Journal of Clinical & Experimental Cardiology
ISSN: 2155-9880

García-Lara et al., J Clin Exp Cardiolog 2013, 4:10
DOI: 10.4172/2155-9880.1000270

Research Article Open Access

Lack of Peri-Procedural Myocardial Necrosis Reduction from Abciximab in Patients on Dual Antiplatelet Therapy Revascularized with Rotational Atherectomy

Juan García-Lara*, Eduardo Pinar-Bermúdez, Javier Lacunza-Ruiz, Raúl Valdesuso-Aguilar, José A Hurtado, Juan R Gimeno and Mariano Valdés-Chávarri

Servicio de Cardiología, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

Abstract

Rotational atherectomy allows plaque remodeling in severely calcified lesions and, prior to the adoption of clopidogrel as standard therapy, small trials showed that abciximab reduces transient hypoperfusion associated with the procedure. However, no studies have evaluated it among patients receiving dual antiplatelet therapy. This study aimed to evaluate whether abciximab reduces procedure-related myocardial injury in a non-selected population of patients receiving dual antiplatelet therapy. The study comprised a retrospective review of a non-selected cohort of 139 consecutive procedures of rotational atherectomy performed in patients pre-treated with dual antiplatelet therapy. Abciximab was administered in 48 (34.5%) patients, whereas 91 (65.5%) did not receive it. The only difference between groups was a higher rate of diabetes mellitus in the abciximab group (89% vs. 51%, *p*=0.001). The rate of procedural complications was 10.5% for patients with abciximab vs. 6.2% for patients without (*p*=0.537). After 24 hours, the peak of biomarkers of myocardial damage (CKmb and TnT) did not differ, and the rate of procedure-related myocardial injury was 23.9% with abciximab and 20.7% without (*p*=0.664). In a restricted analysis to diabetic patients (n=84), the rate of myocardial injury was 27.5% with abciximab vs. 18.6% without, (*p*=0.435). After adjusting by clinical and procedural parameters in a logistic regression model, abciximab use did not confer any significant reduction on procedure-related myocardial injury. In conclusion, in a non-selected cohort of patients receiving dual antiplatelet therapy, the administration of abciximab in the setting of rotational atherectomy did not reduce the incidence of procedure related myocardial injury.

Keywords: Abciximab; Antiplatelet therapy; Rotational atherectomy; Coronary

Introduction

Coronary calcium is commonly found, being present in 50% to 80% of individuals and increasing with age [1-3]. In the setting of percutaneous coronary interventions (PCI), the presence of severely calcified lesions difficult the dilatation and may result in stent under expansion; therefore, severely calcified lesions are associated with a greater complication rate and worse long-term results [4-6]. To deal with this limitation, rotational atherectomy (RA) allows plaque remodeling and facilitates stent implantation with a higher success and lower complication rates [7,8].

In this context, the use of abciximab during RA has been shown to reduce procedural morbidity as well as the incidence, extent and severity of transient hypoperfusion [9,10]. However, this evidence is supported by small trials performed prior to the adoption of clopidogrel as the standard therapy in patients undergoing PCI [11,12]. Therefore, the role of abciximab in the current scenario of rotational atherectomy in patients receiving dual antiplatelet therapy has not been assessed.

This study was conducted to evaluate whether abciximab is associated with a reduction in procedure-related myocardial injury, in a consecutive series of patients pretreated with clopidogrel who underwent RA and stent implantation in severely calcified lesions.

Methods

Study population

The study population comprised a retrospective review of all consecutive procedures of RA performed in the cardiology department of a university centre, in a time period of 36 months. RA was chosen as the treatment option by the interventionist, after confirming the presence of severely calcified lesions and prior to any lesion dilatation attempt. Severely calcified lesion was defined according to the SYNTAX classification [13], as the presence of persistent multiple opacifications of the vascular wall visible in more than one projection and completely surrounding the vessel of the area of the lesion. All the patients received treatment with 150-300 mg/day of acetyl salicylic acid and clopidogrel (300 mg as loading dose and 75 mg/day as maintenance dose), at least 24 hours before the procedure according to guidelines [14,15].

