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ORIGINAL RESEARCH

Release r - The Saviour Sirolimus Stent

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Abstract

Background: Using a sirolimus-eluting stent following percutaneous coronary revascularization considerably lowers the incidence of restenosis, according to preliminary results of studies involving uncomplicated coronary lesions. The aim of present study is to assess the effectiveness and safety of the Release R sirolimus-eluting stent in patients with native coronary artery lesion.

Material & methods: The prospective study was conducted among 450 subjects and at a tertiary care center that were eligible for the placement of stent during the one year of study period. Patients visited the hospital after six months for an angiographic review and clinical evaluation. Results were analyzed using SPSS version 23.0 keeping level of significance less than 0.05.

Results: Mean age of patients was 56±10.64 years. 71.7% were male and 28.2% were female. maximum patients (43.7%) had 80-70% occlusion. 55% diseased vessel were of LAD category and minimum (0.5%) were in LM category. Out of all the patients 6.8% had minor edge dissection , 1.1% had no reflow, 0.8% had cardiogenic shock and 0.2% had recurrence symptoms.

Conclusion : The use of a sirolimus-eluting stent reduced the incidence of restenosis and related clinical events in all subgroups examined in this trial involving patients with complicated coronary lesions.

Keywords :biodegradable polymer, drug-eluting stent , drug release, sirolimus, stents

INTRODUCTION

The non-surgical, minimally invasive procedure known as percutaneous coronary intervention (PCI) is used to treat vascular disease. The groundbreaking PCI method known as balloon-expanded bare-material stents (BMSs) was created in the 1980s [1]. Metals including stainless steel, cobalt-chromium, and platinum-chromium are frequently used to create BMSs. These alloys have qualities that support the durability and form of stents. However, the implantation of BMSs results in endothelial damage and in-stent restenosis [2-4]. Drug-eluting stents (DESs) were created as a result in order to lower the rate of restenosis [5]. The first-generation DES (Cypher, Cordis Corporation, Hialeah, FL, USA) was made up of a durable polymer layer that eluted sirolimus on top of a stainless steel platform [6]. The antiproliferative medication sirolimus interacts with the mammalian target of rapamycin (m TOR), which is important in cell growth and proliferation, through a complex it forms with the FK binding protein (FKBP12) [7]. Sirolimus is categorized as a class II medicine under the BCS (biopharmaceutics classification system) due to its high permeability and low water solubility (2.6 g/mL) [8]. Sirolimus, however, has better kinetics than other anti-proliferative medications, a wider therapeutic index, and does not cause cell death even at greater dosages [9]. As a result, sirolimus loading onto DES is a popular technique for preventing cell overgrowth and lowering restenosis after stent insertion. Release R is a sirolimus eluting cobalt chromium coronary stent system with open and closed cell design. Completely biodegradable, Biocompatible polymer PLGA is being used as a carrier. 90 % of sirolimus drug is released within 90 to 120 days. 6 μm of uniform coating thickness ensures programmed release kinetics. Inhibits In- stent Restenosis (ISR) and late thrombosis with adequate re- endothelization. Mounted on Veda PTCA catheter, which has trifolded / fourfolded balloon for safe crimping and optimal unfolding upon inflation. Designed for utmost safety- Release-R displays one of the lowest entry profiles. Better side branch access due to hybrid cell design and has a hydrophilic coating on the delivery system to reduce transitional force.

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There are very few studies present in literature which focus on application and function of Sirolimus Stents and in those specifically Release R. Hence the present study was conducted to assess the effectiveness and safety of the Release R sirolimus-eluting stent in patients with native coronary artery lesion.

