Title: Comparative effects of integrated physical training with high protein diet versus low protein diet in COVID-19 asymptomatic older adults with Sarcopenia symptoms.

Clinical trial registration number: NCT05224453

Date: 12/02/2022

Study Protocol

Background: Sarcopenia is the major health concern and common consequence of COVID-19 in the aging population. Moreover, this clinical condition has not been considered in usual physical rehabilitation practice and nor its optimal protein requirement in food is well defined, which requires a meaningful study in this field.

Objective: To find and compare the clinical and psychological effects of integrated physical training with a high protein diet versus low-protein diet in community dwelling COVID-19 asymptomatic older adults with Sarcopenia symptoms.

Design: It is a single-blinded, randomized, experimental study performed during March -2020 to November-2021. The trial received acceptance from the department of ethical committee (DEC), Prince Sattam bin Abdulaziz University, Al-Kharj, Saudi Arabia with an approval number of RHPT/020/51. The DEC approved the subject consent form, treatment protocols and the outcome parameters measured in the trial. The trial was executed in accordance with the ethical guidelines laid down in the 1964 Declaration of Helsinki and was registered in the clinical trial registry with registration number NCT05224453. The finally selected subjects for the trial were asked to fill the written subject consent form and underwent measurements for pre interventional personal and anthropometric data. A two block simple random sampling method was used to randomize and allocated the participants into two treatment groups. The group A was treated with integrated physical training with high protein diet (n = 38) and the group B was treated the same integrated physical training with low protein diet (n = 38) for a duration of eight weeks.

Subjects

Subjects for the study were received from local and government hospitals in Al-Kharj and Riyadh region of Saudi Arabia. Positively diagnosis of asymptomatic COVID-19 male patients

with 60 – 80 years of age was recruited for the study. Appendicular skeletal muscle mass index (ASMI< 7.0 kg/m^2) was used to identify sarcopenia (skeletal muscle loss). Sarcopenia was diagnosed according to the guidelines given by the Asian working group for Sarcopenia (AWGS). Patients with less muscle mass, low hand grip strength (< 24 kg) and decrease walking speed (< 0.7 m/sec) were involved. Subjects with a history of physical workout, taking medicines, recent surgeries and joint problems in leg, heart and lung problems, neurological issues, any other systemic diseases and contraindications for physical training were eliminated from the study. The fig-1 depicts the methods and procedure of involving study subjects in this trial.

Intervention

Subjects in group-A and Group-B (n=38) underwent integrated physical training for 8 weeks. A trained physiotherapist executed the training protocols under proper COVID instructions. The training protocol was recorded in treatment logbook and was assessed each session by the study supervisor. Prior to the start of exercise training, the basic tests such as; body temperature, blood-pressure, oxygen saturation rate, heart beat and physical fitness were recorded. If these scores exceeded the normal values such as, like body temperature > 38.0^{o}C, blood-pressure > 150/100mmHg and heart beat>90 beat per min or < 50 beat per min, subjects were asked to refrain from training on that session.

The maximum heart rate (MHR) was used to measure the intensity of the given exercise. It was found by reducing the subject's age from number 220. Aerobic training was given with 40 to 50 percent of maximum heart rate for all the subjects, which is considered as low-intensity aerobic training (LAT). Every day, the intervention started with 10mins of stretching of upper and lower limb muscles. Subsequent to stretching, the subjects were asked to do 30 mins of LAT; consisting of 20 mins of treadmill (Axos, Kettler Runner, China) and 10 mins of cycle ergometer (Axos, Kettler Runner, China), then with 10 mins of cool down.

All the participants, in both the groups, were prescribed with strength training exercises with resistance depends upon each subject's individual muscle assessment. The ideal resistance for each muscle groups were measured based on 1 repetition maximum (1RM) principle. The important muscle groups in the spine, upper and lower limb were trained. Each muscle group was undergone training for 3 sets consisting 10 repetitions in each set, with a relaxation of 5 mins rest between sets. The weight was gradually increased as per the subject and therapist needs and the exercise was performed for 4 days in a week for 8 weeks.

