

The Outcome of Six-month Clinical Trial with Eucatax Paclitaxel Eluting Stent Compared With Eucastflex Bare Metal Stent in Patients Undergoing De Novo Coronary Stenting

MA Ostovan, M Rezaie, J Kojuri

Cardiovascular Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Background: Superiority of paclitaxel-eluting stents over bare metal stents in angiographic and clinical outcomes have been shown in many trials. Eucatax stents is a newly developed paclitaxel eluting stent using biodegradable polymer matrix. To our knowledge there have been no studies directly comparing Eucatax paclitaxel eluting stents with EucaSTSflex bare metal stents. The aim of this study is to evaluate short-term benefits of Eucatax in comparison with EucaSTSflex in patients undergoing denovo coronary stenting.

Methods: A retrospective comparison of Eucatax versus EucaSTSflex was conducted among 89 consecutive patients (44 Eucatax, 45 EucaSTSflex) in Kowsar heart institute, with at least one successfully deployed stent in de novo lesions over a 6-month period. Outcomes included death, nonfatal MI, CABG, late stent thrombosis at six month, as well as functional evidence of ischemia evaluated by exercise treadmill test(ETT) or cardiac scan(SPECT).

Results: From April to July 2008, a total of 89 patients (44 Eucatax, 45 EucaSTSflex) were evaluated after PCI for de novo coronary lesions.

After six month follow up no difference was observed in term of death, MI, CABG and late stent thrombosis between Eucatax compared with EucaSTSflex. Also a non-statistically significant lower rate of positive ETT (or SPECT) was found in Eucatax group after six month.

Conclusion: Paclitaxel eluting stents(Eucatax)are not superior to bare metal stents(EucaSTSflex) in regard to short-term clinical outcome.

Key Words: Paclitaxel, Eucatax, Bare Metal Stents, PCI

Introduction

Drug-eluting stents (DES) have emerged as one of the most promising technologies in the field of interventional cardiology in recent years.¹

Several randomized trials have shown that DES are associated with a significant reduction in restenosis and TVR in both elective and patients with STEMI as compared to bare metal stents (BMS).² Concerns have emerged on the potential higher risk of stent thrombosis and death with DES, which might be even more pronounced among patients with STEMI.³

Paclitaxel was selected as the pharmacologic

component for the paclitaxel-eluting stents (PES) because of its ability to target the key events in the cascade of restenosis and its physicochemical properties which make its systemic delivery a nightmare but are very favorable for stent-based delivery.⁴

Although paclitaxel-eluting stents have been shown to be highly effective in a number of randomized clinical trials which in largest one TAXUS IV study implantation of paclitaxel-eluting stents resulted in 27% reduction in ischemia-driven TLR compared with bare metal stents at nine month,⁵ but there are numerous paclitaxel-eluting stents which can be used in patients with de novo coronary lesions.

In present study we compared Eucatax paclitaxel-eluting stents (Eucatech GMBH) which is a second generation of DES with biodegradable polymer

Correspondence:

M Rezaie

Cardiovascular Research Center, Faghihi Hospital, Zand Street, Shiraz, Iran.

Tel/Fax: +98-711-2343529

E-mail: mrezaie@sums.ac.ir

matrix to EucaSTSflex stent which is an uncoated BMS with stainless steel 316LVM.

Patients and Method

All 89 consecutive patients (44 Eucatax, 45 EucaSTSflex) undergoing revascularization with PCI at the Kowsar heart institute (Shiraz, Fars) entered into a database registry that included prospectively collected demographic, clinical, procedural, angiographic and in-hospital outcome details, consisting of death, recurrent nonfatal myocardial infarction (MI), CABG and late stent thrombosis.

A retrospective comparison of Eucatax with EucaSTSflex was conducted among all consecutive patients at the institution, with at least one stent successfully deployed in de novo lesions over a 6-month period. Patients undergoing primary or rescue PCI, those presenting with cardiogenic shock and subjects with a dual stents (i.e., combination of EucaSTSflex and Eucatax) or presenting with restenosis were excluded from the study. All patients under investigation provided informed consent to be followed up after stenting, and the study had been approved by the institution's research ethics board.

