[1]MPT in Cardiovascular and Pulmonary Science, RK University, Rajkot, Gujarat, India

[2]Dean, Faculty of Medicine, Director, School of Physiotherapy, RK University, Rajkot, Gujarat, India

Corresponding author: Jigna Pansuriya, [1]MPT in Cardiovascular and Pulmonary Science, RK University, Rajkot, Gujarat, India,
jigna.pansuriya95@gmail.com

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The impact of physiotherapy intervention in patients with peripheral arterial disease (PAD): an experimental clinical trial

Jigna Pansuriya[1], Priyanshu Rathod[2]

Abstract:

Background: The peripheral arterial disease affects more than 202 million people worldwide. It happens when the arteries in the legs and feet become clogged with fatty Plaque. This can lead to pain, Ischemia, intermittent claudication and many other symptoms.

Objectives: 1. To evaluate the impact of physiotherapy intervention on ABI and walking performance in patients with mild and moderate peripheral arterial disease. 2. To analyses the effect of patient's specific and severity-based exercise protocol in peripheral arterial disease.

Methodology: In this experimental clinical trial 30 patients with PAD distributed according to the severity of PAD based on ABI in Group A (n=15): Mild PAD (ABI-0.94 to 0.75) and Group B (n=15): Moderate PAD (ABI-0.74 to 0.50). Exercises were prescribed under the category of supervised and home-based exercises. Supervised exercise- treadmill walking was given 3 days a week for 4 weeks. Home Exercise- calf raising exercise was given 3 times a day, every day for 6 weeks. Patient's specific and severity-based protocol was given. Outcomes ABI and WIQ were taken on day 1, end of 2nd, 4th and 6th week.

Results: The data was analyzed using SPSS version 21. The result shows significant improvement ($p < 0.05$) in intragroup comparison in ABI and WIQ after 2nd, 4th and 6th week for both group A-mild PAD and group B-moderate PAD.

Conclusions: severity based, and patient's specific physiotherapy intervention are beneficial for improving the physical and functional performance of patients with mild and moderate PAD.

Keywords: Peripheral Arterial Disease (PAD), Ankle Brachial Index (ABI), Walking performance, intermittent claudication (IC), Physiotherapy intervention, Exercise

Introduction:

The peripheral arterial disease affects more than 202 million people worldwide which is a condition of partial or complete occlusion of one or more non-coronary arteries i.e., superficial femoral artery, popliteal artery etc. In PAD peripheral arteries blood flow is reduced which leads to ischemia due to atherosclerosis and endothelial dysfunction. [1-3] In general Indian population > 45 years of age is 18% and it increases with age and > 70 years of age is 29%. [16] The symptoms depend on the degree of vascular stenosis/ occlusion, obstruction and location of the lesion. Clinical manifestation varies from a complete absence of symptoms to atypical symptoms, pain in the lower extremity with exertion, and most severe form-critical limb ischemia (rest pain, ulceration and gangrene). [5, 6] According to severity, there is mild, moderate and severe PAD. In which ankle brachial index is reduced <0.94. [2] In patients with mild and moderate PAD, primary symptom reported is intermittent claudication. [4,7] In IC cramping and aching pain in the lower extremity in calf, thigh and buttocks while walking due to increased oxygen demand in working muscles secondary to physical activity. Which forces the patient to interrupt the exertion which subsides with rest. [4] Pain most commonly develops to distally from site of occlusion and atherosclerotic changes of arteries. Which affects walking performance and compromise functional activities of Daily Living (ADLs) which further affects the quality of life. [1-3,15] Risk factors include age, diabetes, smoking and hypertension.[3] Ankle-brachial index (ABI) is a non-invasive assessment of the degree of occlusion and sensitive, specific and cost-effective diagnostic as well as a prognostic tool for predicting PAD compared to another diagnostic tool. An abnormal ABI below 0.9 is an independent marker of cardiovascular risk. [6,7,20] Walking impairment questionnaire is a PAD-specific measure which includes walking distance, speed and severity of symptoms and used for evaluating walking impairment in patients with PAD. [12,13,14] Structural exercise may have a role in micro capillarization and increase oxygen-carrying ability to enhance ADLs, which further improve QOL. [1, 9] Some studies suggest that exercise in patients with PAD manages the improvement in the walking performance. Supervised treadmill walking and home-based calf raise exercise are efficient, effective and responsible for the improvement in physical and functional performance. Which is easily manageable and possible for the patients and have a role in increased vasodilatation for better improvement in walking ability. [8, 26] So aim of the study is to evaluate the impact of physiotherapy intervention in patients with peripheral arterial disease.

