

Original research article

A prospective study of Benefits and risk of paclitaxel drug in the treatment of femoropopliteal artery disease:

Dr. Mohammed Hidayathulla^{1*}, Dr. Azhar Ali Syed², Dr. Syeda Tasneem Kausar³

^{1*} Assistant Professor, Dept. of Cardiology, Deccan College of Medical Sciences, Kanchanbagh

Santosh Nagar, Hyderabad (India).

² Assistant Professor, Dept. of General Medicine, Deccan College of Medical Sciences, Kanchanbagh

Santosh Nagar, Hyderabad (India).

³ Assistant Professor, Dept. of Anatomy, Mallareddy Medical College, Hyd (India).

Corresponding Author: Dr. Mohammed Hidayathulla

Abstract

Introduction: Femoro-popliteal arterial disease is a common vascular condition and Various methods of revascularization have been tried which includes simple balloon angioplasty, debulking techniques, stent implantation, and recently the drug eluting balloons. Paclitaxel drug eluting balloons are more promising in the approach to treat femoro-popliteal arterial disease.

Material and Methods: The present study from march 2016 to january 2018 was conducted on 25 cases prospectively in patients admitted to the Department of cardiology sri jayadeva institute of cardiovascular sciences and research center, Bangaluru (Karnataka). femoral artery using cross over sheath VasuQol – 6 disease specific health related quality of life questionnaire post procedure.

Results: A success rate of 92% was recorded and patients treated with DCB showed significantly higher primary patency of the affected vessel. The current study reveals that vasuQoL-6 score used to assess the quality of life of the patient with peripheral arterial disease before and after the intervention improved and it is statistically significantly.

Conclusion: We conclude that Use of paclitaxel drug coating balloon is safe and efficacious in treating femoro-popliteal arterial disease. Restenosis which was noted in 8% of our cases can be successfully managed with percutaneous transluminal angioplasty using same DCB.

Keywords: Femoro-popliteal arterial disease, paclitaxel drug eluting balloon, colour duplex ultrasound scan, smoking

Introduction

Femoro-popliteal arterial disease is a common vascular condition and Various methods of revascularization have been tried which includes simple balloon angioplasty, debulking techniques, stent implantation, and recently the drug eluting balloons. Paclitaxel drug eluting balloons are more promising in the approach to treat femoro-popliteal arterial disease. In cases with extensive disease or after failed endovascular approaches, endarterectomy of focal common femoral lesions or femoro-popliteal bypass surgery is done as required. It has been found that 65–75% of patients with PAD are asymptomatic, the classic presenting symptom is Intermittent claudication which is

usually described as muscle cramps, fatigue or pain in the lower legs by the patients, induced by exercise and rapidly relieved by rest; often the symptom location indicates the level of arterial involvement. Risk factors for atherosclerosis include race, male gender, elderly age, smoking, diabetes mellitus, hypertension, dyslipidaemia, hypercoagulable and hyper viscous states, hyperhomocysteinaemia, systemic inflammatory conditions and chronic renal insufficiency. The presence of symptoms in PAD depends on the metabolic demands of the ischemic tissue during exercise, the degree of collateral circulation and the size and location of the affected artery. The patients may commonly present with intermittent claudication, rest pain, ulcers, discoloration of skin. Patients may also present with critical limb ischemia. The European Society of Vascular Surgeons defined critical limb ischemia (CLI) as a recurring ischemic rest pain requiring analgesia for 2 weeks or ulceration or gangrene of foot or toes with ankle systolic pressure of 50 mm Hg or toe systolic pressure of 30 mm Hg with Fontaine's III and IV grade symptoms¹. Fontaine's classification, proposed in 1954, remains a popular way of staging PAD. It divides patients into groups according to their clinical presentation. A similar clinical classification developed more recently by Rutherford has the advantage of including hemodynamic data, helping to ensure that any rest pain or tissue loss is directly related to PAD². Treatment of femoro-popliteal artery disease by percutaneous transluminal angioplasty is limited by high rates of restenosis (40% to 60%) 6-12 months after procedure³. Paclitaxel is in the taxane family of medications⁴. It works by interference with the normal function of microtubules during cell division. Paclitaxel is used as an antiproliferative agent for the prevention of restenosis (recurrent narrowing) of coronary and peripheral stents; locally delivered to the wall of the artery, paclitaxel coating limits the growth of neointima within stents⁵. Lifestyle modification, exercise therapy are very useful tools in the management of PAD. Modification of risk factors such as diabetes, smoking, hypertension and weight reduction is essential. Pharmacological agents such as cilostazol, a phosphodiesterase III inhibitor, has also been used with some improvement in walking distance as evidenced by the CASTLE study (Cilostazol: A Study in Long-Term Effects)⁶. REVASCULARISATION----- the Zilver PTX trial compared a polymer free paclitaxel-coated nitinol drug-eluting stent with PTA and provisional BMS placement in patients with femoro-popliteal disease. The study suggested that treatment with the paclitaxel-eluting stent was associated with a superior primary patency (83.1 versus 32.8%; P, 0.001) and 12-month event-free survival (90.4 versus 82.6%; P ¼ 0.004) compared with PTA and provisional BMS placement⁷.

