



A STUDY ON THE OUTCOME OF COMBINATION THERAPY OF ASPIRIN AND ATORVASTATIN IN IMPROVEMENT OF ANKLE BRACHIAL PRESSURE INDEX AMONG PATIENTS WITH PERIPHERAL VASCULAR DISEASE IN A TERTIARY CARE CENTRE, SOUTH KERALA

Medicine

Dr. P. Anish Immanuel	Assistant professor, Department of general surgery, Dr SMCSI Medical College, Karakonam, Kerala
Dr. Naraintran. S	Associate professor, Department of general surgery, Dr SMCSI Medical College, Karakonam, Kerala
Dr. Madhumitha. M	Associate Professor, Department of Community Medicine, Kanyakumari Government medical college, Kanyakumari.
Dr. Sandeep Kumar David. S	Professor, Department of general surgery, Dr SMCSI Medical College, Karakonam, Kerala
Dr. Punitha Thetraravu Oli M	Professor, Department of general surgery, Dr SMCSI Medical College, Karakonam, Kerala

ABSTRACT

Background: Peripheral Artery Disease is quite common in the old age group patients in our population. This has to be detected in a early stage so that starting of prophylactic medication with Aspirin and Statin will prevent further progression of the disease , it also prevent the death due to cardiac events in our population.

Objectives

1. To study the outcome of combination therapy of Aspirin and Atorvastatin in PAD patients by improvement in ankle brachial pressure index
2. To find the correlation between cholesterol level and ABPI in peripheral arterial disease.

Materials and methods: A hospital-based observational study involving 55 patients was conducted in the Department of General surgery, Dr. SMCSI Medical College Karakonam, Trivandrum during December 2013 to October 2015. Data about the patient's age, sex, clinical symptoms, co morbidities, additions and ABPI in each month, after starting Aspirin and Atorvastatin are collected with informed consent from the patient. Cholesterol level in the initial and after 6 months was compared. **Results:** A total of 55 adult male or female participants ≥ 31 years of age (mean age: 62.76 ± 10.79) years; 67.3% male and 32.7% female) were evaluated. Among the total participant 26.9% the affected side was right. 37.3% the affected side was left and for 35.8% both the sides were affected. In this study the mean difference between Ankle Brachial Pressure Index of first and sixth month is 0.12 with SD = 0.09 (P value <0.001). Thus, there was significant improvement both statistically and clinically in the Ankle Brachial Pressure Index (p value <0.001). **Conclusion:** Effect of combination therapy with Aspirin and Atorvastatin has a major role in treating PAD patients. It also reduces the incidence of cardiac problems like angina, myocardial infarction.

KEYWORDS

Peripheral Vascular Disease, Ankle Brachial Pressure Index, Cholesterol levels

INTRODUCTION

Peripheral Artery Disease (PAD) is narrowing of the blood vessels due to the formation of plaque in the lumen leading to decreased blood supply to the limbs. Narrowing of blood vessels of heart is known as coronary artery disease and narrowing of the cerebral vessels is known as cerebrovascular disease. It is also known as Peripheral Vascular Disease (PVD), Peripheral Occlusive Vascular Disease (POVD), and Peripheral Obliterative Arteriopathy.

Most of the time peripheral artery disease is asymptomatic. Patients with symptomatic PAD have pain in the lower limbs during work out due to inadequate supply of oxygen to muscles which is also termed as claudication and this pain then improves after rest. This claudication may progress to acute limb ischemia (ALI) or critical limb ischemia (CLI) depending on the severity of disease. Acute ischemia of leg is defined as inadequate blood flow for less than two weeks to the limb and signaled by 6 PS pain, paleness, pulselessness, poikilothermia, paresthesia and paralysis. Chronic ischemia is defined by decreased blood perfusion for long-term (≥ 2 weeks) and is signaled by ischemic pain at rest, unhealed lesions, or gangrene in one or both limbs which is ascribed to PAD. The quality of life of patients with symptomatic PAD decreases significantly as the patient being not able to discharge their normal functions owing to intermittent claudication and in extreme cases lower limbs may have to be severed.

