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Comparative Study between Immediate and Mid-Term Results of Coronary Angioplasty Using Two Different Types of Drug-Eluting Stents

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ABSTRACT

Background: The development of sirolimus-eluting stents (SES) was an important step in treating coronary artery disease (CAD). SES could decrease the angiographic restenosis and target vessel revascularization (TVR) as compared to bare-metal stent (BMS) and drug-eluting stent (DES). Nonetheless, there is scarce data regarding SES's outcomes in Egyptians receiving DESs.

Objective: We aimed to assess the effectiveness of SES vs. Paclitaxel-eluting stent (PES) in treating CAD and identifying severe adverse cardiovascular and cerebrovascular events.

Patients and method: Data collected from 44 patients admitted to Cardiology Department of National Heart Institute from January 2004 and December 2005 and followed up for 3 months, who were scheduled to percutaneous intervention (PCI) due to severe angiographic stenosis (> 50 %) in a native coronary artery. Participants in this study were then divided into 2 groups: SES and PES groups.

Results: The differences between both groups regarding the immediate angiographic outcomes like diameter of residual stenosis (DS%) and acute gain were non-significant. Stent characters including flexibility, deliverability, conformability and side branch preservation ability did not also show significant differences among groups. Similarly, no significant differences were found between both groups in the 3 months clinical follow up. Regarding the percentage of binary restenosis and the late luminal loss at follow-up angiography, both values were higher in group "B" than in group "A" but without a significant difference.

Conclusion: We can conclude that it is better to utilize SES but not to the degree to recommend its utilization over the PES.

Keywords: CAD, DES, PES, Coronary angioplasty.

INTRODUCTION

Individuals with diabetes mellitus (DM) are at high risk of CAD [(1)]. It has been recently shown that prevalence of DM is increasing worldwide. Therefore, its role in CAD is also increased [(2)]. Earlier research has shown that DM had an association with worse outcome in those having percutaneous coronary intervention (PCI), including greater re-stenosis rates, myocardial infarction (MI) and mortality [(3)]. As DM is linked to a greater possibility of advanced CAD, the type of intervention is important in the determination of long-term outcomes [(4)].

The FREEDOM study reported that coronary artery bypass grafting (CABG) was better than PCI as it reduced mortality rates and MI, with a high risk of stroke [(5)]. However, FREEDOM trial did enroll cases with STEMI and a recent study has demonstrated that only few cases with STEMI undergo emergency CABG, which limits the treatment choices for diabetic cases with complex CAD [(6)].

In the previous 2 decades, modern DESs have been significantly utilized in STEMI patients [(7)]. DESs are better than BMS leading to lower TVR rates and, in many reports, lower rates of reoccurrence of MI [(8)]. However, there is little information on the effectiveness of DESs in diabetics having advanced CAD and acute MI.

Through our study, we aimed to assess and compare the safety and immediate results of 2 types of DESs in CAD of patients with and without DM.

PATIENTS AND METHOD

Study population: This prospective comparative study included 44 cases scheduled for PCI due to a significant angiographic stenosis (> 50 %) in a native coronary artery. Cases were divided into 2 groups (22 each): **Group A** received SES (Cypher®, Cordis, Johnson and Johnson) and **group B** received PES (Taxus ®, Boston Scientific).

Exclusion criteria: NYHA class IV or heart failure, severe dysrhythmias or conduction abnormalities, type "C" lesions based on AHA and ACC classification, left main trunk lesions, lesions of arterial graft or venous graft and complete occlusion, lesions of instent restenosis and MI i.e. primary PCI.

Data collection and follow-up:

Initially, we collected data including demographics, history, lab tests, symptoms or signs, PCI information, medications, and outcome. Angioplasty and stent implantations were carried out through femoral approach either direct stenting or following pre-dilatation (depending on the criteria of each lesion). A successful procedure was defined as residual stenosis of dilated segment of < 20% in the worse of the 2 orthogonal views as evaluated by quantitative analysis.

Patient underwent follow-up in the hospital for 24 h post-intervention for any clinical findings of stent thrombosis including chest pain, new ECG abnormalities or neurovascular complications. Each patient was instructed before discharge for drug

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treatment and was followed up for 90 days post-procedure for chest pain and major adverse cardiac events (MACEs) i.e. MI or mortality. **Follow-up angiography** was performed for any asymptomatic patient after 90 days and earlier if the person had chest pain or acute coronary events before 90 days.

Following DES implantation, all cases received Clopidogrel 75 mg per day for 12 months. They also received statins (atorvastatin 20–40 mg per day). All cases with DM received anti-diabetic medications.

Study end points and definitions: The primary end point was a composite of MACEs (cardiac death, recurrent MI, and stented TLR). The secondary end points comprised the individual components of MACEs, all-cause mortality and ST. Binary restenosis was considered significant if it was > 50% restenosis in stented area and within the margins 5 mm. proximal and distal to stent edges. The late luminal loss was measured as a difference between minimal luminal diameter (MLD) post-intervention and at the follow up angiography.

