EFFICACY OF THREE- MODAL EXERCISE PROGRAM THROUGH TELEREHABILITATION ON FATIGUE AND QUALITY OF LIFE IN PEOPLE WITH PARKINSON'S DISEASE DURING THE COVID- 19 PANDEMIC LOCKDOWN

¹Deepa. S, ²Kumaresan. A, ³Prathap Suganthirababu

¹Research Scholar, Saveetha College of Physiotherapy, Saveetha Institute of Medical and Technical sciences, Thandalam, Chennai – 602105, Tamil Nadu, India, ORCiDs: - 0000-0002-3414-3443.

Abstract

Background: - Excessive daytime fatigue had been unattended and unidentified by the patients, caregivers, and medical – rehabilitation team. Fatigue in Parkinson's Disease has worsened the quality of life and has increased the disability. With the outbreak of the pandemic in 2019, medical and rehabilitation services have become inaccessible. Telerehabilitation is attempting to bridge this gap. Aim and objective: - In this study, we have evaluated the probable effects of the Three-Modal Exercise program administered through video conferencing (telerehabilitation) on fatigue and quality of life in people with Parkinson's Disease. Methods: - We conducted a randomized controlled trial in which patients with Parkinson's Disease voluntarily participated based on the inclusion and exclusion criteria. The patients were randomly assigned to the Three-Modal Exercise program as group A and Conventional exercise group as group B. Both the groups received 36 sessions of 1 hour each day for 6 days/ week for 6 weeks through zoom online. Fatigue in both the groups was measured with the Fatigue severity scale and quality of life was measured with Parkinson's Disease questionnaire – 39. Results: -Both fatigue (P< 0.001) and quality of life(P< 0.001) improved more significantly in the Three-Modal Exercise program intervention group A than the conventional control group B. Conclusion: -Three Mod- Exercise Program can be used as an effective intervention for the patients with Parkinson's Disease through telerehabilitation thus enhancing the need of self-management among these patients.

Keywords: Parkinson's Disease, fatigue, Three Modal - Exercise program, Telerehabilitation, non-motor symptom, Quality of life, Covid -19 pandemic, Abbreviations: - PD = Parkinson's Disease, FSS= Fatigue severity scale, PDQ- 39 = Parkinson's Disease Questionnaire.

INTRODUCTION

Fatigue is understood to be arising from different aspects including the complex interplay of central and peripheral control systems along with the environment1, among the available effective symptomatic therapies for motor symptoms, the non-motor symptoms especially fatigue has become the major prognostic factors determining the overall

disease burden and ADL in PD2. As the patients with Parkinson's disease require a long-term rehabilitation with extensive inputs from the therapist, patient commitments, with financial burden and care giver strain, caused severe difficulty in getting these facilities 3. Cumulative evidence from empirical studies have shown reduction in physical activity, increased in fatigue increased sleep disturbances, increased

²Professor, Saveetha College of Physiotherapy, Saveetha Institute of Medical and Technical sciences, Thandalam, Chennai – 602105. Tamil Nadu, India, ORCiDs: - 0000-0002-5424-5463.

³Professor, Saveetha College of Physiotherapy, Saveetha Institute of Medical and Technical sciences,

Thandalam, Chennai– 602105, Tamil Nadu, India, ORCiDs: - 0000-0002-1419-266X.

Deepa. S 4220

anxiety and stress, increase in disease severity during the Covid- 19 crisis4,5.

With 68% reduction in rehabilitative care, 78% reduction in physical therapy during lockdown, 40 % reported tiredness which is defined as a feeling of exhaustion and absence of energy as fatigue, that is a multifactorial symptom6. Fatigue is the most common disability symptom reported by the patients with PD, it has shown to be aggravated due to immobility and less access to rehabilitation care 7,1.

The Covid- 19 pandemic has caused global health care disruptions, whichhave direct as well as indirect effects on the patients with Parkinson's disease. With the medical staffs and therapists under the danger of exposure they have opted for virtual sessions, hence reaching out to a greater number of patients, but it comes with its own disadvantage8. Many patients have now understood the importance and have switched over to the telerehabilitation especially synchronising with the video conferencing5.