The focus of treatment of PAD patients should be to improve the symptoms of the disease and increased locomotor function along with reduction of risk of cardiovascular events. To reduce cardiovascular events, cardiovascular risk factors, especially tobacco consumption must be controlled, while restoration of blood flow should be put aside for symptomatic patients.

Various studies have shown that reduction in levels of low-density lipoprotein cholesterol (LDL-C) decreases the chances of increased

complicacy in legs along with reduces chances of developing cardiovascular events. All current guidelines on management of PAD strongly recommend lipid-lowering therapy. Most of the time peripheral artery disease is neglected by both patient and the doctors as management of cardiovascular risk factors in these patients is difficult compared to people who have had a myocardial infarction or stroke. This is the reason behind little to no change in mortality from PAD in past three decades.

Aspirin is also useful in treatment of PAD owing to its anti thrombotic and anti-inflammatory action.

Therefore, present study was undertaken to estimate the percentage of improvement in patients with peripheral vascular disease with a combination of statin and aspirin.

MATERIALS AND METHODS

Study Design- Observational study (prospective)

Study Setting- Department of surgery, Dr SMCSI Medical College, Karakonam.

Study Period- 2 years

Study Subjects- Patients with PAD attending the General Surgery OPD were enrolled in the study after obtaining informed written consent.

Inclusion criteria- All the patients with clinically proven peripheral vascular disease.

Exclusion criteria

- Arterial occlusion due to trauma
- Bilateral Amputee.

- Patients with bleeding due to Aspirin.
- Patients receiving anticoagulation therapy (e.g., warfarin).
- Patients allergic to Aspirin or Statin.
- Patients who were already taking Aspirin or Statin

Method Of Data Collection:

Socio demographic details were obtained from the patient. Ankle Brachial Pressure Index was monitored using hand-held Doppler (ratio of systole blood pressure of lower limb to the systole blood pressure of upper limb). Cholesterol levels were obtained from laboratory reports. Arterial Doppler findings were obtained from radiology department. The patients were advised to consume Aspirin 75 mg after food in the noon and Statin 10 mg at night daily till the end of study period and ABPI was monitored every month and at the end of 6 months cholesterol was also estimated.

Sample size:

In this study we aimed to determine the percentage of participants who increased there ABPI, 0.15 during the study period. From previous studies and from a preliminary available data in our department the prevalence is about 12% . We calculated required sample size for the study using

$$n = \frac{t^2 \times p(1-p)}{m^2}$$

p- Estimated prevalence, m is the marginal error and t is the confidence limit.

We calculated sample size for prevalence 12 % with 95% confidence interval and effect size 9 ABPI. We reached to a sample size 50.08, approximately 55. So we decided to recruit 55 participants for our study.

Data Analysis

Data was analyzed using SPSS 18.0V. Mean Ankle Brachial Pressure Index (ABPI) at different visits were calculated. The significant differences were tested using paired "t" test for various assessment schedule on ABPI as well as cholesterol levels. We also looked for possible correlation (r) between ABPI and cholesterol.

Variables used in the study:

- 1) Ankle Brachial Pressure Index: Difference in Ankle Brachial Pressure Index (Increase in ABPI more than 0.15 is significant).
- 2) Cholesterol level.

RESULTS

Table 1: Angle Brachial Pressure Index Score according to Gender (n=67)

Gender	Mean	Standard Deviation	t – value	P value
Male	0.1262	0.0893	1.563	0.123
Female	0.0895	0.0919		

We compared the mean ankle brachial pressure score according to gender using t-test and found that it was not significant. (p=0.123) .

Table2. Comparison of Angle Brachial Pressure Index score according to first and sixth month evaluation (n=67)

ABPI	Mean	Standard Deviation	t - value	P value
First month	0.6206	0.1978	- 10.251	<0.001
Sixth month	0.7348	0.2002-		

Ankle brachial pressure index score was compared between first month and sixth month using paired t-test. At sixth month ankle brachial pressure index score was significantly higher (p<0.001) than first month.

