EARLY TREATMENT AFTER TIA OR MINOR STROKE - THE CASE FOR DUAL ANTIPLATELET THERAPY

Jonathan Streifler
Head of the Neurology unit and the stroke program, Rabin Medical Center, Petach Tikva and Tel Aviv University, Israel

Stroke is a major cause of death and disability thus leading to a huge burden (medical & economical) on the society. Not all strokes are disabling; more than 50% of the victims are independent in ADL by 3 to 12 months. Yet previous stroke, in particular non-disabling, is a major risk factor for subsequent stroke

Transient ischemic attacks (TIA's) are very important in identifying stroke risk and high risk TIA patients carry high early risk of stroke.

Thus both patients' groups (i.e. - non-disabling strokes and high risk TIA's) need urgent therapeutic approach, as effective stroke prevention measures are available and invaluable; disabling strokes should be prevented by all means!

In recent years it has been shown that the high early stroke risk can be identified by clinical and investigational means; Scores such as ABCD2, ABCD3 and ABCD3-I were developed for TIA patients and by appropriate immediate approach up to 80% of the stroke risk can be eliminated!

A key factor is the immediate medical treatment including antiplatelet (AP) agents. These were proven to be effective in preventing and reducing stroke risk. Of all AP agents, aspirin alone, clopidogrel alone and the combination of dipyridamole with low dose aspirin are all recommended for secondary stroke prevention with relative stroke risk reductions ranging from 22 to 37%. These results are based on studies which emphasize long term treatment while the key issue (with the current knowledge) is how early do these agents become effective and exert their protective effects.

Clopidogrel is a pro-drug given in a single daily dose of 75 mg. Earlier effective drug levels can be achieved by the administration of a loading dose (300-600 mg).

The combination of clopidogrel and aspirin was found useful in patients with unstable angina and before stent implantation in reducing the risk of cardiac events and stent thrombosis. However, studies in secondary stroke prevention in which this combination was used and compared- the MATCH and SPS3 studies- found no beneficial effect throughout the studies' periods (1.5 & 3.4 years respectively), mainly due to bleeding side effects. Both studies, however, did not aim for the very early post TIA/ stroke period- the period when the risk is the highest!

Small studies comparing this combination early on in patients with symptomatic carotid disease (CARESS, CLAIR) demonstrated a significant reduction in emboli production and subsequent meta-analyses of outcome data from these studies along with data taken from larger studies (for those patients recruited very early) as well as from newer, relatively small, studies (FASTER, EARLY) have shown beneficial effect for dual AP regimen in reducing risks of stroke and death early on. These meta-analyses refer also for the combination of dipyridamole and aspirin.

Lately, the CHANCE study, done in China, found that a combination of clopidogrel and aspirin given for 3 weeks was useful in preventing stroke and death at 3 months.

Similar studies are still ongoing in other parts of the world.

In this debate I will discuss this issue and indicate the potential role and the importance of dual AP early on in patients with stroke or TIA.