

The Effects of Below Knee Compression Garments on Functional Performance in Individuals with Parkinson Disease

Veronica Southard,^{1*} Joanne DiFrancisco-Donoghue,² James Mackay,³ Stephanie Idjadi,⁴ Neil Wright⁵

^{1*}Associate Professor Department of Physical Therapy, School of Health Professions, New York Institute of Technology, Building 500, Room 501, Old Westbury, NY 11568.

²New York Institute of Technology School of Osteopathic Medicine, Academic Health Care Center, Department of Physical Therapy, Riland Building, Old Westbury, New York 11568.

^{3,4,5}New York Institute of Technology, Building 500, Room 501, Old Westbury, NY 11568.

Abstract

Background: Symptoms of Parkinson's disease (PD) include bradykinesia, gait abnormalities, balance deficits, restless leg syndrome, and muscular fatigue. Compression garments (CG) have been shown to improve performance in athletes by increasing venous return and reduce lactic acid.

Objective: Assess the effect of compression garments on the performance of 3 standardized functional tests in persons with PD.

Methodology: The functional tests selected represented strength, endurance, and mobility measures in individuals with PD. Nineteen males and 2 females (age 48-85) with PD participated in this cross-over design study. Subjects were randomly assigned to test under two conditions on two separate days: 1) wearing below knee CG 2) wearing sham stockings. Outcome measures included 5 Times Sit to Stand (5XSTS), gait speed, and 6 Minute Walk Test (6MWT). There were seven days between trials.

Results: A paired t-test was used for each dependent variable. Significance was set at $p < 0.05$. There were no significant differences found between the CG and sham socks for all outcome measures. Paired t-tests for the dependent variables were Gait Speed $p=.729$; 5XSTS $p=.880$; 6MWT $.265$; RPE $p=.100$.

Conclusion: Data to support the use of compression garments for enhanced proprioception, muscle power, speed, and endurance is in need of further study with the PD population. In particular, it is recommended that future studies assess the possible physiological benefits of compression garments when worn during exercise interventions.

Key words: Parkinson's disease, Knee Compression.

Corresponding Author:

Veronica Southard, PT, DHSc, GCS,
Associate Professor Department of Physical Therapy,
School of Health Professions,
New York Institute of Technology,
Building 500, Room 501,
Old Westbury, NY 11568,
516 686 7671,
516 686 7699 Fax
vsouthar@nyit.edu

Introduction

Parkinson's disease (PD) is a progressive movement disorder diagnosed in 1% of the US population over age 65. ^(1, 2) This disease presents as a progressive loss of neurons in the substantia nigra of the midbrain; thus altering the nigrostriatal neural conduction. ⁽³⁾

Clinical presentations of PD vary markedly between individuals. Typical motor symptoms include rigidity, resting tremors, bradykinesia, and postural instability. ⁽⁴⁾ Other symptoms individuals with PD often have are speech disorders, gait deficits, postural adaptations, muscular weakness, fatigue, and reduced function. ⁽⁵⁻⁷⁾ In addition, over 20% of individuals with PD suffer from Restless Leg Syndrome (RLS). ⁽⁸⁾ RLS causes leg discomfort in some people with PD that affects the ability to sleep and causes daytime drowsiness, fatigue, chronic insomnia, sleep maintenance insomnia, intense dreaming, and low quality of life. ⁽⁸⁾

The cause of fatigue and decreased endurance is unknown but thought to be associated with disease processes involving injuries to the basal ganglia and RLS. Bradykinesia also increases fatigue by prolonging the time required to complete activities and tasks. The individual must work harder to carry out simple movements or tasks. Muscles that do not move well or are poorly conditioned, atrophy. ⁽⁹⁾ Loss of muscle strength increases fatigue and decreases endurance. ⁽¹⁰⁾

Over the last decade, compression garments (CG) have become popular among athletes and fitness enthusiasts. Compression garments can be whole body or part specific (i.e. socks, shorts, pants, sleeves), that provide continual external pressure to the body. ^(11, 12)