Evidence from large, randomized, controlled peripheral artery disease trials reporting long-term outcomes using drug-coated balloons (DCBs) is limited. Previously, the DCB showed favorable 1-year outcomes compared with conventional percutaneous transluminal angioplasty (PTA), this study sought to investigate the longer-term outcomes of a paclitaxel-eluting DCB compared to PTA for femoro-popliteal lesions. 331 patients with symptomatic (Rutherford 2 to 4) femoro-popliteal lesions up to 18 cm in Length were enrolled for the trial. Patients were randomly assigned in a 2:1 ratio to treatment with DCB or PTA. The 24-month assessments included primary patency, freedom from clinically driven target lesion revascularization (CD-TLR), major adverse events, and quality of life and functional outcomes as assessed by the Euro QOL-5D quality-of-life questionnaire, walking impairment questionnaire, and 6-min walk test. The 24-month outcomes from the trial demonstrate a durable and superior treatment effect of DCB versus PTA with significantly higher primary patency, lower CD-TLR, and similar functional status improvement with fewer repeat interventions¹⁵. New development over the last several

years include drug eluting balloons (DEB), these are designed to reduce restenosis and to improve long term – outcomes. Various trials have been carried out using drug eluting balloons for management of femoro – popliteal diseases and very satisfying results have been obtained. With the introduction of DCB many trials are ongoing to study the long term effects and efficacy of DCB, both the THUNDER trial and the Fem Pac trial demonstrated proof – of – concept that a short - term exposure of injured femoral arteries to paclitaxel may be sufficient to inhibit restenosis¹⁶.

Material and Methods

The present study from march 2016 to january 2018 was conducted on 25 cases prospectively in patients admitted to the Department of cardiology sri jayadeva institute of cardiovascular sciences and research center, Bangaluru (Karnataka). Patients selected for this study based on the inclusion and exclusion criteria were subjected to peripheral angioplasty using paclitaxel drug eluting balloon through antegrade femoral approach or from contra lateral femoral artery using cross over sheath. Follow – up was done at regular interval by clinical examination, examination of the peripheral pulses, and duplex ultrasound along with VascuQol – 6 disease specific health related quality of life questionnaire post procedure. Under strict aseptic precautions, patients were given these treatment

Methodology

The present study from march 2016 to january 2018 was conducted on 25 cases prospectively in patients admitted to the Department of cardiology sri jayadeva institute of cardiovascular sciences and research center, Bangaluru (Karnataka). Patients with femoro – popliteal disease presenting with intermittent claudication and / or critical limb ischemia were included in the study. Patients selected for this study based on the inclusion and exclusion criteria were subjected to peripheral angioplasty using paclitaxel drug eluting balloon through antegrade femoral approach or from contra lateral femoral artery using cross over sheath. Follow – up was done at regular interval by clinical examination, examination of the peripheral pulses, and duplex ultrasound along with VascuQol – 6 disease specific health related quality of life questionnaire post procedure

Inclusion criteria

All adults more than 18 years of age with symptomatic peripheral arterial Disease (intermittent claudication or chronic limb ischemia) caused by $\geq 70\%$ stenosis of superficial femoral artery or popliteal artery or femoro – popliteal artery

Exclusion criteria

Patients with the following were excluded from this study:
Untreated ipsilateral iliac artery stenosis
Ongoing dialysis
Acute thromboembolic disease of the leg
Infrainguinal aneurysmal disease.