Telemedicine is the use of technology for the application of medicine, tele neurology is the practice of neurology through telemedicine and telerehabilitation is the offshoot of telemedicine. Telerehabilitation is the recent development and is defined as the set of interventions and protocols designed to deliver rehabilitation at a distance virtually using digital technologies9. Keeping in mind the lockdown restrictions and fear of patient exposure to covid- 19, the focus of this study was to give the patients rehabilitation ideally through video conferencing.

The age-related prevalence and increased vulnerability due to comorbidities, makes PD patient's protection a priority. The geriatric population with chronic diseases as Parkinson's disease depend mostly on the community resources as outpatient clinics, exercise programmes etc, which was hampered due to the lockdown rules imposed in each country. They rely on the social network for their mental health and wellbeing6. The social support through family and socializing event in family gathering also was put to an end due pandemic lockdown10.11.

Therapeutic interventions as slow-paced walking, treadmill training, energy conservation techniques, massage, strengthening, balance training, following a good diet were the options

suggested in the studies conducted. Two studies investigated the effect of exercise on fatigue compared with usual care. It was found to be low quality evidence for the effect of exercise on reducing the impact of fatigue on ADL or fatigue severity12,16,29.

Questions still arise on the legitimacy of the optimal exercise programs due to the varied nature of the disease. Diversified presentation of the disease has rendered results of Three Modal – Exercise Programme moot on motor symptoms and very little have been known its effects on fatigue in PD 13-15. In this article, we report a study conducted on the patients with Parkinson's disease at their home setting through video conferencing. The purpose of this study was to test the hypothesis that Three Modal – Exercise Program can be an effective and optimal treatment fatigue intervention and will improve the quality of life in patients with PD when administered through video sessions.

METHODS: -

Study Design: -

We conducted an assessor blinded prospective Randomized control trial of a 6-week video conferencing through zoom online. We investigated whether the Three Modal - Exercise program would be effective on fatigue and quality of life through telerehabilitation into the homes of the people with PD during the pandemic lockdown.

When prescribing exercise, falling was the most compromised balance issue in Parkinson's disease, hence while administering the therapy sessions through video conferencing it was taken care that the patients were accompanied with one care giver beside the participants for the whole 1-hour session17.

Sample Size: - We calculated the sample size to detect the minimum effect size of 0.5, a power of 80% and 5% types I error using Sigma Plot software version 14.5. The total sample size was estimated to be 50 participants with 25 participants each group.

Participants and recruitment: -

The participant's recruitment was done on the basis of selection criteria through invitation explaining about the study and an informed consent was taken. After selection a zoom meeting was arranged with the participants, where queries about the study was addressed during the meeting. The participants were present with the care givers during the assessment who would accompany during the therapy sessions also18. Twenty-five patients were conveniently allocated to one of the two groups. An assessor therapist who was not involved in the trial took the baseline measurement of the participants through zoom meeting before the commencement of the therapy sessions. The study was conducted from June 2021 to November 2021

Selection criteria: -

Participants were selected by the inclusion criteria as Mild to moderate stage I to III on the basis of Hoehn and Yahr scale, age between 50 - 80 years, both male and female, with stable response to levodopa, all the participants complaining of fatigue, on Fatigue severity scale (FSS) minimum score of 4 (cut off score for extreme fatigue), a score of > 23 on mini mental scale examination, able to walk minimum of 10 feet with or without assistance, stable systemic illness e.g., BP, DM, etc., The participants were excluded who had unpredicted fluctuations or dyskinesias not controlled by medications who had severe cardiovascular disorders, vestibular disorders, musculoskeletal conditions, who had undergone recent surgeries, Participation in other trials16.

OUTCOME MEASURES: -

Primary outcome measure: -Fatigue severity score 19 is a 9-item scale used to measure the severity of fatigue, its effect on person's activity and life style in patients with variety of disorders. It's a patient reported outcome measure, The items are scored on a 7- point scale, 1= strongly agree to 7= strongly disagree. Minimum = 9, maximum score = 63, higher the score greater the fatigue. It takes about 5 minutes to administer the scale.

Secondary outcome measure:-Quality of life: Parkinson's Disease Quality of Life Questionnaire-3920 is used to assess the disease specific health related quality of life, experiences on 8 dimensions of quality of life, functioning and wellbeing It is a patient reported outcome measures, it has 39- multiple choice

questions on 8 dimensions, uses 5-point ordinal scoring 0= never to 4 = always the time to administer takes around 10 - 20 minutes.