Compression garments improve venous return by decreasing transmural pressure. ⁽¹³⁾ This leads to local dilation of arteries and decreases capillary resistance, which subsequently increases blood flow. The improved oxygenation and lactate removal allows a person to train at a higher intensity for longer periods of time. ⁽¹⁴⁾ Compressive garments also attenuate muscle oscillation during exercise. This excessive movement leads to a higher oxygen requirement, increased lactic acid production, and increases the potential for fatigue related injuries. Compression reduces this vibration in the

muscle, thus conserving energy, reducing lactic acid production, improving performance and endurance. ^(15, 16) Compression has also shown some evidence of improving RLS symptoms. ⁽¹⁷⁾

Other evidence suggests that CG, improve joint awareness, and alters submaximal oxygen usage during exercise. During post exercise recovery it has been shown to alter local blood flow and protein or metabolite clearance, reduce swelling and reduce perceived muscle soreness. ⁽¹²⁻²³⁾ These events may lead to decreased delayed onset muscle soreness. Little is known about the performance effects of CG's on those with health conditions such as PD. To date, the majority of research on CG has been done using athletes as participants. Until there is a cure, interventions that improve the signs and symptoms or slow down the symptom progression of PD have merit.

The purpose of this study was to assess the possible benefit of CG on functional test results in individuals with PD when compared to sham stockings. We also assessed for any changes on Borg rate of perceived exertion (RPE) during these activities, between the sham stockings and compression garments. We hypothesized that wearing a lower leg compression garment would improve functional performance and gait in individuals with PD.

Methodology

The study was organized and conducted at the Adele Smithers Parkinson's Disease Treatment Center of the New York Institute of Technology, College of Osteopathic Medicine (Old Westbury, NY). A flyer was placed on the bulletin board in the clinic area. The study was also introduced at an exercise class. The study was approved by the New York Institute of Technology Institutional Review Board, and all participants signed written informed consent. Twenty-one Caucasian participants (19 male, 2 female) who were diagnosed with PD by a neurologist were consented to participate in this study. The mean age of participants was 69.7 SD +/- 7.8 years. The mean Unified Parkinson Disease Rating Scale (UPDRS) motor score was 40.5 SD +/- 10.7. All of the participants were on PD medications. One male subject withdrew due to illness. The inclusion criteria included participants with an age range between 48-85 years old; Hoehn

and Yahr scale stages 1-3; pain no greater than a 3/10 grossly; independent in ambulation with or without a device for six minutes; and able to follow the instructions. Exclusion criteria included persons with fluctuating response to PD medications; disabling dyskinesia; cognitively impaired; any other significant neurological, cardiovascular or musculoskeletal condition; participants who were unable to walk six minutes; BP > 140/90 or < 90/50; previous poor tolerance to compression. Using the table for sample sizes, it was determined that 20 subjects would be necessary for a power of 80 with an alpha of .05.⁽¹⁸⁾

A repeated measure design with a Latin Square was used in order to randomize the treatment conditions. Each participant performed all outcome measures on two separate trials separated by 7 days, during which they randomly wore either below knee compression garments or sham stockings. The sham socks were a regular pair of black cotton polyester knee high socks, which were cut at the ankle and did not provide any compression to the lower extremity. See figure 1. Randomization of the participants was based on the date of the initial visit. If the assessment date was an even number, the participant received compression garments. The participant performed 6 Minute Walk Test (6MWT) a measure of functional endurance, gait speed (GS) overall mobility, and 5 Times Sit to Stand (5XSTS) lower extremity strength, wearing either the compression garments for the experimental condition or sham stockings for the control condition.

Figure 1. Compression and sham socks



Demographic data was recorded on each participant, which included; age, sex, height, weight, UPDRS, past medical history, medication time, personal physician and a calf girth measurement. In order to determine the stride length for the pedometer, the participants were asked to ambulate 10 steps at a comfortable pace. The total distance ambulated was divided by 10 in order to calculate stride length. The stride length was entered in to the pedometer before the subject initiated the 6MWT.

The calf girth was measured in centimeters at the greatest circumference to determine the size of the compression garment based on the manufacturer's guidelines. Prior to administering the tests and afterwards, the participants were asked to close their eyes while researchers donned/doffed the garments on each of the participants. The participants performed the 6MWT, Gait Speed, and 5SXTS in a randomized order.