Statistical Analysis:

All the data collected would be tabulated and subjected to appropriate statistical analysis using the SPSS software and the results thereby analyzed

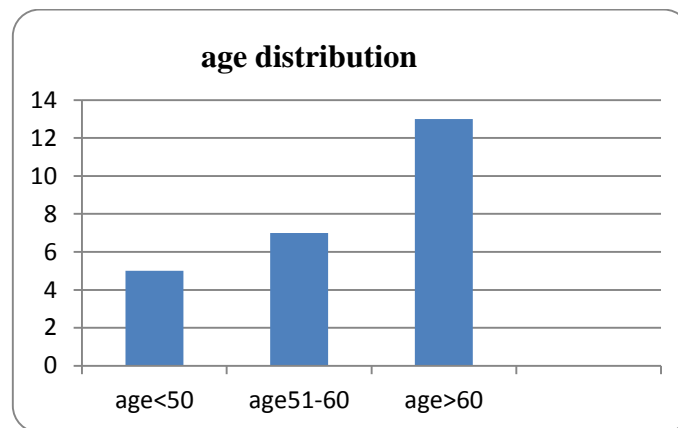
Results

Demographic Parameter:

The total numbers of patients enrolled were 25, the data regarding them was entered systematically and analysed statistically using SSPS software. The following results were obtained.

Table 1: Age Distribution

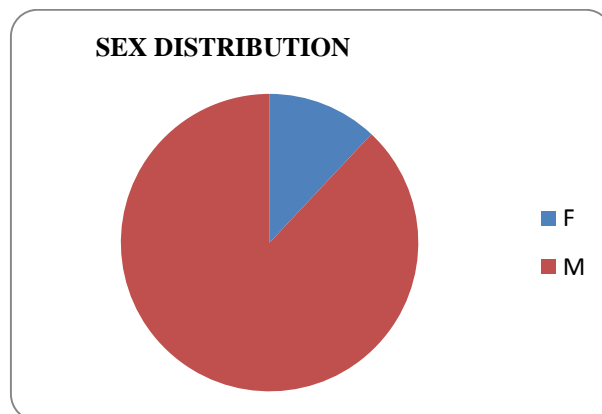
AGEGROUP	FREQUENCY	PERCENT
<50	5	20.0
51-60	7	28.0
>61	13	52.0
Total	25	100.0



The frequency of PVD was found to be higher i.e. about 52% cases in the age group of >61 years, 28% in the age group of 51-60 years of age, and 20% cases of <50 years age group.

Table 2: Sex distribution

sex	Frequency	Percent
M	22	88.0
F	3	12.0
Total	25	100.0



With respect to the gender, the frequency of PVD was more common in males it was 88% as compared to females where it was 12%.

Table 3: Claudication Distance

claudication distance by Fontaine grade	Frequency	Percent
<200 meters	20	80.0
> 200 meters	5	20.0
Total	25	100.0