Intervention

All procedures were performed according to standard techniques. The use of periprocedural antithrombotic agents at the time of PCI was at the discretion of the interventional cardiologist. Angiographic success was defined as residual stenosis of less than 20% in the presence of Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow.

Recommended postprocedural medications included lifelong acetylsalicylic acid and clopidogrel 75 mg/day for one year. The 600 mg loading dose of clopidogrel was used during present study

Definitions and follow-up

The primary outcome was defined as death, recurrent nonfatal MI, CABG or late stent thrombo-

Table 1. Angiographic characteristics

Lesion type	Eucatax	EucaSTSflex	P value
Type A	14 (31.8)	16 (35.6)	0.925
Type B	15 (34.1)	15 (33.4)	
Type C	15 (34.1)	14 (31.1)	
Diseased vessel			
SVD	30 (68.2)	28 (62.2)	0.8224
2VD	12 (27.3)	15 (33.4)	
3VD	2 (4.5)	2 (4.4)	

SVD=single vessel disease 2VD= two vessel disease
3VD=three vessel disease

sis at six month. In-hospital MI was defined as recurrent chest pain with ischemic electrocardiogram changes (mainly ST segment elevation), and/or elevation of total creatine kinase(CK-MB) to twice the upper limit of normal and a positive troponin-I, as per local standards. A diagnosis of recurrent nonfatal MI after discharge required the presence of two of ischemic symptoms, creatine kinase(CK-MB) elevation twice the upper limit of normal with a positive troponin result, or diagnostic Q waves on subsequent electrocardiograms.

Secondary outcomes included the individual events of death, MI, CABG, late stent thrombosis (according to ARC definition) and exercise tolerance test or cardiac SPECT after six month interval.

ARC definition of stent thrombosis was angiographically documented complete occlusion or flow-limiting thrombus of a previously treated artery.

In-hospital outcomes were verified by review of hospital charts.

Six month outcomes were corroborated by telephone calls using standardized questionnaires. Whenever patients had repeat hospitalizations for chest pain or cardiac catheterization, details of the admission were obtained for verification of outcomes. At six month, all patients included in the study were visited and underwent exercise treadmill test(ETT) or cardiac scan(SPECT) in patients with baseline ST depression, WPW, LBBB or physical disabilities not eligible for ETT.

Statistical analysis

Data were analyzed using SPSS software V.11.5. Chi-square and Fisher-exact tests were used to compare the results of two groups. The P value for the variables was less than the prespecified alpha level of 0.05.

RESULTS

A total of 89 patients (44 Eucatax, 45 EucaSTSflex) who underwent PCI for de novo lesions between April 2008 and July 2008, and who met inclusion criteria were evaluated in the present study.

Table 1 shows the baseline characteristics of the patients under study.

The mean age in Eucatax group was 55.4 years and that of EucaSTSflex group was 53.9 years. As for gender, 72.7 % of Eucatax and 77.7% of EucaSTSflex groups were males. Also 34% of Eucatax and 31.1% of EucaSTSflex groups had diabetes.

Dyslipidemia was seen in 63.6% of Eucatax and 60% of EucaSTSflex groups and 36.3% of Eucatax group and 33.3% of EucaSTSflex group had hypertension.