Vital signs including blood pressure, respiration rate, heart rate and Borg RPE were documented pre and post the 6MWT. Each subject sat quietly for 10 minutes prior to taking resting vitals. The 6MWT test is considered a sub maximal test that measures a person aerobic capacity. It was completed on a 30-meter course using two cones to mark the boundaries. It was administered to measure functional endurance and determines the distance a person can walk in 6 minutes. According to Steffen et al,⁽¹⁹⁾ this test has high test retest reliability Interclass Correlation Coefficient (ICC= 0.95-0.96) for individuals with PD, also, the Minimal Detectable Change (MDC) for individuals with PD is 82m. For the 6MWT, the clinician affixed the pedometer to the subject's waist. The Digi-Max pedometer model used in this study has been shown to be a valid distance measure in persons with PD.⁽²⁰⁾ Following the recommendations of the American Thoracic Society guidelines for the 6MWT, the participants were instructed to cover as much distance as possible in 6 minutes at a continuous and comfortable pace.⁽²¹⁾ All participants were experienced with this test. Participants completed this test individually one time under each condition. Researchers managed the time and informed the subject at one-minute intervals. At the completion of the 6MWT, the distance on the

pedometer was recorded; vital signs and the Borg RPE were repeated immediately.

The 5XSTS test was used as a measure of the strength of the lower body. ⁽²²⁾ There are numerous studies that support the reliability of this tool with this population. ^(23, 24) Two studies done with 5XSTS for persons with PD demonstrated excellent test-retest reliability of ICC=0.76 and inter-rater reliability of 0.99 ⁽¹⁹⁾ ICC= 0.91 (0.82-0.96) ⁽²²⁾ respectively. Duncan et al, ⁽²³⁾ assessed the criterion validity between quadriceps maximal voluntary isometric contraction, (MVIC) and 5XSTS, found a correlation of $r^2 = 0.548$. The MDC for 5XSTS has not been established in PD population however, the MDC for healthy community dwellers is 4.2 sec. ⁽²⁵⁾ During the 5XSTS, a standard chair was used (chair height 43cm) with no armrest. Each participant completed a single STS to demonstrate an understanding of the test. The participants completed one trial of this test under the supervision of the researchers. The participants were instructed to move to the center of the chair, cross their arms, and perform a complete sit to stand, 5 times, as quickly as possible. The time began as soon as the participants' buttocks left the chair and stopped when the participants' buttock touched the chair on the fifth repetition.

Gait speed is considered a reliable measure of an individual's overall walking performance and mobility status. ⁽²⁶⁾ Gait speed is a reliable and responsive test for measuring walking speed in patients with PD (ICC= 0.81). ⁽²⁷⁾ The concurrent validity between Berg Balance Scale and gait speed showed a correlation of $r^2 = 0.73$ and 0.64. ⁽¹⁹⁾ The MDC for gait speed

in the PD population is 0.18 m/s. ⁽¹⁹⁾ During gait speed measurement, three trials were conducted in which the participants were asked to walk 3 meters at a comfortable pace, acceleration and deceleration were accounted for with a 2 meter walk on and off. ⁽²⁶⁾ Out of three trials, the best two were averaged to calculate the comfortable gait speed.

The Borg RPE scale 6-20 was used as a measure of perceived effort. Eaton and colleagues, ⁽²⁸⁾ found the Minimal Clinically Important Difference (MCID) for the Borg RPE 10 point scale to be 1 unit. This is a 10% change. Their participants were pulmonary patients. Effect size changes in Eaton's study were based on the Borg RPE score during trials with and without supplemental oxygen during the 6MWT. In addition, a retrospective review, Reis et al ⁽²⁹⁾ also reviewed MCID, using the 10 point scale for the Borg RPE and found that for large effect sizes of .8 or greater improvements in the Borg RPE changes 2 units or more was required. The participants were guarded for safety each trial.

Results

Descriptive analysis of the participants was completed. Paired t tests were used to assess for differences in outcomes of 6MWT, gait speed, and 5XSTS. The mean, standard deviation and the standard error mean from the paired sample t test for the sham and experimental scores for the variables are presented in table 1. None of the mean differences of the variables met the $p = .05$ or less value qualification and therefore, these differences in means were considered insignificant.

