Role of tirofiban in treatment of stent thrombosis

Stent trombozunun tedavisinde tirofibanin rolü

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Stent thrombosis (SAT), defined as acute when developed within 24 hours of the procedure and as subacute after 24 hours to 30 days, can be seen within 30 days of stent implantation and may end up with acute myocardial infarction (61%) and death (12%) (1). Tirofiban is a highly specific inhibitor of glycoprotein (GP) IIb/IIIa receptor located on the surface of the platelets and is effective during percutaneous coronary interventions, especially in the setting of acute coronary syndromes (2,3).

We described the outcome of 5 patients presented with early stent thrombosis (Table 1). Stent thrombosis was defined as the sudden onset of chest pain associated with ischemic electrocardiographic changes in the distribution of the stented artery. Angiographic stent thrombosis was defined as intraluminal filling defects resulting in either complete or partial vessel occlusion.

All patients received aspirin, heparin (with 250-300 sec activated clotting time (ACT) level during the procedure), ticlopidine (500mg/day) or clopidogrel (75mg/day with a preloading dose of 300mg). After documenting the stent thrombosis, tirofiban (Aggrastat, Merck, West Point, PA, USA) infusion (10mcg/kg bolus over 3 minutes followed by 0,15mcg/kg/min infusion) was started in all patients. One patient (20%) underwent emergency bypass surgery due to ongoing ischemia and TIMI 2 coronary flow. Quantitative analyses of all angiographic data before and after the procedure were performed. The luminal diameter of the coronary artery was measured before and after the procedure. The angiographic data and stent diameters are shown in Table 2. There was no death, however 3 patients (60%) experienced myocardial infarction with a mean peak CK of 1244±559 U/L.

Randomized trials demonstrated differing efficacy of the different GP receptor blockers in-patients with acute coronary syndromes (4). Use of abciximab with early interventional therapy was demonstrated to be beneficial (5,6). Tirofiban, small molecule with a short half-life and abciximab, a large antibody with a prolonged half-life have different effects on GP IIb/IIIa receptors. Tirofiban has marked specificity for the glycoprotein IIb/IIIa receptor and abciximab acts to the α v β 3 integrin (vitronectin) receptors, so only abciximab has the potential to influence the adhesion of platelets and endothelial cells and of platelets and white cells. In TARGET trial the dose of tirofiban could not provide a level of platelet-aggregation inhibition similar to that induced by abciximab (7). In our trial we didn't measure the platelet inhibitory effect of tirofiban therefore we could not be sure that we used tirofiban in optimal doses. We did not have a control group with a small study group which was the other limitation of our study.

The only reported data regarding the role of GP receptor blockers in coronary stent thrombosis was by Casserly et al (8). They used abciximab in 10 patients with PTCA in 8, and alone in 2 patients presenting with early stent thrombosis. They concluded that abciximab in the management of stent thrombosis is associated with a better clinical outcome compared to conventional therapy. We achieved TIMI 3 grade coronary flow in 60% (3 patients) of our patients, which was lower than the rates reported by Casserly et al (8). The low success rate achieving TIMI3 flow compared to abciximab could have been due to tirofiban treatment without preloading dose (4,8). Abciximab might have been a better choice in this setting regarding the acute benefit demonstrated with this agent (6), however, it is not available in our market. Although the TIMI 3 flow rate in this study is also lower than the conventional treatment group in the study by Casserly et al (8), we had no death, and only 1(one) emergency

Table 1. Patient characteristics

Patient demographics	n=5
Men/women	3/2
Age, years	65.8±13.4
Coronary bypass surgery	0
Clinical status	
stable angina	1
unstable angina	3
recent MI	1
Diabetes mellitus	3
Systemic hypertension	3
Hyperlipidemia	2
Cigarette smoking	1
Multivessel disease	3
Ticlopidine	3
Clopidogrel	2

MI- myocardial infarction

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Table 2. Pre- and postprocedural angiographic flow status and quantitative coronary angiographic analysis of patients with stent thrombosis

	Pre-procedural	Post-procedural
TIMI 0, n(%)	4 (80)	1 (10)
TIMI 2, n(%)	-	1 (10)
TIMI 3, n(%)	1 (20)	3 (60)
Minimal luminal diameter, mm*	0.70 ± 0.46	2.46 ± 0.20
Reference diameter, mm*	2.14 ± 0.28	2.90 ± 0.31

* p< 0.05

bypass surgery in our study. Our cohort also consisted of high-risk patients with the majority having acute coronary syndromes, which might have benefited from the pre-procedural GP receptor blocker infusion.

There seems to be a benefit in means of death, randomized trials with larger patient population should be conducted to clarify the potential role of these agents in the treatment of this dreadful complication.

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