Table 3 Comparison of cholesterol values according to first and sixth month (n=67)

Cholesterol values	Mean	Standard Deviation	t – value	P value
First month	239.78	62.9	13.184	<0.001
Sixth month	161.78	26.45		

Mean cholesterol level variation between first and sixth month was analyzed using paired t-test. Cholesterol level at sixth month was significantly lower (p<0.001) in comparison with first month

Figure1: Ankle Brachial Pressure Index of affected side Right (n=18)

About 26.9% of the participants the affected side was right. The other side was disease free for this group of participants.

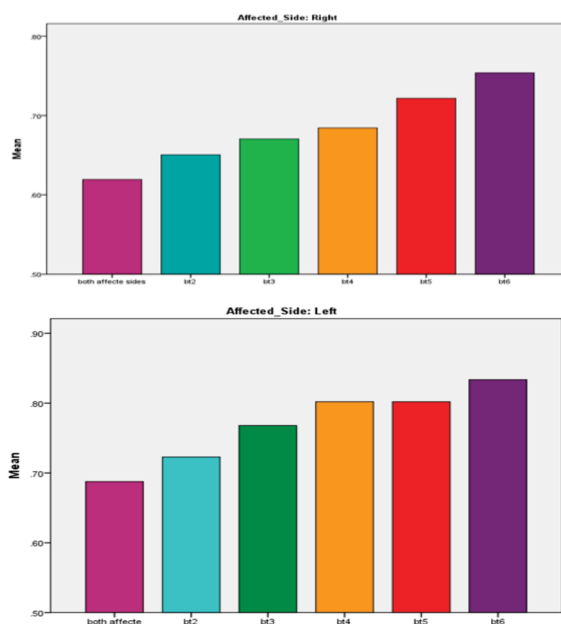


Figure 2: Ankle Brachial Pressure Index of affected side Left (n=25)

About 26.9% of the participants the affected side was right. The other side was disease free for this group of participants.

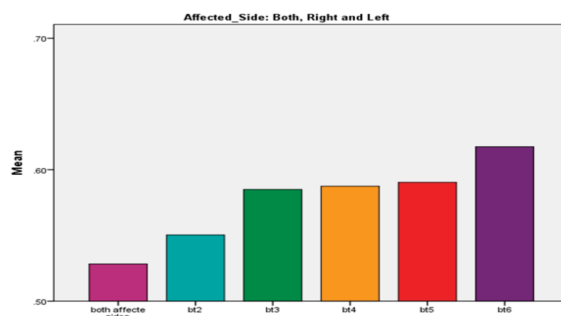


Figure 3: Ankle Brachial Pressure Index of affected side both (n=24)

It was observed that 35.8% participants were affected by peripheral arterial disease on both sides.

DISCUSSION

This study was conducted in a tertiary center at Dr. SMCSI Medical College, Karakonam in patients having peripheral arterial disease. In this study we observed that there is significant improvement in ABPI (P <0.001) among patients with PAD who had taken Aspirin and Statin combination. For persons with asymptomatic peripheral arterial disease (PAD), Vandvik et al, in "Primary and Secondary Prevention of Cardiovascular Disease" has suggested aspirin 75 to 100 mg daily over no aspirin therapy .

In the study Adherence to guideline-recommended therapies among patients with diverse manifestations of vascular disease by Armstrong E et al, with 1,114 patients with vascular disease they found that use of aspirin in 936 (84%), statins in 753 (68%) showed benefit . In our study mean difference between Ankle Brachial Pressure Index of first and sixth month is 0.12 with SD = 0.09 which denotes significant improvement in the ABPI thereby stating that the use of combination therapy with statin and aspirin has a positive effect in the study population.