MATERIAL & METHODS: The prospective study was conducted among 450 subjects and at a tertiary care center that were eligible for the placement of stent during the one year of study period. Total 519 stents were placed during the study. Patients were eligible for the study if they had a clinical indication for ACS. On visual estimation, percent diameter stenosis had to be ≥60%; vessel size, between 2.5 and 3.0 mm; and lesion length, 45 mm. Principal exclusion criteria were total occlusion at the site of in-stent restenosis; previous brachytherapy; lesion in the unprotected left main; myocardial infarction within the preceding 14 days; contraindication to aspirin, clopidogrel, or heparin; and severe concomitant disease interfering with follow-up. Every patient signed an informed consent form. With the aid of conventional balloon angioplasty procedures, all lesions had to be predilated. After that, one or two sirolimus-eluting stents were placed over the lesion (Release R). Sirolimus-eluting stents with lengths of 8, 18, or 33 mm and diameters of 2.5 or 3.0 mm were offered for the study. There was a limit of 2 stents. Except when they occurred early within the first four months, focal restenoses were treated by placing a confined stent. All patients got aspirin 100 mg/d for life and clopidogrel 75 mg/d for three months following stent insertion. For 48 hours following the operation, the plasma concentrations of creatine kinase and its MB isoenzyme were routinely assessed. Patients visited the hospital again after six months for an angiographic review and clinical evaluation. Continuous data were given as mean± SD, while discrete variables were reported as counts (percentages). By using the general linear model, we evaluated the impact of covariables on late loss. The best predictors of restenosis were found using a logistic regression analysis. The multivariate models contained all baseline variables. In the 2-tailed test, a value of $P < 0.05$ was considered significant.

RESULTS: The baseline demographics and clinical characteristics of patients were noted and it was found that mean age of patients was 56±10.64 years. 71.7% were male and 28.2% were female. The number of active smoker was 15% and 54.2 % had hypertension, 32.8% had diabetes mellitus and 15.5% had dyslipidemia as a risk factor. 11.1% patients had previous history of cardiac ailment as seen in table 1.

Table 1 : shows baseline demographic and clinical characteristics

Variable	Frequency (%)/ Mean± SD
Age (in years)	56±10.64
Male	323 (71.7)
Female	127 (28.2)
Smoker	67 (15)
Hypertension	244 (54.2)
Diabetes mellitus	148 (32.8)
Dyslipidemia	70 (15.5)
Previous history of cardiac ailment	50 (11.1)
Status post PTCA	33 (7.3)

Baseline angiographic and procedural characteristics were noted and it was found that maximum patients (43.7%) had 80-70% occlusion. 55% diseased vessel were of LAD category and minimum (0.5%) were in LM category. 18.6% had TIMI 0, 23.1% had TIMI 1, 42.2% had TIMI 2 and 14.6% had TIMI 3. Single diseased vessel was found in 45.1% patients , 35.5% had double vessels diseased and 17.1% had TVD as seen in table 2.

Table 2 : shows baseline angiographic and procedural characteristics

Variable		Frequency (%)/ Mean± SD
Stenosis	90% occlusion	88 (19.5)
	80-70% occlusion	197 (43.7)
	Total occlusion	84 (18.6)
	Subtotal occlusion	17 (3.7)
Diseased vessel	LAD	249 (55.4)
	LCx	94 (21)
	RCA	93 (20.8)
	LM	2 (0.5)
TIMI	0	84 (18.6)

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	1	104 (23.1)
	2	190 (42.2)
	3	66 (14.6)
Number of diseased vessel	Single	203 (45.1)
	Double	160 (35.5)
	TVD	77 (17.1)
Balloon dilatations	Pre	98 (21.7)
	Post	20 (4.4)
	Both	40 (8.8)
	None	98 (21.7)

Out of all the patients 6.8% had minor edge dissection , 1.1% had no reflow, 0.8% had cardiogenic shock and 0.2% had recurrence symptoms as seen in table 3.