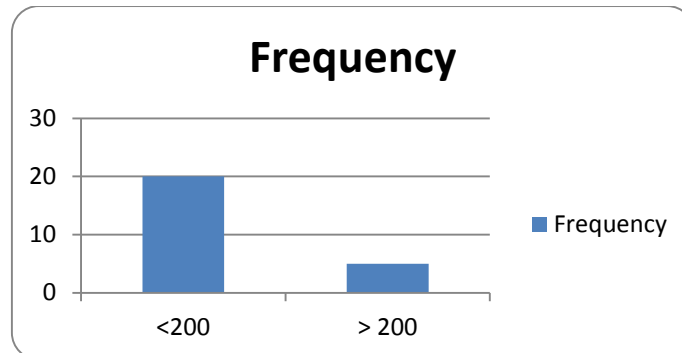


Table 4: Rest Pain

REST PAIN	Frequency	Percent
YES	16	64.0
NO	9	36.0
Total	25	100.0

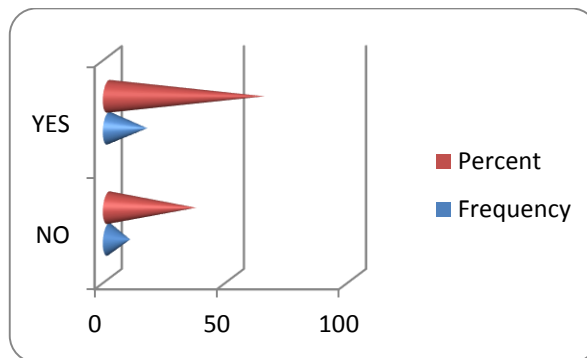
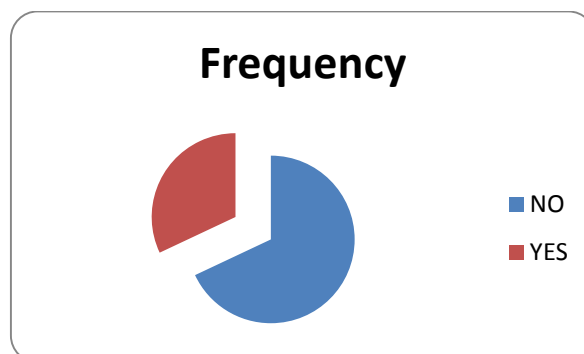


Table 5: Ulcer

ULCER	Frequency	Percent
NO	17	68.0
YES	8	32.0
Total	25	100.0



Of the 25 patients, 8 patients presented with ulcers which were non-healing i.e 32% of cases.

Table 6: Rutherford Class

RUTHERFORD CLASS	NUMBER OF PATIENTS	PERCENT
2	5	20%
3	4	16%
4	8	32%
5	7	28%
6	1	4%
TOTAL	25	100

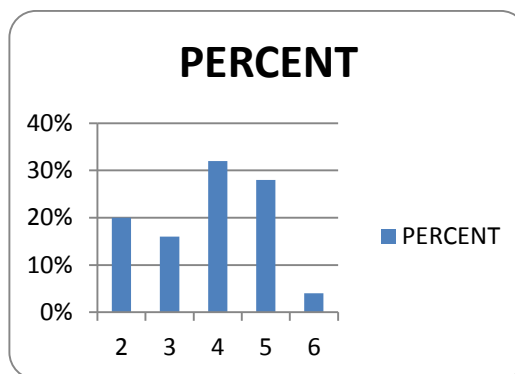
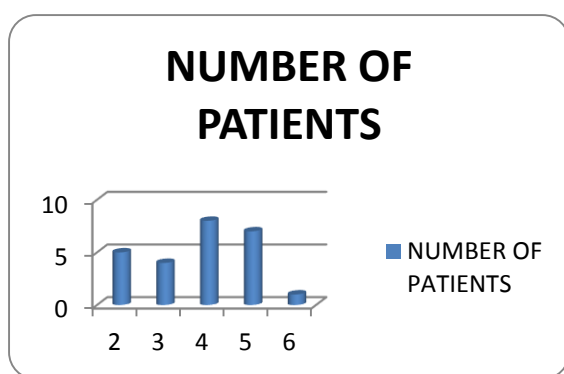
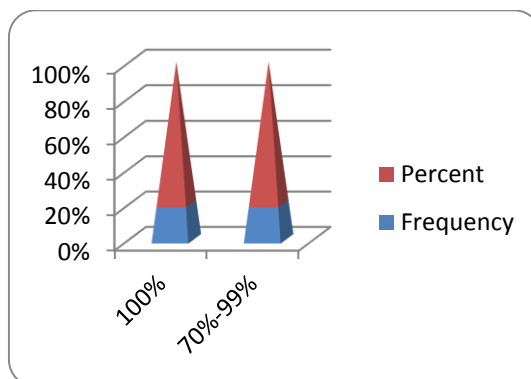


Table 7: Percentage of Stenosis

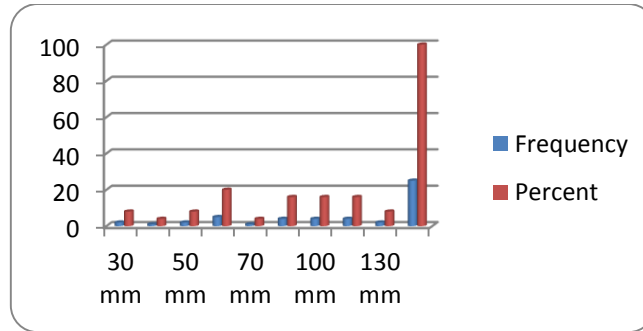
% of stenosis	Frequency	Percent
100%	17	68.0
70%-99%	8	32.0
Total	25	100.0



100% stenosis was noted in 68% of patients, rest of the patients had stenosis in the range of 70%-99%.

