

## **STATINS ARE MORE EFFECTIVE THAN ASPIRIN IN SECONDARY STROKE PREVENTION – NO**

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Antithrombotics, and in particular anti platelet (AP) agents have been, and still are the cornerstone treatment following acute stroke or TIA (i.e.- in secondary stroke prevention). Of all AP, acetyl salicylic acid (ASA) is the mainstay; this was established about 40 years ago following the completion of several large randomized studies that compared ASA with placebo and reported a relative risk reduction (RRR) of around 30% in the stroke and death rates. The ASA dose that was used then was higher than what is currently recommended, ranging from 975 to 1300 mg. per day. With much lower doses (50- 75 mg/day) the RRR was only 17-18%. Low doses of ASA may be associated with normal platelets function- explaining in part possible low effects of such doses. Metaanalysis of all trials (antithrombotic trialists collaborators 2002) found the RRR to be around 22%.

The positive effects of ASA treatment can be appreciated by looking at another view point; It has been shown that discontinuation of (even) low dose ASA was associated with increased stroke risk of about 40% within 6 months.

ASA effect can be augmented by adding other AP agents. The ESPS2 study have shown that the combination of sustained release dipyridamole with low dose ASA was associated with 37% RRR and other small studies in the acute phase have shown an additive effect of dual AP agents given for a short term period. This last effect was particularly demonstrated in patients with symptomatic carotid stenosis.

Hyperlipidemia and in particular high cholesterol (LDL-C) level is a well known risk factor for cardiovascular diseases and therefore effective treatment in lowering its levels is a mainstay in its prevention. However this was not the case for cerebrovascular diseases as a whole and studies along the years have failed to show a positive association. It was only after the development of the statin group of drugs that put cholesterol (and especially its treatment) back as one of the risk factors for stroke. Many trials with different types of statins have shown a significant stroke risk reduction of about 21% yet these studies were done in patients with primarily cardiovascular diseases and not in stroke patients. Following these results a large study was design for stroke patients, cardiovascular disease naïve: The SPARCL study compared 80 mg. atorvastatin with placebo and found only 16% RRR in favor of the treated patients after a long follow up. A second study- the HPS trial, in which some of the recruited patient shared the same characteristics, didn't show any clear benefit in this group!

It seems however that for a specific subgroup of stroke patients – those with large artery atherosclerosis, the benefit is somewhat better. This group, however, constitute only 15-20% of all stroke patients. It is believed that statins have a plaque stabilizing effect and studies in patient with symptomatic carotid stenosis have consistently shown a positive effect, including a reduction in the peri-procedural (endarterectomy or stenting) complication rate. Yet no studies so far provided clear evidence for an early effect in patients with symptomatic carotid stenosis and a study in TIA and minor stroke patients (FASTER study) which assessed also early administration of statins didn't show any protective effect.

On the other hand, as stated, AP treatment is a first line treatment for more than 75% of patients, except the cardio-embolic group in which anticoagulants (AC) are more effective. Yet even in this group, for patients unable to take AC AP treatment, given as ASA alone or in combination with clopidogrel, is recommended as a reasonable alternative.

The most feared side effect of AP is hemorrhagic complication – especially in the brain, yet patients on effective statin therapy are also exposed to this risk!

Lastly, in real life discontinuation/ non-compliance of statin treatment is more prevalent. This is due to a combination of side effects and high cost of even the cheapest statin medication while ASA is a very cheap drug.

In summary, while statin treatment have a clear role in the treatment of patients with stroke or TIA their effectiveness is not uniformly distributed and thus AP, which provide a wider effect in various patients' groups and situations, remain the mainstay of treatment.