Cássio Lamas Pires[1]
https://orcid.org/0000-0001-8052-0898

Lucas Rodrigues Mentz[2]
https://orcid.org/0009-0002-0144-8715

Nicholas Kostopoulos Cardoso[3]
https://orcid.org/0009-0005-6989-6065

Anne Sordi[4]
https://orcid.org/0000-0002-4629-1646

Franciele Ramos Figueira[4]
https://orcid.org/0000-0002-9919-6722

Felipe Barreto Schuch[5]
https://orcid.org/0000-0002-5190-4515

Eduardo Lusa Cadore[3]
https://orcid.org/0000-0003-4397-9485

Combined physical training associated with multidisciplinary intervention in the treatment of alcohol use disorder: a study with n of 1

O treinamento físico combinado associado à intervenção multiprofissional no tratamento do transtorno por uso de álcool: um estudo com n de 1

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ABSTRACT

Objective: Substance misuse can lead to several consequences for physical and mental health. Physical exercise is an important ally to pharmacological and psychotherapeutic treatment for substance use. However, the literature is still scarce regarding long-term interventions. Thus, this study aims to describe the acceptability and effects of combined physical training intervention (aerobic and strength). **Methods:** This study comprises an n-of-1 clinical trial that was performed with a 64-year-old male individual with alcohol use disorder. The treatment lasted 12 weeks and evaluated the association of multidisciplinary interventions on quality of life, depressive symptoms, cognitive impairment, and anxiety. **Results:** The participant improved general quality of life (12.5%), no alterations were found for depressive symptoms, there was an improvement in cognition (20%), as well a reduction in the trait (16.2%) and state (14.7%) anxiety symptoms of the participant. **Conclusions:** These findings allude to the importance of non-drug therapeutic resources such as structured physical exercise, associated with other offers in the treatment of alcohol use disorder.

KEYWORDS:

Alcohol-related disorders, alcoholism, exercise, quality of life, and mental health.

RESUMO

Objetivo: O uso de substâncias psicoativas pode levar a diversas consequências à saúde física e mental. O exercício físico é um importante aliado ao tratamento farmacológico e psicoterápico para o uso de substâncias. No entanto, a literatura ainda é escassa em relação às intervenções de longa duração. Dessa forma, este estudo objetiva descrever a aceitabilidade e os efeitos de uma intervenção de treinamento físico combinado (aeróbico e força). **Métodos:** Este estudo compreende um *n-of-1 clinical trial* que foi realizado com um indivíduo do sexo masculino, de 64 anos de idade, com transtorno por uso de álcool. O tratamento teve a duração de 12 semanas e avaliou a associação de intervenções multiprofissionais sobre a qualidade de vida, sintomas depressivos, comprometimento cognitivo e ansiedade. **Resultados:** O participante melhorou a qualidade de vida geral (12,5%), não foram encontradas alterações para sintomas depressivos, houve melhora na cognição (20%), bem como redução nos sintomas de ansiedade traço (16,2%) e estado (14,7%) do participante. **Conclusões:** Esses achados aludem à importância de recursos terapêuticos não medicamentosos como o exercício físico estruturado, associados às demais ofertas no tratamento para o transtorno por uso de álcool.

PALAVRAS-CHAVE:

Transtornos relacionados ao uso de álcool, alcoolismo, exercício físico, qualidade de vida, saúde mental.

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1 Federal University of Rio Grande do Sul (UFRGS), Post-Graduated Program in Human Movement Sciences; Hospital de Clínicas in Porto Alegre, Porto Alegre, RS, Brasil.
2 School of Public Health of Rio Grande do Sul (ESP-RS), Porto Alegre, RS, Brasil.
3 Federal University of Rio Grande do Sul (UFRGS), School of Physical Education, Physiotherapy, and Dance, Porto Alegre, RS, Brasil.
4 Hospital de Clínicas in Porto Alegre, Porto Alegre, RS, Brasil.
5 Federal University of Santa Maria (UFSM), Department of Sports Methods and Techniques, Santa Maria, RS, Brasil; Federal University of Rio de Janeiro (UFRJ), Institute of Psychiatry, Rio de Janeiro, RJ, Brasil; Universidad Autónoma de Chile, Faculty of Health Sciences, Providencia, Chile.
Address for correspondence: Cássio Lamas Pires. E-mail: cassilhano@gmail.com

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INTRODUCTION

The use of alcohol is associated with several physical and mental health problems, especially among middle-aged and older adults[1]. The consequences of individual health abuse of alcohol are numerous, reducing overall functionality and well-being, and having clinical, family, and social repercussions. Further, substance misuse is associated with a higher risk for HIV infection, and liver diseases including hepatitis, cancer, and cirrhosis, conditions that may lead to an increased risk of premature death[2]. There is also high psychiatric comorbidity rates[3]. In Brazil, the prevalence of alcohol use disorder (AUD) among adults is 17,1%[4], similar to 16% of the worldwide population[5].