Materials and Methods:

In this experimental clinical trial total 30 patients were selected through purposive sampling from Dekiwadia institute of vascular science, Rajkot. Patients were first evaluated and diagnosed by physician or surgeon then patient's consent and assessment were taken. In this study age 25-75 years, male and female, ABI 0.94 to 0.50 in either leg and patients having intermittent claudication and pain in lower extremity and who was willing to participate included.[1,8,27,28]   Patients

having ulcer in the lower limb and critical limb ischemia and history of hospitalization in last 6 months were excluded[29]. 30 patients allocated according to severity of PAD according to Ankle Brachial Index in to two groups in group A 15 patients having mild PAD- ABI 0.94 to 0.75 and in group B 15 patients having moderate PAD- ABI 0.74 to 0.50. Then counselling of patients was done, and exercise was monitored by a logbook. And exercise protocol was given along with medication.

Group A and B received supervised exercise treadmill walking 3 days/ week for 4 weeks and home-based exercise calf raising exercise 3 times a day: every day for 6 weeks. However, an intervention was given according to severity. Within-group patient's specific exercise was given in which frequency, intensity and duration were selected according to the patient's need. Intervention was given in Group A- Mild PAD: Supervised exercise: 3 days/ week for 4 weeks [1] :Warm-up exercise include marching on a place and walking (2-3 minute), treadmill walking at speed produce claudication pain grade- 3 (which was intense pain) within 5 to 10 minute with grade 0% followed by rest (30 minutes) Cool-down exercise include stretching of major muscle group (2 minutes), Every week speed was increased 0.3 km/m or grade by 1%. Home-based exercise was given 3 times a day; every day for 6 weeks [8]includes Calf raising exercise – repeated until the pain in calf following initiation of pain perform extra five repetitions for secured ischemia. Intervention was given in group B- Moderate PAD: Supervised exercise: 3 days/ week for 4 weeks [1,19] Warm-up exercise including marching on a place and walking (3-4 minute), treadmill walking at

a speed produce claudication pain grade- 2 (which was moderate pain- patient can be distracted) within 5 to 6 minute with grade 0% followed by rest (40 minute), Cool-down exercise including stretching of major muscle group (2 minute), Every week speed was increased 0.3 km/m or grade by 1%. Progressive relaxation exercise involved tensing the specific muscle groups for 7 to 10 second followed by relaxing for 15 to 20 second as per Jacobson's protocol (2-3 minute) Home-based exercise were 3 times a day; every day for 6 weeks [8]. Exercise included was Calf raising exercise – repeated until the pain in calf following initiation of pain perform extra five repetitions for secured ischemia.

Outcome measures:

Ankle Brachial Index: [6,21,24]: The ankle-brachial index is defined as a ratio of highest systolic pressure of 2 ankles and highest systolic pressure of upper limb it was measured by highest systolic pressure of lower limb arteries (either anterior tibial artery, posterior tibial artery or dorsalis pedis artery) and higher 2 systolic pressure of upper limb. ABI is a non-invasive, easily performed, cost effectiveness and clinically valid assessment method used as a diagnostic tool for predicting lower extremity PAD. ABI < 0.9 interpreted as a PAD in which ABI 0.94 to 0.75 predicted as mild PAD, 0.74 to 0.50 predicted as moderate PAD and < 0.5 predicted severe PAD.

Walking Impairment Questionnaire [13,14,22]: WIQ is used to measure walking performance in PAD patients. It is a scoring of 0 – 100 and two part which measure walking distance and walking speed. In which 100 is the maximal physical ability

and greater walking performance and 0 is extreme limitation and lower walking performance. Higher the score suggests greater walking performance. It is a dependable (sensitivity 0.90 and specificity 0.73) and valid clinical tool which is used to check the effectiveness of intervention given to the patients.

Result:

Data was Analyzed using statistical software SPSS version 21. Descriptive statistics included computation of means and standard deviations. Intragroup analysis for both group A and group B were done using Repeated measures ANOVA test. Confidence interval (CI) was 95%, and the level of significance was considered < 0.05.

As the table 2 and 3 shows p value < 0.05 suggests significant improving in ABI and WIQ after the 2nd, 4th and 6th week of intervention in group A and B.

Discussion:

The aim of the study was to evaluate the impact of physiotherapy intervention on physical and functional performance of mild and moderate peripheral arterial disease patients.

In this study total 30 patients allocated according to severity of PAD into two groups in which group A was mild PAD and group B was moderate PAD and in both groups total 6 weeks of exercise protocol was given. The changes in physical and functional performance were seen with ABI and WIQ before and after 2nd, 4th and 6th week of the intervention in both mild and moderate PAD group.