Table 3 : shows data at follow-up

Variable	Frequency (%)
Minor edge dissection, plaque shift	31 (6.8)
No reflow	5 (1.1)
Cardiogenic shock	4 (0.8)
Recurrence symptoms	1 (0.2)

DISCUSSION

The preferred approach of percutaneous revascularization, the implantation of a coronary stent, has been shown to be clinically useful and safer than balloon angioplasty due to lower rates of restenosis. The frequency of restenosis, however, may be more than 30% in a number of patient subgroups despite the use of coronary stents, including populations with diabetes mellitus, narrow coronary arteries, and lengthy lesions.[10,11] In the past two decades, efforts to employ locally or systemically administered pharmacological medicines to decrease restenosis following angioplasty have generally failed. Recently, it was demonstrated in small registry studies and randomized clinical trials that sirolimus, a cytostatic macrocyclic lactone with both anti inflammatory and antiproliferative properties, delivered from a polymer-encapsulated stent, could lower the risk of restenosis in patients who were at low risk for restenosis.[12,13] The present study was done to assess the effectiveness and safety of the Release R sirolimus-eluting stent in patients with native coronary artery lesion. In our study the average age of patients was 56±10.64 years and number of male patients (71.7%) were more in number as compared to female patients (28.2%). The results were comparable to study done by Neumann FJ et al where average age was 62.9 years and umber of male patients was 68.5%. This shows that 55-65 years is the most common age of having coronary artery disease and it is more prevalent in male patients.[14] In our study 70-80% occlusion of vessels was common in 43.7% patients.55.4% patients had disease in LAD. Out of all 45.1% patients had only one vessel involved and these findings were similar to study done by Neumann FJ et al.[14] Sirolimus-eluting stent implantation was successful, with a long-term angiographic success rate of over 90%. Notably, reintervention was not necessary in the roughly Among patients who experienced recurrence because the stenosis was not severe enough to be deemed clinically relevant. A low rate of clinical and angiographic re-restenosis resulted from the low late loss following sirolimus-eluting stents for in-stent restenosis. Following the implantation of sirolimus-eluting stents, serial angiographic and intravascular sonographic follow-up demonstrated no risk of late restenosis and validated that 6-month angiography accurately represents the minimal neointimal formation within sirolimus-eluting stents.[15] However, in order to fully define the clinical effect of sirolimuseluting stents in the treatment of in-stent restenosis, longer follow-up times and more patients are required. Although there was a tendency for bigger late losses to occur with longer lesions, we were unable to find any clinical, angiographic, or procedural characteristics that were linked to a significant decline in the efficacy of sirolimus-eluting stents. On the other hand study was not powered to identify weak predictors of recurrence after treatment with sirolimus-eluting stents. Additional clinical trials involving patients with disease in a bifurcation, chronic total occlusions, saphenous-vein graft disease, restenosis after stenting, failure of vascular brachytherapy, lesions in the left main coronary artery, and multivessel disease are needed to determine the sirolimus-eluting stents' ultimate clinical usefulness. The results of 450 patients' one-year follow-up exams after receiving sirolimus-eluting stent treatment are optimistic since they show that the angiographic and clinical efficacy is still present.[15] A precise integration of the stent design, drug-carrier vehicle, and therapeutic agent is necessary for a clinically effective drug-eluting stent system. Release R, a well-known

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chemotherapeutic drug that reduces microtubule dynamics and is given via a polymer-matrix formulation, has produced promising preliminary stent-based results [16,17].The findings of our study show that the sirolimus-eluting stent has managed to strike a delicate balance between improved efficacy and conserved safety, and as a result, has the potential to change the future of coronary therapy.

CONCLUSION

Sirolimus is a conventional antiproliferation drug and is the most widely used drug in DESs. Sirolimus-release behavior affects endothelialization and thrombosis formation after DES implantation. In this study where we involved patients with complex coronary lesions, the use of Release R sirolimus-eluting stent had a consistent treatment effect, reducing the rates of restenosis and associated clinical events in all subgroups analyzed.

DISCLAIMER

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