The treatment of people with AUD usually includes a multidisciplinary intervention with a multidisciplinary health team such as psychiatrists, nurses, and psychologists[6]. This study took place in a specialized treatment service for addictions and also includes occupational therapists, nutritionists, and exercise science professionals. This team develops approaches in relapse prevention, emotional regulation, social skills training, motivation for treatment, nutritional education, physical exercise program, and well-being. In this way, there is evidence that exercise can reduce depressive symptoms and increase physical fitness[7], as demonstrated by improvements in cardiorespiratory conditioning, resting heart rate, and muscular strength[8]. Regular physical exercise can also positively influence mood, decrease anxiety symptoms, improve cognitive function, and helps with alcohol cravings[9]. However, most of the studies evaluated only the effects of aerobic exercise, and there is limited evidence on adding up the combination of aerobic and strength exercises to a usual multidisciplinary intervention. In addition, there is a scarcity of data on the benefits of combined strength and endurance training on the mental health of older adults with alcohol dependence. Lastly, there is a paucity of interventions prescribing exercise with progressive workloads.

In this sense, this study aimed to describe the effects of combining progressive workload strength and aerobic exercises to the usual care multidisciplinary intervention in a set of outcomes. Specifically, we sought to evaluate the effects on quality of life, depression, anxiety, and cognition in one outpatient with alcohol dependence.

METHODS

This study was carried out by the Physical Education and Occupational Therapy Service and the Addictions and Forensic Psychiatry Service of the Hospital de Clínicas in Porto Alegre (HCPA). The protocol was approved by the research ethics committee of HCPA (number 4.556.680). The participant agrees to participate in this study and signs the informed consent form.

This study is an "n-of-1 clinical trial" with a 64-year-old male individual with higher education, with AUD, a design that has been increasingly widespread in the health field, intending to determine the ideal intervention for a biological specificity in each person, enhancing the results from the intervention[10]. The participant had been under treatment for over a year when we proposed the study. Our protocol is characterized by an intervention of combined aerobic and strength training associated with a multidisciplinary intervention for 12 weeks, totalizing 24 sessions. Nonetheless, the 12-week intervention protocol needed to be extended to 18 weeks to allow the participant to complete 24 combined training sessions. This period change was the consequence of the research participant's circumstances, such as health problems and professional commitments. The exercise sessions were divided into 2 moments, 30 minutes of aerobic exercise, performed on an ergometric treadmill in a gym inside the hospital and 30 minutes of strength exercises, continuously, with no break between them. The exercise intensity progressed throughout the intervention. In strength training, a rest of 45 seconds to 1 minute was established between sets. The muscle strength exercises were prescribed using loads relative to the one repetition maximum (1 RM) values, and the aerobic exercise training progression was based on % of maximal heart rate measurement (Table 1). During strength training, six exercises were prescribed targeting the upper and lower limbs and trunk. During the combined training period, the research participant maintained contact with an outpatient clinic, participated in a motivational group, conducted by Physical Education and Nursing professionals, and participated in individual psychotherapy consultations. The quality of life was assessed using the WHOQL-BREF[11] questionnaire. This 24-question instrument divides them into four domains, namely: physical, psychological, social relationships, and environment, in addition to the individual's self-perception regarding their quality of life and satisfaction with their own health. Depressive symptoms with the Beck Depression Inventory (BDI)[12] questionnaire. Cognitive impairment with the Montreal Cognitive Assessment (MoCA)[13], the instrument has a maximum of 30 points and the cut off point for normal cognition is 26 points. Trait and state-level anxiety were assessed using the State-Trait Anxiety Inventory (STAI)[14].

The patient was already on the usual treatment for AUD before starting the intervention and he was instructed not to perform physical activity outside the intervention protocol.

He attended an online motivational group, an advantage relapse prevention group, individual psychotherapy consultations, and a multifamily group together with his wife and other families. The questionnaires were applied by a trained exercise science professional before and after the intervention. The combined training sessions were conducted by another exercise science professional who was blinded to the test results. Data were presented with means of pre and post and percentage of change.