Rotational atherectomy procedure

A 0.09-inch guide wire was used directly or after exchange using a coaxial microcatheter or balloon. RA was carried out using the Rotablator® device (Boston Scientific-Scimed Corp, Natick, MA) at a rotation speed of 140,000-180,000 rpm, with the intention of using just one burr, in relation of less than 0.7 to the artery. Only when a first burr advance did not allow a correct balloon dilatation, a second burr was used. The advances were short (a maximum of 10 seconds), and saline was infused with heparin, nitroglycerin, and verapamil

***Corresponding author:** Juan García-Lara, MD, Servicio de Cardiología, Hospital Universitario Virgen de la Arrixaca, Murcia 30120, Spain, Tel: +34 968 369 893; Fax: + 34 968 369 893; E-mail: jgarciadelara@gmail.com

Received August 20, 2013; **Accepted** September 10, 2013; **Published** September 13, 2013

Citation: García-Lara J, Pinar-Bermúdez E, Lacunza-Ruiz J, Valdesuso-Aguilar R, Hurtado JA, et al. (2013) Lack of Peri-Procedural Myocardial Necrosis Reduction from Abciximab in Patients on Dual Antiplatelet Therapy Revascularized with Rotational Atherectomy. J Clin Exp Cardiolog 4: 270. doi:10.4172/2155-9880.1000270

during the atherectomy. All the patients received at least one stent after balloon pre-dilatation. DES was used in all cases, except those that showed contraindications for prolonged double antiplatelet therapy. The stent was post dilated when residual stenosis was greater than 20%. Unfractionated heparin (70-100 U/kg) was administered to all the patients and abciximab was applied as a coadjuvant medication at the operator's discretion. When abciximab was required, at operator discretion based on clinical evidence, immediately before the procedure of RA patients received abciximab (0.25 mg/kg of body weight bolus, followed by a 10 μg/kg per minute infusion for 12 hours), plus unfractionated heparin, 70 U/kg.

After the procedure, dual antiplatelet therapy with aspirin (100-300 mg/day) and clopidogrel (75 mg/day) was prescribed for at least 12 months in the case of patients treated with DES, and for at least one month in patients treated with conventional stents.

Angiographic success was defined as a <30% diameter obstruction at the end of the procedure.

Myocardial necrosis and procedural complications

Procedural complication was defined as the occurrence of death, perforation, acute vessel closure, slow reflow (>5 beats to refill the vessel) or significant (>2 mm) branch loss. The presence of myocardial damage was monitorized after the procedure, at 8, 12, and 24 hours. Blood samples were processed and the markers of myonecrosis measured were TroponinT (TnT, Roche Diagnostics. Germany), Creatine Kinase (CK) and the MB-fraction (CK-MB). Procedure-related myocardial injury was defined, as recently proposed: "the increase five times upper the normal limits [16], what result in a concentration higher than 0.5 ng/mL". Major and minor bleeding was defined according to well known TIMI bleeding classification [17].

Statistical analysis

The continuous variables were expressed as mean ± SD. When non-normal distribution was observed, continuous variables were expressed as median and interquartile range (IQR). The categorical variables were expressed as number and percentages. Comparisons between continuous variables were conducted using t-test (or Mann-Whitney when normal distribution was not assumed). Categorical variables were compared with chi-square (or F-Fisher exact test when normal distribution not assumed). The statistical analysis was carried out using the SPSS 15.0 software (SPSS-IBM inc., Chicago, IL).

Results

Study population and characteristics

Among the 4832 procedures of PCI performed in the 36 months study period, a total of 139 (2.9%) were RA and represent the study population. Abciximab was used in 48 (34.5%) patients, as co-adjuvant therapy to the RA, and represent the abciximab group. All of 139 patients were on dual antiplatelet therapy at the time of the RA. The indication for the procedure was stable coronary disease in 43 (31%) and acute coronary syndrome in 96 (69%). The main demographic data are shown in Table 1. The mean age was 72 ± 8 years-old, 100 (72%) were men and 84 (60.5%) were patients with diabetes. No statistically significant differences were found between both groups, except for a higher prevalence of diabetes mellitus in the group of patients who received abciximab (50.6% vs 89.4%, p=0.001). The procedure characteristics are showed in Table 2, and no differences were found between patients who received abciximab and those who did not. A mean of 1.07 ± 0.3 vessels per patients were treated, including 37 with left main disease. The procedures were, on average, complex requiring large amounts of contrast and fluoroscopy (Table 2).

Abciximab	No (n=91)	Yes (n=48)	p
Age	71 ± 8.7	69 ± 8.7	0. 763
Male	67 (73.6)	32 (66.7)	0. 481
BMI	28 ± 3.4	28 ± 4	0. 136
Hypertension	65 (77.4)	39 (83)	0. 391
Dyslipidemia	48 (57.1)	29 (61.7)	0. 877
Diabetes Mellitus	42 (50.6)	42 (89.4)	0. 001
Smoker	29 (34.5)	16 (34.8)	0. 777
Previous MI	41 (49.4)	19 (40.4)	0. 593

BMI: Body Mass Index

Table 1: Baseline population characteristics.