Table 8: Length of Stenosis

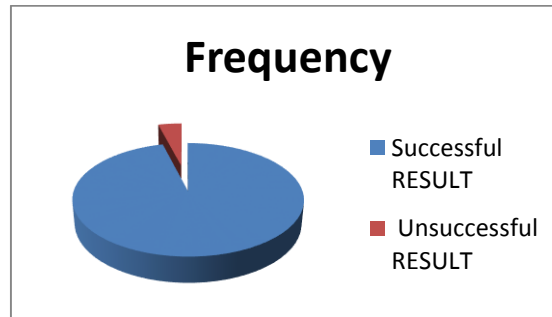
length of stenosis	Frequency	Percent
30 mm	2	8.0
40 mm	1	4.0
50 mm	2	8.0
60 mm	5	20.0
70 mm	1	4.0
80 mm	4	16.0
100 mm	4	16.0
120 mm	4	16.0
130 mm	2	8.0
Total	25	100.0



With regard to the length of the lesion, 20% of patients had 30-50mm lesion. 20% of patients had 60 mm of length, 60% of them had length in the range of 70-130mm.

Table 9: Procedural Result

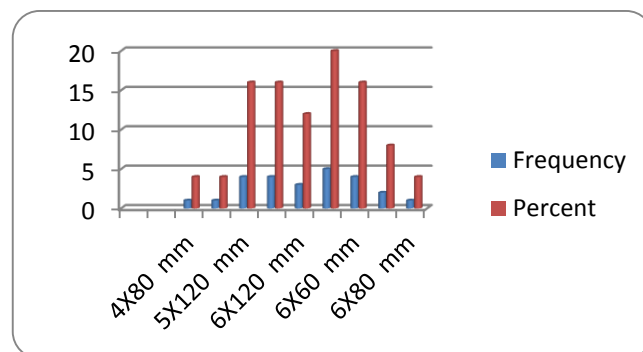
Procedure done/result	Frequency	Percent
Successful result	24	96.0
Unsuccessful result	1	4.0
Total	25	100.0



The overall results of the patients after the post-procedure were about 96% success rate

Table 10: Size of DEB used in our study.

size of DEB	Frequency	Percent
4X80 mm	1	4.0
4X120mm	1	4.0
5X120 mm	4	16.0
5X150 mm	4	16.0
6X120 mm	3	12.0
6X150 mm	5	20.0
6X60 mm	4	16.0
6X80 mm	2	8.0
6X80 mm	1	4.0
Total	25	100.0



The most commonly used size of DEB is between 4mm to 6mm in diameter and 80 mm to 150 mm in length.

Discussion

In this study we enrolled 25 cases, 52% were of >61 years of age group which indicates that the incidence of PAD is more common in older people of >60 years of age, 28% of patients belonged to the 51-60 years of age group, 20% cases belonged to <50 years of age group. Peripheral artery disease refers to atherosclerosis involving the aorta, iliac, femoral, popliteal, infrapopliteal arteries and is associated with significant morbidity and mortality. The incidence of the disease is on a significant rise because of the risk factors such as smoking and lifestyle.