RESULTS

During the intervention period the research team, attentive to fluctuations in the participant's motivation, used motivational techniques, such as educational approaches on the benefits of regular physical exercise, clarifying the process of physical conditioning, and strengthening the importance of regular practice for health gains, through words of encouragement to self-perceive in his disposition, mood, discomfort or pain. We observed improvements in the patient in the following outcomes: self-evaluation of quality of life (14.2%), in the physical domain (20.8%), in the psychological domain (13.6%), in social relationships (10%), and in the environment (6%). The assessment of the general quality of life increased by 12.5% in the WHOQOL-Bref. The differences in scores in the pre-and post-intervention assessment in the different optimized training domains are seen in Table 2. The patient was below the cutoff point for the presence of levels of depressive symptoms throughout the intervention, scoring 6 (six) in the pre-assessment and 3 (three) points after the application of the BDI. Anxiety symptoms, as measured by the STAI-S, decreased from 34 in the pre-intervention to 29 in the post-intervention points (14.7% decrease). In STAI-T, the score was 37 in the pre-intervention and decreased to 31 in the post-intervention, achieving a reduction of 16.2%. In MoCA for cognitive impairment, the participant scored 22 out of a maximum of 30 points pre-intervention, increasing to 26 points post-intervention (20% reduction).

DISCUSSION

This study found improvements in all assessed outcomes. Regarding depressive symptoms, the questionnaire did not classify the patient as a depressed individual. In quality of life, the differences in scores in the pre-and-post-intervention assessment in the different domains are apparently clinically significant[15]. In the trait and state anxiety questionnaires, the participant had a decrease in both levels when comparing the pre-and post-intervention responses. These findings are in agreement with results of the studies mentioned in the meta-analysis[7]. The changes reached about 15% in both types of anxiety, which demonstrates substantial improvement induced by a protocol of 24 sessions of combined training associated with multidisciplinary interventions. One study suggests cutoffs between 39-40 points to detect significantly relevant anxiety problems[16]; however, another study[17] considered 54-55 a cutoff point closer to reality in older adults and that it decreases the incidence of false positives. Combined training as an intervention for anxiety symptoms is scarce among selected studies in systematic reviews[7,18].

Table 1. Progressions of the intensity of aerobic training and muscular endurance

Weeks	% HRmáx	% Rep-Max	Volume
1, 2	55-65%	50-55%	2 sets of 15 repetitions
3, 4, 5, 6	65-75%	60-65%	2 sets of 15 repetitions
7, 8, 9, 10	75-80%	70-75%	2 sets of 10 repetitions
11, 12	80-90%	80%	2 sets of 10 repetitions

Table 2. The score for Quality of Life through WHOQOL-BREF

	General WHOQOL	Physical domain	Psychological domain	Social relations domain	Environmental domain	Self-evaluation QL	Health satisfaction
Pre	14.76	13.71	14.66	13.33	16.5	14	3
Post	16.61	16.57	16.66	14.66	17.5	16	4
Amplitude	1.85 (+12.5%)	2.86 (+20.8%)	2 (+13.6%)	1.33 (+9.9%)	1 (+6.06%)	2 (+14.2%)	1 (+33.3%)

Thus, combined training associated with multidisciplinary interventions may have contributed to a slight reduction in anxiety symptoms, helping the patient to remain below the cutoff point for the presence of symptoms during the intervention period[5]. Although the literature already supports these antidepressant and anxiolytic effects in alcohol users, this case study suggests that combined training associated with multidisciplinary interventions can reproduce these effects. In addition, it has been shown that people with depressive and anxiety symptoms have elevated inflammatory markers and physical exercise is a protective factor in reducing these markers[19].

The research participant also showed significant improvement in the cognitive domain, reaching almost a 20% reduction in the total score. As already seen in the results, in the pre-intervention moment, the participant scored for "mild cognitive impairment" and after the combined training protocol associated with multidisciplinary interventions, its score changed to the category "without cognitive impairment" (26 is suggested as the cutoff point for normal cognition)[14]. This finding converges with evidence that physical exercise stimulates brain neuroplasticity and may improve cognitive performance[7].

A limitation of the study was concerning the abstinence control of the participant, as no abstinence monitoring technique was applied throughout the study, such as the use of a breathalyzer. Although the participant had an extensive history of alcohol abuse, his social condition favors treatment adherence and collaborates with a good performance in most tests, since he demonstrates to have broad family support and good income, facilitating access to psychotherapy, means of leisure, and social interaction. Therefore, the sample in question physiologically represents an individual with AUD. However, his family and social support are far from the reality of the majority of the population that seeks treatment for AUD in the Health Unic System. It is important to emphasize that the results obtained in the study cannot be extrapolated to other patients, but it is presented as a possibility of a protocol since it proved to be effective and can serve as a model for different patients with AUD. Moreover, the results obtained from the instruments take into account all the multidisciplinary interventions that the patient received, along with factors such as medication use, time of abstinence, and family and work relationships. On the other hand, this report demonstrates the expected outcomes in a real-life scenario.

This study suggests that the combined training protocol associated with multidisciplinary interventions can improve quality of life, alleviate anxiety symptoms and improve cognitive performance in people with AUD. Since this activity can disseminate the substitution of pleasures and routine structuring, needs to be linked to the logic of relapse prevention.