Abciximab	No (n=91)	Yes (n=48)	p
Baseline stenosis	74.88 ± 12.3	76.47 ± 9.2	0. 446
Poststent stenosis	14.87 ± 16.1	15.40 ± 12.8	0. 851
Reference lumen diameter	2.77 ± 0.6	2.86 ± 0.6	0. 423
Maximum stent diameter	3.04 ± 0.5	2.94 ± 0.3	0. 273
Ostial lesion	20 (22)	14 (29)	0. 510
Bifurcated lesion	35 (38.5)	24 (50)	0. 347
IABP	1 (1)	2 (4)	0. 499
Pacemaker	2 (2.2)	1 (2.1)	0. 718
Fluroscopy (min)	28 ± 12	33 ± 16	0. 055
Contrast (ml)	319 ± 126	291 ± 113	0. 249
DES	77 (84.6)	40 (83.3)	0. 844
Number of treated vessel	1.033 ± 0.2	1.06 ± 0.2	0. 487
Stent length	45.28 ± 26	45.6 ± 27	0. 947
Burr Size	1.65 ± 0.21	1.58 ± 0.16	0. 086
LM Treated	25 (27.5)	12 (25)	0. 698
Inotropes	4 (4.4)	1 (2.1)	0. 710
Slow/No reflow	3 (3.3)	0	0. 444
Branch loss (>2 mm)	2 (2.2)	2 (4.2)	0. 718

DES: Drug Eluting Stent; IABP: Intraortic Balloon Pump

Table 2: Procedural characteristics.

Myocardial necrosis and procedural complications

Procedural success was achieved in 127 (91.4%) patients with no significant difference between naive and abciximab treated patients (90% vs 94%; p= 0.537). The rate of procedural complication was 8.6%. Only 3 patients required temporal pacemaker (2.2%). Significant (>2 mm) branch loss was observed in 3 patients (2.2%) and slow-flow/no-reflow was detected in 3 cases (2.2%). One patient who did not received abciximabdied during the procedure due to cardiac tamponade after coronary perforation. Regarding to safety issues, 1 (1.2%) minor bleeding was detected in those who did not received abciximab and 1 (2.1%) in those who were treated with abciximab (p>0.999). In addition, 1 (1.2%) major bleeding was found in those with no abciximab and another one (2.1%) in patients treated with abciximab (p>0.999).

As shown in Figure 1, the peak of myocardial damage biomarkers was: CK, median 147 ng/mL (IQR 56; 130); CKmb, median 15.37 ng/mL (IQR 3.68; 12.1); TnTmedian 0.35 ng/mL (IQR 0.02; 0.41) (Figure 1). No statistical differences were found between those who received abciximab and those who did not. The incidence of procedure-related myocardial injury in patients who received abciximab and patients who did not was 22.9% vs 20.9% (p=0.664). Baseline and procedural characteristics according myocardial injury occurrence are listed in Table 3.

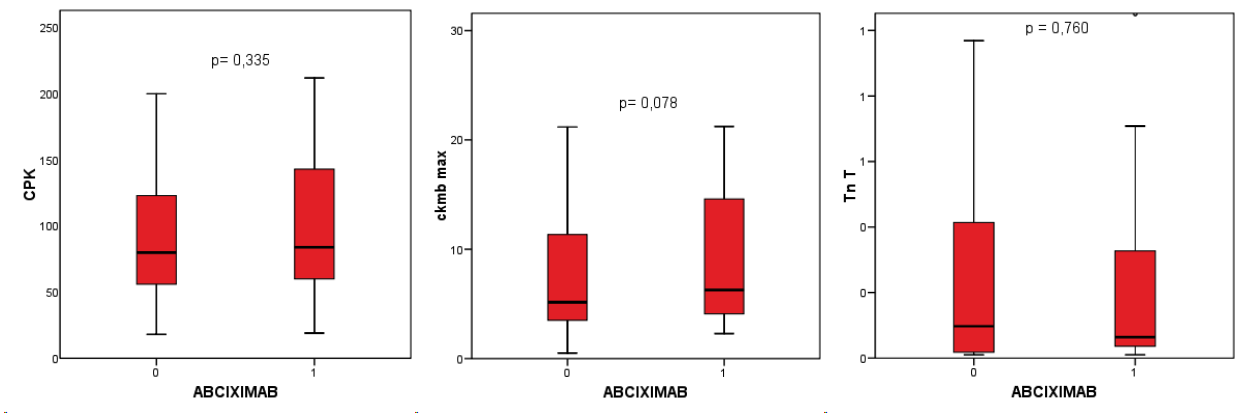

Figure 1: Myocardial Damage Biomarkers according to treatment.