Binary restenosis %= reference vessel diameter (RVD) at follow up ⁻ MLD at follow up.

Ethical approval: Our study was performed according to Helsinki Declaration after being approved by The Ethical Committee at Faculty of Medicine, Ain Shams University. Informed consents were signed by all cases.

Statistical analysis

SPSS software version 22.0 was utilized for data analysis. Continuous data were represented as means ± SDs, and the comparison between 2 groups was performed by Student t-test. Categorical data were represented as frequencies (percent) and comparisons between two groups were performed by Chi-square test or Fisher's exact test. P values ≤ 0.05 were regarded significant.

RESULTS

In our study, 44 cases were enrolled and then allocated into two groups (22 each): Group A: received SES **(Cypher®)**, and **group B:** received PES **(Taxus ®)**. The age group "A" patients was 36 - 72 years (mean = 51.68 ± 9.25). The age of group "B" patients was 38 - 68 years (mean= 52.27 ± 8.38). Males in groups "A" and "B" were 59.1% and 63.6% respectively. No significant differences in patients age and gender were found between both groups (p > 0.05= NS).

Table (1): Demographics of studied groups

Criteria	Group A	Group B	P- value
Age			
Range	36-72	38-68	p>0.05=
Mean ± SD	51.68 ± 9.25	52.27 ± 8.38	NS
Sex			
Male [N (%)]	13/22 (59.1%)	14/22 (63.6%)	p>0.05=NS
Female [N (%)]	9/22 (40.9%)	8/22 (36.4%)	p>0.05= NS

Risk Factors analysis (Table 2): No significant differences in the number (percentages) of cases with DM, cases with hypertension (HTN), cases with dyslipidaemia and smokers were found between the 2 groups (p > 0.05).

Table (2): Risk factors in studied groups

	Group A (n=22)	Group B (n=22)
DM	17 (77.3%)	17 (77.3%)
HTN	13(59.1%)	10 (45.5%)
Dyslipidemia	9 (40.9%)	10 (45.5%)
Smoking	12 (54.5%)	14 (63.6%)

Clinical presentation (Table 3): 22 patients had anterior MI (11 in each group). 7 patients had inferior MI (3 in group "A" vs. 4 in group "B"). 7 patients had unstable angina (3 in group "A" vs. 4 in group "B"). 2 patients from group "B" presented with NSTEMI. 6 patients had chronic stable angina (5 in group "A" vs. 1 in group "B").

Table (3): Clinical presentation of patients in study groups

Clinical Presentation	Group		Total
	A	B	
Anterior MI	11	11	22
Inferior MI	3	4	7
Unstable Angina	3	4	7
NSTEMI	0	2	2
Chronic stable Angina	5	1	6

Angiographic data (Table 4): No significant differences were found between the 2 groups regarding lesion length, RVD before angioplasty, MLD before angioplasty, MLD post-angioplasty, DS% pre-angioplasty, residual DS% post-angioplasty, acute procedural gain and stent diameter and length. Regarding flexibility, deliverability and conform-ability there were no significant difference noticed during angioplasty between the 2 types of the stents used in our study.

Table (4): Angiographic findings in study groups

Characteristics	Group A	Group B	p-value
Lesion length (mm)	21.23 ± 8.35	21.68 ± 4.38	NS
RVD pre-angioplasty	3.18 ± 0.39	3.21 ± 0.36	NS
MLD pre-angioplasty	0.29 ± 0.14	0.26 ± 0.1	NS
MLD post-angioplasty	2.95 ± 0.39	2.92 ± 0.32	NS
DS% pre-angioplasty	90.32 ± 3.78	91.32 ±3.37	NS
Residual stenosis% post-angioplasty	6.77 ± 2.02	8.05± 3.03	NS
Acute Gain (mm)	2.66± 0.34	2.66 ± 0.35	NS
Stent diameter (mm)	3.05 ± 0.38	3.11 ± 0.38	NS
Stent length (mm)	21.86 ± 6.53	23.54± 4.53	NS

In hospital follow up: No complications of acute stent thrombosis (chest pain, ECG abnormalities or neurovascular complications) were reported in the first 24 h of hospital stay post-intervention. No significant differences existed between group A and group B in the follow-up because MACEs occurred in 2 patients (one in each group) in the form of unstable angina with significant in-stent restenosis.

Statistical analysis of the follow up angiographic data: (Table 5)

1- Minimal luminal diameter at follow up (MLD):

The difference 1n MLD at follow up among studied groups was insignificant (p > 0.05).

2- Binary restenosis %:

Binary restenosis % was greater in group "B" than in group "A" but without a significant difference between both groups (P value > 0.05).