INTERVENTIONS: -

The Three Modal — Exercise Program protocol21were performed for 60 min each day for 6 days a week for 6 weeks comprising of total of 36 sessions22. This group performed cardiovascular, strengthening and balance exercise where the frequency of each mode of exercise was twice a week. The exercise prescription for number of sets, repetition, frequency, duration followed the ACSM guidelines for Parkinson's Disease 13,14,23. The control group carried out conventional exercises which was based on the symptoms complained by the patients and there was no proper protocol fixed for the same.

A telephonic interview was done to fix the timings for therapy sessions, a day before the start of the therapy, participants underwent complete Physiotherapy neurological assessment and was given a Zoom link each by the attending therapist, the same link was followed throughout the 6 weeks.

Both the groups underwent 5 minutes of warm up exercise and cool down exercises. The exercises were recorded as videos which were shared on the screen during the Zoom session and while the therapist gave verbal instructions explaining the exercises. The patient in presence of a care giver with proper safety measures completed the set of exercises. Frequent rest were given to the participants to avoid exercise induced fatigue.

The intervention group followed a protocol consisting of 40 minutes of cardiovascular, balance and strengthening where cardiovascular involved walking inside the house or community (within Covid -19 precautions), walking was progressed with dual motor tasks (tray with glass) and cognitive tasks (counting number) 24-26. Strengthening exercises involved upper limb, lower limb, abdominal, back 27-29. Balance exercises involved single leg stance, tandem walking, tandem stand, turning, static and dynamic exercises, oculomotor exercises 27,28,30. The exercises were designed in reference with previous literature reviews and ACSM guidelines proposed for geriatric

<u>Deepa. S</u> 4222

population31,. The intervention as Three Modal- Exercise programme was well tolerated by the patients. The exercises were progressive and every week was reviewed for duration, intensity, repetitions that were achieved and by the principal investigator based on Heart rate maximum with a pulse oximeter, strengthening with 1- Repetition Maximum and balance progression was measured by Timed up and go test every two weeks 29, 30. These tests were not included for statistical inferences and were only used for tracking progression during the 6 weeks therapy duration32,33.

The conventional exercises were not designed as a framework but was randomly selected, which did not follow a pattern. The exercises were just walking, simple balance and strengthening exercises 27,28.

The participants were also encouraged to participate in 36-day challenge for 36 sessions where they were guided to do their leisure activities like gardening, reading daily newspaper, household chores, indoor and outdoor games34, reciting Tamil literature like Thirukural, adopting and caring a plant, crosswords, writing poems and stories. A video of the participants performing these activities were sent to the principal investigator. These recreational activities were not a part of their 1-hour Physiotherapy sessions35-37.

STATISTICAL ANALYSIS: -

All statistical analyses on output and outcome measure were performed using Sigma Plot 14.5 software Descriptive statistics were employed to evaluate efficiency and effectiveness data. To evaluate the adherence, we computed the percentage of subjects who reached at least the 70% of the complete sessions.

RESULTS: -

Group A and B age mean values are 68.96 and 67.12 respectively, Group A gender ratio Male/Female is 18/7 and Group B is 14/11. Average disease duration reported in Group A was 5.5 years and group B is 6 years.

Paired t- test was used to analyse the within the group A and Group B pre- test and post- test of Fatigue severity scale (FSS) and Parkinson's

Disease questionnaire (PDQ- 39). The mean value with in the group A of pre- test FSS is 44.280 and post- test value is 26. 720. The standard error value pre- test is 1.423 and post-test is 0.861, with pre- test standard deviation of 7.115 and post- test value of 4.306. The t- value is 10.726 with p value of < 0.001.

The mean value with in the group B of pre- test FSS is 46.720 and post- test value is 42.960. The standard error value pre- test is 1.483 and post-test is 1.212, with pre- test standard deviation of 7.414 and post- test value of 6.059. The t- value is 6.931 with p value of < 0.001.

