Updating Predictors and Prevention of Acute Stroke

Essay submitted for partial fulfillment of the Master Degree in Neuropsychiatry

Presented by:

Mohammad Badawy Mohammad Khier

MB Bch. South Valley University

Under the supervision of:

Prof. Dr. Mahmoud Hemeda El - Rakawy

Professor of Neuropsychiatry,
Faculty of Medicine,
Ain Shams University.

Dr. Ayman Mohamed Nassef

Assistant Professor of Neuropsychiatry,
Faculty of Medicine,
Ain Shams University.

Dr. Lobna M. El-Nabil

Lecturer of Neuropsychiatry,
Faculty of Medicine,
Ain Shams University.

Faculty of Medicine
Ain Shams University.
Cairo 2008.

الجديد في متنبئات السكتة الدماغية الحادة وكيفية الوقاية

رسالة مقدمة توطئة للحصول على درجة
الماجستير في الأمراض
العصبية و النفسية

مقدمة من:

الطبيب محمد بدوى محمد خير
بكالوريوس الطب و الجراحة ، جامعة جنوب الوادي

تحت إشراف:

الأستاذ الدكتور/ محمـود حميـدة الرقــاوى
أستاذ الأمراض العصبية و النفسية
جامعة عين شمس

الدكتور/ أيــمــن محمــد نــاصـــــف
أستاذ مساعد الأمراض العصبية و النفسية
جامعة عين شمس

الدكتور / لبني محمد النبيل السيد
مدرس الأمراض العصبية و النفسية
جامعة عين شمس

كليـــــة الطـــب
جامعة عين شمس
القاهرة ٢٠٠٨

Acknowledgement

First of all thanks to **ALLAH**

I wish to express my deepest thanks, gratitude and profound respect to my honored professor, ***Prof. Dr. Mahmoud Hemeda El – Rakawy,*** *Professor of Neuropsychiatry, Faculty of Medicine, Ain Shams University, for his meticulous supervision. I consider myself fortunate to work under his supervision. His constant encouragement and constructive guidance were of paramount importance for the initiation, progress and completion of this work.*

No words can describe the effort and help of ***Dr. Ayman Mohamed Nassef,*** *Assistant Professor of Neuropsychiatry, Faculty of Medicine, Ain Shams University, for his great support, facilities, careful supervision and continuous advice and guidance, which were the cornerstone for this work.*

I am also deeply grateful and would like to express my sincere thanks and gratitude to ***Dr. Lobna M. El-Nabil,*** *Lecturer of Neuropsychiatry, Faculty of Medicine, Ain Shams University for her great help and continuous contributions with the accomplishment of this work.*

List of Contents

ACE	angiotensin converting enzyme
ADH	antidiuretic hormone
AGT	angiotensinogen
APCR	activated protein C receptor
AST	Serum aspartate aminotransferase
BPSD	behavioral and psychological symptoms of dementia
CADASIL	cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
CBS	cystathionine beta synthase
CHD	coronary heart disease
CKD	chronic kidney disease
CRP	C-reactive protein
cSVD	cerebral small vessel disease
CT	computed tomography
CVD	cardiovascular disease
CWT	color-word test
DD	deletion/deletion
eNOS	endothelial nitric oxide synthase
EPCR	endothelial cell protein C receptor
ESRD	end-stage renal disease
ETs	endothelins
FSRP	Framingham stroke risk profile
GFR	glumerular filteration rate
GHQ	general health questionnaire
GLA	a-galactosidase gene
GP	glycoprotein
GWB-D	general well-being schedule
HbC	hemoglobin C
HbF	fetal hemoglobin

HbS	hemoglobin S
HDL	high density lipoprotein
HPL	Human Population Laboratory
HUS	uremic syndrome
I/D	insertion/deletion
ICAM	intercellular adhesion molecule
I/I	insertion/insertion
IMT	intima-medial wall thickness
LA	leukoaraiosis
LD	linkage disequilibrium
LDL	low density lipoprotein
LI	lacunar infarction
LP	lipoprotein
MBP	mean blood pressure
MELAS	mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes
MI	myocardial infarction
MRFIT	multiple risk factor intervention trial
MRIs	magnetic resonance images
MTHFR	5.10-methylene tetrahydrofolate reductase
NSTE-ACS	non-ST-segment elevation acute coronary syndrome
PAI1	plasminogen activator inhibitor 1
PDAY	pathobiological determinants of atherosclerosis in youth
PDE4D	phosphodiesterase 4D
PICH)	primary intracerebral hemorrhage
PPET	preproendothelin
RAAS	renin-angiotensin-aldosterone system
RAS	renin-angiotensin system

