SHOULD ASPIRIN-RESISTANCE BE ROUTINELY APPLIED TO TAILOR STROKE PREVENTION?

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Aspirin (Acetylsalicylic acid, ASA) is one of the most important and widely used drug for the primary and secondary prevention of atherothrombotic disease.

Aspirin irreversibly inhibits cyclooxygenase – 1 (COX-1) in platelets by acetylating its serine-529 residue, thereby blocking thromboxane 2 (TXA2) and other eicosanoid production from arachidonic acid. Aspirin induced COX-1 inhibition is rapid and irreversible (1). After a single dose, a peak value is reached in about 1 hour and then declines gradually, with a half-life of about 2-3 hours at antiplatelet doses (2). The overview analysis of an indirect comparisons between the various doses of aspirin suggests that aspirin doses as low as 30 mg per day to as high as about 1300 to 1500 mg per day have the same point estimate of efficacy for recurrent stroke prevention, but lower-dose aspirin use is associated with fewer side effects.

The Aspirin Trialists' Collaboration1 suggests that the use of aspirin provides an overall 25% risk reduction of secondary thrombotic events (5). Despite strong evidence in preventing thrombotic events, a lot of patients still fail to respond to aspirin therapy. Aspirin resistant patients are at about a fourfold increased risk of non-fatal and fatal cardiovascular, cerebrovascular, or vascular events while taking aspirin than their aspirin sensitive counterparts (4).

In a recent meta-analyses of 20 studies (n=2930) patients with cardiovascular disease 810 patients (28%) were classified as aspirin resistant. The results of meta-analyses suggest that patients who were resistant to aspirin were at a greater risk of clinically important cardiovascular morbidity long term than patients who were sensitive to aspirin. And the prevalence of nonresponsiveness to aspirin was statistically higher in those patients who suffered recurrent cerebral ischemia while taking aspirin ($P < 0.5$) compared with patients who remained without new ischemic symptoms (4).

Till now there is no agreed universal definition of aspirin resistance. The failure of aspirin to prevent clinical events or failure of aspirin to inhibit platelet aggregation, ex vivo and in vitro, is known as aspirin resistance. The term **clinical aspirin failure** (clinical "resistance", treatment failure) refers to those patients who have had recurrent ischemic events while on aspirin therapy. The term **platelet nonresponsiveness to aspirin** (laboratory "resistance", biochemical aspirin resistance) describes the inability of aspirin to inhibit platelet aggregation to arachidonic acid and/or collagen (6, 7).

The prevalence of platelet nonresponsiveness to aspirin has been reported with frequencies ranging from 5,5% to 60% of patients treated (8-13). This wide range is due to clinical differences in the patient populations reported and differences in the methodology used to assess responsiveness to aspirin therapy.

The measurement of "aspirin resistance" with various methods and its clinical usefulness is still debatable.