PRMI	No (n=109)	Yes (n=30)	p
Age	71.49 ± 8	72.79 ± 7	0.470
Male	82 (75.2)	17 (56.7)	0.05
BMI	28.4 ± 4	28.09 ± 4	0.758
Hypertension	78 (71.5)	26 (86.6)	0.159
Dyslipidemia	65 (59.6)	12 (40)	0.179
Diabetes Mellitus	66 (60.5)	18 (60)	0.577
Smoker	36 (33)	9 (30)	0.988
Previous MI	45 (41.3)	15 (50)	0.381
Abciximab	35 (32.1)	13 (43.3)	0,356
Baseline stenosis	75.34 ± 11.6	76.45 ± 9.5	0.676
Poststent stenosis	15.49 ± 13.9	14.48 ± 20.8	0.784
Ostial lesion	23 (21.1)	11 (36.6)	0.215
Bifurcated lesion	43 (39.4)	16 (53.3)	0.459
Pacemaker	2 (1.8)	1 (3.3)	0.051
Contrast (mL)	305.8 ± 114	310 ± 120	0.874
DES	93 (85.3)	24 (80)	0.266
Treated Vessel	1.05 ± 0.25	1.04 ± 0.2	0.889
Stent Length	41.63 ± 23	60 ± 32	0.002
Burr Size	1.62 ± 0.21	1.65 ± 0.12	0.491
LM Treated	26 (23.8)	11 (36.7)	0.204
Inotropes	3 (2.7)	2 (6.6)	0.255
Branch Loss (>2 mm)	1 (0.9)	3 (10)	0.015

BMI: Body mass index; LM: Left main;DES: Drug eluting stent

Table 3: Baseline and procedural characteristics according to procedure-related myocardial injury.

A subanalysis restricted to diabetic patients was also performed. The incidence of procedure-related myocardial injury in diabetics was 27.5% in those who received abciximab vs. 18.6 % in those who did not received the drug (p=0.435).

In a logistic regression analysis including age, gender, hypertension, diabetes, dyslipidemia, abciximab use, stent length, renal dysfunction, burr diameterand unstable condition, only the stent length was predictor of peri-procedural MI (OR 1.026, CI 1.006-1.047; p<0.011). After adjusting for the aforementioned clinical and procedural parameters, the use of abciximab did not show to reduce periprocedural myocardial damage.

Discussion

The main finding of this observational study is that the use of abciximab in the setting of RA did not reduce the procedure-related myocardial injury when patients were receiving dual antiplatelet therapy. Previous published studies showed that rotablation induces platelet activation, thus leading to platelet aggregation [18]. Small randomized trials found the benefit of abciximab during rotational atherectomy in reducing procedural morbidity, CK-MB elevation, as well as the incidence, extent and severity of transient hypoperfusion, as assessed by single-photon emission computed tomography [9,10].

Nonetheless, this evidence is prior to the generalization of clopidogrel as coadjuvant therapy. In our study, the administration of intravenous abciximab in patients pretreated with clopidogrel showed no benefit in terms of procedure-related myocardial injury in a population of complex patients/complex lesions. There was no reduction in the peak of biomarkers, which seems to be even higher in those receiving abciximab. This could be attributed to the higher number of diabetics patients in the group who received abciximab. However, in the subgroup of diabetics, this difference was still remarkable. The rate of procedural success and complications was otherwise similar in both groups.

The role of abciximab after clopidogrel pretreatment in patients undergoing PCI has been in discussion with controversial results in different trials [19,20]. Specially striking is the fact that, in patients with diabetes the protective effect of abciximab was absent, and even a higher level of myocardial damage markers was observed. This result is probably explained, in part, by the administration of abciximab in more severe patients due to the non randomized nature of the study, although no benefit was observed in patients with diabetes in previously released clinical trials on non -STEMI patients such as ISAR-REACT 2 [20]. Nonetheless, to the best of our knowledge, this is the first study addressing the effect of abciximab in patients treated with rotablation and dual antiplatelet pretreatment. No other studies exist for comparing the findings of the presented study. Some limitations are recognized, as the non- randomized and single center nature. The non-randomized and retrospective methodology of our study, the number of patients included, as well as the use of abciximab according to operator election limits the conclusions to be drawn. However, this study provides new findings and improves the knowledge according with the current standard therapy that incorporates dual antiplatelet therapy in all patients. In whole, further confirmatory studies including large populations should be addressed in order to confirm these findings.