To evaluate the impact of physiotherapy intervention on ABI and walking performance in patients with mild and moderate peripheral arterial disease The within-group comparison of both outcome measures ABI and WIQ Were done using statistical test Repeated Measures ANOVA. Result shows statistically significant improvement ($p < 0.05$) in ABI and WIQ score from day 1 to end of 2nd, 4th and 6th week in group A and B and mean difference suggests that between 2nd to 4th week there is more improvement. In patients with PAD due to atherosclerosis and endothelial dysfunction vasomotor tone is disturbed, it causes the hemodynamic changes in the leg that affects ABI therefore walking performance is also affects.

Due to exercise causes changes in muscle metabolism and it improves intramuscular vasodilatation because of muscle cannot keep contraction without oxygen and because of oxygen deficit causes release of vasodilators substance include adenosine, potassium, ions, ATP etc. that improves vasomotor tone and leads to local arteriolar vasodilatation. And during exercise all the capillaries opens and this opening of dormant capillaries diffuse oxygen and other nutrients from capillaries to muscle fibers and improve micronutrients supply to the muscle through the plasma protein by microcapillaries. All the changes improve the arterial pressure therefore improvement in ABI occurs that also improve walking performance. [11]

In mild and moderate PAD Treadmill walking increases exercise tolerance and it shows the improvement in walking performance. Calf raising exercise also improves walking performance. [1, 25]

Table 1: Demographic distribution of group A and group B

Demographic data		Group A	Group B
Age (years)	**Mean ± SD**	58.93 ± 7.00	61 ± 7.16
No. Of patients in each age level	**Age 25- 41**	0 (0%)	0 (0%)
	AGE 42- 58	9 (60%)	5 (33.33%)
	AGE 59-75	6 (40%)	10 (66.66%)
Gender (**male: female**)		14: 1	12: 3
Smoking status	**Smoker**	9 (60%)	11(73.33%)
	NON-SMOKER	6 (40%)	4 (26.66%)
Onset of claudication (In months)	**Mean ± SD**	6.86 ± 3.33	9.06 ± 2.34

Interpretation: The above table shows that mean value and standard deviation of age, smoking status, the onset of claudication (in months) and gender distribution of group A and B.

Table 2: Intragroup pairwise comparison of ABI and WIQ in group A

		ABI		WIQ	
TIME (I)	**TIME(J)**	**MEAN (I-J) DIFFERENCE**	**p VALUE**	**MEAN (I-J) DIFFERENCE**	**p VALUE**
DAY 1	**6th WEEK**	0.242	0.000	30.56	0.000
DAY 1	**2nd WEEK**	0.014	0.021	4.06	0.000
2nd WEEK	**4th WEEK**	0.123	0.000	15.39	0.000
4th WEEK	**6th WEEK**	0.105	0.000	11.10	0.000

Interpretation: p value < 0.05 suggests significant improvement in ABI and WIQ score after 2nd, 4th and 6th week of intervention in group A and between 2nd to 4th weeks there is more improvement.

Table 3: Intragroup pairwise comparison of ABI and WIQ in group B

		ABI		WIQ	
TIME (I)	**TIME(J)**	**MEAN (I-J) DIFFERENCE**	**p VALUE**	**MEAN (I-J) DIFFERENCE**	**p VALUE**
DAY 1	**6th WEEK**	0.353	0.000	31.93	0.000
DAY 1	**2nd WEEK**	0.065	0.001	6.197	0.000
2nd WEEK	**4th WEEK**	0.151	0.000	14.50	0.000
4th WEEK	**6th WEEK**	0.137	0.000	11.22	0.000

Interpretation: p value < 0.05 suggests significant improvement in ABI and WIQ score after 2nd 4th and 6th week of intervention in group B and between 2nd to 4th weeks there is more improvement.

Treadmill training causes changes in the metabolism of the muscles because of increase muscle blood flow during exercise because of intramuscular vasodilatation caused by direct effects of improving muscle metabolism. In the working muscle, it reduces the anaerobic muscle activity that reduces the level of lactate. These cause an increase in the formation of ATP that rises the exercise capabilities. Treadmill training also helps in reducing blood viscosity and increases the flexibility of erythrocytes. And improve walking performance. [2, 10, 11]

Calf raising exercise increases mitochondrial activity and perfusion of blood flow to the calf muscle. During the calf muscle contraction vasodilators released and citrate synthesis activity improve. Muscle work output increases oxygen consumption and dilate muscle blood vessels. So, muscle mitochondrial respiration improves and may be exercise causes stretch of capillaries that activates stretch receptors and stimulus the stretch reflex and releases the vasodilators that dilate the blood vessels and blood perfusion improves so it improves the arterial pressure and improves the ABI. Hence it reduces intermittent claudication and improves walking ability. [8, 11]

