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EFFICACY OF CILOSTAZOL IN PERIPHERAL ARTERY DISEASE PATIENTS

Prince J.*[1],
Venkateswaramurthy. N[1], Perumal. P[1]

[1]J K K Nattaraja College of Pharmacy, Komarapalayam, Tamilnadu, India.

ABSTRACT

The objective of study was to study Peripheral artery disease relate intermittent claudication, ulceration, and critical limb ischemia results substantial morbidity contribute to increased hospital stay and culmina in limb loss for some patients. Evaluation of the efficacy of cilostazol peripheral artery disease patients with diabetic foot ulcer is carried out b comparing the Walking impairment questionnaire scores of patien treated with cilostazol and patients not treated with cilostazol.The metho used is Walking Impairment Questionnaire (WIQ) is a disease-specif questionnaire validated in patients with intermittent claudication. consists of four subcategories: pain, distance, walking speed, and sta climbing. Dr Lee WIQ is used to find quality of life in PAD patients. Th results of WIQ are compared and statistical significance is found. It resu that study included 82 Peripheral artery disease subjects, out of whom 4 treated with cilostazol and 40 not treated with cilostazol.. Compared wi cilostazol group, the non cilostazol group PAD patients exhibite significantly lower scores for all four sub scales of the WIQ; indeed th results are not statistically significant. More specifically, pain (cilostaz group- 56.36±14.93, Non cilostazol- 51.3±17.21), distance (cilostaz group- 51.9±14.94, non cilostazol- 51.37±16.4), and speed (cilostazo 55.6±15.08, non cilostazol- 53.9±14.01, with the pain subscale being th strongest) appear to be the WIQ subscales that more thoroughly describ the ambulation related limitations of PAD patients. The study can conclud that The WIQ results indicated reduced functional status in PAD patien not treated with cilostazol compared with patients who receive cilostazol.And the group of PAD Patients treated with Cilostazol ha improved QOL than the patients not treated with cilostazol. Thus the stud can be concluded that cilostazol may be used as a drug of choice in PAD.

Correspondence to Author

Prince J.

J K K Nattaraja College of Pharmacy, Komarapalayam, Tamilnadu, India

Email: prinz.pharm@gmail.com

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INTRODUCTION

Diabetes mellitus is one of the most important risk factor for peripheral artery disease (PAD). The goal of treatment of patients with intermittent claudication is twofold, to identify, treat, and prevent or delay progression of atherosclerotic disease as a systemic entity, and to improve functional status and exercise tolerance. Cilostazol, a phosphodiesterase 3 inhibitor, was approved in the United States in 1999 for use in patients with PAD and intermittent claudication. Recent meta-analyses, including all but one recent unpublished study, have shown that cilostazol significantly improves maximal walking distance (MWD) or peak walking time, quality of life measures, and lipid profiles. Far, detailed subgroup analyses, which might assist physicians in identifying the patients most likely to benefit, have not been performed, and no prior meta-analyses have compared the relative time course of benefit and the durability of treatment response to cilostazo[1].

Antiplatelet therapy is an essential part of management therapy for PAD patients. Cilostazol, a specific inhibitor of cyclic adenosine monophosphate phosphodiesterasehas an antiplatelet function and vasodilating effects. Therefore it is necessary to determine the optimal antiplatelet regimen and comparison of aspirin alone and combined therapy has importance[2]. Antiplatelets delay the rate of PAD progression; reduce the need for intervention and the rate of graft failure following revascularization procedures[3]. Antiplatelet therapy reduces the risk of adverse cardiovascular outcomes anddeath in patients with cardiovascular disease by approximately 25%[4]. Adding cilostazol may also be a way to further inhibit platelet aggregation and the risk ofthrombosis[5]. Cilostazol may be an attractive addition for antiplatelettherapy, compared with the new antiplatelet drugs prasugrel and ticagrelor, when drug cost is a consideration or for patients at high risk for bleedingcomplications[6].Walking Impairment Questionnaire is a qualitative measure for assessing Physical function and health-related QOL. The overall and combined scores were calculated as the average of the subscores[7,8].