In our study patients belonging to Rutherford, class 4 were 32%, class 5 were 28%, class 2 were 20%, class 3 were 16%, class 6 were 4%. Majority of the patients had rest pain. In the present study, 68% of patients had total occlusion, 32% of the patients had stenosis ranging from 70%-90%. In 24 months INPACT SFA trial, the total occlusion was seen in 25.8% of cases. The length of lesion in our study was found to be in the range of 30-130mm. Fourteen societies representing disciplines in medicine, vascular surgery, interventional radiology, and cardiology from Europe and North America came together in 2000 to form a consensus in the classification and treatment of patients with PAD. The focus was to provide recommendations in the epidemiology of PAD, clinical evaluation, diagnosis, treatment, and follow-up of patients with intermittent claudication, ALI, and chronic limb ischemia. The resulting document was referred to as the Trans-Atlantic Inter-Society Consensus Document (TASC). In 2007, the consensus was updated and involved additional representatives from Australia, South Africa, and Japan and is referred to as TASC II. TASC II is comprehensive in reviewing the literature relating to PAD up to 2007. While TASC II addresses all aspects of PAD, the anatomic classification detailed in TASC II has received the significant focus of the review as well as considerable criticism of the recommendations. Specific categories are assigned treatment algorithms (surgical vs endovascular) based on lesion classification. TASC II divides anatomic distribution of lesions into aorto-iliac and femoral popliteal. Lesion patterns are grouped into A-D lesions. Based on this group recommendation, TASC A lesions are those that should have excellent results from endovascular management alone. TASC B lesions are those that should have good results from endovascular management, and endoluminal interventions should be the first treatment approach. TASC C lesions are those for which surgical management provides superior long-term results and endovascular techniques should be reserved for patients who are surgically high risk. TASC D lesions should be treated by open surgery. While TASC II provides a framework to compare therapeutic techniques, advancement of endovascular techniques have led to many trials suggesting that endovascular management of TASC II C and D lesions is a potential alternative treatment to open strategies⁸. All DCBs available today utilize paclitaxel in combination with different carriers and excipients. The presence of a drug carrier plays a central role in the transfer of paclitaxel into the vessel wall from the surface of a balloon. Iopromide is the first-generation DCB. This hydrophilic x-ray contrast, apart from serving as a coating matrix for the antiproliferative drug, has been shown to facilitate the rapid transfer of paclitaxel into the vessel wall (< 60 seconds)^{9, 10}. Of the 25 cases, 1 case after 24 hours of procedure developed ischemic rest pain and on examination distal pulses were absent, duplex ultrasound revealed absent wave forms distal to left mid SFA, so this patient had to undergo femoro-popliteal bypass. Another patient

after 8 months of procedure developed rest pain, ischemic ulcer, gangrene of the toes and had to undergo redo procedure with the drug eluting balloon. This patient had uncontrolled diabetes and renal dysfunction secondary to diabetic nephropathy. One more patient after 12 months of procedure presented with lower limb rest pain without ulceration. This patient was diabetic, continued to smoke and was a default with the medications and hence had to undergo redo procedure. The success rate in the present study is 92%. In 24 month trail the results revealed that 78.4% success rate was obtained with paclitaxel drug eluting balloon. In levanta 2 trail 83.9% success rate was obtained with paclitaxel drug eluting balloon. The success rate in our study is good compared to other trails. In a multi –ethnic study conducted with respect to the incidence of peripheral arterial disease in association with the blood groups , it was concluded that blood type A and the A allele count were significantly associated with prevalent peripheral arterial disease¹¹. VasQOL-6 is a reliable and valid score in patients with peripheral artery disease in clinical practice before and after treatment . The main advantage is , it's a compact format that offers a possibility of routine use in busy clinical setting¹² . There was a significant increase in the score after intervention in our study with the significant p-value . This score can be used in patient with peripheral artery disease before and after the intervention. Percutaneous transluminal angioplasty is a minimally invasive therapy for the treatment of patients with peripheral artery disease who suffer from intermittent claudication or critical limb ischemia . The main advantage of the endovascular approach is a low complication rate ranging between 0.5% - 4% , a high success rate approaching 90% even in long occlusions and an acceptable clinical outcome ^{13, 14}.

Conclusion

The present study of paclitaxel drug eluting balloon in femoro-popliteal arterial disease showed positive results with a success rate of 92%, so use of paclitaxel drug coating balloon is safe and efficacious in treating femoro-popliteal arterial disease. All these patients should be emphasized on controlling risk factors such as cessation of smoking, good diet, exercise, control of blood pressure and blood sugar. Restenosis which was noted in 8% of our cases can be successfully managed with percutaneous transluminal angioplasty using same DCB . The current study reveals that vascuQoL-6 score used to assess the quality of life of the patient with peripheral arterial disease before and after the intervention improved significantly . The score is valid , reliable and can be used routinely while assessing the patient with PAD .

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