In the longitudinal observational study conducted in China by Wilson Y Leung et al, aspirin use was associated with a hazard-ratio of 2.2 (1.53, 3.15, p < 0.001) of GI bleeding and 1.71 (1.00, 2.95, p = 0.051) of hemorrhagic stroke. The absolute risk of aspirin-related GI bleeding was 10.7 events per 1,000 person-years of treatment . But in our study no patients developed any gastric complication due to the intake of

Aspirin. This is achieved by taking the drug along with food. In the study Role of ankle-brachial pressure index as a predictor of coronary artery disease severity in patients with diabetes mellitus conducted by Shih-Tai Chang et al, in China showed comparisons of sex distribution among study groups with PAD revealed that it has the highest percentage of men population. In our study also the predominance of male patients is more. It may be due to the higher incidence of atherosclerosis, smoking habits and the hormonal protection in females. We compared the mean ankle brachial pressure score according to gender using t-test and found that it was not significant. ($P=0.123$)(Table.1).

In a cross-sectional study of community-dwelling Korean men, they assessed the association of cumulative smoking exposure and duration of smoking cessation with peripheral arterial disease (PAD) and found the odds ratio with 95% confidence interval was 2.31 (1.20-4.42) for past smokers and 4.30 (2.13-8.66) for current smokers, after adjusting for other cardiovascular disease risk factors. There was a significant dose-response relationship between pack-years of smoking and PAD. Compared with those who had never smoked, the multivariate-adjusted ORs of PAD for smokers of 0.1-20.0, 20.1-40.0, and >40.0 pack-years were 2.15 (1.06-4.38), 2.24 (1.08-4.65), and 2.93 (1.41-6.09), respectively.

There was a significant reduction in Peripheral Artery Disease risk as the number of years of quitting smoking increased. The multivariate-adjusted Odds Ratios of PAD for 11-20 and ≥ 21 years smoking cessation were 0.41 (0.19-0.86) and 0.49 (0.24-0.98), compared with current smokers. The association of risk factors of PAD like diabetes and hypertension are more in our study like all other studies conducted in other population group. Hence treatment with aspirin and statin not only prevents PAD it also prevents the incidence, progression, and helps in the treatment of CAD and CVA.

We also compared the ankle brachial pressure index score between first month and sixth month using paired t-test. At sixth month ankle brachial pressure index score was significantly higher ($P < 0.001$) than first month (Table 2) indicating that the combination therapy with Statin and Aspirin is having positive effect in the study population. Mean cholesterol level variation between first and sixth month using paired t-test was significantly lower in this study denoting that the medication not only reduces the chance of plaque formation and stabilizes the plaque in PAD but also helps in controlling the lipid profile (Table 3) ($p < 0.001$).

There is significant improvement in the Ankle Brachial Pressure Index during the study with a difference of 0.12 with SD = 0.09. This is also significant amount raise in ABPI as per the literature.

In our study we found that there is very minimal correlation ($r = 0.1$, p value = 0.419) between improvement in ankle brachial pressure index and control of cholesterol level after a period of six month of treatment with Aspirin and Statin. Which is similar to the study conducted by Kumeo Ono et al in Japan concluding that there is no correlation between the levels of ABPI and the cholesterol level.

CONCLUSION

Peripheral Artery Disease is quite common in the old age group patients in our population. It is caused by multiple factors like uncontrolled diabetes, hypertension, hyperlipidemia, smoking and sedentary lifestyle. It is usually associated with coronary artery disease, cerebrovascular events. This has to be detected in a early stage so that starting of prophylactic medication with Aspirin and Statin will prevent further progression of the disease, it also prevent the death due to cardiac events in our population. There should be a strict control of other associated factors, exercise and good food habits. Treatment in the initial period will help to improve the quality of life of the patient.

The simple way of detecting the disease is routine examination of all pulses in the outpatient department and the best non invasive screening tool for peripheral artery disease is Ankle Brachial Pressure Index. In our study we found that there is positive effect of the combination therapy with Statin and Aspirin in peripheral artery disease, patient showing better compliance and improvement in symptoms.

Recommendations

Very few studies are done with the combination effect using Aspirin and Atorvastatin. Hence larger studies should be conducted for

generalization of the study findings.

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