METHODS

It is a retrospective study. The study comprised of 42 PAD patients who are treated with cilostazol. Patients are recruited from Monica Diabetic centre, Erode. Patients specifically evaluated and screened. This includes a detailed history and a direct assessment of the patient walking impairment. The clinical laboratory values assessed involve HbA1c, Blood sugar levels, blood pressure and lipid profile. Clinical data includes HbA1c, Blood sugar levels, blood pressure and lipid profile are also collected.

The WIQ is a disease-specific questionnaire validated in patients with intermittent claudication. It consists of four subcategories: pain, distance, walking speed, and stair climbing.

Patient not treated with cilostazol.

The study recruited 40 PAD patients who are not treated with cilostazol. Clinical data also collected from patient not treated with cilostazol. The WIQ is a disease-specific questionnaire validated in patients with intermittent claudication. It consists of four subcategories: pain, distance, walking speed, and stair climbing.

Patient of either sex more than 40 years old and type 2 diabetes patient with PAD are included in the study. Patient of either sex less than 40 years old and Patient with heart failure are excluded from the study.

RESULTS

Demographic

The distribution of age, sex, food habits, and smoking habits among PAD patients treated with cilostazol and not treated with cilostazol were not significant. The average age (years) of patients in the study is 50 – 60. The study have male as major population (62.19%).

The number of smokers (39.92%) was less when compared to the studies performed other

countries[9,10]. Most of the other studies had more number of smokers than nonsmokers.

Table 1. Averaged demographic details among PAD patients

Demographic characteristic	Cilostazol group	Non cilostazol group	P value
Age(years)	55.2381± 9.524832	56.65 ± 9.07673	0.6728
BMI	24.49286± 3.443206	26.34667 ± 3.100611	0.0124

Dosage

57.14% of PAD Patients were treated with cilostazol 50mg in BD dose and 30.95% treated in HS dose. Whereas only 2.38% of patients receivedcilostazol100mg in BD dosage. 88.09% out of over all patients were treated with cilostazol 50mg out of which 57.14% of patient taken it as BD dose. 9.52% and 2.38% of patients were treated with cilostazol 100mg BD and cilostazol 100mg HS respectively.

Table 2. Cilostazol Dosage administered in PAD patients.

Dosage	**Number of patient used as BD dose**	**Number of patient used as HS dose**	**Total**
Cilostazol 50 mg	24(57.14)	13(30.95)	37(88.09)
Cilostazol 100 mg	1(2.38)	4(9.52)	5(11.90)

Aniplatelet drugs and cilostazol

Among cilostazol group, 35.37% patients used cilostazol alone as antiplatelet agent. In remaing 63.6% ,6.09% of the patients used aspirn, 3.65% used clopidogrel and 4.87% used pasuagrel along with cilostazol.

Other than cilostazol the antiplatelet used are aspirin (9.75%), clopidogrel (6-09%), Pasuagrel (6.09%) or clopidogrel and aspirin combination (31.7%). 35.37% of patients were treated only with cilostazol. According to Antony[11], cilostazol is safe to use with other platelet inhibitors. As Anthony,s study, the study shows there is a significant use of cilostazol in combination with other platelet inhibiting agents. Cilostazol given in combination with aspirin (6.09%), clopidogrel (3.65%) and pasuagrel (4.87%).

Table 3. Antiplatelet combinations used among PAD patients.

Drugs	**Number of patients (%)**
Cilostazoland aspirin	5(6.09)
Cilostazol and clopidogrel	3(3.65)
Cilostazol and pasuagrel	4(4.87)
Cilostazol alone	29(35.37)

Antihypertensive therapy

Among all PAD patients 59.75% were found to be having hypertension. HOPE study showed that ACE inhibitors significantly decreased cardiovascular events in those with symptomatic PAD and in those with asymptomatic PAD. Whereas in the study 20.71% of patient was treated with Angiotensin receptor blockers, 7.29% with beta blockers, 9.75% with calcium channel blockers, 8.52% with diuretics and 3.65% with ACE inhibitors.

