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Remote versus face-to-face home-based exercise programme in people with amyotrophic lateral sclerosis: protocol for a randomised clinical trial

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ABSTRACT

Introduction Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease with variable and complex clinical manifestations that requires a multidisciplinary approach. However, face-to-face treatment in this population may experience barriers, such as difficulty accessing physical therapists or other professionals. As a result, strategies (eg, telerehabilitation) emerged to facilitate treatment and physical therapy monitoring. This study aims to evaluate the effects of remote versus face-to-face home-based exercise programmes on clinical outcomes and treatment adherence of people with ALS.

Methods and analysis This is a single-blind randomised clinical trial protocol that will include 44 people with clinical diagnosis of ALS at any clinical stage and aged between 18 and 80 years. Participants will be randomised into two groups after face-to-face evaluation and perform a home-based exercise programme three times a week for 6 months. A physical therapist will monitor the exercise programme once a week remotely (phone calls—experimental group) or face-to-face (home visits—control group). The primary outcome measure will be functional capacity (Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised). Secondary outcomes will include disease severity (Amyotrophic Lateral Sclerosis Severity Scale), fatigue (Fatigue Severity Scale), pain (Visual Analogue Scale and body pain diagram), adverse events and adherence rate. Outcomes will be initially evaluated face-to-face and revaluated remotely every 2 months and 1 month after interventions. Linear mixed models will compare outcome measures between groups and evaluations (α=5%).

Ethics and dissemination This study was approved by the research ethics committee of Hospital Universitário Onofre Lopes/Universidade Federal do Rio Grande do Norte (no. 3735479). We expect to identify the effects of an exercise programme developed according to ALS stages and associated with remote or face-to-face monitoring on clinical outcomes using revaluations and follow-up after interventions.

Trial registration number Brazilian Registry Clinical Trials (RBR-10z9pgfv).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Single-blind randomised clinical trial.
⇒ Clinically important outcomes.
⇒ Specific home-based exercises for each stage of amyotrophic lateral sclerosis (ALS).
⇒ Analysis of face-to-face versus remote exercise monitoring.
⇒ The rapid evolution of ALS may hinder long-term monitoring.

INTRODUCTION

Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease that results in the loss of upper and lower motor neurons.[1] The clinical manifestation may include limb (eg, muscle weakness, fasciculations, reduced movement speed and muscle atrophy) or bulbar symptoms (eg, facial muscle weakness, respiratory disorders, dysphagia and dysarthria), which may lead to death due to respiratory failure.[2 3] Muscle weakness is progressive from the initial stages and reduces functional performance and quality of life.[4]

A multidisciplinary approach is essential for the effectiveness of interventions due to disease complexity, and physical therapy is an important component of this approach.[1] Individualised physical therapy is generally prescribed to delay progressive impairments and maintain the functionality of people with ALS.[5]

Physical exercise benefits people with ALS and improves functional independence and quality of life.[6–8] When appropriately prescribed, physical exercise also promotes physiological and psychological benefits in this population.[9] Although one can affirm that active exercise causes fatigue by overuse,

Table 1 Proposed exercise protocol according to disease stage

Stage	Exercises
0 (no impairment or very mild impairment)	Aerobic, resistance and stretching exercises
1 (mild impairment)	Aerobic, resistance or active-assisted and stretching exercises
2 (mild to moderate impairment)	Aerobic, resistance (unaffected muscles), active or active-assisted (affected muscles) and stretching exercises
3 (moderate impairment)	Aerobic (if possible), active-assisted, passive mobilisation and stretching exercises
4 (moderate to severe impairment)	Stretching and passive or active-assisted mobilisation

its benefits on muscle weakness and atrophy by disuse must be strongly considered.[10]

Literature regarding physical therapy programmes for improving motor function of people with ALS is scarce.[7 8] However, resistance and aerobic exercises may be useful to these patients, especially in the middle stage of the disease.[7] Active or assistive exercises, passive exercises and stretching exercises have also been considered in the middle and advanced stages.[5]

