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Six-Month Clinical and Angiographic Results of Paclitaxel Eluting Simpax Stent

Paklitaksel Kaplı Simpax Stentin Altı Aylık Klinik ve Anjiyografik Sonuçları

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ABSTRACT

Introduction: *We aimed to evaluate the safety and efficacy of the simpax stent in the treatment of different patient groups.*

Patients and Methods: *Forty-five patients were treated with the simpax stent. Of these patients, 23 patients gave consent for six months of follow-up by quantitative coronary angiography (QSA) and six patients were evaluated by exercise electrocardiographic test. Only the patients having lesions with stenosis > 50% of diameter and lengths > 16 mm with reference diameters < 2.75 mm were included.*

Results: *The device success rate was 100% and procedure success rate was 97.7%. The mean stent length was 24.6 ± 7.3 mm and stent size was 2.54 ± 0.24 mm. The overall six months incidence of major adverse cardiac events (MACE) was 8.8%. MACE was consisted of two cases of non-Q wave myocardial infarction and two cases of repeated revascularization of the target lesion. MACE rate was higher in chronic total occlusion (CTO) group than non-CTO group (respectively 33.3% and 5.1). Also when compared to stent size, MACE rate was 25% in < 2.5 mm, 0% ≥ 2.5 mm. The QSA results at six months showed in-stent late lumen loss witha diameter of 0.25 ± 0.15 mm in 17 patients.*

Conclusion: *The six month results in this study demonsrated excellent procedural and device success. Simpax stent was associated with a low in-stent late lumen loss. Also this study showed simpax stent was a safe and effective device in non-CTO group with stent size ≥ 2.5 mm.*

Key Words: *Drug eluting stents; paclitaxel; coronary restenosis.*

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ÖZET

Giriş: *Bu çalışmadaki amacımız farklı hasta gruplarında simpax stentin etkinliği ve güvenilirliğini değerlendirmektir.*

Hastalar ve Yöntem: *Kırk beş hasta simpax stent ile tedavi edildi. Altı aylık takipte 23 hasta kantitatif koroner anjiyografi (QSA) ve altı hasta egzersiz elektrokardiyografi testiyle değerlendirildi. Çalışmaya > %50 çap daralması olan ve uzunluğu > 16 mm ile referans damar çapı < 2.75 mm olan hastalar dahil edildi.*

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Bulgular: *Cihaz başarı oranı %100, prosedür başarı oranı %97.7 idi. Ortalama stent uzunluğu 24.6 ± 7.3 mm ve stent çapı 2.54 ± 0.24 mm idi. Altı aylık majör istenmeyen kardiyak olayların (MACE) genel insidansı %8.8 olarak bulundu. MACE oranı kronik total oklüzyon (KTO) grubunda KTO olamayan gruba göre daha fazlaydı (sırasıyla %33.3 ve %5.1). Ayrıca, stent çaplarına göre karşılaştırıldığında, MACE oranı çapı < 2.5 mm olan stentlerde %25; > 2.5 mm olan stentlerde %0 olarak bulundu. On yedi hastadaki altıncı ay QSA sonuçları stent içi geç lümen kaybını 0.25 ± 0.15 mm olarak gösterdi.*

Sonuç: *Çalışmanın altı aylık sonuçlarına göre prosedür ve cihaz başarı oranı mükemmeldi. Simpax stent düşük stent içi geç lümen kaybı ile ilişkili bulunmuştur. Ayrıca bu çalışma simpax stentin, kronik total oklüzyonu olmayan ve stent çapı > 2.5 mm olan grupta güvenli ve etkili olduğunu gösterdi.*

Anahtar Kelimeler: *İlaç kaplı stent; paklitaksel; koroner restenoz.*

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INTRODUCTION

Drug eluting stents (DES) decrease the risk of clinical and angiographic restenosis compared with bare-metal stents (BMS)[1,2]. The use of DES also reduces the need of coronary by-pass operation. But the benefit of revascularization with DES is reduced in presence of high-risk lesion and in the group of patients with diabetes, diffuse or multivessel disease, chronic renal failure, left main disease or ostial disease and chronic total occlusion[3]. Their use in acute myocardial infarction still is controversial due to thrombus burden. But a number of randomized clinical trials previously tested the safety and the efficacy of DES used in patients with ST elevation myocardial infarction (STEMI)[4-6]. DES was designed with the primary purpose of inhibiting restenosis after percutaneous coronary intervention (PCI). Early data from pivotal randomized studies had proven the efficacy of DES in reducing restenosis and target vessel revascularization (TVR) compared with BMS. However, long-term (two years or longer) observations demonstrated the "late catch-up" phenomenon 23 of first-generation DES, namely, an increased rate of very late restenosis or TVR[7]. New generation stents have usually thinner struts. In stents with thinner struts, restenosis and repeatedintervention are observed less frequently. This effect may be due to more rapid re-endothelialisation, reducing vascular injury and inflammation[8,9]. The Simpax stent consists of anti-proliferative agent paclitaxel and the low profile, thin strut multicellular cobalt-chromium stent platform. Strut thickness is 65 micron. Simpax stent is based on SFU-polysulfan Polimer Matrix system which aids in the control of drug release and supports biocompatibility. This system also reduces the risk of inflammatory response and thrombosis of stent. Polymer coating system has asymmetric features which help to complete endothelization and release the drug in accordance with the vessel wall. The paclitaxel dose is 1 μ per mm^2 of stent surface. The drug is completely eluted by 30 days. Our aim this study is to investigate the safety and efficacy of the simpax stent produced in Turkey in different patient groups.

