

**Clopidogrel versus ticlopidine after the placement of coronary artery stents**

David Rott

*J. Am. Coll. Cardiol.* 2003;42;772  
doi:10.1016/S0735-1097(03)00793-9

**This information is current as of July 10, 2009**

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://content.onlinejacc.org/cgi/content/full/42/4/772>

**JACC**

*JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY*



**Gerald M. Reaven, MD**

Falk CVRC  
Stanford Medical Center  
300 Pasteur Drive  
Stanford, California 94305  
E-mail: greaven@cvmed.stanford.edu

**Philip S. Tsao, PhD**

doi:10.1016/S0735-1097(03)00791-5

**REFERENCES**

1. Facchini FS, Hollenbeck CB, Jeppesen J, Chen Y-DI, Reaven GM. Insulin resistance and cigarette smoking. *Lancet* 1992;339:1128-30.
2. Eliasson B, Attvall S, Taskinen MR, Smith U. Smoking cessation improves insulin sensitivity in middle-aged men. *Eur J Clin Invest* 1997;27:450-6.
3. Assali AR, Beigel Y, Schreiber R, Shafer, Z, Fainaru M. Weight gain and insulin resistance during nicotine replacement therapy. *Clin Cardiol* 1999;22:357-60.
4. Jee SH, Lee SY, Nam CM, Kim SY, Kim MT. Effect of smoking on the paradox of high waist-to-hip ratio and low body mass index. *Obes Res* 2002;10:891-5.
5. Seppala-Lindroos A, Vehkavaara S, Hakkinen AM, et al. Fat accumulation in the liver is associated with defects in insulin suppression to glucose production and serum free fatty acid suppression independent of obesity in normal men. *J Clin Endocrinol Metab* 2002;87:3023-8.

## Clopidogrel Versus Ticlopidine After the Placement of Coronary Artery Stents

In a study published recently in *JACC*, Mueller et al. (1) compared treatment with clopidogrel and aspirin to ticlopidine and aspirin in patients undergoing coronary stent placement. Both drugs were started after the procedure and continued for four weeks. Ticlopidine was given as a 500-mg loading dose followed by 250 mg twice daily thereafter; however, clopidogrel was given without loading: 75 mg daily. The results suggested that clopidogrel was inferior to ticlopidine in terms of cardiovascular mortality. In other studies involving clopidogrel, a loading dose of 300 mg was given initially followed by 75 mg daily thereafter (2,3). A loading dose of 300 mg of clopidogrel is needed in order to achieve timely platelet inhibitory effect (4). The lack of clopidogrel loading clearly delays the effect of clopidogrel and, therefore, may cause a higher thrombotic stent occlusion (TSO) rate (the TSO rate was not reported by Mueller et al.). Use of a clopidogrel loading dose in this instance may show clopidogrel not to be inferior to ticlopidine (3).

**David Rott, MD**

The Heiden Department of Cardiology  
Bikur-Cholim Hospital  
5 Strauss St.  
Jerusalem 91004  
Israel  
E-mail: drott@012.net.il

doi:10.1016/S0735-1097(03)00793-9

**REFERENCES**

1. Mueller C, Roskamm H, Neumann FJ, et al. A randomized comparison of clopidogrel and aspirin versus ticlopidine and aspirin after the

placement of coronary artery stents. *J Am Coll Cardiol* 2003;41:969-73.

2. Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet* 2001;358:527-33.
3. Atmaca Y, Dandachi R, Gulec S, Dincer I, Oral D. Comparison of clopidogrel versus ticlopidine for prevention of minor myocardial injury after elective coronary stenting. *Int J Cardiol* 2003;87:143-9.
4. Gurbel PA, Cummings CC, Bell CR, et al. Onset and extent of platelet inhibition by clopidogrel loading in patients undergoing elective coronary stenting: the Plavix Reduction Of New Thrombus Occurrence (PRONTO) trial. *Am Heart J* 2003;145:239-47.

**REPLY**

We fully agree with Dr. Rott that the lack of a loading dose of clopidogrel is an important issue in interpreting our data. After completion of our study, two major clinical trials, Clopidogrel for the Reduction of Events During Observation (CREDO) (1) and ISAR-REACT (2), were reported that highlight the need for a loading dose of clopidogrel. In CREDO, the best clinical outcome was seen in those patients who achieved the full antiplatelet effect of clopidogrel at the time of intervention, which was 6 h after a loading dose of 300 mg. Based on clinical observations (3) and *ex vivo* analysis of platelet function (4), the ISAR-REACT trial used an even higher loading dose of clopidogrel, 600 mg, which enables the full antiplatelet effect of clopidogrel within 2 h (4). With this loading scheme, the antithrombotic efficacy in patients undergoing elective interventions could not be further improved even with abciximab, as shown by the composite 30-day end point of death, myocardial infarction, and urgent revascularization (2).

In light of these new findings, we cannot exclude that the results of our trial, as well as those of other trials suggesting inferiority of clopidogrel compared with ticlopidine (5), would have been different had an appropriate loading dose been used. Notably, a high loading dose may overcome the other potential explanation of our findings, which is the interference of statins. Although the issue has not been completely settled, preliminary reports indicate that attenuation of the antiplatelet effect by statins is not detectable after a 600-mg loading dose (6).

**Christian Mueller, MD**

University Hospital Basel  
Department of Internal Medicine  
Petersgraben 4  
Basel, 4031  
Switzerland  
E-mail: chmueller@uhbs.ch

**Heinz J. Buettner, MD****Franz-Josef Neumann, MD**

doi:10.1016/S0735-1097(03)00794-0

**REFERENCES**

1. Steinhilber SR, Berger PB, Mann JT 3rd, et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. *JAMA* 2002;288:2411-20.
2. Schömig A. Glycoprotein IIb/IIIa inhibition with abciximab in patients undergoing coronary stenting after pretreatment with a high loading dose of clopidogrel. Late-breaking clinical trial. Presented at the Late-Breaking Clinical Trial Session, March 30, 2003, at the 52nd

## Clopidogrel versus ticlopidine after the placement of coronary artery stents

David Rott

*J. Am. Coll. Cardiol.* 2003;42:772

doi:10.1016/S0735-1097(03)00793-9

**This information is current as of July 10, 2009**

<b>Updated Information &amp; Services</b>	including high-resolution figures, can be found at: <a href="http://content.onlinejacc.org/cgi/content/full/42/4/772">http://content.onlinejacc.org/cgi/content/full/42/4/772</a>
<b>References</b>	This article cites 4 articles, 1 of which you can access for free at: <a href="http://content.onlinejacc.org/cgi/content/full/42/4/772#BIBL">http://content.onlinejacc.org/cgi/content/full/42/4/772#BIBL</a>
<b>Rights &amp; Permissions</b>	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://content.onlinejacc.org/misc/permissions.dtl">http://content.onlinejacc.org/misc/permissions.dtl</a>
<b>Reprints</b>	Information about ordering reprints can be found online: <a href="http://content.onlinejacc.org/misc/reprints.dtl">http://content.onlinejacc.org/misc/reprints.dtl</a>