Effect of Prestroke Use of Angiotensin-Converting Enzyme Inhibitors Alone Versus Combination With Antiplatelets and Statin on Ischemic Stroke Outcome

Yahaya Hassan, PharmD,* Samah W. Al-Jabi, MSc,†‡ Noorizan Abd Aziz, PharmD,*
Irene Looi, MBBS, MRCP,§ and Sa'ed H. Zyoud, MSc‡||

Background: Angiotensin-converting enzyme inhibitors (ACEIs), antiplatelets (APs), and statin are increasingly being prescribed for ischemic stroke prevention.

Objectives: The objective of the study was to examine whether previous combination therapy of ACEI with AP and/or statin has additive effect compared with ACEI alone on functional outcome after ischemic stroke. Furthermore, factors associated with improving functional outcome were investigated.

Methods: Ischemic stroke patients attending a Malaysian hospital in 2008 were categorized according to Barthel Index at discharge. Favorable outcome was defined as Barthel Index of 75 or greater. Data included demographic information, clinical characteristics, and previous medications with particular attention to ACEI, AP, and statin.

Results: Overall, 505 patients were included. Variables associated with good functional outcome were younger age ($P = 0.002$), first-ever attack ($P = 0.016$), lacunar ($P = 0.015$) or posterior circulation infarct stroke subtype ($P = 0.034$), minor Glasgow Coma Scale ($P < 0.001$), and previous use of ACEI alone or combined with AP and/or statin ($P = 0.002$). Using ACEI alone as the reference for ACEI + AP, ACEI + statin, or ACEI + AP + statin combinations, there was no significant difference among combinations on improving functional outcome ($P = 0.852$).

Conclusions: Prestroke use of ACEI either alone or combined with AP and/or statin was associated with better functional outcome. Previous use of ACEI in combination with AP and/or statin did not significantly differ from ACEI alone in their effect on outcome. Our study provides a potential rationale for optimizing the use of ACEI among individuals at risk of developing ischemic stroke.

Key Words: angiotensin-converting enzyme inhibitors, antiplatelets, Barthel Index, functional outcome, ischemic stroke, statin

Annually, about 16 million first-ever strokes occur worldwide, with a death toll of approximately 5.7 million people per year.[1] In addition, stroke is the major cause of morbidity among adults, with up to half of all patients who survive after the stroke failing to regain independence and needing long-term health care.[2]

Angiotensin-converting enzyme inhibitors (ACEIs) have shown promising effects in reducing the incidence of ischemic stroke in populations at risk[3] and in alleviating ischemic stroke severity and improving its outcomes.[4,5] Although their main effect is on hypertension treatment, the main modifiable vascular risk factor for ischemic stroke, previous evidence has shown that these drugs can decrease the severity of ischemic stroke by other mechanisms including neuroprotective properties, beneficial properties on the endothelium, and an anti-atherosclerotic effect.[3,6]

Antiplatelets (APs) have been prescribed for secondary ischemic stroke prevention[7] and are increasingly being prescribed for primary prevention since their effectiveness for primary stroke prevention is still uncertain.[8] Several studies have evaluated the role of APs, mainly aspirin, in reducing stroke severity and therefore enhancing outcome. These studies have shown conflicting results, with some finding a positive effect of AP use,[9,10] whereas others have found that previous AP use has no significant effect on stroke severity.[11,12] Moreover, statins are widely used for the treatment of dyslipidemia and secondary prevention in patients with ischemic heart disease (IHD). These agents have been proven to significantly reduce the risk of ischemic stroke in populations at risk[13] and improve stroke-related mortality and outcomes.[14,15]

Does previous combination therapy of ACEI with AP and/or statin have an additive effect compared with ACEI therapy alone in improving the functional outcome of ischemic stroke patients as measured by the Barthel Index (BI)? To the best of our knowledge, none of the studies performed to date have taken into account the comparison between previous ACEI-only use and its combination with AP and/or statin on ischemic stroke outcome at discharge. We performed this observational study to evaluate the impact of ACEI alone versus combination of ACEI with AP and/or statin on BI scores at discharge and to identify the factors associated with improving functional outcome of ischemic stroke patients, including demographic, risk, and clinical factors in addition to previous medications.

MATERIALS AND METHODS

Patients, Setting, and Study Design

We retrospectively reviewed the collected acute ischemic stroke data of patients admitted to a 1200-bed hospital located in northern Malaysia over the year period of 2008. Before starting the study, permission for the use of patient clinical information was obtained from the local health authorities and medical ethics committee.

The study patients were identified according to the *International Classification of Diseases, 10th Revision*. Using a computer-generated list obtained from the hospital record office, patients with diagnostic codes I63.0 to I63.9 (acute ischemic stroke) were included in the study. Case verification was supplemented by

*Department of Pharmacy Practice, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, Bandar Puncak Alam, Selangor Darul Ehsan; †Clinical Pharmacy Program, School of Pharmaceutical Sciences, Universiti Sains Malaysia (USM), Penang, Malaysia; ‡Faculty of pharmacy, An-Najah National University, Nablus, Palestine; §Clinical Research Centre, Hospital Pulau Pinang; and ||National Poison Centre, Universiti Sains Malaysia (USM), Penang, Malaysia.

Address correspondence and reprint requests to Yahaya Hassan, PharmD, Department of Pharmacy Practice, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, Bandar Puncak Alam 42300, Selangor Darul Ehsan, Malaysia;
E-mail: dryahaya2909@puncakalam.uitm.edu.my