IJC Heart & Vessels 1 (2013) 37–41

Contents lists available at ScienceDirect

IJC Heart & Vessels

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vessels

Clinical Efficacy and Safety of SeQuent Please Paclitaxel-Eluting Balloon in a Real-World Single-Center Registry of South-East Asian Patients☆,☆☆

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ARTICLE INFO

Article history:
Received 3 November 2013
Accepted 18 November 2013
Available online 27 November 2013

Keywords:
Drug-eluting balloon
Percutaneous coronary intervention
South-East Asia
Registry
Outcomes

ABSTRACT

Background: Drug eluting balloon (DEB) is a new therapeutic option for treatment of obstructive coronary lesions in percutaneous coronary intervention (PCI). There is limited data on the safety and efficacy of DEB in Asian patients in contemporary clinical registries. We evaluated the clinical efficacy and safety of SeQuent Please paclitaxel-eluting balloon in our cohort of South-East Asian patients in real world clinical practice.

Methods: Between January 2010 to November 2012, 320 patients (76% male, mean age 61.3 ± 11.2 years) with a total of 337 coronary lesions were treated with SeQuent Please drug-eluting balloon (DEB). The primary endpoint was major adverse cardiac events (MACE) ie a composite of cardiovascular death, target vessel related myocardial infarction (MI) and target lesion revascularization (TLR) at 9 months follow-up.

Results: The majority of patients presented with acute coronary syndrome (76%).The most common indication for the use of DEB was small vessel disease (54%) followed by instent restenosis (21%), bifurcation lesions (6%) and others (19%). An average of 1.23 ± 0.5 DEB were used per patient, with mean DEB diameter of 2.6 ± 0.6 mm and average total length of 24.0 ± 11.1 mm.

At 9 months follow-up, 5.3% of patients developed MACE. MACE was mainly driven by TLR(4%) followed by target vessel related myocardial infarction (2.6%) and cardiovascular death (1%).

Conclusion: SeQuent Please DEB was a safe and effective treatment modality in our cohort of South-East Asian patients with a low incidence of MACE observed at 9 months follow-up.

1. Introduction

Drug-eluting balloon [1] (DEB) has emerged as a new therapeutic option to treat obstructive coronary artery disease (CAD) in percutaneous coronary intervention (PCI). Non-stent-based local drug delivery using DEB has several advantages as it:

1) inhibits excessive neointimal hyperplasia following balloon angioplasty of a diseased native coronary artery without leaving a permanent metallic frame
2) avoid a "stent-in-stent" approach in previously stented arteries
3) eliminate the risk of stent thrombosis
4) reduce the duration of dual anti-platelet therapy (DAPT).

The clinical efficacy of DEB has been well proven in randomized controlled trials [2,3] in the treatment of bare metal stent instent restenosis (BMS ISR) when compared to uncoated balloon/paclitaxel-coated stent with sustainable results [4] observed at long term follow-up. Favourable results are also seen with the use of DEB in drug-eluting stent (DES) ISR [5,6] although robust data is lacking for the combined use of DEB and BMS [7,8] in routine PCI and also in specific lesions subsets [9–11] like small vessel, bifurcation lesion, etc. Similar to DES, DEB has been used in "off-label" indications in the "real world" and there is limited data [12] on its clinical efficacy and safety in Asian patients in contemporary clinical registries. We therefore sought to evaluate the clinical efficacy and safety of SeQuent Please DEB (B. Braun, Melsungen, Germany) in our cohort of South-East Asian patients in "real world" clinical practice.

2. Materials and Methods

2.1. Study Population

From January 2010 to November 2012, a total of 320 symptomatic patients with native coronary lesions, instent restenosis (ISR) and saphenous venous graft lesions (total of 337 lesions) were treated with SeQuent Please DEB at our institution.

