Does Abciximab Improve the Prognosis of Diabetics After Percutaneous Coronary Intervention?

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**Introduction and objectives.** It is known that the outcome of percutaneous coronary intervention is worse in diabetics than in non-diabetics. The aim of our study was to determine whether abciximab therapy could improve clinical outcome in an unselected diabetic population that underwent percutaneous coronary interventions.

**Material and methods.** We analyzed retrospectively 198 diabetic patients who underwent PTCA from January 1997 to January 2000. Seventy-three patients (36.7%) were treated with abciximab and the remaining 125 patients (63.3%) did not receive abciximab. The mean follow-up was 12.6 months. The events considered were death, non-fatal myocardial infarction, any revascularization procedure (including the target vessel), and hospital admission for unstable angina.

**Results.** Patients who received abciximab had more frequent previous myocardial infarction (67.1 vs. 52.8%; p = 0.04), worse left ventricular function (0.53 vs. 0.59%; p = 0.02), more frequent angiographic thrombus (67.1 vs. 36.8%; p < 0.001), more complex lesions (B2/C) (76.4 vs. 55.8%; p = 0.004), and less frequent location in left anterior descending artery (34.2 vs. 60.8%; p = 0.002). The indication for PTCA in patients who received abciximab was most often related to myocardial infarction. There were no differences between the groups in sex, age and distribution of diabetes treatment. Events were more frequent in diabetics not treated with abciximab than in those who were treated with abciximab (38 vs. 22%; p < 0.037). The patients not treated with abciximab suffered more frequently target vessel revascularization (22.7 vs. 7.2%; p < 0.007). There were no significant differences in the frequency of death or non-fatal myocardial infarction, but hospital readmissions for unstable angina were significantly more frequent in diabetics not treated with abciximab (29.1 vs. 15.9%; p = 0.045). Multivariate analysis identified abciximab as a predictor of the absence of complications during follow-up (CR: 0.45; p = 0.03).

**Conclusion.** Abciximab treatment seems to reduce events in unselected diabetic patients undergoing percutaneous coronary intervention, particularly target vessel revascularization.

**Key words:** Coronary angioplasty. Diabetes mellitus. Revascularization. Prognosis.

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¿El abciximab mejora el pronóstico de los diabéticos tras la intervención coronaria percutánea?

**Introducción y objetivos.** Se sabe que los pacientes diabéticos tienen peor pronóstico tras la intervención coronaria percutánea que los no diabéticos. El propósito de nuestro estudio fue determinar si el tratamiento con abciximab puede mejorar los resultados clínicos en una población diabética no seleccionada.

**Material y métodos.** Analizamos retrospectivamente a 198 pacientes diabéticos sometidos a intervención coronaria percutánea (ICP) desde enero de 1997 a enero de 2000. Setenta y tres pacientes (36,7%) fueron tratados con abciximab y los restantes 125 (63,3%) no recibieron abciximab. El seguimiento medio fue de 12,6 meses. Consideramos como episodios: la muerte, el infarto no fatal, cualquier revascularización (incluyendo el vaso diana) y el ingreso hospitalario por angina inestable.

**Resultados.** Los pacientes que recibieron abciximab tenían mayor incidencia de infarto de miocardio previo (67,1 frente a 52,8%; p = 0,04), peor función ventricular izquierda (0,53 frente a 0,59%; p = 0,02), mayor incidencia de trombo angiográfico (67,1 frente a 36,8%; p < 0,001), mayor incidencia de lesiones complejas B2/C (76,4 frente a 55,8%; p = 0,004) y menor proporción de afectación de la coronaria descendente anterior (34,2 frente a 60,8%; p = 0,002). La indicación de angioplastia en los pacientes con abciximab se relacionaba en mayor medida con el ingreso hospitalario por infarto agudo de miocardio. No había diferencias entre los grupos respecto al sexo, edad y distribución del tratamiento diabético. Los episodios fueron más frecuentes en los diabéticos que no recibieron abciximab frente a aquellos que lo recibieron (38 frente a 22%; p < 0,037). Asimismo, los pacientes que no recibieron abciximab necesitaron más revascularización del vaso diana (22,7 frente a 7,2%; p < 0,01) du-
rante el seguimiento. No hubo diferencias significativas en lo concerniente a la muerte e infarto de miocardio no fatal, pero sí en la necesidad de ingreso hospitalario por angina inestable (29,1 frente a 15,9%; p = 0,045). El uso de abciximab era un factor predictor de ausencia de complicaciones en el seguimiento (OR = 0,45; p = 0,03).