3- Late Luminal loss in mm. (late loss):

Late loss at follow-up angiography was greater in group "B" than in group "A" but without a significant difference.

Table (5): Follow up angiography of studied groups

Mean	Group A	Group B	p value
MLD(mm)	2.69 ± 0.47	2.49 ± 0.55	NS
Binary restenosis (%)	10.27 ± 11.14	18.05 ± 15.21	NS
Late loss (mm)	0.26 ± 0.34	0.43 ± 0.32	NS

DISCUSSION

The complication and death rates are elevated in cases with DM following PCI or CABG, making it essential to choose the ideal therapeutic strategy for those having multivessel or left main disease [(9)]. In the pre-DES era, PCI was not recommended for diabetic cases because of the increased risk of mortality [(10)]. After DES introduction, rates of ischaemic complications have considerably decreased, and PCI has proven safety for diabetic cases that have complex CAD [(11)]. In the last decade, the implantation of DES for the prevention of restenosis and some anti-proliferative agents like Sirolimus, (immunosuppressive drug) and Paclitaxel (antineoplastic), has been coupled with a polymer that elutes or slowly releases this growth inhibitor from the stent [(12)].

The present study included 44 patients admitted at Cardiology Department National Heart Institute. The patients were allocated into equal 2 groups: Group A received SES (Cypher®), and group B received PES (Taxus ®). The mean age of group "A" patients was 51.68 ± 9.25 years. The mean age of group "B" patients was 52.27 ± 8.38 years. Male patients were 59.1% and 63.6% in groups "A" and "B" respectively. The differences in patients' age and sex in both groups under study were insignificant (p > 0.05= NS).

We found no significant differences in the number of diabetic patients, hypertensive patients, dyslipidemic patient and smokers between both groups (p > 0.05). The diabetic patients were 77.3% in group "A" and "B" and hypertensive patients were approximately about 50%. 22 patients had anterior MI, 7 patients had inferior MI, 7 patients had unstable angina, 2 patients presented with NSTEMI and 6 patients had chronic stable angina.

Similarly, the ISAR-DESIRE 2 study enrolled 450 cases that were equally divided into either SES or PES. Among all patients, 162 patients were diabetics and 83 patients presented with ACS. The mean age in SES group and PES group was 66.4 and 67.1 years respectively with no significant difference in patients' age, sex, DM, HTN, hyperlipidemia, previous MI and C/P in both groups (p value > 0.05= NS) [(13)].

The prevalence of diabetes was 39%, in the study of **Seth *et al.*** [(14)], slightly higher compared to 23% at the study of **Lemos *et al.*** [(15)], and prevalence of hypertension was 35% in both studies.

Additionally, no significant differences were existed among studied groups regarding lesion length, RVD before angioplasty, MLD post-angioplasty, MLD pre-angioplasty, DS% before angioplasty, residual DS% post-angioplasty, acute procedural gain and stent diameter and length. Regarding flexibility, deliverability and conform- ability there were also no significant differences noticed during angioplasty between the 2 types of the stents used in our study.

In hospital follow up during our study, no complications of stent thrombosis (chest pain or ECG abnormalities or neurovascular complications) were reported in the first 24 h of hospital stay post-intervention. No significant differences existed between both groups in the clinical follow-up because MACEs occurred in one patient of each group (in the form of unstable angina with significant in-stent restenosis).

As regards the follow up of angiographic data, we found non-statistically significant difference in MLD at follow up between groups A and B (p > 0.05). Binary restenosis was greater in group "B" vs. group "A" without a significant difference (P value >0.05).

Also, late luminal loss at follow-up angiography was greater in group "B" versus group "A" without significant difference ($p > 0.05$).

In agreement with our findings, and as regards the primary angiographic end point, **Mehilli *et al.*** [16] found a non-significant difference among both groups. Late losses were 0.40 ± 0.65 mm and 0.38 ± 0.58 mm in "SES" group and "PES" group, respectively ($p= 0.85$). There was also insignificant difference ($p=0.69$) among both groups as regards binary restenosis.

LIMITATIONS

It was a nonrandomized observational analysis with a small sample size, a single-center study that can have a selection bias. We also did not look at the risk scores of the study population as it was out of the study's objectives, and study follow-up was a 3 months only due to protocol boundaries. The drug and antiplatelet regimen compliance of these patients to medications has not been recorded, which is a very important factor in recurrent events post-stenting. Furthermore, no intravascular imaging intravascular ultrasound/optical coherence tomography was done either during initial angioplasty or among those who presented with ISR or repeat cardiac events.

CONCLUSION

It is more preferred to utilize SES but not to the degree to recommend its utilization over the PES. SES and PES had a similar anti-restenotic efficacy and safety. The relatively higher late loss in PES in our study indicated that drug resistance had a role in PES restenosis.

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