☆ Declaration of Interest: The authors report no conflicts of interest.
☆☆ This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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http://dx.doi.org/10.1016/j.ijchv.2013.11.008

2.2. Interventional procedure

All PCIs were performed using standard techniques and according to contemporary practice guidelines. All patients were treated with aspirin 100 mg prior to the procedure and indefinitely thereafter. Patients also received clopidogrel (an oral loading dose of 600 mg followed by 75 mg daily) before the procedure, followed by a minimum of 1 month in patients who received DEB alone and a minimum of 3 months in patients who received BMS implantation in combination with DEB. Additional duration of clopidogrel treatment was at the discretion of the attending physician.

2.3. Use of DEB during PCI

The SeQuent Please DEB catheter was loaded with paclitaxel 3 ug/mm2. The length of the DEB catheter was chosen to exceed the target lesion for at least 2 mm (at both proximal and distal ends). The catheter(s) was inflated for 30 to 60 s with a minimum of 7 atm. Predilation of the diseased coronary segment with a uncoated balloon/scoring balloon/cutting balloon before the use of DEB was encouraged. BMS was implanted if the angiographic result after DEB alone therapy was not satisfactory due to significant recoil/residual stenosis or dissection (Type C-F). For those opting for the combined use of DEB and BMS as primary therapy, the length of DEB had to exceed the length of the implanted BMS (this principle was also applied for bail-out stenting).

2.4. End-Points and Definitions

The primary end-point was major adverse cardiac event (MACE) ie a composite of cardiovascular (CVS) death, target vessel related myocardial infarction (MI) and target lesion revascularization (TLR) at 9 months follow-up. Secondary end-points include individual components of MACE and target lesion thrombosis.

Death from CVS causes was defined as death due to acute MI, cardiac perforation or tamponade, arrhythmia, a complication of the PCI procedure or as any death in which a CVS cause could not be ruled out.

Target-vessel related MI was defined as the presence of new Q waves in at least 2 contiguous leads on electrocardiogram (concordant with the intervened target lesion) with elevation in cardiac troponin or in creatine kinase/creatine kinase-MB above the upper limit of the normal range, or in the absence of pathologic Q waves, MI was diagnosed in the presence of an elevation in cardiac troponin or in creatine kinase > 2 times the upper limit of normal. TLR was defined as any repeat revascularization (percutaneous or surgical) secondary to a stenosis > 50% within the stent or within 5 mm proximal or distal to the stented segment. Target lesion thrombosis was defined according to the Academic Research Consortium [13] criteria for definite and probable stent thrombosis. In our study, we defined native coronary artery as small vessel when reference vessel diameter ≤ 2.8 mm and as *de novo* lesion when reference vessel diameter > 2.8 mm. Our retrospective study conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the institution's human research committee.

2.5. Statistical analysis

Continuous variables were expressed as mean ± standard error of mean. Dichotomous variables were expressed as counts and percentages. Statistical comparisons were performed using Student's t test or Fisher's exact test, as appropriate. Multivariate regression analysis was performed (using an enter regression model) to evaluate predisposing factors for TLR, in which each entered variable had p value < 0.1 based on univariate analysis. Calculations were performed using SPSS software (version 16.0; SPSS, Inc., Chicago, Illinois). All *p*-values were 2-sided and *p*-values < 0.05 were considered statistically significant.

3. Results

Table 1 show the baseline clinical characteristics of the study patients. The mean age of the patients at presentation was 61.3 ± 11.2 years with male preponderance (76%).

Diabetes mellitus (DM) was present in 155 patients (48.4%) and 137 patients (43%) had history of prior stenting. The mean left ventricular function was 45 ± 13 %. The majority (76%) of patients presented with acute coronary syndrome (ACS).

Table 2 shows the angiographic features and procedural data of our patients. The majority of patients (78 %) had multi-vessel disease on coronary angiography. The most common target vessel for PCI with DEB was left anterior descending artery (37%), right coronary artery (18%), left circumflex artery (17%) and others (28%). "Others" include side branches (mostly diagonals followed by posterior descending arteries/posterior left ventricular branches, obtuse marginals), saphenous venous grafts (all seven cases involved distal venous graft anastomosis) and left main lesions (2 patients).