The median values within the group A for PDQ- 39 pre- test is 54.000 and post- test is 38.000. The 25% values pre- test are 48.000 and post- test are 38.000, 75% values pre- test are 74.500 and 42.000. The W value is -325.000, the z value is -4.375 and the p value is <0.001. The median values within the group B for PDQ- 39 pre- test is 56.000 and post- test is 51.000. The 25% values pre- test are 48.000 and post- test are 41.000, 75% values pre- test are 74.500 and 64.000. The W value is -325.000, z value is -4.379 and the p value is <0.001.

Comparison between the group A and group B for Fatigue severity scale (FSS) and PDQ- 39 Group A and Group B Mann- Whitney Rank sum Test was applied. The median values between the group A and group B for FSS pretest is 28.000 and post- test is 41.000. The 25% values pre- test are 24.000 and post- test are 36.000, 75% values pre- test are 30.500 and 49.000. The T value is 325.000, and the p value is < 0.001. The median values between the group A and group B for PDQ- 39 pre- test is 38.000 and post- test is 51.000. The 25% values pre- test are 32.000 and post- test are 41.000, 75% values pre- test are 42.500 and 64.000. The T value is 415.000, and the p value is < 0.001.

DISCUSSION: -

The aim of this study was to investigate the effects of Three Modal-Exercise program which is multimodal on fatigue and quality of life, it was efficient to improve cardio vascular endurance, muscle strength and balance which where the key components leading to disability. The results of this study are in agreement with previous studies, as to have included the multimodal exercise program to improve fatigue

and quality of life. The median values between the group A and B were 28.000 and 42.000 for Fatigue severity scale and the median values for the group A and B were 38.000 and 51.000 for the Parkinson's disease questionnaire- 39. This showed considerable reduction in the Group fatigue levels and Quality of life in people with Parkinson's disease.

A meta – analysis study conducted by Cusso, M. E et al in 2016 covered 20 randomized controlled trial showed significant improvement in non- motor symptoms as fatigue, mood disorders, neurocognitive manifestations by extensive physical therapy regime. Ellis, T. & Rochester, L 2018 according to their study PD has different degrees of severity, types and subjectively varying degrees of motor and nonmotor symptoms and has become clear that single type of training cannot affect meet the multiple requirements of the patients with PD which support this study for taking up an intervention which is multi modal. Hall, M. E. & Church, F. C 2020 in their study have suggested using moderate intensity exercise in contrast to high intensity exercise, as moderate intensity exercise has the cell and cytokine- based effect on the immune system and this was kept in mind in this study while planning the exercise protocol for the 6 weeks of Three Modal -Exercise program for the intervention group.

It is important to attest that the intervention administered had no adverse event and it indicates towards safe application on people with PD. The current study brings a new pragmatic approach that physical exercise can offer in the field of telerehabilitation in PD during the pandemic situation. However, they are no or very few studies analysed the effect of multimodal exercises on fatigue that too in short term program through video conferencing.

Orcioli-Silva et al in 2014 analysed the effects of multimodal exercise program onthe functional capacity of Parkinson's diseasepatients considering disease severity and gender before and after 6 months, where this long term might prove to be a burden to follow up, we in this study did a 6 weeks study which gave the same results as 6 months result, where the post-test mean in the Three- Modal Exercise group A reduced to 26.720 from 44.280 pre-test. Group B which underwent conventional exercises showed changes post- test to pre- test mean as 46.720 to 44.960. The PDQ- 39 scores

within the group A pre- test to post- test was median of 54.000 to 38.000 which showed considerable reduction as compared with the group B where the median values showed pre-test to post-test as 56.000 to 51.000.

An overwhelming body of evidence shows that Multi – Modal physical therapy offers beneficial preventive and moderating effects on the course of PD. The multi – modal training has a vital mainstay effect on the treatment covering multidimensional symptoms and its associated mortality, which is seen in this study where the intervention was administered through video conferencing on the zoom based online platform.

Even though evidence supports this kind of training in motor symptoms, little or no evidence is known about its effects on fatigue in individual with PD. A range of studies have shown the characteristics of multimodal program were responsible for increased mobility, maintenance of balance, cognitive performance, reduction in falls frequency, improvement in gait parameters, quality of life. Paradoxically, fatigue should have been a more controlled non- motor symptom but rather got trigger due to physical inactivity and reduction in wellbeing.

The association between subjective exhaustion and reduced physical activity is provided credence by the finding that being confined to the house and lack of rehabilitative support systems triggered the fatigue more than before.

