Letter to the Editor

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Letter by Schlachetzki et al Regarding Article, “Endovascular Stroke Therapy: Tirofiban Is Associated With Risk of Fatal Intracerebral Hemorrhage and Poor Outcome”

To the Editor:

The current study by Kellert et al1 stirs up the debate on the potential of glycoprotein IIb/IIIa antagonists in the therapy of ischemic stroke, and at first sight seems disappointing, especially, to interventional neuroradiologists.

Blocking the fibrin-binding site at the C by integrin αIIbβ3−blocking agents has been attempted in ischemic stroke therapy in various settings with and without recombinant tissue-type plasminogen activator (rtPA): the Abciximab in Emergency Treatment of Stroke Trial-II in patients exceeding the time limit for IV rtPA used an monoclonal antibody 7E3 fragment2 and was prematurely terminated because of an excess of hemorrhage. The use of the highly specific nonpeptide tyrosine derivate tirofiban within 3 to 22 hours of stroke onset in the Safety of Tirofiban in acute Ischemic Stroke (SaTIS) trial, however, was safe but did not result in better outcome. The Combined Approach to Lysis Utilizing Eptifibatide and rtPA in Acute Ischemic Stroke trial compared low-dose rtPA followed by standard dose of the nonpeptide glycoprotein IIb/IIIa antagonist eptifibatide with standard rtPA. The study demonstrated comparable safety of the combinational therapy and only a trend for increased efficacy in the rtPA only group.3

Our own experiences with tirofiban during 2004 and 2008 in patients with tirofiban either as monotherapy (n=34) in patients not amendable for IV rtPA, to prevent reocclusion after partial recanalization using IV or IA thrombolysis (n=13), or as a bridging therapy started before interventional revascularization (n=13) indicated acceptable safety for this drug. In 4 instances, asymptomatic intracerebral hemorrhages occurred and 7 patients were found to have minor, not life-threatening extracerebral bleeding complications leading to termination of tirofiban therapy. Overall, tirofiban treatment was found to be quite safe.

This first study on the safety in the context of endovascular embolectomy is of great importance given the widespread use in interventional neuroradiology to prevent thromboembolic complications (ie, during aneurysma coiling or arterial stenting).4,5 However, selection criteria in administration of adjunct platelet inhibitors is critical. In the published study by Kellert et al,1 tirofiban was given within a standard operational procedure stating, “if stenting is performed or relevant endothelial damage is feared, eg, because of multiple thrombectomy passages.” The use of a standard operational procedure in acute stroke treatment suggests some degree of standardization; however, there was no difference between the tirofiban and non-tirofiban group, in general 2 passages. In addition, how did the interventionalists assess endothelial damage? Perhaps, the bias resulting in increased intracerebral hemorrhage was introduced by the interventionalist administering tirofiban in patients felt to be at higher risk of unfavorable outcome during the intervention. This may be indicated by the high number of stenting in the tirofiban group (22, 44%) versus (9, 8%) in the nontirofiban group, although stent deployment was not a risk factor for bad outcome. Also, very critical, a variety of catheters/devices (N=20, among them 3 different stent retriever, 4 different intracranial, and a single extracranial stents) were used during the study period, all of which might have different effects on endothelial cells.

We agree that further studies on glycoprotein IIb/IIIa antagonists should be performed, but in a controlled manner and with a single type of device, randomization before the procedure and the aid of biomarkers, related to endothelial damage, such as matrix metalloproteinases 2 and 9, or cellular fibronectin.6 Before such a study is not performed, it is too early to close the chapter on glycoprotein IIb/IIIa antagonists in ischemic stroke, a still very promising class of substances.

Disclosures

None.

Ulrich Bogdahn, MD
Felix Schlachetzki, MD
Department of Neurology
University of Regensburg
University Hospital & Bezirksklinikum Regensburg
Regensburg, Germany

Gerhard Schuierer, MD
Center for Neuroradiology
University Hospital Regensburg & Bezirksklinikum Regensburg, Germany

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Ulrich Bogdahn, Felix Schlachetzki and Gerhard Schuierer

*Stroke*. 2013;44:e112; originally published online August 8, 2013; doi: 10.1161/STROKEAHA.113.002340

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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http://stroke.ahajournals.org/content/44/9/e112

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