Table

Table 4. Antihypertensive used In PAD patients.

Drug	Patients receiving Cilostazol	Patients not receiving Cilostazol	Total (%)
Olmesartan	4	5	9(10.97)
Losartan	1	1	2(2.43)
Telmisarten	4	2	6(7.31)
Metoprolol	2	2	4(4.87)
Atenolol	0	1	1(1.21)
Carvedilol	0	1	1(1.21)
Amlodipine	4	4	8(9.75)
Furesamide	1	2	3(3.65)
Torlactone	3	0	3(3.65)
Aldosterone	1	0	1(1.21)
Ramipril	1	2	3(3.65)

Statins

Elderly patients with PAD and hyper-cholesteroemia should be treated with statins to reduce PAD progression. Based on the Heart protection study, persons with PAD should be treated with statin regardless of age, gender, or initial serum lipid levels. A population of 17.5% patients in non cilostazol group was found to be used atorvastatin and rosuvastatin respectively. And among cilostazol group 21.42% used atorvastatin and 19.04% patients used rosuvastatin.

Table 5. Lipid lowering therapy used in PAD patients.

Drug	Patients receiving cilostazol(%)	Patients not receiving cilostazol (%)
Atorvastatin 40 mg	9(21.42)	7(17.5)
Rosuastatin 10mg	8(19.04)	7(17.5)

Cilostazol

The WIQ results indicated reduced functional status in PAD patients not treated with cilostazol compared with patients who received cilostazol. Compared with cilostazol group, the non cilostazol group PAD patients exhibited significantly lower scores for all four subscalesof the WIQ. Furthermore, the WIQ is the qualitative measure that best reflects actual ambulatory performance of the PAD patients. More specifically, pain

(cilostazol group- 56.36±14.93, Non cilostazol- 51.3±17.21), distance (cilostazol group- 51.9±14.94, non cilostazol- 51.37±16.4), and speed (cilostazol- 55.6±15.08, non cilostazol- 53.9±14.01, with the pain subscale being the strongest) appear to be the WIQsubscales that more thoroughly describe the ambulation related limitations of PAD patients. The WIQ may be the most specific questionnaire to capture both the physiologic and quantitative ambulatory dysfunction associated with PAD and claudication. However, may not be reflective of the overall PAD population because claudicant patients frequently have comorbidities, such as osteoarthritis, neurogenic claudication, and peripheral neuropathy, that affect walking invarying degrees. Although WIQ is a disease-specific measure, the study shows that questionnaires can be useful in providing information about the QOL of PAD patients. In the absence of SF-36 data, WIQ can adequately reflect an overall drop in QOL in claudicant patients.

Table 6. Walking Impairment Questionnaire score given to PAD patients

WIQ Subscale	Cilostazol	Number of patients	Non Cilostazol	Number of patients	P value
Pain	56.36±14.93	42	51.3±17.21	40	0.1585
Distance	51.9±14.94	42	51.37±16.4	40	0.8787
Speed	55.6±15.08	42	53.9±14.01	40	0.5998
Stair	56.49±19.28	42	56.25±19.87	40	0.9559

CONCLUSION

The study demonstrates that WIQ pain, speed, distance, and stair subscales are the qualitative parameters best describe ambulatory limitation of claudicant patients and also closely relate to their QOL. TheWIQ results indicated reduced functionalstatus in PAD patients not treated with cilostazol compared with patients who received cilostazol. And the group of PAD Patients treated with Cilostazol has improved QOL than the patients not treated with cilostazol. Thus the study can be concluded that cilostazol may be used as a drug of choice in PAD.

Proper diagnosis and treatment of peripheral artery disease can prevent threatening limb complication in diabetic patients. Future studies focusing on the subject may show tremendous improvement in quality of life among diabetic foot ulcer patients.

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