Conclusiones. El tratamiento con abciximab podría reducir los episodios a medio plazo en los diabéticos sometidos a intervención coronaria percutánea especialmente debido a una menor necesidad de revascularización en el seguimiento en una población no seleccionada.


INTRODUCTION

A high percentage of patients who undergo percutaneous coronary intervention procedures are diabetic. It is known that this type of patient has a higher morbidity-mortality rate following coronary revascularization, whether it is percutaneous or surgical, than non-diabetic patients.1-4 Even now, in the era of the stent, worse results are observed in diabetic patient groups.5-6 Powerful plaque inhibition with glycoprotein IIb/IIIa inhibitors has been shown to improve the results following percutaneous coronary intervention (PCI),7-11 and this effect may be even greater in diabetic patients, as the changes in plaque function may be 1 of the mechanisms responsible for worse results in the diabetic population.12

Recently, the clinical results of the subgroup of diabetic patients in 3 large tests that used abciximab (EPIC, EPILOG and EPISTENT) were analyzed, and a decrease in the mortality rate of patients who received anti IIb/IIIa versus diabetics who did not receive it was observed.13 The aim of our study was to analyze our series of diabetic patients and observe the medium-term clinical results with regard to whether or not abciximab treatment was used.

MATERIAL AND METHODS

Study population

Between January, 1997 and January, 2000 198 consecutive diabetic patients underwent PCI in our unit with angiographic success. Of these, 73 patients (36.7%) received concomitant abciximab treatment, and the remaining 125 patients (63.3%) did not. We selected those patients with a prior diagnosis of diabetes mellitus, who were already being treated with insulin, or oral agents, or whose diabetes was controlled by diet. The patients were considered diabetic if they had been diagnosed previously, if they had been in treatment with oral anti-diabetic medication or insu-
TABLE 1. Patient baseline clinical characteristics

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Diabetes+ abciximab (N=73)</th>
<th>Diabetes− abcimab (N=125)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64±7.9</td>
<td>65±8.2</td>
<td>.44</td>
</tr>
<tr>
<td>Men</td>
<td>41 (56.2)</td>
<td>82 (65.6)</td>
<td>.18</td>
</tr>
<tr>
<td>Hypertension</td>
<td>42 (57.5)</td>
<td>66 (52.8)</td>
<td>.51</td>
</tr>
<tr>
<td>Smoking</td>
<td>31 (42.5)</td>
<td>55 (44)</td>
<td>.83</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>30 (41.1)</td>
<td>51 (40.8)</td>
<td>.96</td>
</tr>
<tr>
<td>Type of diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet-controlled</td>
<td>17 (23.3)</td>
<td>41 (32.8)</td>
<td>.11</td>
</tr>
<tr>
<td>Oral agents</td>
<td>35 (47.9)</td>
<td>57 (45.6)</td>
<td>.51</td>
</tr>
<tr>
<td>Insulin</td>
<td>21 (28.8)</td>
<td>27 (21.6)</td>
<td></td>
</tr>
<tr>
<td>EF</td>
<td>0.53±0.17</td>
<td>0.59±0.14</td>
<td>.028</td>
</tr>
<tr>
<td>Previous infarct</td>
<td>49 (67.1)</td>
<td>65 (52.8)</td>
<td>.049</td>
</tr>
<tr>
<td>Indication for PCI indication</td>
<td></td>
<td></td>
<td>.005</td>
</tr>
<tr>
<td>Stable angina</td>
<td>8 (11)</td>
<td>22 (17.6)</td>
<td></td>
</tr>
<tr>
<td>Unstable</td>
<td>20 (27.4)</td>
<td>56 (44.8)</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>45 (61.6)</td>
<td>47 (37.6)</td>
<td></td>
</tr>
<tr>
<td>Previous PCI</td>
<td>1 (1.4)</td>
<td>6 (4.8)</td>
<td>.20</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>2 (2.7)</td>
<td>6 (4.8)</td>
<td>.47</td>
</tr>
</tbody>
</table>