Table 1. Mean Scores for Paired Variables

Dependent Variables	Mean ±SD	N	p-value
Experimental gait speed (meters/sec)	0.782±0.887	20	0.729
Sham gait speed	0.769±0.530	20	
Experimental 5x sit to stand (sec)	16.41±12.182	20	0.880
Sham 5x sit to stand	16.26±12.259	20	
Experimental. 6 min walk test (meters)	110.93±123.94	20	0.265
Sham 6 min walk test	101.37±140.46	20	
Experimental Rate of Perceived Exertion (6-20 scale)	12.20±1.576	20	1.000
Sham Rate of Perceived Exertion	12.20±2.093	20	

Discussion

To date, the majority of research on compression garments has included athletes as participants. To our best knowledge, this is the first study to analyze the benefits of compression garments on individuals with PD. This study sought to address this gap in knowledge by testing the effects of compression garments on the motor symptoms of PD, through single performances on three standard outcomes; which included, the 5-Times Sit-to-Stand Test, the 6-Minute Walk Test, and the gait speed test.

In consideration of the 5-Times Sit-to-Stand test, we likened our short burst of sit-to-stand to previous studies on volleyball players, who completed 10 vertical jumps. ⁽³⁰⁾ This study failed to demonstrate that compression garments increase vertical jump height; however, the participants were able to maintain the power of the jump on the following jump efforts. It is believed that the enhanced performance, in this power-based activity, is due to increased proprioception. ⁽³⁰⁾ Compression garments are thought to refine our proprioceptive abilities. ⁽³⁰⁾ Better proprioception improves efficiency of movement by reducing the number of muscles that are activated, thus decreasing the demand on the muscle. ⁽³⁰⁾ The volleyball study found a

reduction in muscle oscillation when wearing the compression shorts. ⁽³⁰⁾ It has been suggested that excess muscle oscillation can contribute to fatigue and interference to optimal muscle recruitment. ⁽³¹⁾ Our participants wore below knee compression garments, which may not have provided enough protection to reduce muscle oscillations or improve proprioception of the lower extremity. Compression shorts might have been a better choice for this test. The mean difference in time between the two trials in the 5XSTS was below the minimal detectable change of 4.2 seconds.

The 6-Minute Walk Test was used as a performance based measure of exercise capacity and endurance in community dwelling older adults. ⁽²¹⁾ Its original purpose was to assess exercise tolerance of patients diagnosed with chronic respiratory disease and heart failure. ⁽²¹⁾ Our study demonstrated that wearing below knee compression garments did not statistically improve the 6-minute walk distance. However, participants completing the compression garment trial completed a mean of 31.09 meters greater distance than the sham stockings trial. The minimal detectable change for subjects with PD is 82 meters. ⁽¹⁹⁾ Although some studies have shown compression garments to improve endurance in athletes, studies supporting the endurance

enhancing abilities of compression garments are inconclusive.⁽³⁰⁾ Most studies discussing the benefits of compression garments focused on improvements in blood flow; however, these results don't specifically improve exercise endurance.⁽³¹⁻³³⁾ The enhancements in overall circulation help more with the speed of muscle recovery time post-exercise and delayed onset muscle soreness.⁽³⁴⁾ Bringard et al.⁽³³⁾ found that compression garments can improve circulation, allowing the body to use less energy at the same running speed. However, the sample size in this study was small and the results were completely self-reported by the participants.

There is a void in the literature that concerns the assessment of compression garments and gait speed measurements. Contrary to the supportive findings of gait speed by Lim,⁽²⁷⁾ other research supports that the gait speed test may not be an appropriate gait speed parameter for patients with Parkinson's disease.⁽³⁵⁾ This is because the test does not appropriately distinguish those participants who had freezing and hesitation from those who walked slowly without hesitations and freezing.⁽³⁵⁾ Therefore, it should be noted that there can be variability in spatiotemporal gait measures, like the gait speed test. We note however, that freezing of gait was not evidenced with any of the participants in this study. The mean time difference between the two trials in the gait speed test was below the minimal detectable change (.18 m/s) for those with PD.⁽¹⁹⁾

While no performance differences were observed in our study, the results are subject to several considerations. Firstly, our study under-recognized the potential importance of the non-motor symptoms (cognitive impairment, depression, anxiety, psychosis, apathy, compulsive disorders, sleep disorders) associated with the disease. Our study was limited in that it did not screen for the non-motor symptoms from trial one to trial two. Given the knowledge that non-motor symptoms can cause considerable physical burden on patients with PD, it is important to establish that the intensity of these non-motor symptoms remains consistent through both trials in order to properly depict our results.