In the rehabilitation context, difficult access to health services reduces adherence of people with ALS,[11] which may lead to the advent of new strategies (eg, telerehabilitation). Telerehabilitation consists of remote evaluation, monitoring, health education and exercise intervention.[12] This strategy prevents displacement (relevant for patients with limited mobility), reduces costs and time, and provides convenient and flexible scheduling.[12]

Adherence to telerehabilitation may vary among patients and types of intervention and monitoring.[13] A high rate of non-adherence was observed in people with Parkinson's disease when exercises were performed at home without face-to-face supervision.[14] Conversely, another study conducted with the same population observed that face-to-face programmes with minimal supervision (ie, once a week) improved participant engagement.[15]

Face-to-face follow-up by physical therapists may positively influence time, frequency and correct execution of exercises.[16] In contrast, home-based exercises prescribed by the therapist and performed at home without professional supervision stimulate self-management and improve performance.[17 18] Patients under remote monitoring are expected to contact therapists more frequently, allowing the team to conduct individualised therapy.[18] Nevertheless, remote and face-to-face treatment and monitoring are possibly equivalent when considering scientific evidence, professional experience, and patient preference.[17]

Although evidence regarding telerehabilitation for ALS is limited, studies suggest it as an alternative approach, especially for patients with difficult access to health services.[19 20] Evidence from other neurological conditions (ie, stroke) suggests that telerehabilitation is not inferior and has a lower cost for implementation than face-to-face rehabilitation.[21]

Considering the benefits of physical exercise and the need of patients with ALS for full-time care, this study aims to evaluate the effects of face-to-face versus remote home-based exercise programmes on functional capacity, fatigue, disease severity, pain and treatment adherence of people with ALS.

METHODS

Study design

This is a single-blind randomised clinical trial protocol developed according to the Standard Protocol Items: Recommendations for Interventional Trials.[22]

Participants

This study will include definite, probable or possible participants with ALS of both sexes, diagnosed by a neurologist (*El Escorial*[23] criteria), aged between 18 and 80 years, and able to understand and perform simple motor instructions according to verbal commands. Bedridden participants under continuous use of non-invasive ventilation and those who need but do not have caregivers available will be excluded from the study.

Recruitment

Participants will be recruited and initially evaluated at the Ambulatory of Neuromuscular Diseases of the Onofre Lopes University Hospital (Federal University of Rio Grande do Norte, Natal, Rio Grande do Norte, Brazil). Demographic and clinical data (ie, age, weight, sex, marital status, symptom onset, date of diagnosis, initial symptom, chief complaint, dominant side and most affected site) will be collected, and a trained physical therapist blinded to allocation of experimental and control groups will assess functional physical capacity, disease severity, fatigue and pain. Participant enrolment will occur between November 2021 and December 2022.

Randomisation and allocation concealment

An external researcher will randomise participants into two groups (ie, experimental and control) of 22 participants each using the website www.randomization.com. A restricted randomisation with four blocks of eight and two blocks of six participants will be used. The same researcher will maintain the randomised sequence in numbered and sealed envelopes and keep it confidential until the end of the study. Therapists will open envelopes only before the training of each participant. Therapists and participants will not be blinded due to intervention characteristics, whereas researchers responsible for statistical analyses will be blinded. Also, participants will not be informed about interventions applied to the other group.

Intervention groups

After the initial evaluation, a trained physical therapist will teach exercises to participants and caregivers,

Box 1 Supervision questionnaire to monitor exercise performance

Monitoring questionnaire

⇒ How many times a week (how often) did you perform the exercises?
⇒ Did you have any difficulties performing the movements?
⇒ Did you feel the need to take a break to rest? If yes, how many times and for how long?
⇒ Did you feel muscle fatigue, pain, discomfort, shortness of breath or any other symptom during or after exercises?
⇒ Did you feel the need to use non-invasive ventilation before, during or right after the exercises?

according to disease stage (table 1). The proposed exercises will be tested with the participant and adjusted to ensure a correct execution. Participants and caregivers from experimental (EG) and control groups (CG) will also receive a guideline with type, frequency and duration of exercises. Participants of both groups will perform the same home-based exercise programme with specific exercises for each stage of the disease, three times a week, for 6 months, and with the assistance of caregivers.