The data is expressed as the number of patients and the percentage of the total in parentheses or as mean±standard deviation. PCI indicates percutaneous coronary intervention; EF, ejection fraction.

Statistical analysis

For data analysis we used the SPSS (Statistical Package for Social Sciences, version 8.0 for windows) statistical package. The quantitative variables appear as mean±standard deviation (SD). The qualitative values appear as percentages. To compare the qualitative variables, we used the χ² test (or Fisher test, if the expected frequencies were <5). The quantitative variables were compared using the Student t test. We used multivariate logistical regression analysis to evaluate the factors that contributed to the final goal in both groups. The variables included in the logistical regression model were age, ventricular function, indication for angioplasty, involvement of the descending anterior artery, and the use of abciximab. A test was considered statistically significant when P<.05.

RESULTS

Baseline clinical characteristics of both groups are shown in Table 1. There was no difference with respect to age or sex. Both groups had a very similar cardiovascular risk profile. In the abciximab group, there was a higher percentage of insulin-dependent patients (28.8% versus 21.6%), and in the group without abciximab there was a greater number of patients with diet-controlled diabetes (32.8% versus 23.3%), (P=.29). The indication for percutaneous coronary revascularization was related to complications following an infarct in 45 diabetics treated with abciximab (61.6%); 30 presented with residual post-infarct ischemia (either spontaneous or after ergometry); 9 had cardiac insufficiency; 4 in recovery chest angioplasty, and in 2 patients primary angioplasty was performed secondary to fibrinolysis being contraindicated.

The patients who received abciximab had worse left ventricular function (0.53 versus 0.59) and greater infarct frequency (recent or old) (67.1% versus 52.8%; P<.049). In the same manner, diabetics treated with abciximab had more complex lesions, smaller luminal diameter, and less involvement of the anterior descending artery (Table 2).

Similar medium-term follow-up was carried out for both groups of 12.6±9.7 months; follow-up was completed for 88.7% of the diabetic patients who received abciximab and for 90.8% of patients who did not (90.4% overall). We found a reduction in episodes per patient during this period in the patients treated with abciximab (38% versus 22%; P=.037) (Table 3). There was no significant difference with regard to mortality rate (7.3% versus 5.8%) and non-fatal infarct (3.2% versus 6.8%) between the 2 groups, but we did find there was a significant difference in the need for hospital admission due to unstable angina, which was 29.1% in those patients who did not take abciximab and 15.9% in those who did (P=.045), and the need for revascularization of the target vessel, which decreased
multiple factors such as hematological anomalies (in-

and a lesser need for revascularization of the target

treated with abciximab (39.6% versus 23.7%;

gard to major clinical episodes in favor of the group

administered, with the same significant difference with re-

used in 86.2% of the cases where abciximab was not

respect to the use of coronary stents, this device being

There were no differences between the 2 groups with

The data is expressed as the number of patients and the percentage of the to-

tal is given in parenthesis.

TABLE 4. Multivariate analysis of predictive factors

episodes during follow-up

<table>
<thead>
<tr>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.98 (0.94-1.03)</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.99 (0.97-1.01)</td>
</tr>
<tr>
<td>Post-infarct PCI indication</td>
<td>0.92 (0.81-1.05)</td>
</tr>
<tr>
<td>PCI of anterior descending</td>
<td>1.07 (0.83-1.39)</td>
</tr>
<tr>
<td>Use of abciximab</td>
<td>0.45 (0.21-0.94)</td>
</tr>
</tbody>
</table>

LVEF indicates left ventricular ejection fraction; PCI, percutaneous coronary

from 22.7% in those patients not treated with abcxi-

mab to 7.2% in those treated with abciximab (P<.01).

