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Optimal Platelet Inhibition following Acute Ischemic Stroke

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The activation of platelets during cerebral ischemia, which can contribute to ischemic damage, has been recognized for decades [1]. Early aspirin treatment following ischemic stroke produces a modest clinical benefit, with minimal risk of hemorrhagic transformation [2]. It has also been noted that patients who are on aspirin before the onset of acute stroke have an improved outcome compared to patients not on aspirin. Thus, variability in prestroke aspirin usage may have influenced clinical trials [3]. Aspirin is now commonly given to acute ischemic stroke patients, but neither the degree and duration of platelet inhibition nor the effect of prestroke aspirin dosage has been studied.

We have new data that 300 mg of aspirin inhibits arachidonic acid-induced platelet activation by light-induced platelet aggregometry within 3 h of aspirin dosage in patients with recent acute stroke [4]. This corresponds with decreased thromboxane B2 (TXB2) levels at 3 h. In spite of the 'irreversible' inhibition of COX-1 by aspirin, TXB2 levels had increased significantly within 24 h in patients who had not been treated with low-dose aspirin prior to the onset of ischemic stroke. Patients previously taking aspirin maintained platelet inhibition at 24 h [4].

This study has important implications for aspirin dosage in acute stroke patients. Patients who have not been on aspirin have higher TXB2 levels following stroke and may need a second dose of aspirin earlier than 24 h to maintain platelet inhibition. Other platelet inhibitors have not been adequately studied in the acute stroke setting. It is clear we do not know the optimal platelet in-

hibitor following stroke, nor do we know the appropriate loading regimen or dosage interval to maximize platelet inhibition and patient outcome.

The same problem exists with platelet inhibition for secondary stroke prevention following TIA. The Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) trial, comparing clopidogrel (600 mg load followed by 75 mg daily) with aspirin (50–325 mg) within 12 h of the event, is expected to provide important data in the acute TIA and minor stroke setting.

Given variables including aspirin resistance, variable genetic factors in clopidogrel metabolism and prestroke platelet inhibition, maximizing platelet inhibition for individual stroke patients will require the ability to quickly and accurately measure platelet inhibition, as pointed out by Richard et al. [4]. Reliable 'point of service' measures of platelet inhibition are not widely available, and the development of such devices should be a high priority given the importance of platelet activity in ischemic stroke.

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