Safety and Efficacy of Ticlopidine After Stent Placement

To the Editor:

We have read with interest the article by Dr Berger and colleagues regarding safety and efficacy of ticlopidine for only 2 weeks after successful intracoronary stent placement. The authors conclude that “in patients receiving intracoronary stents, the discontinuation of ticlopidine therapy 14 days after stent placement is associated with a very low frequency of stent thrombosis and other adverse events.” In our opinion, 3 major points need to be discussed regarding this conclusion.

First, the authors point out that intravascular ultrasound study (IVUS) was used “to facilitate stent placement in 73 patients (8.8%).” IVUS led to additional treatment (additional balloon inflation or placement of additional stents) in 36 patients. This point is crucial and needs to be discussed. Colombo and coworkers first demonstrated that optimization of stent implantation was a key issue in the prevention of subacute occlusion. Aliberto et al demonstrated that stent thrombosis and other adverse events were not significantly different between the aspirin and the ticlopidine-plus-aspirin groups when stent expansion, controlled by IVUS, was adequate. The reasons that led to IVUS examination are not clearly defined in the article by Berger et al. We can hypothesize that IVUS was performed when the result was not satisfactory, eg, suboptimal final result, persistent slow flow or dissection, or persistent intraluminal defect. Therefore, several patients with a high risk of stent thrombosis before IVUS could be treated with aspirin alone after optimization.

Second, the rate of unstable coronary syndromes is not clearly mentioned in the article by Berger et al. Abciximab was used in 312 patients (38%). We can hypothesize that abciximab was administered in patients with a high risk of thrombotic events (for clinical or angiographic reasons). We cannot be sure whether the use of abciximab in combination with ticlopidine plus aspirin explains the low rate of thrombosis observed in the study. The EPISTENT study has shown that abciximab associated with ticlopidine-plus-aspirin treatment significantly decreases the risk of cardiac adverse events.

Third, as pointed out in the discussion, the authors cannot make conclusions about the frequency of stent thrombosis because there was no systematic angiographic control.

Therefore, the following conclusion could be more appropriate: in patients receiving intracoronary stents, in combination with the use of IVUS or abciximab when needed, the discontinuation of ticlopidine therapy 14 days after stent placement is associated with a very low frequency of adverse events.

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Response

We thank Drs Henry and Beverelli for their interest in our article and the opportunity to address the important issues they raise.

The importance of full stent expansion, initially demonstrated by Colombo using intravascular ultrasound (IVUS), is clear, but whether routine IVUS during stent placement is essential is not. IVUS was used in only 8.8% of our patients for the reasons that Drs Henry and Beverelli hypothesized. Without IVUS, the event rate might have been higher, but because stent thrombosis usually occurs in the first several days, a higher frequency of stent thrombosis after 14 days would not be expected. The correspondents suggest that aspirin alone is sufficient with an optimal result confirmed by IVUS. However, aspirin was less effective than aspirin and ticlopidine in 2 randomized trials, whether or not IVUS was used.1,3 We do not advocate monotherapy with aspirin.

Drs Henry and Beverelli are correct that the use of abciximab in 38% of our patients was based on clinical and angiographic assessment of procedural risk. It is possible that abciximab may have reduced stent thrombosis in our study. However, although they are correct in stating that abciximab reduced adverse events in EPISTENT, the frequency of stent thrombosis was not reported.4 The reduction in EPISTENT in death, Q-wave infarction, and repeat procedures (surrogates of stent thrombosis) within 30 days by abciximab was only 0.3%, 0.5%, and 0.8% in absolute terms, and these were not mutually exclusive. Furthermore, if IIb/IIIa inhibitors do reduce stent thrombosis, one might theorize that late stent thrombosis after the effects of abciximab had worn off might actually be increased; this was not seen. It was the rarity of late stent thrombosis, after ticlopidine (and abciximab) had been discontinued, that was the focus of our study.

Regarding the concern that lack of angiographic follow-up may have led to underestimation of the frequency of stent thrombosis, we addressed this in the article. No studies evaluating the frequency of stent thrombosis performed routine angiography at 30 days. Stent thrombosis is usually not subtle, resulting in Q-wave infarction or death in most patients.5

We can conclude that the risk of stent thrombosis when ticlopidine is discontinued after 14 days is less than the risk of neutropenia and thrombotic thrombocytopenic purpura if the drug is continued. However, the most appropriate duration of therapy with a thienopyridine remains to be determined if clopidogrel is used, which does not cause these hematological side effects.

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