatment consists of individualised general care.[11] Regarding pharmacological treatment, the small number of drugs approved by the Food and Drug Administration acts modestly on the drastic effects of the disease.[12] The clinical treatment is complex and requires a multidisciplinary approach to cover all difficulties faced by patients. Physical therapy is fundamental for the multidisciplinary team and must be adapted to the needs and objectives of the individual. The physical therapist must also focus on treating symptoms, maximising

functions and activities and participation and providing quality of life to patients with ALS.[13]

Patients with ALS widely accept physical activity involving range of motion and stretching exercises. Resistance exercises for the unaffected muscles (or affected muscles with strength of at least grade 3 or higher) using low to moderate loads and aerobic activities at submaximal levels (ie, 50%–65% of heart rate reserve), such as swimming, walking and stationary cycling, can be safe and effective to achieve therapeutic goals.[14] Aerobic and resistance exercises should be prescribed early after diagnosis and may be more suitable for patients with slow disease progression and those in the initial or intermediate stage of ALS.[13]

The prescription of an intervention plan can be challenging for physical therapists due to the diverse clinical phenotypes, individual prognosis and the rapid, progressive and deteriorating nature of the disease.[15] In this sense, the effects of therapeutic exercises (ie, resistance and aerobic exercises) in patients with ALS remain controversial in the literature. Nevertheless, the hypothesis that properly prescribed exercises applied in the early stages benefit patients with ALS is being increasingly accepted.[16] Furthermore, most studies evaluating physical therapy exercises or motor techniques in ALS demonstrated improved physical function, quality of life and fatigue.[9 17 18] Therefore, this review aims to critically assess whether physical therapy interventions are effective for improving functional capacity, quality of life and fatigue of individuals with ALS.

METHODS AND ANALYSIS

This systematic review protocol was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)[19] and registered in the International Prospective Register of Systematic Reviews (PROSPERO).

Eligibility criteria

Study types

We will include randomised clinical trials (RCTs) involving motor physical therapy for patients with ALS and control groups (any other non-physiotherapeutic method or technique, placebo, no intervention or minimal intervention (eg, minimum guidance and booklets)). Data from the first phase of cross-over studies will also be included if a random allocation of interventions has been conducted. We will exclude quasiexperimental and non-randomised studies.

Participants

We will include participants of both sexes, with a clinical or probable diagnosis of ALS at any stage of the disease, without any other neurological disease, aged 18 or above and who have undergone motor physical therapy methods or techniques in RCTs.

Interventions and comparators

We will consider intervention as any physical therapy practice acting on motor symptoms of patients with ALS: therapeutic exercises, stretching, aerobic exercises, relaxation techniques, massage therapy, electrostimulation and energy conservation techniques. Any other non-physiotherapeutic method or technique, placebo, no intervention or minimal intervention (eg, minimum guidance and booklets) will be considered for the control group.

Outcome measures

1. The primary outcome measure will be the assessment of global function using the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised.[20]
2. Secondary outcomes will include quality of life (36-Item Short Form Health Survey,[21] ALS Assessment Questionnaire,[22] ALS Specific Quality of Life-Revised[23] or McGill Quality of Life Questionnaire),[24] fatigue (Modified Fatigue Impact Scale,[25] Fatigue Severity Scale[26] or Neurological Fatigue Index-Motor Neurone Disease[27]) and adverse events related to the intervention during the study period.

Moment of evaluation

We will extract outcome data from baseline, end of the intervention (immediate effects) and follow-up (medium and long-term effects). The medium-term effects will be those collected between 1 week after the end of the intervention and 6 months after the treatment, whereas the long-term effects will be considered if collected more than 6 months after treatment.

Search method

We will select studies according to eligibility criteria and without language, geographical area or publication date restriction. We will use four databases: MEDLINE, EMBASE, Cochrane Library (CENTRAL) and Physiotherapy Evidence Database (PEDro). Searches will also be conducted on ClinicalTrials.gov (www.clinicaltrials.gov/) and the reference list of included studies. After full-text reading, we will remove studies not meeting inclusion criteria, and reasons for exclusion will be registered. We plan to conduct the searches between October and December 2022.