In addition to the integrated physical training exercises, group A received a high protein diet in the range of 1.1 – 1.3 g/kg protein/ ideal body weight/day (>1 g/kg aBW/d) and group B received low protein diet in the range of 0.7 – 0.9 g/kg protein/ ideal body weight/day (<1 g/kg aBW/d) as prescribed by a qualified nutritionist.

Outcome measures

Hand grip strength: The test is easy to perform and a less expensive one. It measures the strength of upper extremity by using a device handheld dynamometer. The participant was instructed to press the hand piece of the dynamometer to the maximum of his ability and the values shown on the display were recorded. Three values were noted for each participant and the mean value was considered for interpretation and it is a reliable and valid tool to measure the strength of upper extremity.

Muscle cross sectional area - *CSA:* Muscle CSA is measured with Magnetic resonance imaging (MRI) scan and it is an expensive measurement. The CSA of three major muscle such as;half way at arm - biceps, thigh - quadriceps and calf muscles were measured and included for analysis.[23]

Kinesiophobia: TSK – 11; Tampa scale of kinesiophobia questionnaire was administered to find the level of fear of movement of participants. The questionnaire has eleven items, which measures the mindset at various activities in four point likert scale. Maximum score indicates high level of fear whereas the minimum score indicates low level of fear during activities.

Quality of life: Sarcopenia quality of life (SarQol) questionnaire was used to measure the subjects' wellbeing. The participants filled the questionnaire themselves and it is a robust tool to measure Qol.

Sample size

The sample size for the study was decided based on the report from the study by Yoo Jet al. Thirty-five subjects in each group were found by assuming forty percentage mean improvement in handgrip strength with standard deviation of 2. By accepting 10% drop of subjects at 6 month follow up, two subjects were added in each group. Hence, N=76 subjects were selected and divided into two groups with n=38. The sample size was calculated with the statistical power at 80% with α level of 0.05. The whole analysis was done with G*Power - version 3.1.9.7 software.

Statistical analysis plan

Subjects' personal and anthropometric measurements were calculated through Kolmogorov–Smirnov test for testing homogeneity and the data were represented in tabular form. The measurements were taken before intervention, during intervention at 4 weeks, after intervention at 8 weeks and after 6 months follow up. The data were shown as mean and standard deviation with 95% confidence interval (CI) with upper and lower limit. The time and group (4 × 2) multiple analysis of variance (MANOVA) of primary and secondary variables are reported between group A and group B at various intervals. Student's t test was used to calculate inter-group effects and repeated measures (rANOVA) was used to calculate the intra-group effects. IBMSPSS – online version 20 was used to do all the statistical tests and α level was set at 0.05.

Informed Consent Form

Name of patient: Age/Gender:

Study Title: "Comparative effects of integrated physical training with high protein diet versus low protein diet in COVID-19 asymptomatic older adults with Sarcopenia symptoms"

Introduction and Purpose of Study: You have been selected to take part in a study Comparing the effects of integrated physical training with high protein diet versus low protein diet in COVID-19 asymptomatic older adults with Sarcopenia symptoms.

Study Information

Outline of Procedures: At first consultation you will be screened and evaluated for suitability of the study. You are requested to attend 4 consultations a week for 4 weeks' period. If you are taking any medication or undergoing any other form of treatment for your back pain, you may be excluded from the study.

Risks and Discomfort: The treatment is safe and is unlikely to cause any adverse side effects. All treatments will be performed by qualified physiotherapist.

Benefits of the study: This study will assist the physiotherapy profession in expanding its knowledge of this condition and thus making future treatment of patients suffering from chronic low back pain more effective.

Withdrawal from the Study: You are free to withdraw at any stage with no negative repercussions to your health care.

Remuneration: Patients taking part in the study will not be offered any other form of remuneration for taking part in the study.

Costs of Study: Treatment for the duration of the research process will be free of charge.

Confidentiality: All patient information and results will be kept confidential and can be shared for research purpose if required.

I have been explained about this research in which I agreed to participate. I know that I am giving this consent without any force. I can discontinue the study any time without any reason and that will not affect my treatment that I have been informed. My identity can be disclosed for any

other follow up research.

Signature of Patient **Signature of Researcher**

I certify that I have explained to the participant about nature, purpose, potential benefits & possible risk of the indicated procedure. The information collected will be kept confidential.

Signature of Witness **Signature of Researcher**