Lai B et al 2020, in their study demonstrated that the adults with Parkinson's Disease exercising through a tele rehab system have opened a channel to self-manage them at times when they are devoid of sessions. Their findings supported our study that human- interactive support is required to overcome specific impediments in terms of patient participation, tele- video conferencing and availability of a caregiver.

With pandemic lockdown the availability of health care system was at stake which was taxing on the disease severity. Our study which created an impact on lives of people with PD with an adherence of 70% during the session, also was supportive to study findings of SaraIsernia et al 2020 where they had more than 80% of adherence to the HEAD treatment in clinic and home was reported.

Deepa. S 4224

With respect to fatigue and quality of life, our study protocol Of Three Modal Exercise program was effective when administered through video conferencing. The PD participants obtained positive results on all the 8 dimensions of the PDQ- 39 questionnaire, fatigue severity scale scores. The scale score represented the subjective wellness. Our results also provided support in favor of using multimodal exercise protocol even in mild to moderate stages of PD which coincided with the study done by Van der Kolk NM et al 2019.

A key and innovative feature of this multimodal exercise protocol was the inclusion of exercise that were patient oriented and those who complained about undefined fatigue. This multimodal exercise program intended to focus combination of cardiovascular, strengthening and balance where the key components as endurance, muscle strength and balance (frequent falls) resulting in excessive energy expenditure and hence excessive day time fatigue. There has been no established evidence of motor symptoms causing fatigue whichoccurs earlier than the disease diagnosis and has been shown to worsen with the disease duration. After an initial evaluation, the staff was able to change the composition of the exercises on the basis of level, intensity and mode of exercises.

Out of 5 RCTs only 3 studies showed improvement in fatigue which does not rule out the fact that exercise benefits the population having fatigue related Parkinson's Disease. Ghahari, S et al 2010 in their study compared a self-management group with information being provided to another group, the study concluded improvement in fatigue but not significantly. Winward et al 2011 in their study used supervised gym-based program and compared with a standard care, where fatigue did not improve. Canning et al 2012 compared semisupervised home-based program of treadmill walking with the advice group and showed improvement in fatigue scale. Three groups higher-intensity treadmill exercise, lowerintensity treadmill exercise andstretching and resistance were compared which showed improvement in Gait speed, VO2, muscle strength but not in non-motor symptoms in a study conducted by Shulman, L. M et al. Amirabas Abasi et al in 2020 compared vestibular rehabilitation and conventional

exercises where fatigue and activities of daily living improved.

Altogether these findings highlighted and supported the role of an established protocol to handle Fatigue in the PD population to enhance and maintain physical functioning and allowing the continuity of self-management. Participants feedback that they were physiotherapy sessions independently with the handouts given and by the caregiver assistance, even after the study was over. This added to the goal of the study to accomplished that a feasible protocol should reach the community where in future these pandemics do not cause serious adverse situation to the people with Parkinson's Disease and patients can self-manage themselves.

Future studies should aim at including a salivary cortisol as an objective biomarker as an outcome measure with an aim to reduce fatigue levels which is a major disability concern for patients and care givers.

The limitations of this study were due to teleconferencing they were frequent internet instability issues, the PD geriatric population had difficulty in connecting through the online link provided even after providing a training session before the start of the study. The teleconferencing device laptop camera had its own flaws as the participants moved out of the screen while performing exercises. But the recorded exercise videos and handouts provided made them learn better and perform in the next sessions.

CONCLUSION: -

The Covid- 19 pandemic has left the lives of people more vulnerable to living with disability and compromised quality of life among people Parkinson's Lockdown Disease. restrictions has put a considerable strain on the health professional and patients who were unable to reach each other. But the concept of telerehabilitation though having its own challenges has eased the strain and allowed the dynamics between health infrastructure and patient's needs by video consultation and video rehabilitation. This study has reduced the gap created by the Covid- 19 Pandemic lockdown. This study has given better understanding on delivering the Three Modal - Exercise Program through telerehabilitation to improve fatigue and quality of life in people with Idiopathic Parkinson's Disease which not yet been used in previous studies. The video conferencing has shown to improve their mental health as they met the therapist on daily basis.

