Does Intracoronary Abciximab Improve the Outcome of Percutaneous Coronary Interventions? A Randomized Controlled Trial

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Introduction and objectives. It has been clearly demonstrated that abciximab is useful in percutaneous coronary interventions. However, it is not known if intracoronary administration of the initial abciximab bolus improves outcome. Moreover, there may be safety concerns.

Methods. The study was a single-center prospective randomized trial that included all patients undergoing coronary angioplasty involving the use of abciximab. Patients were randomized to either intracoronary or intravenous administration of the abciximab bolus. The primary endpoint was the incidence of major adverse cardiac events (i.e., death, myocardial infarction, or the need for revascularization); secondary endpoints were hemorrhagic complications and the troponin-I level.

Results. The study included 137 patients; 72 received an intracoronary abciximab bolus and 65, an intravenous bolus. Clinical characteristics and baseline angiographic findings were similar in the 2 groups. All patients underwent coronary stent implantation. No difference was observed between the intracoronary bolus group and the intravenous bolus group in type of stent used (drug eluting stent 47.2% vs 50.8%, respectively), total stent length, or final TIMI flow grade (3 vs 2.97, respectively). The intervention success rates were also similar (98.5% vs 99%, respectively). No complication associated with the administration route was reported. However, the level of the myocardial injury marker troponin I increased significantly in the intravenous bolus group. Clinical follow-up at 1 year did not reveal any difference in the incidence of major adverse cardiac events: 8.5% in the intracoronary bolus group versus 6.2% in the intravenous bolus group.

Conclusions. Intracoronary administration of an abciximab bolus did not appear to be less safe or effective than intravenous administration. Less postprocedural myocardial damage was observed in the intracoronary bolus group.

Key words: *Abciximab. Platelet aggregation. Stent. Prospective randomized trial.*

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¿Mejora el uso de abciximab intracoronario el resultado del intervencionismo percutáneo? Estudio prospectivo y aleatorizado

Introducción y objetivos. La utilidad del abciximab en el intervencionismo coronario percutáneo se ha demostrado plenamente. Sin embargo, se desconoce si la administración intracoronaria del bolo inicial puede aportar ventajas. Igualmente, podría haber dudas acerca de su seguridad.

Métodos. Estudio en un solo centro, prospectivo y aleatorizado, en el que se incluyó a todos los pacientes en los que se realizó un intervencionismo coronario percutáneo con abciximab. Se aleatorizó a los pacientes para recibir un bolo de abciximab (ABX) intracoronario o intravenoso. Se analizaron la incidencia de MACE (muerte, reinfarto y necesidad de revascularización) como variable principal y las complicaciones hemorrágicas y las concentraciones de troponina I como variables secundarias.

Resultados. Se incluyó a 137 pacientes (72 con ABX intracoronario y 65 con ABX intravenoso). Las características clínicas y los hallazgos angiográficos fueron similares en ambos grupos. Todos recibieron *stents.* No hubo diferencias en el tipo de *stent* utilizado (recubierto activo del 47,2 frente al 50,8%), la longitud total del *stent* y el flujo TIMI final (3 frente a 2,97). Los resultados del intervencionismo coronario percutáneo fueron similares: se realizó con éxito en el 98,5% de los pacientes del grupo ABX intracoronario y en el 99% del grupo ABX intravenoso. No se detectaron complicaciones derivadas de la vía de administración. En el grupo ABX intravenoso se observó una elevación significativa posprocedimiento de la troponina I. En el seguimiento clínico al año no se hallaron diferencias significativas en la incidencia de MACE (el 8,5% en el grupo ABX intracoronario frente al 6,2% en el grupo ABX intravenoso).

Conclusiones. La administración intracoronaria del bolo de abciximab no parece menos segura que la intravenosa y es, al menos, igualmente eficaz. Se observó un menor grado de daño miocárdico posprocedimiento en el grupo ABX intracoronario.

Palabras clave: *Abciximab. Agregación plaquetaria.* Stent. *Ensayo prospectivo y aleatorizado.*

ABBREVIATIONS

ABX: abciximab.
AMI: acute myocardial infarction.
PCI: percutaneous coronary intervention.
MACE: major adverse cardiac event.
ACS: acute coronary syndrome.