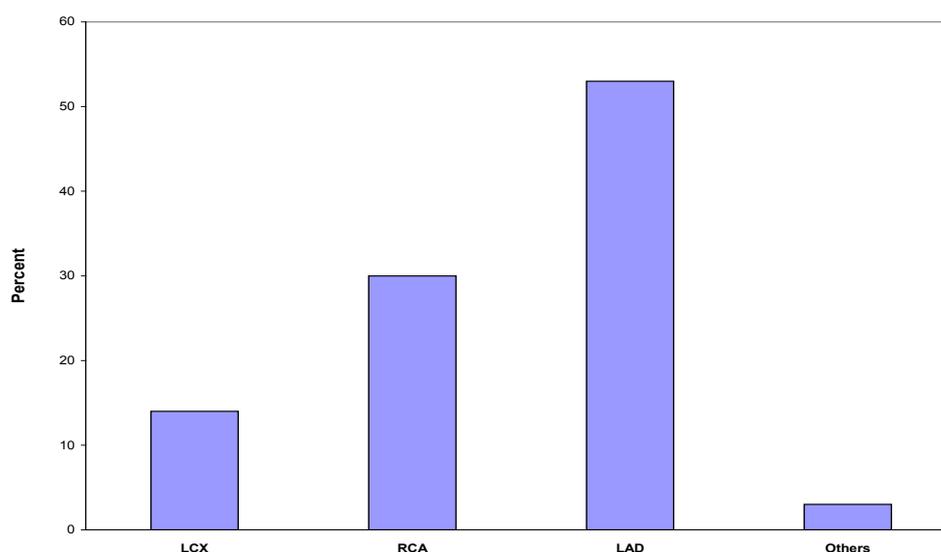


Figure 1. Coronary Artery Profile(All Patients)

Table 2. Procedure's characteristics

	Min	max	Mean
Lesion length	6	36	18.70±10.6
Reference diameter	2.4	4	2.85±0.8
Stent length	8	28	19.62±6.2

There were no significant differences with respect to aforementioned baseline characteristics.

Key angiographic characteristics are shown in Table 1, where 31.8% of Eucatax group and 35.6% of EucaSTSflex group had type A lesion. Also 34.1% of Eucatax group and 33.4% of EucaSTSflex group had type B lesion. Type C lesion was seen in 34.1% of Eucatax group and 31.1% of EucaSTSflex group.

Overall, in regard to the foregoing values, there were no significant differences between two groups.

The culprit coronary vessel was LAD in 53%, RCA in 30%, LCX in 14% of cases and the remaining 3% belonged to other vessels (SVG). (Fig. 1)

In patients of both groups, the mean length of

Table 3: Demographic data

	Eucatax	EucaSTSflex	P value
Age (yr)	55.4 ±5.3	53.9 ±4.5	0.150
Gender (male)	72.7%	77.7%	0.760
Diabetes	34.0%	31.1%	0.940
Dyslipidemia	63.6%	60.0%	0.820
Smoking	34.0%	35.5%	0.940
Hypertension	36.3%	33.3%	0.940
Positive ETT (or SPECT)	9.0%	15.5%	0.545

lesion was 18.70 ± 10.6 with a mean reference vessel diameter of 2.85 ± 0.8 and the mean length of deployed stents being 19.62 ± 6.2 .

Among 44 cases of Eucatax group 30, 12, and 2 patients had 1, 2 and 3 vessel disease respectively. The respective number among 45 cases of EucaSTSflex group were 28, 15, and 2 patients with one, two, and three vessel disease ($P=0.8224$).

After 6 month clinical follow up there were no death, non fatal MI and late stent thrombosis in Eucatax group and there was only one death in patient of Eucatax group (2.2%) which was statistically non-significant ($P=0.494$).

There was no CABG as a result of Eucatax or BMS group after 6 month clinical follow up.

Evaluation of functional ischemia by ETT or SPECT showed 9% positive ETT (or SPECT) in Eucatax group compared with 15% in EucaSTSflex (Table 3, $P=0.545$).

Discussion

Although paclitaxel eluting stents have been shown to be superior to Bare metal stents in many trials;⁸⁻¹¹ Our study, the first to compare Eucatax and EucaSTSflex, showed that Eucatax is not superior to EucaSTSflex considering 6 month clinical outcomes.

