**Impact of the Additive Effect of Angiotensin-Converting Enzyme Inhibitors and/or Statins with Antiplatelet Medication on Mortality After Acute Ischaemic Stroke**

Yahaya Hassan¹, Samah W. Al-Jabi²,³, Noorizan Abd Aziz², Irene Looi⁴ and Sa’ed H. Zyoud⁴,⁵

¹Department of Pharmacy Practice, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, Bandar Puncak Alam, Selangor Darul Ehsan, Malaysia, ²Clinical Pharmacy Program, School of Pharmaceutical Sciences, Universiti Sains Malaysia (USM), Penang, Malaysia, ³Faculty of Pharmacy, An-Najah National University, Nablus, Palestine, ⁴Clinical Research Centre, Hospital Pulau Pinang, Penang, Malaysia, and ⁵National Poison Centre, Universiti Sains Malaysia (USM), Penang, Malaysia

(Received 23 April 2011; Accepted 17 October 2011)

Abstract: There has been recent interest in combining antiplatelets, angiotensin-converting enzyme inhibitors (ACEIs) and statins in primary and secondary ischaemic stroke prevention. This observational study was performed to evaluate the impact of adding ACEIs and/or statins to antiplatelets on post-stroke in-hospital mortality. Ischaemic stroke patients attending a hospital in Malaysia over an 18-month period were evaluated. Patients were categorized according to their vital status at discharge. Data included demographic information, risk factors, clinical characteristics and previous medications with particular attention on antiplatelets, ACEIs and statins. In-hospital mortality was compared among patients who were not taking antiplatelets, ACEIs or statins before stroke onset versus those who were taking antiplatelets alone or in combination with either ACEIs, statins or both. Data analysis was performed using srs version 15. Overall, 637 patients met the study inclusion criteria. After controlling for the effects of confounders, adding ACEIs or statins to antiplatelets significantly decreased the incidence of death after stroke attack by 68% (p = 0.036) and 81% (p = 0.010), respectively, compared to patients on antiplatelets alone or none of these medications. Additionally, the addition of both ACEIs and statins to antiplatelet medication resulted in the highest reduction (by 94%) of the occurrence of death after stroke attack (p < 0.001). Our results suggest that adding ACEIs and/or statins to antiplatelets for patients at risk of developing stroke, either as a primary or as a secondary preventive regimen, was associated with a significant reduction in the incidence of mortality after ischaemic stroke than antiplatelets alone. These results might help reduce the rate of ischaemic stroke morbidity and mortality by enhancing the application of specific therapeutic and management strategies for patients at a high risk of acute stroke.

Stroke, a global health problem, is one of the leading causes of morbidity and mortality worldwide. Annually, about 16 million first-ever strokes occur worldwide, with a death toll of approximately 5.7 million people per year [1]. Over the past few decades, post-stroke mortality has declined in most developed countries. This beneficial trend was because of the better control of modifiable risk factors and improvements in medical care [2].

Previous studies resulted in conflicting data regarding the role of antiplatelet therapy, especially in the primary prevention of ischaemic stroke. Some studies reported that patients who suffer ischaemic stroke while taking aspirin have less severe strokes and more favourable outcomes [3,4]. However, others suggested that aspirin has no effect on stroke severity or its outcomes [5,6]. In the Women’s Health study, a randomized primary prevention clinical trial, 10-year follow-up of 39,876 apparently healthy women

health professionals to evaluate the benefits of aspirin in the primary prevention of stroke and cardiovascular diseases, was performed. The result showed that women taking aspirin experienced an overall 17% reduction in the risk of stroke [relative risk (RR) = 0.83; 95% confidence interval (CI) = 0.69–0.99; p = 0.04], mostly due to significant reductions in ischaemic stroke (RR = 0.76; 95% CI = 0.63–0.93; p = 0.009). In the subgroup analyses, aspirin significantly reduced the risk of ischaemic stroke among women aged 65 years or older. On the other hand, the trial found a non-significant increase in the risk of haemorrhagic stroke (RR = 1.24; 95% CI = 0.82–1.87; p = 0.31) [7]. As a secondary end-point, there was no significant difference between the groups in the risk of fatal stroke (RR = 1.04; 95% CI = 0.58–1.86; p = 0.90), but the aspirin group had a decreased risk of non-fatal strokes (RR = 0.81; 95% CI = 0.67–0.97; p = 0.02), as compared with the placebo group [7].

Angiotensin-converting enzyme inhibitors (ACEIs) and statins are being increasingly prescribed for ischaemic stroke prevention. Recent studies indicate that previous use of ACEIs and statins can reduce the incidence of ischaemic stroke in populations at risk [8,9] and that their use may be...