Conclusion

In conclusion, this study showed that, in a cohort of patients on dual antiplatelet therapy who underwent coronary percutaneous

revascularization with rotablation and stent implantation, the administration of abciximab was not associated with a benefit in terms of procedure-related myocardial injury reduction. This is the first study addressing the issue of IIb/IIIa inhibitors as ancilliary medication in rotablation since the generalization of clopidogrel pretreatment.

Acknowledgement

The authors report no financial relationships or conflicts of interest regarding the content herein.

References

1. Wexler L, Brundage B, Crouse J, Detrano R, Fuster V, et al. (1996) Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association. Writing Group. Circulation 94: 1175-1192.
2. Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, et al. (2006) Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 114: 1761-1791.
3. de la Torre Hernandez JM, Laso FS, Ruisanchez C, Zueco J, Figueroa A, et al. (2005) Coronary angiography with flat panel digital detectors significantly increases the sensitivity for calcium detection in relation to conventional fluoroscopy: comparison of both systems with intravascular ultrasound. J Invasive Cardiol 17: 365-368.
4. Ellis SG, Roubin GS, King SB 3rd, Douglas JS Jr, Weintraub WS, et al. (1988) Angiographic and clinical predictors of acute closure after native vessel coronary angioplasty. Circulation 77: 372-379.
5. Hoffmann R, Mintz GS, Kent KM, Pichard AD, Satler LF, et al. (1998) Comparative early and nine-month results of rotational atherectomy, stents, and the combination of both for calcified lesions in large coronary arteries. Am J Cardiol 81: 552-557.
6. Wilensky RL, Selzer F, Johnston J, Laskey WK, Klugherz BD, et al. (2002) Relation of percutaneous coronary intervention of complex lesions to clinical outcomes (from the NHLBI Dynamic Registry). Am J Cardiol 90: 216-221.
7. Moussa I, Moses J, Di Mario C, Busi G, Reimers B, et al. (1998) Stenting after optimal lesion debulking (sold) registry. Angiographic and clinical outcome. Circulation 98: 1604-1609.
8. Doshi SN, Kini A, Kim MC, Payne N, Kamran M, et al. (2003) A comparative study of rotational atherectomy in acute and stable coronary syndromes in the modern era. Am J Cardiol 92: 1404-1408.
9. Koch KC, vom Dahl J, Kleinhans E, Klues HG, Radke PW, et al. (1999) Influence of a platelet GPIIb/IIIa receptor antagonist on myocardial hypoperfusion during rotational atherectomy as assessed by myocardial Tc-99m sestamibi scintigraphy. J Am Coll Cardiol 33: 998-1004.
10. Kini A, Reich D, Marmur JD, Mitre CA, Sharma SK (2001) Reduction in periprocedural enzyme elevation by abciximab after rotational atherectomy of type B2 lesions: Results of the Rota ReoPro randomized trial. Am Heart J 142: 965-969.
11. Mehta SR, Yusuf S, Peters RJ, Bertrand ME, Lewis BS, et al. (2001) Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 358: 527-533.
12. Cavusoglu E, Kini AS, Marmur JD, Sharma SK (2004) Current status of rotational atherectomy. Catheter Cardiovasc Interv 62: 485-498.
13. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, et al. (2005) The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 1: 219-227.
14. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, et al. (2011) 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation 124: e574-e651.
15. Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS); European Association for Percutaneous Cardiovascular Interventions (EAPCI), Wijns W, Kolh P, Danchin N, Di Mario C, et al. (2010) Guidelines on myocardial revascularization. Eur Heart J 31: 2501-2555.
16. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, et al. (2012) Third universal definition of myocardial infarction. Eur Heart J 33: 2551-2567.
17. Chesebro JH, Knatterud G, Roberts R, Borer J, Cohen LS, et al. (1987) Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 76: 142-154.
18. Williams MS, Coller BS, Väänänen HJ, Scudder LE, Sharma SK, et al. (1998) Activation of platelets in platelet-rich plasma by rotablation is speed-dependent and can be inhibited by abciximab (c7E3 Fab; ReoPro). Circulation 98: 742-748.
19. Mehilli J, Kastrati A, Schühlen H, Dibra A, Dotzer F, von Beckerath N, et al. (2004) Randomized clinical trial of abciximab in diabetic patients undergoing elective percutaneous coronary interventions after treatment with a high loading dose of clopidogrel. Circulation 110: 3627-3635.
20. Kastrati A, Mehilli J, Neumann FJ, Dotzer F, ten Berg J, Bollwein H, et al. (2006) Abciximab in patients with acute coronary syndromes undergoing percutaneous coronary intervention after clopidogrel pretreatment: the ISAR-REACT 2 randomized trial. JAMA 295: 1531-1538.