There were no differences between the 2 groups with

from the use of coronary stents, this device being

used in 86.2% of the cases where abciximab was not

administered and 84.7% of cases where it was admi-

istered, with the same significant difference with re-

gard to major clinical episodes in favor of the group

treated with abciximab (39.6% versus 23.7%; P<.04),

and a lesser need for revascularization of the target

vessel on follow-up (21.9% versus 6.8%; P<.01). On

multivariate analysis (Table 4) the use of abciximab is

shown to be a protective factor with regard to compli-

ations on follow-up (OR=0.45; P=.03).

DISCUSSION

Diabetic patients have particular characteristics that

differentiate them from other patients with ischemia.

The greater age of diabetic patients and the greater

number of risk factors associated with the disease, as

well as the increased difficulty of revascularizing all

the arterial territories and the increased progression

of heart disease, means that diabetic patients with is-

chemic heart disease have a worse long-term prognosis

than non-diabetic patients.14 The progression of coro-

nary disease in these patients seems to be related to

multiple factors such as hematological anomalies (in-

creased plaque aggregation, increased synthesis of

procoagulant factors such as fibrinogen, factor VII,

and von Willebrand factor, and fibrinolysis attenuated

by the increase in type I plasmingenic inhibitor),15 en-

dothelial dysfunction with increased risk of vasos-

pasm and coronary thrombosis, and it has even been

suggested that exogenous insulin could have a dele-

terious effect, as in in vitro studies elevated concentra-

tions of insulin induce the formation of atheromatous

plaques.16

Although it has been established that following ba-

loon angioplasty diabetic patients have a higher inci-

dence of re-stenosis due to greater neoimtial hyper-

plasia and a higher mortality-morbidity rate as com-

pared to non-diabetic patients,17 there is no conclusive

evidence that these differences are maintained fol-

lowing placement of a coronary stent. Some authors

have reported a greater rate of re-stenosis in diabetic

patients,18 but others have not found diabetes to be a

predictive factor of re-stenosis when a stent is used.19

They have associated the poor prognosis of diabetic

patients after PCI exclusively to those who are insulin-

dependent20 and to incomplete percutaneous revascu-

larization.21-23

We found a significant difference in the combined

clinical objective on follow-up (38% in patients who

received abciximab versus 22% in those who did not; 
P=.037), a decrease in the necessity for revascular-

ization of the target vessel (22.7% versus 7.2%; 
P<.01) at medium-term follow-up of 12.6 months.

There were no differences between the 2 groups with

regard to mortality rate or non-fatal myocardial in-

farct. The small size of both groups made it difficult to

obtain results in this sense, a situation that also oc-

curred in the substudy of diabetic patients in the EPIS-

TENT study,10 while in the metaanalysis of the EPIC,

EPILOG, and EPISTENT studies,24 of 1462 diabetic

patients treated with abciximab in the 3 studies they

found a significant decrease in the mortality rate of

diabetic patients treated with abciximab, which was

decreased in non-diabetic patients taking placebo.

The use of abciximab is associated with the presen-

cence of angiographic thrombus on coronary angiography.

