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JOURNAL OF THE AMERICAN HEART ASSOCIATION

Antiplatelet Activity Should Be Measured Routinely. No

Philip M.W. Bath

Stroke published online Apr 30, 2009;

DOI: 10.1161/STROKEAHA.108.537647

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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ISSN: 1524-4628

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Controversies in Stroke

Section Editors: Geoffrey A. Donnan, MD, FRACP, and
Stephen M. Davis, MD, FRACP

Antiplatelet Activity Should Be Measured Routinely No

Philip M.W. Bath, MD, FRCPath, FRCP

Antiplatelet agents such as aspirin, clopidogrel, and dipyridamole are effective in secondary stroke prevention with single agents reducing risk by 15% to 20%¹⁻³; the addition of a second agent (eg, combining aspirin and dipyridamole) doubles this benefit.³ As with other vascular prevention strategies, eg lowering blood pressure and cholesterol, antiplatelet agents reduce, not abolish, risk. Despite this, the concept of “aspirin failure” (ie, where a further event occurs despite aspirin) is discussed widely; this contrasts with other prophylactic strategies in which events occurring on antihypertensive or lipid-lowering therapy are not described as failures. In parallel, another concept, resistance to antiplatelet agents (eg, “aspirin resistance,” “clopidogrel resistance”) has come to the forefront⁴; here, some patients may be less sensitive to an antiplatelet agent than other patients. Such variation in response is widely recognized and accounted for in guidelines⁵ for other vascular prophylactic strategies such as antihypertensive agents; for example, younger patients are more sensitive to angiotensin-converting enzyme inhibitors than older subjects with the reverse being true for calcium channel blockers and diuretics.

The concepts of “antiplatelet failure” and “antiplatelet resistance” have led to the question of whether measuring the functional activity of antiplatelet agents might predict response to treatment and efficacy in vascular prevention. When using antihypertensive agents, we know that lowering blood pressure acts as a reliable surrogate for the resulting reduction in stroke and myocardial infarction.⁶ However, unlike blood pressure, there is no global measure of platelet function, although cutaneous bleeding time⁷ has been proposed; unfortunately, it does not assess platelet function in high-pressure/high-shear conditions, is influenced by non-platelet factors (such as hematocrit), and is very dependent on both operator and measurement environment. Similarly, platelet size, a determinant of platelet function and predictor of recurrent stroke events,⁸ does not appear to be satisfactory because antiplatelet agents such as aspirin do not alter it.

In the absence of a suitable global measure of platelet function, interest is growing in assessing specific aspects of platelet function, in particular those relevant to the antiplatelet agent being used. So, response to aspirin might be assessed using platelet aggregation after stimulation with arachidonic acid or assay of thromboxane metabolites (eg, urinary thromboxane B₂). Similarly, sensitivity to clopidogrel can be assessed using platelet aggregation in response to adenosine 5'-diphosphate. It is more problematic to measure the effects of dipyridamole because it is a stimulator of endogenous platelet inhibitory systems, whereas most measures of platelet function rely on activating them. However, these measures do not replicate the environment that platelets see in the arterial tree. To overcome this, a number of semiautomatic cartridge-based systems have been developed that create shear by forcing blood over a platelet-activating surface, eg, containing collagen and either adenosine 5'-diphosphate or epinephrine (as used in the PFA-100 system).

If specific measures of platelet function were strongly related to subsequent stroke and other vascular events, their use might be warranted. However, such evidence is lacking and the evidence that so-called aspirin- or clopidogrel-resistant people are more likely to go on to have a clinical event is weak. Furthermore, the tests are expensive both financially and in time.

By analogy with hypertension, using specific assessments of platelet function is akin to measuring blood norepinephrine or renin levels rather than blood pressure. What we really need for monitoring the effects of antiplatelet agents is a global measure of platelet function. Until such a measure can be identified, the routine measurement of platelet function using specific assessments such as aggregation or shear-based systems cannot be recommended. Clearly, the use of these approaches in research remains valid, both to address the issues raised here and to support and continue the search for a true global measure. In the meantime, if events occur on

Received September 28, 2008; accepted October 3, 2008.

From the Stroke Trials Unit, University of Nottingham, City Hospital Campus, Nottingham, UK.

Correspondence to Philip M.W. Bath, MD, FRCPath, FRCP, Stroke Trials Unit, University of Nottingham, City Hospital Campus, Hucknall Road, Nottingham NG3 5LX, UK. E-mail philip.bath@nottingham.ac.uk

(*Stroke*. 2009;40:00-00.)

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DOI: 10.1161/STROKEAHA.108.537647

monotherapy, add rather than substitute another antiplatelet as is done with antihypertensive agents.

Disclosures

None.

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KEY WORDS: antiplatelet agents ■ antiplatelet drugs ■ antiplatelet RX ■ aspirin ■ prevention



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