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The Twelve-Month Outcome of Biolimus Eluting Stent with Biodegradable Polymer Compared With an Everolimus Eluting Stent with Durable Polymer

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ABSTRACT

Introduction Drug-eluting stents (DES) have significantly decreased the need for repeat coronary revascularization but concerns remain regarding the safety of first and second generation DES. We compared the safety and efficacy of a biolimus-eluting stent (with biodegradable polymer) with an everolimus-eluting stent (with durable polymer) one.***Methods***: We performed a randomized trial to compare the two types of stents. Two hundred patients undergoing PCI for de novo lesions were randomly assigned 1:1 to treatment with either biolimus-eluting (BioMatrix) or everolimus -eluting (Xience V) stent. The primary endpoint was a composite of cardiac death, myocardial infarction, and clinically driven target vessel revascularization within 12 months. ***Results***: Demographics, clinical, and lesion characteristic were comparable between two groups. The 30-day major adverse cardiac event (MACE) rate was 2% in BioMatrix group versus 0% in Xience group ($p > 0.05$). After 12 months, the rates of cardiac death (0% in both groups), MI (2% versus 0%, $p=0.49$) and clinically –driven target vessel revascularization (0% in both groups) were similar for BioMatrix and Xience. No stent thrombosis was reported at 1, 6, 9 or 12 months after intervention in either group. ***Conclusion***: BES (Biolimus-eluting stent) with biodegradable polymer and EES (Everolimus-eluting stent) with durable polymer appear similar with respect to MACE and stent thrombosis in this patient population. Many studies with longer follow up are needed to define better the role of BES with biodegradable polymer in treatment of coronary artery lesions.

Introduction

Compared to bare metal stents (BMS), drug-eluting stents (DES) have reduced instent restenosis and so repeat revascularization rate. However, long-term safety of first and second-generation drug –eluting stents (DES) has been questioned due to late stent thrombosis risk. [1-3] Durable polymer may play a key role in this terrible phenomenon as a substrate for persistent inflammation and delayed vascular healing .[4] In recent years, new generation stents have been designed to improve safety and efficacy profile of previous DES. Ones and clinical trials have been performed to assess use of these new devices, which are also known as third-generation DES. Biolimus is a sirolimus analogue. It binds to the mammalian target of rapamycin and inhibits proliferation of smooth muscle cells. The BioMatrix biolimus-eluting stent (Biosensors, Switzerland) has a stainless steel platform with a strut thickness of about 112 µm and drug concentration of 15.6 µg per mm stent length and an abluminal biodegradable polymer, poly lactic acid (PLA). Previous studies largely compared Biolimus-eluting stent (BES) with sirolimus–eluting stent(SES).[5-8] Our aim was to compare the safety and efficacy of the biolimus-eluting stent (BioMatrix, Biosensors, Switzerland) with a widely used everolimus-eluting stent (Xience V, Abbott Vascular, Santa Clara, CA, USA).

Materials and methods

Study design

This study was a single-center, prospective, randomized trial. The study design randomly assigned 200 patients undergoing PCI in Shahid-Madani Heart Hospital, Tabriz, Iran in a 1:1 proportion to either BioMatrix stent or Xience V stent between February 2010 and March 2011.

Patient inclusion/exclusion criteria

Patients aged 18 years or older with stable angina or acute coronary syndromes, including non-ST elevation

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and ST-elevation MI and unstable angina, were considered eligible if they had at least one de novo lesion with a diameter stenosis of 50% or more that was suitable for coronary stent implantation in a vessel with a reference diameter ranging from 2.25 to 3.5 mm. Major exclusion criteria included: known allergy to acetyl salicylic acid, clopidogrel, heparin, stainless steel, everolimus, biolimus or contrast agent and pregnancy.

Procedure and follow up

A loading dose of heparin (70 units/kg) was administered intravenously before the procedure. Patients were given 100 mg of aspirin and 300 mg of clopidogrel before stenting. The balloon angioplasty and stent implantation were done according to standard techniques where direct stenting was allowed and no mixture of drug-eluting stents was allowed in any patient. The concentration of creatine kinase, creatine kinase-MB, and troponin at baseline, 6h and 18h after procedure were assessed. All patients were discharged on aspirin 100 mg daily indefinitely and clopidogrel 75 mg daily for at least 12 months. Concomitant medication was prescribed at the physician´s discretion. Clinical follow up were conducted by outpatient visits at 1month, 6months and 12 months post stent implantation. The patients were monitored for major cardiovascular events and for the need for additional revascularization of the target lesion.

Study Endpoints

The endpoints of the study was major adverse cardiac events including death, Q-wave or non-Q wave MI, CABG or PCI repetition on target lesion or vessel and stent thrombosis at 30 days, 6 months, and 12 months after the index procedure. The Q-wave MI was defined as development of new Q waves in ≥ 2 continuous leads with post procedural CK-MB elevation 3 times above normal. A non-Q wave MI was defined like the mentioned one, without development of new Q wave on the surface electrocardiogram.

Statistical Analysis

Data are presented as mean ± SD or frequencies. Categorical data were compared with Fisher´s exact test and continuous variables with student´s t test. A p-value of < 0.05 was considered significant. The statistical analysis was performed using SAS version 16.

Results

Two hundred patients were recruited in this trial. Two study groups had similar baseline clinical and angiographic characteristics (Tables 1 and 2). There were a greater number of Diabetic and Dyslipidemic patients in Xience V group (p > 0.05). No difference between the type of clinical presentation was observed in two groups. The LV function was similar in BioMatrix group and Xience V group (46.6 ± 9.3 vs. 46.3 ± 8.8). Number of patients with mono vessel, two vessel, and three vessel disease was similar between two groups (Table 2).