Acknowledgement: - Nil

Conflict of interest: - Nil

Authors contribution: - All the authors have contributed to the work and have agreed to the present findings.

Reference

- [1] Kostić VS, Tomić A, Ječmenica-Lukić M. The pathophysiology of fatigue in Parkinson's disease and its pragmatic management. Mov Disord Clin Pract. 2016;3(4):323-330.
- [2] Ravan A, Ahmad FMH, Chabria S, Gadhari M, Sankhla CS. Non-motor symptoms in an Indian cohort of Parkinson's disease patients and correlation of progression of non-motor symptoms with motor worsening. Neurol India. 2015;63(2):166-174.
- [3] Lahiri D, Ardila A. Covid-19 pandemic: A neurological perspective. Cureus. 2020.
- [4] Kumar N, Gupta R, Kumar H, et al. Impact of home confinement during COVID-19 pandemic on sleep parameters in Parkinson's disease. Sleep Medicine. 2021;77:15-22.
- [5] Amatya B, Khan F. Covid-19 in developing countries: A rehabilitation perspective. The Journal of the International Society of Physical and Rehabilitation Medicine. 2020;3(2):69.
- [6] Hall M-FE, Church FC. Exercise for older adults improves the quality of life in Parkinson's disease and potentially enhances the immune response to COVID-19. Brain Sciences. 2020;10(9):612.
- [7] Helmich RC, Bloem BR. The impact of the COVID-19 pandemic on parkinson's disease: Hidden sorrows and emerging opportunities. Journal of Parkinson's Disease. 2020;10(2):351-354.
- [8] Yogev-Seligmann G, Kafri M. Covid-19 social distancing: Negative effects on people with Parkinson disease and their associations with confidence for self-

- management. BMC Neurology. 2021;21(1).
- [9] Elbeddini A, To A, Tayefehchamani Y, Wen C. Potential impact and challenges associated with Parkinson's disease patient care amidst the COVID-19 Global Pandemic. Journal of Clinical Movement Disorders. 2020;7(1).
- [10] Dhamija RK, Garg D. Tele neurorehabilitation for Parkinson's disease: A panacea for the Times to come? Annals of Indian Academy of Neurology. 2020.
- [11] Ambrosio L, Portillo MC, Rodriguez-Blazquez C, et al. Influencing factors when living with Parkinson's disease: A cross-sectional study. Journal of Clinical Nursing. 2019;28(17-18):3168-3176.
- [12] Fasano A, Antonini A, Katzenschlager R, et al. Management of advanced therapies in Parkinson's disease patients in times of humanitarian crisis: The covid 19 experience. Movement Disorders Clinical Practice. 2020;7(4):361-372.
- [13] Elbers RG, Verhoef J, van Wegen EEH, Berendse HW, Kwakkel G. Interventions for fatigue in Parkinson's disease. Cochrane Database of Systematic Reviews. 2014.
- [14] Radder DL, Lígia Silva de Lima A, Domingos J, et al. Physiotherapy in Parkinson's disease: A meta-analysis of present treatment modalities. Neurorehabilitation and Neural Repair. 2020;34(10):871-880.
- [15] Vaartio-Rajalin H, Rauhala A, Fagerström L. Person-centered home-based rehabilitation for persons with Parkinson's disease: A scoping review. International Journal of Nursing Studies. 2019; 99:103395.
- [16] Klucken J, Krüger R, Schmidt P, Bloem BR. Management of Parkinson's disease 20 years from now: Towards Digital Health Pathways. Journal of Parkinson's Disease. 2018;8(s1).
- [17] Orcioli-Silva D, Barbieri FA, Simieli L, Rinaldi NM, Vitório R, Gobbi LT. Effects of a multimodal exercise program on the functional capacity of Parkinson's disease patients considering disease severity and gender. Motriz: Revista de EducaçãoFísica. 2014;20(1):100-106.
- [18] Lai B, Bond K, Kim Y, Barstow B, Jovanov E, Bickel CS. Exploring the uptake and implementation of Tele-monitored home-

<u>Deepa. S</u> 4226

exercise programs in adults with Parkinson's disease: A mixed-methods pilot study. Journal of Telemedicine and Telecare. 2018;26(1-2):53-63.