PATIENTS and METHODS

This trial is a prospective, single center, non-randomised, single-arm study of the use of the simpax stent to treat 45 patients with symptomatic ischemic heart disease or acute coronary syndrome. Study was set up as a prospective trial in consecutive patients undergoing angioplasty and stenting during six months period. The exclusion criteria were as follows; vessel diameter > 2.75 mm and/or lesion lengh < 16 mm, in-stent restenosis and patients refusing to give consent. The mean age of patients was 56.9 ± 10.9 years (range 40-85 years). Clinical presentation was stable angina pectoris in 8 (17.7%) cases, unstable angina pectoris in 22 (48.8%), STEMI in 12 (26.6%) and non-ST-elevation myocardial infarction in 2 cases (NSTEMI, 4.4%). Of these patients, 13.3% had chronic total occlusion (CTO) and 86.6% had non-CTO. Stents were implanted according to the following guidelines. Patients received acetyl-salicylic acid (ASA) (at least 75 mg daily, started 24 hours before the procedure and continued post-procedure; 300 mg in STEMI) and clopidogrel (≥ 300 mg loading dose at least four hours before procedure, 600 mg in STEMI and then 75 mg daily for a minimum of six months post- procedure). All patients were followed clinically for six months. Dual antiplatelet therapy with ASA and clopidogrel was prescribed for six months. Of these patients, 23 consented to a six month follow-up evaluation by quantitative coronary angiography (QCA), six patients evaluation by exercise

electrocardiographic test, other 16 patients didn't accept coronary angiography and exercise electrocardiographic test but no cardiac symptoms occurred in these patients. Only one lesion per patient was treated. Only lesions with diameter stenosis ≥ 50% and with lengths ≥ 16 mm in vessel with reference diameter ≥ 2.25 mm to ≤ 2.75 mm were included. The primary endpoint of this trial was six month in-stent late lumen loss, defined as the difference between post procedure minimal lumen diameter and follow-up minimal lumen diameter, as measured by QCA. Secondary endpoints include major adverse cardiac events (defined as death, myocardial infarction, emergent cardiac surgery, or repeat revascularization of target lesion); acute device and procedure success. The study was conducted according to the Declaration of Helsinki; the local ethical committees approved the study protocol.

RESULT

Baseline clinical characteristics of all patients and 23 patients undergoing six-months QCA examination were presented in Table 1. Prior PCI and CABG rate was greater in CTO group than non-CTO group. Six patients were evaluated by exercise electrocardiographic test which were all negative. Procedural and lesion characteristics-were presented in Table 2. For the entire study group, the device success rate was 100%, and the procedural success rate was 97.7%. The mean stent length was 24.6 ± 7.36 mm. Clinical follow-up at six months of all the 45 patients were presented in Table 3. The overall six months incidence of major adverse cardiac events (MACE) was 8.8%, in non-CTO group 5.1% and in CTO group 33.35%, which consisted entirely of two cases of non-Q wave myocardial infarction and two cases of percutaneous intervention. Non-Q wave myocardial infarction only occurred in patients with in-stent chronic total occlusion before stent placement. In the both patients who underwent PCI

Table 1. Patient characteristics for the non-CTO and CTO group

Characteristic	Total (n= 45)	Non-CTO (n= 39)	CTO (n= 6)
Age (years)	56.9 ± 10.9	57.8 ± 11.2	51.1 ± 5.8
Male sex (%)	84.4	82.0	100
Female sex (%)	15.5	17.9	-
Diabetes mellitus (%)	28.8	33.3	-
Hypertension (%)	51.1	53.8	33.3
Hyperlipidemia (%)	57.7	53.8	83.3
Current smoker (%)	46.6	51.2	16.6
Prior PCI (%)	37.7	30.7	83.3
Prior CABG (%)	8.8	5.1	33.3
Stable angina (%)	17.7	12.8	50
Unstable angina (%)	48.8	48.7	50
STEMI (%)	26.6	30.7	-
NSTEMI (%)	4.4	5.1	-