Glycoprotein IIb/IIIa inhibitors were administered in 232 patients (73%). The most common indication for the use of DEB in our registry was small vessel disease (54%) followed by ISR (21%), bifurcation lesions (6%), *de novo* lesions (5%) and others (14%). Of the 72 ISR, DEB intervention was performed for 56% BMS ISR and 44% DES ISR. Based on Mehran classification for ISR, DEB was largely used for focal ISR (Mehran type I: 56%) followed by Mehran type II (28%), Mehran Type IV (12%) and Mehran Type III (4%).

DEB alone therapy was the predominant approach (82% of patients) during PCI whereas DEB followed by bare metal stenting was performed for the remaining 18% of patients. An average of 1.23 ± 0.5 DEB were used per patient, with mean DEB diameter of 2.6 ± 0.6 mm and average total length of 24.0 ± 11.1 mm.

For the initial 320 patients, 5 patients died during index hospitalization and 11 patients were lost to follow-up. Table 3 summarizes the clinical outcomes of 304 patients at 9 months follow-up. A total of 16 patients (5.3%) developed MACE at 9 months follow-up.

MACE was mainly driven by TLR (4%) followed by target vessel related MI (2.6%) and CVS death (1%). There was no reported target lesion thrombosis. Factors associated with TLR by univariate analysis (TLR group vs non-TLR group) were older age at presentation (67.2 ± 11.2 years vs 60.6 ± 10.9 years, p = 0.04), diabetes mellitus (75% vs 47%, p = 0.07), DES ISR (25% versus 8.6%, p = 0.08), DEB alone therapy during PCI (58.3% vs 83%, p = 0.04), mean number of DEB per patient (1.5 ± 0.67 vs 1.23 ± 0.47, p = 0.06) and total DEB length (31.7 ± 14.6 vs 23.9 ± 11 mm, p = 0.02). However no independent predictors of TLR were identified by multi-variable analysis. Figs. 1 to 7 illustrates our clinical experiences with the use of DEB in "real world"clinical practice.

4. Discussion

To our knowledge, this is the largest registry in the South-East Asian region evaluating the use of DEB in an all-comer group of patients in the "real world". We found that the use of SeQuent Please DEB was a safe and effective treatment modality for South-East Asian patients in the "real world" setting. The intermediate term clinical outcomes in our cohort of patients were good with a low incidence of MACE.

In recent years, DEB has emerged as a viable therapeutic option for treating CAD as the current DES technology [14] has limitations like late stent thrombosis and prolonged DAPT.

Paclitaxel is the drug of choice for all the commercially available DEB manufacturers because of its highly lipophilic properties which allows rapid diffusion into the vessel wall and sustained anti-proliferative effect despite its short contact with the vessel wall. The largest clinical evidence [2–9,11,12] has been reported for DEB coated with paclitaxel-iopromide with > 3000 patients evaluated in randomized

Table 1
Baseline Clinical Characteristics of Patients.

	N = 320
Mean age (years)	61.3 ± 11.2
Male:Female,n, %	242: 78 (76 : 24)
Ever smokers,n,%	173 (54.1)
Diabetes,n, %	155 (48.4)
Hyperlipidemia,n,%	261 (81.6)
Hypertension,n,%	257 (80.3)
Previous myocardial infarction,n,%	102 (32.0)
Previous PCI,n,%	137 (42.8)
Previous CABG,n,%	24 (7.5)
LVEF(%)	45 ± 13
Presentation:	
STEMI,n,%	48 (15)
NSTEMI/UAP,n,%	194 (61)
Stable angina,n,%	78 (24)

*PCI denotes percutaneous coronary intervention, CABG coronary artery bypass graft, LVEF left ventricular ejection fraction, STEMI ST elevation myocardial infaction, NSTEMI/UAP denotes non STEMI/unstable angina pectoris.