Table 1. Baseline demographics and clinical characteristics

Variables	Biomatrix stent(n=100)	Xience v stent(n=100)	P
Age, years	60.60±9.1	62.38±10.2	0.42
Male	66%(66)	64%(64)	0.76
Diabetes mellitus	28%(28)	32%(32)	0.53
Hypertension	48%(48)	37%(37)	0.05
Hyperlipidemia	36%(36)	44%(44)	0.24
smoking	26%(26)	20%(20)	0.31
Unstable Angina	28%(28)	29%(29)	0.16
Non ST-elevation MI	6%(6)	9%(9)	0.17
Ant STEMI	28%(28)	20%(20)	0.21
INF STEMI	14%(14)	8%(8)	0.09
Stable Angina	24%(24)	34%(34)	0.06
LVEF	46.59±9.3	46.30±8.8	0.82

STEMI, ST-elevation myocardial infarction; LVEF, Left ventricular ejection fraction

Clinical outcomes

Major cardiac events are listed in Table 3. Two patients in BioMatrix group had a Non-Q wave myocardial infarction after stenting and managed conservatively. No other adverse event was seen in either group in hospital course. The 12-month MACE rate was 0% (0 of 100 patients) in the Xience V group compared with 2% (2 of 100 patients) in the BioMatrix group (p > 0.05; Table 3). There were no death, and no patients required any type of repeated revascularization (bypass surgery or PCI) in two groups during 1-year follow-up. No stent thrombosis occurred during follow-up period up to 12 months in either group. After hospital discharge, no other clinical complication occurred in patients receiving BioMatrix stent or Xience V stent.

Discussion

This randomized study has confirmed the similar clinical outcomes of the BES with a biodegradable polymer in compare to EES with a durable polymer during one-year follow-up. There was no early or late stent thrombosis in any study subjects. The MACE rates were low at 30 days, 6 months, and 12 months. To the best of our knowledge, this is the first study that compared a BES (with a biodegradable polymer) with EES (with a durable polymer). Previous studies have shown safety and efficacy of everolimus-eluting stent Xience V in treating simple and complex coronary lesions and it is known as "market leader" in DES world.[9, 10]

The Stealth study was first trial which assessed safety and efficacy of a BES with biodegradable polymer compared with a BMS (bare metal stent) and showed better results in reducing 6 month instent lumen loss and simi-

lar clinical profile.[11]Then, Leaders trial compared BES (with a biodegradable polymer) with a SES (with durable polymer). Three year follow up of this trial recently has been published where it shows similar safety and efficacy of BioMatrix compared to Cypher stent.[5,7] Like Leaders trial, our study has conducted in an "all-comers" population albeit at a small size. More than two-thirds of the patients enrolled in our study had an acute coronary syndrome so the results can be more applicable to routine clinical practice. The low MACE rates seen in our study (2%) compared to Leaders trial (10.6%) could be attributed to several factors. First of them is the small number of patients in our study. Second, less severe and complex coronary artery lesions in our patients. Interestingly, no stent thrombosis was seen for up to 1 year in BioMatrix group (and Xience V group). These low rates of stent thrombosis are consistent with previous studies. In a study conducted by Esteves et al. no stent thrombosis was seen for up to 5 years follow up in BES with biodegradable polymer.[8]

Late and very late stent thrombosis is one of the major concerns about DES. Durable or permanent polymers may play an important role regarding this drawback.[4] Durable polymers can also cause vascular inflammation, hyper-eosinophilia and thrombogenic reaction, which may lead to stent thrombosis.[12]

Biodegradable polymers like PLA as found on the BioMatrix BES stent is located on the abluminal surface of the stent and allows for better-targeted drug release, and reduces systemic exposure to both the polymer and biolimus. The polymer is co-released with biolimus during 6-9 months and biodegrades to carbon dioxide and water, and only a stainless steel (metal stent backbone) remains after 6-9 months of stent deployment. This could reduce the risk of late and very late stent thrombosis.

Table 1. Baseline Angiographic characteristics

	Biomatrix stent(n=100)	Xience stent(n=100)	P
Refrence vessel diameter,mm	2.97±0.22	2.96±0.29	0.1
Stent length,mm	27.6±3.7	28.59±9.1	0.7
Single vessel disease	63%(63)	74%(74)	0.10
Two vessel disease	16%(16)	14%(14)	0.69
Three vessel disease	21%(21)	12%(12)	0.06
Treated vessel LAD	68%(68)	62%(62)	0.08
LCX	10%(10)	18%(18)	0.09
RCA	22%(22)	20%(20)	0.1

LAD, Left anterior descending artery; LCX, Left circumflex artery; RCA, Right coronary artery

Table 3. MACE and stent thrombosis at 1-year follow up

MACE Event	BioMatrix stent(n=100)	Xience V stent(n=100)	P
12 month MACE rate	2%(2)	0%(0)	0.49
Cardiac death	0	0	NA*
Q-wave MI	0	0	NA
Non-Q wave MI	2%(2)	0	0.49
TVR	0	0	NA
Stent thrombosis	0	0	NA

MACE, Major adverse cardiovascular events; TVR, Target vessel revascularization

*indicates not applicable because of zero value.

Conclusion

In conclusion, BES with biodegradable polymer and EES with durable polymer appear similar with respect to MACE and stent thrombosis during 12 months follow up in this study. The BioMatrix may be a good alternative for Xience V stent in patients with coronary artery disease.

Limitations

The present study has several limitations, including the small number of patients, relatively short follow up, no angiographic follow up, single center design and excellent clinical outcomes in control group (Xience stent) which may limit the ability to identify significant differences with the BioMatrix stent.

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Ethical issues

The local ethics committee of Tabriz University of Medical Sciences approved the study and all patients signed informed consent.

Conflict of interests

The authors declare no conflicts of interest

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