Table 2. Procedural and lesion characteristics for entire patient cohort and for the subgroup undergoing examination by quantitative coronary angiography at six months

Characteristic	Total (n= 45)	Non-CTO (n= 39)	CTO (n= 6)
Target artery (%)			
LAD	46.6	53.8	-
RCA	33.3	25.6	83.3
CX	20	20.5	16.6
Average stent diameter (mm)	2.57 ± 0.2	2.57 ± 1.9	2.54 ± 0.24
Average stent length (mm)	24.6 ± 7.3	23.64 ± 7.0	31.3 ± 5.8
Device success (%)	100	100	100
Procedure success (%)	97.7	97.4	-

Device success was defined as < 50% residual in-segment final stenosis with the assigned stent; Procedure success was defined as < 50% residual in-segment final stenosis with the assigned stent without a major adverse cardiac event in 30 days.

Table 3. Major adverse events: in hospital and out of hospital at six months

Variable	Non-CTO (n= 39)	CTO (n= 6)	Total (n= 45)
Any MACE (%)	5.1	33.3	8.8
Death (%)	0.0	0.0	0.0
Myocardial infarction (%)	0.0	33.3	4.4
Q-wave (%)	0.0	0.0	0.0
Non-Q wave (%)	0.0	33.3 (2/6)	4.4
Target lesion revascularization (%)			
CABG (%)	0.0	0.0	0.0
PTCA (%)	5.1	33.3	8.8
Stent thrombosis (%)	0.0	0.0	0.0

MACE: Major adverse cardiac events (defined as death, myocardial infarction, emergent cardiac surgery or repeat revascularization of target lesion), CABG: Coronary artery bypass grafting, PTCA: Percutaneous transluminal coronary angioplasty.

had thin vessels. Average reference vessel diameter was 1.78 mm and both patients had stents with diameter of 2.25 mm. Randomized, controlled studies demonstrated that the long-term effect of DES for CTO was better than that of BMS, DES significant reduces of target vesel revascularisation (TVR) rates[10]. But, still long-term restenosis rates higher than non-CTO lesion[11]. Small vessel and diffuse long lesions, the use of overlap or multiple stents, incomplete revascularization and stent malapposition due to severe calcificationis considered to be the most important mechanisms of high MACE rate[12]. Comparison of the stent sizes were presented in Table 4. The MACE rate was higher in stents with diameter < 2.5 mm compared to stents with diameter ≥ 2.5 mm (25% and 0.0%, respectively). The QCA results at six months for 23 patients were presented in Table 5. Acute gain was 1.64 ± 23 mm, in-stent late lumen loss was 0.25 ± 0.15 mm and binary restenosis was 11% (two patients). Sizes of stents developing binary restenosis were both 2.25 mm.

Table 4. Major adverse events indifferent size of stent in non-CTO group

Variable	< 2.5 mm (n= 8)	≥ 2.5 ≤ 2.75 mm (n= 31)	Total (n= 39)
Any MACE (%)	25	0.0	5.1
Death (%)	0.0	0.0	0.0
Myocardial infarction (%)	0.0	0.0	0.0
Q-wave (%)	0.0	0.0	0.0
Non-Q wave (%)	0.0	0.0	0.0
Target lesion revascularization (%)			
CABG (%)	0.0	0.0	0.0
PTCA (%)	25	0.0	5.1
Stent thrombosis (%)	0.0	0.0	0.0

Table 5. Angiographic result for the undergoing examination by quantitative coronary angiography at six months in non-CTO group (n= 18)

Variable	Angiographic result
Reference vessel diameter (mm)	2.42 ± 0.3
Lesion length (mm)	24.77 ± 9.2
Minimal lumen diameter (mm)	
Pre-procedure	1.1 ± 0.26
Post-procedure	2.74 ± 0.32
Acute gain	1.64 ± 0.23
Minimal lumen diameter, 6 months (mm)	2.49 ± 0.32
Late lumen loss (mm)	0.25 ± 0.15
Binary restenosis (%)	11 (2/18)

Binary restenosis was defined as > 50% diameter stenosis.

DISCUSSION

In summary, despite the fact that we used longer stents and stents with smaller diameters and lesions were more complex compared with the other stent studies, the six-months results demonstrated excellent procedural and device success. Simpax stent was associated with alow in-stent late lumen loss and minimal amount of neointimal hyperplastic in-growth. The incidence of MACE was low at six months, with no cases of death and stent thrombosis. This study showed simpax stent is a safe and effective device in non-CTO group and stent size ≥ 2.5 mm. Further long term follow-up and multicenter, randomized clinical studies are required for the safety and efficacy of this stent.

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