Progressive muscle relaxation exercise works by stimulating the activity of the sympathetic nervous system. In muscles of the body, there is β1 receptors of the sympathetic nervous system, which causes vasodilation of blood vessels and increase the blood flow and oxygen to the muscles. [23]

In the result mean difference suggests in first 2 weeks there is less improvement in both the groups. It may be due to initially body is not adapted to exercise and human body takes time to get adapted with any physical or structural changes. And duration of exercise plays an important role to influence physical and functional performance. Initially may be anaerobic threshold extends due to accumulation of lactic acid in the tissue and anaerobic process become more dominant. That affects the vasomotor tone that is not keep sufficient pressure in arteries and ABI have a less improvement in first 2 week hence, there is also less improvement in walking performance. And there may have insufficient duration to lowering the anaerobic threshold level thereby keeping normal vasomotor tone and these hemodynamic changes may take more than 2 weeks of time to improve physical and functional performance.

To analyses the effect of patient's specific and severity-based exercise protocol in peripheral arterial disease we studied within-group, there is severity so the entire group may not perform the same exercise protocol, so it was given according to the severity of the disease. However, there are number of factors like individual's perception of pain which could differ from patient to patient, and it was based upon the severity of PAD and could not be under control and affect the claudication distance though to reduce this effect in the study claudication pain rating scale and individual's supervision were taken to standardized exercise protocol. According to scale intensity was differ with each patient. So within-group patient's specific exercise was given in which intensity and duration were selected according to the patient's need. And the result suggests it is effective for both mild and moderate PAD group.

The result of this research is incoherent with the result observed by Chaitsi Kirit Jani et al. they compared upper body strength training exercise vs treadmill walking on patients with intermittent claudication in which they concluded that treadmill walking exercise is effective for improving PFWD, HR and WIQ in intermittent claudication. While no significant improvement noted in ABI. [1]

The result of this study is also consentient with the result observed by Michel Van Schaardenburgh et al. they compared calf raising exercise vs traditional walking exercise in patients with intermittent claudication in which they concluded that calf raise exercise improves walking performance and increases biomarker of mitochondrial- volume density and mitochondrial respiration.[8] Maria Szymczak et al. compared walking exercise- treadmill walking and resistance exercise in the patient with chronic limb ischemia and suggested that treadmill walking is effective in the treatment of improving the claudication distance in PAD patients, which supports the result of this study.[5] Additional finding of the study- Demographically mean value of age in group A was 58.93 and in the group B was 61 and there was no any patients in 25 to 41 age in both groups, between 42 to 58 in group A- 60% and in group B- 33.33% patients and between 59 to 75 in group A- 40% and in group B- 66.66% patients. There was in group A – 93.33% male and 6.67% - female and in group B- 80% male and 20% female. There was 60% smoker in group A and 73.33% in group B. hence it can be evaluated that prevalence is higher in male as well as a smoker and above the age of 50 years. Because as the age increase many risk factors are responsible for PAD like decrease vascular reactivity, endothelial dysfunction, vascular wall abnormalities, reduce compliance and loss of elasticity of arterial wall.[17] And components of cigarette smoke, including carbon monoxide and nicotine, affect the endothelial cell's function, increase reactivity and adhesion of platelets causes vasoconstriction. [18]

As both physical and functional parameters affected in both mild and moderate PAD groups. And the result of the study suggests that according to severity based and patient's specific protocol at least 6 weeks of supervised and home-based both form intervention combined, and home exercise alone improves the physical and functional performance of the patients which further improves health status and QOL. So, according to the feasibility of patients, home-based exercise also prescribed. The result shows the similarity between both physical and functional ability. So, it can be evaluated that physiotherapy intervention protocol designed for both mild and moderate PAD groups can be used clinically to improve walking performance.

Further recommendation:

In future advance, the study can be done with different outcome measure like muscle biopsy and cardiac function measurements to know the local and systemic effect of treatment.

Conclusions:

The study concluded that severity based, and patient's specific physiotherapy intervention are beneficial for improving the physical and functional performance of patients with mild and moderate PAD. It may further improve health status and quality of life. Designed patient's specific

exercise programme should be taken into consideration for mild and moderate PAD patients to open new era of physiotherapy practice. Thus, physical and functional exercise which should be based on intensity, frequency and duration remain key factors for exercise to have an impact on mild and moderate PAD.

Conflict of interest: There was no personal or institutional conflict of interest for this study.

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