SBP	systolic blood pressure
SES	socioeconomic status
SHRSP	stroke-prone spontaneously hypertensive rat
SIADH	syndrome of inappropriate ADH secretion
SWISS	siblings with ischemic stroke study
TCD	transcranial doppler ultrasonography
TFPI	tissue factor pathway inhibitor
TGF B	transforming growth factor B
TIAs	transient ischemic attacks
TM	thrombomodulin
TMA	thrombotic microangiopathy
tPA	tissue plasminogen activator
US	united states
VCAM	vascular cell adhesion molecules
VKORC1	vitamin K epoxide reductase complex 1
VNTR	variable nucleotide tandem repeat
vWF	von Willebrand factor
WMHs	white matter hyperintensities

List of tables

List of figures

Introduction

Stroke is rapidly developing clinical symptoms and or signs of focal and at time global loss of brain functions with symptoms lasting more than 24 hours or leading to death , which is thought to be due to inadequate blood supply to a part of the brain or spontaneous hemorrhage into or over the brain substance (***Warlow , 2001)***.Stroke is the third leading cause of death following cardiac disease and cancer related deaths ***(Adams et al., 2003***) . Approximately 29% of patients die within one year following stroke. These percentage rise in patients older than 65 years (***Schneider et al., 2004).***

Acute ischemic stroke refers to stroke caused by thrombosis or embolism and accounts for 80% of all strokes (***Gustafsson , 2003***) .

Large artery atherosclerosis, cardiac embolism, and lacunar disease, which collectively account for 60% to 70% of all causes of stroke, primarily affect older individuals. Stroke in the young usually results from a variety of conditions that, although individually

uncommon, collectively account for approximately 40% of all strokes. Ischemic strokes can be caused by vascular atherosclerotic disease, nonatherosclerotic abnormalities, cardiac emboli, hematologic or coagulation disorders, substance abuse, migraines, oral contraceptives, inflammatory disorders, and many other conditions. The spectrum of causes may differ by geographic distribution ***(Ghandehari and Moud, 2006).***

Ischemic stroke can be caused by a number of monogenic disorders , and in such cases stroke is frequently part of multi system disorder. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL), due to mutation in the notch 3 gene,is increasingly appreciated as of familial subcortical stroke ***(Markus and Hassan, 2000)*** . A notable genetic study found that polymorphisms in the glutathione peroxidase (Gpx-3) gene, perhaps via interactions with conventional vascular risk factors, increase the risk for ischemic stroke in children and young adults .Such polymorphisms affect the gene's transcriptional activity and thereby compromise plasma antioxidant and

antithrombotic activities ***(Voetsch et al., 2007).*** Findings from gene expression profiling studies are leading to new diagnostic and therapeutic strategies that can be applied in medical practice. Promising results of gene expression profiling of the peripheral blood in patients with ischaemic stroke have been obtained in recent pilot studies, demonstrating a partially reproducible gene signature of acute cerebral ischaemia ***(Baird , 2006).***

Depressive symptoms and other psychological factors have a role as predictors of stroke in the elderly .However the main psychological factor of interest was depression. Marital status , social support, social networks, and religiousness were also assessed as potential antecedent or mediating factors. When combined with other significant predictor variables such as age , sex , hypertension , diabetes , physical function, and smoking, neither depression nor religious attendance retained its significance (***Colantonio et al ., 2001).***

Stroke is an uncommon but serious complication after non-ST-segment elevation acute coronary syndrome (NSTE-ACS). This study aimed to identify

predictors of stroke within 30 days in patients who suffered NSTE-ACS. Stroke is a rare complication occurring early after NSTE-ACS, but is associated with high mortality (***Armstrong et al., 2006).***

Although patients with end stage renal disease (ESRD) experience markedly higher rates of stroke, no studies in the US have identified risk factors associated with stroke in this population. It was hypothesized that black race, malnutrition, and elevated BP would be associated with the risk of stroke among patients with ESRD. Adult Medicare-insured hemodialysis and peritoneal dialysis patients without a history of stroke or transient ischemic attack (TIA) were considered for analysis. The primary outcome was hospitalized or fatal stroke (***Seliger et al., 2003).***

Primary prevention involves identification of individuals with high risk for stroke and treatment of modifiable risk factors. Modifiable risk factors include (high blood pressure, smoking and passive smoking, lack of physical activity; and inadequate treatment of atrial fibrillation, carotid artery disease, and heart failure) ***(Goldstein et al., 2001) .***

In general, reduction of modifiable risk factors is the single best preventative action to lessen strokes in both younger and older individuals (***Ning and Furie, 2004***).

Primary prevention guidelines recommend regular screening and appropriate treatment of hypertension and diabetes, smoking cessation for all current smokers, weight reduction in overweight persons, a healthy diet, and regular exercise ***(Goldstein et al .,2001).***

Prevention has a major role in few diseases that predispose to stroke in the young: for example, timely blood transfusions have been shown to reduce the risk for stroke in patients with sickle cell disease ***(Adams et al .,1998).***

A history of drug use and abuse should be sought during patient encounters and appropriate counseling initiated as needed. Caution has also been recommended in women using oral contraceptives with additional risk factors (cigarette smoking or prior thromboembolic events) ***(Bousser et al., 2000)***.

Aim of The Work:

To revise stroke predictors and their impact on stroke prevention.