بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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The Risk of Cerebral Microbleeds in Ischemic Stroke Patients Using Antiplatelet Therapies

Thesis

Submitted for Partial Fulfillment of M.D Degree in Neurology

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Nabil Nasif Saber

Contents

List of Abbreviations

Abb.		Full Term
AD	.....	Alzheimer Disease
ACE	.....	Angiotensin-Converting Enzyme 2
AGES	.....	Age Gene/Environment Susceptibility Study
APs	.....	Antiplatelets
APOE	.....	Apolipoprotein E
ARDS	.....	Acute Respiratory Distress Syndrome
ASPS	.....	Austrian Stroke Prevention Study
Aβ	.....	Beta Amyloid Peptide
BBB	.....	Blood Brain Barrier
CAA	.....	Cerebral Amyloid Angiopathy
CADASIL	.....	Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy
CMBs	.....	Cerebral microbleeds
COVID-19	.....	Coronavirus 2019
CT	.....	Computed Topography
FLAIR	.....	Fluid Attenuated Inversion Recovery
GRE	.....	Gradient Recalled Echo
ICH	.....	Intracerebral Hemorrhage
LACI	.....	Lacunar Infarct
LVMI	.....	Left Ventricular Mass Index
MRI	.....	Magnetic Resonance Imaging
OCSP	.....	Oxford Classification Stroke Project
PACI	.....	Partial Anterior Circulation Infarct
POCI	.....	Posterior Circulation Infarct
SARS-COV-2	.....	Severe Acute Respiratory Syndrome Coronavirus 2
SE	.....	Spin Echo
SWI	.....	Susceptibility weighted images

Abb.		Full Term
SVD	.....	Small Vessel Disease
TACI	.....	Total Anterior Circulation Infarct
TE	.....	Echo Time
TIA	.....	Transient Ischemic Attack
TOAST	.....	Trial of Org 10172 in Acute Ischemic Stroke Treatment
TOF	.....	Time of Flight
WHO	.....	World Health Organization
WMLs	.....	White matter lesions

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Abstract

Background: Interest in cerebral microbleeds (CMBs) has increased based on advances in magnetic resonance imaging (MRI) technology. Both MRI T2-weighted gradient-echo (GRE) and susceptibility-weighted imaging may be sensitive techniques for the detection of past and more recent brain hemorrhage. The prevalence of CMBs in healthy population ranges 3.7–7.7%, whereas in patients with intracerebral hemorrhage is thought to be around 60%.

Objective: To evaluate the prevalence and possible risk of microbleeds among patients with ischemic stroke using antiplatelets (Aps).

Patients and Methods: The observational hospital-based cross-sectional analytical study involved 150 consecutive patients with ischemic stroke (recent or old ischemic strokes or both), from inpatients of neurology departments of Ain Shams University Hospital and Agouza Police Hospital for a period of 15 months from April 2018 to June 2019.

Results: Cerebral microbleeds were present in 13 patients representing 26% of the no AP group, 16 patients representing 32% of the single AP group and 19 patients representing 38% of the double AP group, there was no statistically significant difference between the three groups of patients. Cerebral microbleeds were present in 60% of patients on double APs and 37.5% of patient on single AP for more than two years, compared to 23.3%and 26.9%for the two groups respectively on APs for less than two years, In the current study we found that the significant risk factor for the presence of CMBs was the duration of APs use. There was no statistically significant difference in the laboratory data (including full lipid profile, HbA1c and platelet count) between the three groups.

Conclusion: CMBs are significantly associated with long term use of antiplatelets, so careful clinical and radiological follow up of ischemic stroke patients with CMBs using antiplatelets for risk of future intracranial hemorrhage.

Keywords: Cerebral Microbleeds, Ischemic Stroke, Antiplatelet Therapies

Introduction

In the mid-1990s reports began to appear of small hemorrhagic lesions on magnetic resonance imaging (MRI) studies, Scharf et al. described black dots of signal loss on T2-weighted MRI in patients with spontaneous intracerebral hemorrhage (ICH) and termed these 'hemorrhagic lacunes' ***(Scharf et al., 1994)***.

Subsequent studies using T2*-weighted gradient-echo (T2*-GRE) MRI – a technique with greater sensitivity to the signal loss from magnetic 'susceptibility' effects of blood breakdown products – detected small round black dots which have become known as 'cerebral microbleeds' (CMBs) ***(Offenbacher et al., 1996)***.

CMBs reflect small areas of hemorrhage, and are common in both ischemic stroke and ICH ***(Werring, 2011).***

Stroke was defined according to WHO criteria as a syndrome of rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin. It is subdivided into ischemic stroke (caused by vascular occlusion or stenosis) and hemorrhagic stroke (caused by vascular rupture, resulting in

intra-parenchymal and/or subarachnoid hemorrhage). Ischemic stroke accounts for about 85% of cases and hemorrhagic stroke about 15% ***(Thom et al., 2006).***

Stroke is considered to be one of the important global health problems, 15 millions individual worldwide suffer a stroke annually. Of these, 5 millions die and another 5 millions are left permanently disabled, placing a burden on family and community. It ranks the second most common cause of mortality in the world, and remains the most common cause of long-term disability in adults .Although the incidence of stroke is declining in many developed countries, largely as a result of better control of high blood pressure, and reduced levels of smoking, the absolute number of strokes continues to increase because of the ageing population ***(Taher et al., 2010).***

Based on the data collected by ***Zhang et al. (2012)***, the incidence of stroke in five European countries and the USA ranges from 114 cases per 100,000 persons per year in France for first-ever stroke to 350 cases per 100,000 persons per year in Germany for all strokes; prevalence estimates ranged from 1.5% in Italy to 3% in the UK and USA. A systematic review recorded by ***Kulshreshtha et al. (2012)*** recorded that population-based studies from South Asia have stroke prevalence in the range of 45–471 per 100,000. Because there

have been no epidemiological studies of stroke in Egypt, a community-based three-phase door-to-door study survey was conducted in the Assiut Governorate to estimate the prevalence and risk factors of stroke in our community giving a crude prevalence rate of 963/100,000 ***(Khedr et al., 2013).***

Transient ischemic attack (TIA) is one of the most important factor of acute ischemic stroke (AIS) ***(Amarenco et al., 2016)***. In 2009, the American Heart Association and the American Stroke Association agreed on a new definition of TIA, defined by the absence of a cerebral tissue lesion, and no more by the time from the onset ***(Easton, et al., 2009)***, a similar definition also appears in the upcoming International Classification of Diseases, Eleventh Revision ***(WHO, ICD-11, 2018).***

Transient ischemic attack is a common condition, with an estimated 250,000 to 300,000 events occurring annually in the United States ***(Mozaffarian et al., 2016).*** It precedes stroke in approximately 15% to 26% of patients ***(Rothwell et C.P. Warlow, 2005).*** The majority of strokes occur in the first week after transient ischemic attack, and the first 2 days after an attack are the highest-risk period, in which rates of stroke vary from 4% to 10% ***(C.M. Wu, et al., 2007)***.