CONCLUSIONS

Considering the benefits observed in the participant's mental health and cognitive function, it is recommended that combined aerobic and strength training be encouraged and incorporated as a complementary strategy to treatment already established for people with AUD. The professional must be aware of the necessary adaptations according to each patient's profile, considering the disorder's peculiarities.

REGISTRATION OF STUDY APPROVAL

HCPA Ethics and Research Committee with Opinion of approval under nº 4,556,680.

INDIVIDUAL CONTRIBUTIONS

Cássio Lamas Pires – Contributed to the study design, article writing, results analysis, and discussion.
Lucas Rodrigues Mentz – Contributed to the elaboration of the article, as well as applied the intervention and analysis of the results and discussion.
Nicholas Kosptopoulos Cardoso – Contributed to the application of evaluation instruments and analysis of results.
Anne Sordi – Contributed to the elaboration of the article and analysis of the results and discussion.
Franciele Ramos Figueira – Contributed to the elaboration of the article and analysis of the results and discussion.
Felipe Barreto Schuch – Contributed to the elaboration of the article and analysis of the results and discussion.
Eduardo Lusa Cadore – Contributed to the elaboration of the article and analysis of the results and discussion.

CONFLICTS OF INTEREST

FBS is associate editor of the *Jornal Brasileiro de Psiquiatria* and of the Mental Health and Physical activity. He is also on the editorial board of the Brazilian Journal of Psychiatry. FBS wrote a commercial book on lifestyle psychiatry. FBS has a research project funded by FITXR Limited. FBS received grants from UpJohn to write two mental health guides during COVID-19 pandemic. The other authors state that there are no conflicts of interest.

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COMBINED PHYSICAL TRAINING ASSOCIATED WITH MULTIDISCIPLINARY INTERVENTION IN THE TREATMENT OF ALCOHOL USE DISORDER: A STUDY WITH N OF 1

SPENT 2019 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item Nº	Description	
		Administrative information	
Title	1a	Descriptive title, including "N-of-1 trial" and "protocol". For series: Descriptive title, including "a series of N-of-1 trials" and "protocol"	OK
	1b	For specific guidance on abstracts, see SPENT Guidance for Abstracts. (Appendix table 2)	
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	No
	2b	All items from the World Health Organization Trial Registration Data Set	No
Protocol version	3	Date and version identifier	OK
Funding	4	Sources and types of financial, material, and other support	OK
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	OK
	5b	Name and contact information for the trial sponsor	Not applicable
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Not applicable
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Not applicable
		Introduction	
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention, and rationale for using N-of-1.	OK
	6b	Explanation for choice of comparators	OK
Objectives	7	Specific objectives or hypotheses	OK
Trial design	8	Description of the trial design, including N-of-1 trial or series of trials, and framework (eg, superiority, equivalence, non-inferiority, exploratory). In addition for series: Explanation of the series design including whether the design will be tailored to each participant	OK
		Methods: Participants, interventions, and outcomes	
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	OK
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists). Diagnosis/disorder, diagnostic criteria, co-morbid conditions and concurrent therapies	OK
Interventions	11a	Intervention(s) for each period with sufficient detail to allow replication, including how and when they will be administered, planned number of periods, and duration of each period (including run-in and washout, if applicable).	OK
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Not applicable
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	OK
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	OK
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	OK
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended	Not applicable
Sample size	14	Estimated number of intervention periods and measurements/observations needed to achieve study objectives within an individual N-of-1 trial	Not done
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	OK
		Methods: Assignment of interventions (for controlled trials)	
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability, details of any restrictions (eg, pairs, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Not applicable
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Not applicable
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	OK
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Not applicable
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Not applicable

Section/item	Item Nº	Description	
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	OK
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Not done
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	OK
Statistical methods	20a1	Statistical methods for analyzing primary and secondary outcomes for each individual. Reference to where other details of the statistical analysis plan can be found, if not in the protocol.	OK
	20a2	Statistical methods to account for correlation introduced by the repeated measures and crossover design of N-of-1 studies.	Not applicable
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Not applicable
	20c	Statistical methods to handle missing data (eg, multiple imputation, modelling)	Not applicable
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	No
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	No
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	No
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	No
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Ok
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Ok
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Ok
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Not applicable
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Ok
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Ok
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Ok
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Ok
Dissemination policy	31a	Plans for investigators to communicate each individual's results to the participant. Plans for investigators and sponsor to communicate trial results to participants, health care professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data-sharing arrangements), including any publication restrictions.	Ok
	31b	Authorship eligibility guidelines and any intended use of professional writers	Ok
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Ok
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Ok
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	Not applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.