The benefits seen with athletes wearing compression garments are associated with prolonged use of the compression garments

during training.⁽³⁶⁾ The participants in this study wore the CG only one time. Our participants did not train with the compression garments on. We posit that trials with compression garment use during therapeutic interventions may provide the similar benefits for those with PD. Future studies should include trials with participants exercising while wearing compression garments.

Limitations

A limitation in our study is the time our participants came in for data collection. While still in a therapeutic window of their medications, some participants were unable to come precisely the same time for each trial. The best results would be attained when participants are at their peak dose.⁽³⁷⁾ This varies among individuals. This study was likely to have been affected by the small sample size (n=20). Although our study had power and the size was adequate to detect differences between compression garments vs. sham stockings, a larger sample size may have led to an increased ability to detect differences. Lastly, since there was only one woman that completed the study, no gender differences could be assessed.

Conclusion

This is the first study to observe the effects of compression garments on individuals with PD. Although no benefit was noted in the performance of single trial compression garment use among individuals with PD; future trials with exercise intervention components are warranted based on results seen in the literature with athletes. Therefore, data to support the use of compression garments for enhanced proprioception, muscle power, speed, and endurance is in need of further study with the PD population. In particular, it is recommended that future studies assess the possible physiological benefits of compression garments when worn during exercise interventions.

Acknowledgement

The authors would like to recognize Dipali Patel, Simony Patel, and Jonathan Pavlica for their assistance in this project.

References:

1. Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. *Arch Neurol.* 1999; 56:33-39.
2. Borg G. Perceived exertion as an indicator of somatic stress. *Scand J Rehabil Med.* 1970; 2:92-98.
3. Agid Y. Parkinson's disease: pathophysiology. *Lancet.* 1991; 337:1321-1324.
4. Obeso JA, Rodriguez-Oroz MC, Rodriguez M, Arbizu J, Gimenez-Amaya JM. The basal ganglia and disorders of movement: pathophysiological mechanisms. *News Physiol Sci.* 2002; 17:51-55.
5. Protas EJ, Stanley RK, Jankovic J, MacNeill B. Cardiovascular and metabolic responses to upper- and lower-extremity exercise in men with idiopathic Parkinson's disease. *Phys Ther.* 1996; 76:34-40.
6. Morris ME. Movement disorders in people with Parkinson disease: a model for physical therapy. *Phys Ther.* 2000; 80:578-597.
7. Cano-de-la-Cuerda R, Perez-de-Heredia M, Miangolarra-Page JC, Munoz-Hellin E, Fernandez-de-Las-Penas C. Is there muscular weakness in Parkinson's disease? *Am J Phys Med Rehabil.* 2010; 89:70-76.
8. Ylikoski A, Martikainen K, Partinen M. Parkinson's disease and restless legs syndrome. *Eur Neurol.* 2015; 73:212-219.
9. Milanovic S, Filipovic SR, Radovanovic S, Blesic S, Ilic NV, Kostic VS, et al. Changes in motor cortex excitability associated with muscle fatigue in patients with Parkinson's disease. *Vojnosanit Pregl.* 2013; 70:298-303.
10. Nirenberg MJ. Dopamine agonist withdrawal syndrome: implications for patient care. *Drugs Aging.* 2013; 30:587-592.
11. Born DP, Sperlich B, Holmberg HC. Bringing light into the dark: effects of compression clothing on performance and recovery. *Int J Sports Physiol Perform.* 2013; 8:4-18.
12. MacRae BA, Cotter JD, Laing RM. Compression garments and exercise: garment considerations, physiology and performance. *Sports Med.* 2011; 41:815-843.
13. Ali A, Caine MP, Snow BG. Graduated compression stockings: physiological and perceptual responses during and after exercise. *J Sports Sci.* 2007; 25:413-419.
14. Agu O, Baker D, Seifalian AM. Effect of graduated compression stockings on limb oxygenation and venous function during exercise in patients with venous insufficiency. *Vascular.* 2004; 12:69-76.
15. Bottaro M, Martorelli S, Vilaca J. Neuromuscular compression garments: effects on neuromuscular strength and recovery. *J Hum Kinet.* 2011; 29A:27-31.
16. Bringard A, Perrey S, Belluye N. Aerobic energy cost and sensation responses during submaximal running exercise--positive effects of wearing compression tights. *Int J Sports Med.* 2006; 27:373-378.
17. Scanlan AT, Dascombe BJ, Reaburn PR, Osborne M. The effects of wearing lower-body compression garments during endurance cycling. *Int J Sports Physiol Perform.* 2008; 3:424-438.
18. L Portney MW. *Foundations of Clinical Research Applications to Practice.* 3rd Table C.2 ed.: Pearson Prentice Hall; 2009.
19. Steffen T, Seney M. Test-retest reliability and minimal detectable change on balance and ambulation tests, the 36-item short-form health survey, and the unified Parkinson disease rating scale in people with parkinsonism. *Phys Ther.* 2008; 88:733-746.
20. Southard V, De Francisco-Donoghue J. The 6MWT: Validity of a pedometer and instruction on 15m and 30m courses in adults with Parkinson's disease. *J Geriatrics and Palliative Care.* 2014; 2:4.
21. Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A, et al. The 6-min walk test: a quick measure of functional status in elderly adults. *Chest.* 2003; 123:387-398.
22. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport.* 1999; 70:113-119.
23. Duncan RP, Leddy AL, Earhart GM. Five times sit-to-stand test performance in Parkinson's disease. *Arch Phys Med Rehabil.* 2011; 92:1431-1436.