Horizon's trials presented at TCT2008, showed no difference in death (3.5% vs. 3.5%) and reinfarction (3.5% vs. 4.7%) after 1-year follow up with PES vs. BMS, respectively.⁹

Data from TAXUS I and III rate of death, reinfarction and restenosis was lower in PES group

than BMS patients.^{4,7}

In Passion trial, Laarman et al showed safety of PES in terms of death (4.6% vs. 6.5%) and stent thrombosis(1% vs. 1%) at 1-year clinical follow up, as compared to BMS.¹⁰

In present study we showed that there was no significant difference (P=0.494) between Eucatax and EucaSTSflex in regard to death (1% vs zero) MI(1% vs zero)and late stent thrombosis (1% vs zero).

In a recent study, Martin et al demonstrated that the use of Paclitaxel- eluting stents compared with Bare metal stents in patient who had undergone PCI for single noncomplex de novo lesions not only significantly decreased the overall need for repeat procedures to treat restenosis but also reduced

the need for subsequent CABG by 67%.¹¹ However in our study the rate of CABG after 6 month in both groups was zero which disallowed comparison.

Functional evidence of ischemia evaluated by ETT or SPECT was lower in Eucatax than EucaSTSflex groups (P=0.545).

Paclitaxel- eluting stents(Eucatax) are not superior to bare metal stents(EucaSTSflex) in view of short term clinical outcomes. However, long term follow up and evaluation, for at least one year, are needed to achieve a more comprehensive result.

Acknowledgments

This work was financially supported by Vice Chancellor for Shiraz university of Medical Sciences. The authors declare that they have no conflicts of interest.

References

- 1 Dawkins KD, Grube E, Guagliumi G, Banning AP, Zmudka K, Colombo A, et al. Clinical efficacy of polymer-based paclitaxel-eluting stents in the treatment of complex, long coronary artery lesions from a multicenter, randomized trial: support for the use of drug-eluting stents in contemporary clinical practice. *Circulation* 2005;**112**:3306-13. [16286586]
- 2 Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, et al. Sirolimus- eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;**349**:1315-23. [14523139]
- 3 Lagerqvist B, James SK, Stenestrand U, Lindbäck J, Nilsson T, Wallentin L. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. *N Engl J Med* 2007;**356**:1009-19. [17296822]
- 4 Kamath KR, Barry JJ, Miller KM. The taxus drug- eluting stent: A new paradigm in controlled drug drug delivery. *Adv deliv rev* 2006;**58**:412-36. [16647782]
- 5 Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, et al. TAXUS- IV investigators. A polymer- based paclitaxel- eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;**550**:221-31. [14724301]
- 6 Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, et al. One- year clinical results with slow- release, polymer-based, paclitaxel- eluting TAXUS stent TAXUS- IV trial. *Circulation* 2004;**109**:1942-7. [15078803]
- 7 Grube E, Silber S, Hauptmann KE, Mueller R, Buellesfeld L, Gerckens U, et al. TAXUS I: Six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel-eluting stent for de novo coronary lesions. *Circulation* 2003;**107**:38-42. [12515740]
- 8 Colombo A, Drzewiecki J, Banning A, Grube E, Hauptmann K, Silber S, et al. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stent for coronary artery lesions. *Circulation* 2003;**108**:788-94. [12900339]
- 9 Mehran R, Brodie B, Cox DA, Grines CL, Rutherford B, Bhatt DL, et al. The Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial: study design and rationale. *Am Heart J* 2008;**156**:44-56. [18585496]
- 10 Laarman GJ, Suttrop MJ, Dirksen MT, van Heerebeek L, Kiemeneij F, Slagboom T, et al. Paclitaxel-eluting versus uncoated stents in primary percutaneous coronary intervention. *N Engl J Med* 2006;**355**:1105-13. [16971717]
- 11 Martin JL, Ellis SG, Colombo A, Grube E, Maloney T, Friedman MI, et al. Frequency of coronary artery bypass grafting following implantation of a Paclitaxel-Eluting or a Bare-Metal Stent into a single coronary artery. *Am J Cardiol* 2009;**103**:11-16. [19101222]