Search strategy

We built a search strategy (see online supplemental material 1) using the MEDLINE database and will adapt it to other databases to search for terms referring to ALS motor symptoms, functionality, quality of life and fatigue. Descriptors regarding aspects of ALS, intended outcomes and physical therapy techniques will be included in English.

Data extraction

Two independent authors (STdS and KP) will verify the titles and abstracts of references and exclude irrelevant studies using the Rayyan software (Intelligent

Systematic Review).[28] Researchers will remove duplicates, and authors will be contacted if more than one study included the same sample and did not report it in the text. If confirmed, we will consider the most recent study or that with a complete presentation of data. Inconsistencies will be resolved by discussion or consulting a third author (TSR). We will record this process in a PRISMA flow chart.

The same authors (STdS and KP) will also extract data from the included studies using an extraction form elaborated by the researchers. In case of absence or uncertain data, the authors will be contacted.

Risk of bias assessment

We will use the PEDro scale[29] to assess the quality of included studies. It consists of 11 criteria that determine the methodological quality using a score ranging from 0 to 10. High scores indicate high methodological rigour.

Data analysis and processing

We will use the Review Manager V.5.4 software for statistical analysis. For continuous outcomes, the weighted mean difference will be selected when tools and measurement units are the same, whereas the standardised mean difference will be used when tools and measurement units are different. The 95% CIs will also be calculated. For dichotomous outcomes (adverse events), we will use the OR and 95% CIs to measure treatment effects.

Heterogeneity

Values of χ^2 and I^2 will determine the heterogeneity among studies. In the case of low heterogeneity ($p \geq 0.1$ and $I^2 \leq 50\%$), the fixed-effects model will be used for meta-analysis. If significant heterogeneity is observed between studies ($p < 0.1$, $I^2 > 50\%$), the source of heterogeneity will be explored using subgroup analyses.

Meta-analyses

We will conduct meta-analyses using the Review Manager V.5[30] or a more recent version if clinical and methodological similarities are detected between studies. Studies will be grouped to compare the following effects:

1. Methods and techniques of motor physical therapy versus placebo.
2. Methods and techniques of motor physical therapy versus no therapy.
3. Methods and techniques of motor physical therapy versus educational and orientation programmes.

Dealing with missing data

In the case of missing data (ie, statistical or relevant data related to the study), we will contact the lead author via email for additional information. A descriptive analysis will be conducted in case of data loss or no author reply.

Subgroup analyses

We intend to consider the following variables in subgroup analyses if the number of studies is sufficient:

1. Type of disease onset: spinal or bulbar.
2. Disease duration: less than 5 years or more than 5 years.
3. Age: less than 60 years and above 60 years.
4. Type of treatment: manually or using equipment.
5. Treatment dose: once to twice a week and more than twice a week.

Sensitivity analysis

We will perform sensitivity analyses in case of suspected missing data introducing important biases and exclude studies with low grades during risk of bias assessment (≤5).[31] Heterogeneity caused by peripheral studies will also be assessed.

Assessment of quality of evidence

We will use the five components of the grading quality of evidence and strength of recommendations (ie, study limitations, inconsistency, imprecision, indirectness and publication bias)[32] to assess the quality of studies included in the meta-analyses.[32] When necessary, decisions to reduce or increase the quality of evidence will be justified using footnotes and comments to help the reader understand the review. The quality of the evidence will be classified as high, moderate, low or very low.[32]

Patient and public involvement

Patients will not be involved in this study.

ETHICS AND DISSEMINATION

No ethical approval is required because this study does not involve human beings. Our results will be published in peer-reviewed journals.

DISCUSSION

The prescription of therapeutic exercises is challenging for physical therapists due to the concern that it would accelerate the progressive decline of patients with ALS.[33] Therefore, it is worth gathering scientific evidence to guide the treatment and exploring the effects of reliable physical therapy methods and techniques for motor symptoms in ALS.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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