24. Paul SS, Canning CG, Sherrington C, Fung VS. Reproducibility of measures of leg muscle power, leg muscle strength, postural sway and mobility in people with Parkinson's disease. *Gait Posture*. 2012; 36:639-642.
25. Schaubert KL, Bohannon RW. Reliability and validity of three strength measures obtained from community-dwelling elderly persons. *J Strength Cond Res*. 2005; 19:717-720.
26. Kegelmeyer DA, Kloos AD, Thomas KM, Kostyk SK. Reliability and validity of the Tinetti Mobility Test for individuals with Parkinson disease. *Phys Ther*. 2007; 87:1369-1378.
27. Lim LI, van Wegen EE, de Goede CJ, Jones D, Rochester L, Hetherington V, et al. Measuring gait and gait-related activities in Parkinson's patients own home environment: a reliability, responsiveness and feasibility study. *Parkinsonism Relat Disord*. 2005;11:19-24
28. Eaton T, Garrett JE, Young P, Fergusson W, Kolbe J, Rudkin S, et al. Ambulatory oxygen improves quality of life of COPD patients: a randomised controlled study. *Eur Respir J*. 2002; 20:306-312.
29. Ries JD, Echternach JL, Nof L, Gagnon Blodgett M. Test-retest reliability and minimal detectable change scores for the timed "up & go" test, the six-minute walk test, and gait speed in people with Alzheimer disease. *Phys Ther*. 2009; 89:569-579.
30. Kraemer W, Bush J, Bauer J, Triplett-McBride N, Paxton N. Influence of Compression Garments on Vertical Jump Performance in NCAA Division I Volleyball Players. *Journal of strength and conditioning research / National Strength & Conditioning Association*. 1996; 10:180-183.
31. Doan BK, Kwon YH, Newton RU, Shim J, Popper EM, Rogers RA, et al. Evaluation of a lower-body compression garment. *J Sports Sci*. 2003; 21:601-610.
32. Sperlich B, Born DP, Haegele M, Zinner C, Holmberg HC. Effects of compression textiles on performance enhancement and recovery. *Sportverletz Sportschaden*. 2011; 25:227-234.
33. Dascombe BJ, Hoare TK, Sear JA, Reaburn PR, Scanlan AT. The effects of wearing undersized lower-body compression garments on endurance running performance. *Int J Sports Physiol Perform*. 2011; 6:160-173.
34. Bringard A, Perrey S, Belluye N. Aerobic energy cost and sensation responses during submaximal running exercise--positive effects of wearing compression tights. *Int J Sports Med*. 2006; 27:373-378.
35. Rochester L, Yarnall AJ, Baker MR, David RV, Lord S, Galna B, Burn DJ. Cholinergic dysfunction contributes to gait disturbance in early Parkinson's disease. *Brain*. 2012; 135:2779-88.
36. Partsch H, Mosti G. Thigh compression. *Phlebology*. 2008; 23:252-258.
37. Yeh KC, August TF, Bush DF, Lassetter KC, Musson DG, Schwartz S, et al. Pharmacokinetics and bioavailability of Sinemet CR: a summary of human studies. *Neurology*. 1989; 39:25-38.