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Effectiveness of a home-based, self-administered exercise program for hands in patients with Systemic Sclerosis: a Randomized Controlled, Single-blind, Clinical Trial.

NCT Number:

Study protocol

Objectives

The aim of the study is to investigate the effectiveness of the hand exercise program and demonstrate its influence on hand function, quality of life, as well as anxiety and depression in patients with systemic sclerosis.

Material and Methods

Study design and study population

The current study was designed as a single-blind, prospective, randomized controlled, comparative study with a 2-month follow-up period, conducted in a rheumatology outpatient clinic of a university hospital, between July 2016-June 2019. Female patients with SSc who fulfilled the 2013 ACR/EULAR classification criteria for systemic sclerosis were included in the study. Patients with neurological disorders, arthritis, myositis, amputation of fingers, serious contracture resisting hand grip and history of undergoing hand surgery were excluded from the study. The study protocol was approved by the local ethics committee of Cukurova University (Approval date: 15-July-2016, number: 55). Written informed consent form was obtained from all patients according to the Helsinki declaration.

Evaluation of Patients

The demographic variables and socio-economic status of patients were recorded at the beginning of the study. The time from the beginning of non-Raynaud's phenomenon symptoms was regarded as disease duration. The systemic sclerosis subsets including limited systemic sclerosis and diffuse systemic sclerosis were classified according to the definition of LeRoy et al. The organ involvements including interstitial lung disease, pulmonary arterial hypertension, scleroderma renal crisis, and gastroesophageal reflux disease were recorded based on the medical data. The present or absent of clinical variables such as Raynaud's phenomenon, digital pitting scars, arthralgia, sclerodactyly, calcinosis, color change, and telangiectasiawas noted as well. Patients were questioned about cigarette smoking (package/years), medical drug information (previous and current) and comorbidities causing hand dysfunction (diabetes mellitus, atherosclerosis, thyroid diseases). Additionally, the laboratory results including anti-nuclear antibody, anti-Scl 70 antibody, anti-centromer antibody, complement levels (C3 and C4), erythrocyte sedimentation rate (ESR) (mm/h), and C-reactive protein (CRP) (mg/dl) were recorded.

The evaluation of disease activity and severity was performed by Valentini disease activity index and Medsger disease severity scale. Modified Rodnan Skin Score was used to assess the severity and the extent of

skin involvement. Hand involvement of patients was exhaustively evaluated by means of physical examination and indexes assessing the hand function. The finger range of motion was performed by the measure of finger-to-palm. The functional disability of hand was examined by Hand mobility in Scleroderma (HAMIS) test. Hand function was also evaluated by Duruoz Hand Index (DHI). Handgrip strength was measured by hydraulic hand dynamometer (JAMAR®,USA) according to the standard protocol. The physical function and quality of life were assessed by using Health Assessment Questionnaire-Disability Index (HAQ-DI) and Short-Form 36 (SF-36). Psychological status was evaluated by using Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

Randomization

The computerized block randomization method was used to randomize subjects into groups. Each block contained 10 subjects consisting of 5-intervention and 5-control subjects. We simulated seven blocks with a total of 70 subjects at the beginning of the study. The 6^{th} block was designed to compensate for the study population in terms of loss to follow-up. The 7th block that was designed to use if needed was planned for compensation of the patients who would be excluded from the analysis. Randomization was managed by a physiatrist who trained patients according to which group they were in. The second physician who was blinded evaluated patients.

Sample size

Handgrip strength was determined as the primary outcome measure. According to the literature, handgrip strength has been reported to have a standard deviation between 6 and 7 [35]. Accordingly, standard deviation as 7 and autocorrelation coefficient as 0.3 were accepted in the current study evaluating the average of three consecutive measurements of handgrip strength. The sample size was calculated as 24 participants for each group in order to detect at least 4 kg differences with a 95% confidence interval and 80% power.

DHI was defined as the secondary outcome measure. We calculated the mean standard deviation as the mean of the total DHI for two time-points and two groups (20.20+16.22+17.1+17.85)/4=17.5 [23]. We expected at least 5-6 points regression in the control group and at least >5-6 points improvement in the treatment group, so that, we assumed that there could be at least 12 points differences between groups. The number of observations, to find this difference significant at alpha=0.05 with 80% power, was calculated to be at least 23 per group.

Intervention

The patients were randomized into an exercise (n=25) and a control (n=25) group. Both groups were informed about systemic sclerosis and they received the printed materials that include recommendations such as avoiding cold and trauma. The treatment group participated in a single hand exercise training (isometric hand exercise and self-administered stretching) applied by a physiatrist. Isometric exercise was told as the ball squeeze exercise. Accordingly, patients squeezed the soft small ball for 60 seconds. This repeated 15 times in each set. Three sets were recommended per day. The stretching exercises were as follows; i) forearm supination and pronation, ii) wrist flexion and extension, iii) finger flexion, extension and abduction iv) thumb flexion, extension and abduction. Holding each stretch was recommended for 30 seconds. Thereafter, patients took instructions illustrating the exercises. The 8-week intervention consisted of isometric hand exercise 15-times/3

set and self-administered stretching repeated 10-times/2 set per day. Compliance was assessed by a checklist, which included all information on how to exercise and how many times to do them.

Statistical analysis

Statistical analysis was performed by IBM SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics was used to analyze the demographic and clinical variables. The normality of the variables was checked by Shapiro-Wilk test. Non-parametric values were given as median and interquartile range. Between-group comparisons of continuous and categorical variables were performed by Mann-Whitney *U* test and Chi-square test, respectively. Within-group comparisons over time analyzed by Friedman test. Delta (Δ) values were calculated as the difference from baseline measurement to the second visit measurement. Δ values were compared between groups by Mann-Whitney *U* test. In addition, apart from Δ values, the percentages of improvement or worsening on grip strength, DHI, HAMIS, HAQ-DI, Beck Depression and Beck Anxiety were calculated according to the formula as [(Last assessment−Baseline assessment)/Baseline assessment]X100. Multiple Linear regression analysis was used to define the predictors impacting on the percentages of improvement or worsening of HAMIS, DHI, handgrip strength, and HAQ-DI. The results were considered as statistically significant when p values below 0.05.