We found a similar incidence of acute complications

(acute non-fatal myocardial infarct) in the group trea-

ted with abciximab in spite of there being a greater inci-

dence of angiographic thrombus. Although the pre-

ence of angiographic thrombus has traditionally been

related to a greater incidence of complications during

percutaneous coronary intervention, the situation has

changed considerably since the advent of the coronary

stent and anti- IIb-IIIa agents. Alfonso et al25 showed

the efficacy of the coronary stent for treatment of le-

sions containing a thrombus, obtaining an immediate

angiographic success rate of 96%, although with a rate

of myocardial infarct without Q-wave of 6%, the

majority with data indicating distal embolization. On
the other hand, Musa Khan et al\textsuperscript{26} classified 2099 consecutive patients in the EPIC study in 3 groups according to whether they had a lack of, the possibility of, or clear evidence of angiographic thrombus. Although they found a greater percentage of acute occlusion in the presence of thrombus, at 6 months follow-up there were no differences in the combined clinical outcome (death, acute myocardial infarct [AMI], need for revascularization), and the benefit of treatment with abciximab was observed in the 3 groups. Ellis et al\textsuperscript{27} analyzed the combined data from the EPIC and EPILOG studies with the aim of evaluating whether a differential effect existed with abciximab as a function of the baseline characteristics of the lesion treated, and they found a benefit in all groups, but particularly in more complex lesions such as type B or C in which the risk of death, AMI, or urgent revascularization was reduced by 7.6\% and 5.8\%, respectively. It is worth considering the possibility of an added effect of the physical phenomenon of «sealing» of the thrombus by the stent together with the effect of abciximab on possible distal embolization and the consequent improvement in microcirculation, something that Neumann et al\textsuperscript{28} already demonstrated in the context of AMI, where they found an improvement in the peak velocity of coronary flow measured with a Doppler guide after administration of papaverine in patients treated with abciximab with regard to those who did not receive the drug.

We found a significant decrease in the need for revascularization of the target vessel (RTV), which was, respectively, 7.2\% and 22.7\% in patients who received and did not receive abciximab ($P$<.01). The need for RTV has been considered equivalent to re-stenosis, given that the patients were not routinely studied from an angiographic point of view. In the substudy of diabetic patients in the EPISTENT study, which included 491 patients divided into the 3 types of treatment (balloon angiography+abciximab, stent+ placebo, and stent+abciximab) there was a decrease in RTV from 16.6\% in the stent plus placebo group to 8.1\% in the stent plus abciximab group ($P$=.021). Nevertheless, such a decrease was not found in the general group of patients in the EPISTENT study; nor was it found in other studies with anti-IIb-IIIa in the field of interventional cardiology, with the exception of the EPID study at 3 years, findings that were not confirmed in later studies of treatment with abciximab or other anti-IIb-IIIa agents.

The excessive intimal hyperplasia seems to be the cause of the increased re-stenosis seen in diabetic patients both in the context of balloon angioplasty and after stent implantation;\textsuperscript{29} although in the ERASER study,\textsuperscript{30} which evaluated the possible effect of abciximab on the decrease in re-stenosis, they did not encounter differences between the different groups in plaque volume measured by intravascular echocardiography, although it must be pointed out that there were only 19 diabetic patients in the study so that it was not possible to reach conclusions regarding this type of patient. Perhaps in the diabetic patient, with a greater tendency toward aggregation, a potent IIb-IIIa receptor inhibitor could reduce the presence of non-occlusive peri-procedure thrombi that in turn, could influence neointimal proliferation on follow-up.\textsuperscript{31} If this is the case, we could hope for a similar effect on the diabetic population with other anti-IIb-IIIa agents such as tirofiban and eptifibatide. Another possible mechanism could be the inhibition of abciximab, different from the other anti-IIb-IIIa agents, of the $\alpha_\text{IIb}$ receptor of vitronectin,\textsuperscript{32} which would impede both neointimal proliferation and the migration and production of extracellular matrix. The long-term results in the diabetic population of studies with eptifibatide (ESPRIT) and tirofiban (TARGET) will indicate whether this is an exclusive effect of abciximab or it can be extended to other anti IIb-IIIa agents.

**Study limitations**

This is a longitudinal study of an observational character and it is subject to its own design limitations. There is no homogeneity between the groups compared, although the tendency to present characteristics that classically are considered unfavorable for PCI is close to abciximab treatment. No data exists regarding glycemic control in these patients and its possible influence on the results.

**CONCLUSION**

Abciximab improves the prognosis of a non-selective diabetic population subjected to PCI. This improvement is achieved along with a lesser need for revascularization of the target vessel during follow-up.

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