A physical therapist will conduct face-to-face (visits—EG) or remote (phone calls, video calls or instant messaging app—CG) monitoring of exercises once a week and apply a questionnaire regarding exercise frequency and fatigue after the exercise programme (box 1). Therapists will also answer questions from participants and caregivers and adjust the protocol according to individual responses if needed (eg, changes in load or rest between series).

Participants are currently monitored by a multidisciplinary team of the ambulatory, including a neurologist, physiotherapist, speech therapist, nutritionist, psychologist and nurse. We will record all therapies performed by professionals of the multidisciplinary team and external professionals (eg, respiratory and occupational therapists) and instruct participants to maintain activities throughout the study.

The non-adherence to the programme will be considered if participants do not perform exercises for more than three consecutive days or do not answer phone calls for more than four consecutive days. In the case of adverse events interfering with or caused by exercises (eg, pain, discomfort or falls), patients will be instructed to temporarily suspend the proposed exercise programme and communicate to the therapist responsible for the monitoring. In this case, guidance on managing the condition will be provided.

Statistical analyses

Sample size

Sample size was calculated using an online calculator[24] (www.openepi.com) and considering functional capacity as the primary outcome, assessed using the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-r). A similar study[25] showed a mean functional capacity of 32.8±6.5 and 28.7±7.5 in the EG and CG, respectively, after 6 months of intervention. Based on these data, a sample size of 18 participants per group (total n=36) was estimated to detect a 20% difference between groups (α=5% and 80% of statistical power). A final sample size of 22 participants per group (total n=44) was calculated considering a loss of approximately 20%.

Statistical analysis

Statistical Package for the Social Sciences software V.22 (IBM Corp) will be used for data analysis, and Shapiro-Wilk test will verify data normality. Descriptive statistics will be conducted for sample characterisation, and inferential statistics will consider an alpha of 5%. Linear mixed models will compare outcome measures between groups and evaluation times. In the case of statistical significance, the Bonferroni post hoc test will be applied to identify differences. Intention-to-treat analysis will be considered to analyse participants according to groups. Additionally, data loss will be inferred by repeating values of the previous evaluation.

Patients and public involvement

The public or participants were not involved in planning recruitment and conducting processes. However, we intend to involve participants in the disclosure plan of this study.

OUTCOMES

Outcomes will be evaluated initially face-to-face and revaluated remotely every 2 months during interventions and 1 month after the rehabilitation programme.

Primary outcome

Functional capacity

The ALSFRS-r, validated for the Brazilian population,[26] will assess functional physical capacity to perform activities during an interview with participants or caregivers (in case of impaired speech). This scale is reliable[27] and has 12 items ranging from 0 to 4 points (maximum score of 48 points, higher scores indicate a better functionality). Participants will be classified according to a reduction in the total score, considering 30 points as cut-off (≤30 and >30) and 20%–25% change in ALSFRS-r slope as clinically significant.[27 28]

The ALSFRS-r will also be used to assess disease progression concerning physical capacity. The rate of disease progression (ΔPR) will be calculated by subtracting the total ALSFRS-r score between assessments and dividing by time (in months) since the baseline assessment.[29] ALSFRS-r progression will be classified as slow (ΔPR≤0.5), intermediate (0.5≤ΔPR≤1) or fast (ΔPR≥1), and analyses will be adjusted for the rate of progression.