- [19] Ghahari S, Leigh Packer T, Passmore AE. Effectiveness of an online fatigue self-management programme for people with chronic neurological conditions: A randomized controlled trial. Clinical Rehabilitation. 2010;24(8):727-744.
- [20] Coe S, Franssen M, Collett J, et al. Physical activity, fatigue, and sleep in people with Parkinson's disease: A secondary per protocol analysis from an intervention trial. Parkinson's Disease. 2018; 2018:1-6.
- [21] Marinus J. Health related quality of life in Parkinson's disease: A systematic review of disease specific instruments. Journal of Neurology, Neurosurgery & Description (2002), 1241-248.
- [22] Winward C, Sackley C, Meek C, et al. Weekly exercise does not improve fatigue levels in Parkinson's disease. Movement Disorders. 2011;27(1):143-146.
- [23] Shulman LM, Katzel LI, Ivey FM, et al. Randomized clinical trial of 3 types of physical exercise for patients with Parkinson disease. JAMA Neurology. 2013;70(2):183.
- [24] Pereira MP, Oliveira Ferreira MD, Caetano MJ, et al. Long-term multimodal exercise program enhances mobility of patients with Parkinson's disease. ISRN Rehabilitation. 2012; 2012:1-7.
- [25] Gallo PM, Ewing Garber C. Parkinson's disease. ACSM'S Health and Fitness Journal. 2011;15(4):8-17.
- [26] Ni M, Hazzard JB, Signorile JF, Luca C. Exercise guidelines for gait function in Parkinson's disease: A systematic review and meta-analysis. Neurorehabilitation and Neural Repair. 2018;32(10):872-886.
- [27] Huang Y-Z, Chang F-Y, Liu W-C, Chuang Y-F, Chuang L-L, Chang Y-J. Fatigue and muscle strength involving walking speed in Parkinson's disease: Insights for developing rehabilitation strategy for PD. Neural Plasticity. 2017; 2017:1-9.
- [28] Giardini M, Nardone A, Godi M, et al. Instrumental or physical-exercise rehabilitation of balance improves both balance and gait in Parkinson's disease. Neural Plasticity. 2018; 2018:1-17.
- [29] Cheng Y-C, Su C-H. Erratum: Cheng, Y.-C., et al. evidence supports PA prescription

- for Parkinson's disease: Motor symptoms and non-motor features: A scoping review. int. J. Environ. Res. public health 2020, 17, 2894. International Journal of Environmental Research and Public Health. 2020;17(14):5024.
- [30] Orcioli-Silva D, Barbieri FA, Simieli L, Rinaldi NM, Vitório R, Gobbi LT. Effects of a multimodal exercise program on the functional capacity of Parkinson's disease patients considering disease severity and gender. Motriz: Revista de EducaçãoFísica. 2014;20(1):100-106.
- [31] Fan B, Jabeen R, Bo B, et al. What and how can physical activity prevention function on Parkinson's disease? Oxidative Medicine and Cellular Longevity. 2020; 2020:1-12.
- [32] Cusso ME, Donald KJ, Khoo TK. The impact of physical activity on non-motor symptoms in Parkinson's disease: A systematic review. Frontiers in Medicine. 2016;3.
- [33] Martignon C, Pedrinolla A, Ruzzante F, et al. Guidelines on exercise testing and prescription for patients at different stages of Parkinson's disease. Aging Clinical and Experimental Research. 2020;33(2):221-246.
- [34] Ellis TD, Dibble LE, Peterson DS. Moving beyond effectiveness. Journal of Neurologic Physical Therapy. 2019;43(1):1-2.
- [35] Canning CG, Allen NE, Dean CM, Goh L, Fung VSC. Home-based treadmill training for individuals with Parkinson's disease: A randomized controlled pilot trial. Clinical Rehabilitation. 2012;26(9):817-826.
- [36] Abasi A, Raji P, Friedman JH, et al. Effects of vestibular rehabilitation on fatigue and activities of daily living in people with Parkinson's disease: A pilot randomized controlled trial study. Parkinson's Disease. 2020; 2020:1-7.
- [37] Isernia S, Di Tella S, Pagliari C, et al. Effects of an innovative telerehabilitation intervention for people with Parkinson's disease on quality of life, motor, and nonmotor abilities. Frontiers in Neurology. 2020;11.