INTRODUCTION

The results of percutaneous coronary interventions (PCI) have improved continuously since the technique was introduced. Advances in the procedures and materials have been accompanied by a notable development in associated drug treatments.

The use of abciximab (ABX), a murine-human chimeric antibody fragment (c7E3 Fab) that inhibits platelet aggregation by acting selectively on glycoprotein IIb/IIIa receptors,[1] has been one of the most significant advances in drug treatment, and its effectiveness has been demonstrated for PCI in high-risk patients[2] with complex lesions or requiring multiple stents,[2,3] in the context of acute myocardial infarction (AMI),[4] in diabetic patients,[5,6] with intracoronary thrombus,[7] etc. The efficacy of the drug has been demonstrated both in the short-term for the reduction of thrombotic complications[8] and in the medium- to long-term.[9]

Since platelet inhibition caused by ABX occurs immediately, local administration, in this case intracoronary, may act faster and with a greater intensity than intravenous administration, especially in lesions with a greater thrombus load. Little data is available to address this possibility and the majority of the studies that have been performed are neither prospective nor randomized. We have only found 1 randomized controlled trial on the efficacy of intracoronary ABX, but the study was performed selectively in patients in the acute phase of AMI.[10]

On the other hand, the incidence of bleeding complications in patients treated with ABX is known to be higher than in patients who do not receive the drug.[11,12] However, it is not clear whether this varies according to the route of administration.

A randomized, double-blind, controlled trial was therefore designed to assess the safety, efficacy, and possible prognostic benefits of intracoronary versus intravenous administration of ABX.

METHODS

All patients with acute coronary syndrome (ACS) admitted to our hospital between January 1 and November 10, 2004, and in whom PCI was performed with concurrent administration of ABX were consecutively enrolled in the study. Once the study protocol was accepted by the local ethics committee, the inclusion criteria were as follows: acute coronary syndrome with or without ST-segment elevation in which the use of ABX was indicated and provision of informed consent by the patient.

The exclusion criteria were as follows: *a)* impossibility of stent implantation; *b)* cardiogenic shock; *c)* contraindications for the use of ABX, namely active internal bleeding, hemorrhagic stroke in the last 2 years, recent (2 months) spinal or cranial surgery or trauma, major surgery in the last 2 months, intracranial tumors, aneurysm or arteriovenous malformation, hemorrhagic diathesis or uncontrolled hypertension, preexisting thrombocytopenia, vasculitis, diabetic or hypertensive retinopathy, and severe hepatic or renal failure.

Indication for ABX was assessed on the basis of the guidelines for percutaneous coronary intervention of the European Society of Cardiology[13]:

1. Prior to PCI in high-risk patients with non-ST elevation ACS.
2. High-risk patients with known anatomy 24 hours prior to PCI.
3. All primary PCI, particularly in high-risk patients.
4. In stable angina associated with complex lesions, occlusion or the possibility of occlusion of the vessel, visible thrombus, reduced flow or no-reflow phenomenon, angioplasty with multiple stents, and diabetic patients.

Patients were randomized to receive an initial bolus by intracoronary or intravenous administration. Randomization was performed using a table of random numbers that determined the route of administration of ABX once the indication was established. A double-blind system was used such that neither the patients nor the cardiologists responsible for their assessment and follow-up knew to which group they belonged. In addition, prior to the procedure, the interventional cardiologist who performed the PCI did not know the route of administration of ABX.

The patients included in the study received an initial standard dose of 0.25 mg/kg by intracoronary or intravenous administration. Subsequently, ABX was administered in both groups by intravenous perfusion at a rate of 0.125 µg/kg/min over a 12-hour period.

In all procedures, at least 50 U/kg of unfractionated heparin was provided intravenously and antiplatelet treatment was given with aspirin and clopidogrel. If the patients had not received antiplatelet drugs prior to entering the catheterization laboratory they received 500 mg of aspirin and a 300 mg loading dose of clopidogrel. Treatment with aspirin was continued indefinitely and clopidogrel was continued for at least 6 months.