Secondary outcomes

Disease severity

The Amyotrophic Lateral Sclerosis Severity Scale is a reliable and valid nominal scale used to classify disease severity by identifying the functional independence level of individuals.[30 31] It has four categories (lower extremity,

	STUDY PERIOD					
	Enrollment	Allocation	Post-allocation			Close-out
TIMEPOINT**	$-t_1$	0	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screening	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Control Group			←	—	→	
Experimental Group			←	—	→	
ASSESSMENTS:						
Sociodemographic data	X					
Cognition	X					
Functional Capacity	X		X	X	X	X
Disease severity	X		X	X	X	X
Fatigue	X		X	X	X	X
Pain	X		X	X	X	X
Adverse events			X	X	X	
Adherence rate			X	X	X	

Figure 1 Study schedule. –t1 (initial evaluation); t1 (after 2 months); t2 (after 4 months); t3 (after 6 months); t4 (1 month after interventions).

upper extremity, speech and swallowing) with scores ranging from 1 to 10, considering a decline in function, functional adaptation, auxiliary devices and need for caregiver. The total score ranges from 4 (worst function) to 40 (normal function).[31]

Fatigue

The Fatigue Severity Scale (FSS) is not specific to assess participants with ALS; however, it has acceptable validity and reliability for some neuromuscular conditions[32] and is commonly used to assess fatigue.[33 34] FSS is composed of nine statements influenced by fatigue (eg, motivation, performance, carrying out duties and responsibilities, work, family and social life), in which patients select a score (1–7) that best describes the agreement level for each statement.[35] Total scores range from 9 to 63, and scores ≥28 indicate fatigue.[36] Although FSS may not be sensitive to detect changes in our ALS population, the literature indicates that a 1.9-point difference in total score would reflect a clinically important change.[32]

Pain

Pain intensity will be assessed during static position (static pain) and movement (dynamic pain) using the Visual Analogue Scale (VAS).[37] VAS is a valid and reliable instrument used in studies with people with ALS, and scores range from 0 (no pain) to 10 (maximum supported pain).[38] Additionally, a body pain diagram will determine the pain location reported by participants. This tool provides a reliable representation of 45 body areas where patients can indicate specific painful body areas.[39]

Adverse events

Adverse events will be self-reported weekly during face-to-face or remote monitoring (see Box 1). These adverse events will be classified according to disease severity, and potential associations with the exercise programme will be determined.

Adherence rate

Adherence to the intervention will be calculated using the percentage of participants that performed the entire exercise programme (6 months) at least once a week. Figure 1 shows the study schedule.

ETHICS AND DISSEMINATION

Ethics approval and consent to participate

This project was approved by the research ethics committee of HUOL/UFRN (no. 3735479), according to Resolution 466/12 of the National Health Council and Declaration of Helsinki. Researchers will invite patients and caregivers to participate voluntarily and sign the informed consent form (see online supplemental file 1) to be included in the study.

Consent for publication and confidentiality

Information of all participants will be kept confidential and stored in the laboratory database. Only researchers will access the database, ensuring anonymity, respect and human dignity. Results will be published in peer-reviewed journals and presented at scientific meetings. In case of significant changes in the protocol, we will inform participants, the Brazilian Registry of Clinical Trials and journals. If requested, we will provide a copy of the informed consent form.

Availability of protocol and data

The protocol information is registered and available. The corresponding author will provide the study protocol and data of participants on reasonable request to achieve study goals.

DISCUSSION

Participants need specific and continuous healthcare from the early stages of ALS due to the fast disease progression. This specific healthcare is challenging for rehabilitation professionals, mainly because of difficulties regarding healthcare access. Displacement to treatment centres demands time and funds from the government and participants. Therefore, effective home-based low-cost treatments (eg, physical exercise) should be considered the first choice in rehabilitation programmes.

We expect this study demonstrates the usefulness and applicability of telerehabilitation for patients with ALS, reinforcing the benefits of home-based exercises and remote monitoring. Regarding study limitations, the fast disease progression may lead to sudden complications or death and limit the long-term follow-up of participants.

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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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