Faculty of medicine

Relationship Between Metabolic Disorders And Stroke

Essay submitted for partial fulfillment of the Master Degree in Neuropsychiatry

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2007

كليـــــة الطـــب

الأضطرابات الأيضية وعلاقتها بالسكتة الدماغية

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

مقدمة من

الطبيب: المتولي علي المتولي

بكالوريوس الطب و الجراحة

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جامعة عين شمس

2007

Acknowledgment

First and before all I thank God . I thank him for his great mercy , generous blesses , and for his continuous gifts . I thank him for giving me the ability to achieve this work .

I would like to thank professor ***Dr*** . ***Mahmoud Hemeda*** Professor of Neuropsychiatry ,Faculty of medicine, Ain Shams University , who is always pushing me to accomplish thing I never thought I could do . He had the idea of this study and I owe him choosing me to do it .

I am very grateful to ***Dr : Ayman Mohamed Nassef*** Assistant Professor of Neuropsychiatry, Faculty of medicine, Ain Shams University, for his kind supervision , support , indispensable suggestion and great help through out the course of this study .

Words can never express my sincere thank to ***Dr : HALA EL-KHAWAS*** Assistant Professor of Neuropsychiatry, Faculty of medicine, Ain Shams University , for her continuous encouragement , enthusiatic support indispensable suggestion and great help through out the course of this study .

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List of abbreviation

5-FU	5-fluorouracil
A1C	Glycosylated hemoglobin
ACE inhibitors	Angiotensin converting enzyme inhibitors
aCL	Anticardiolipin antibody
ACTH	Adrenocorticotropic hormone
ADH	Antidiuretic hormone
AF	Atrial fibrillation
AGEs	Glycosylation end products
AHA	American Heart Association
ApoE4	Apolipoprotein E 4
ATP	Adenosine triphosphate
AVMs	Arteriovenous malformations
BBB	Blood brain barrier
BG	Blood glucose
BMI	Body mass index
Ca	Calcium
CAA	Cerebral amyloid angiopathy
CAD	Coronary Artery Disease
CADASIL	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
CH	Cerebral haemorrhage
CBS	Cystathionine B-synthase
CBV	Cerebral blood volume
CHD	Coronary Heart Disease
CHS	Cardiovascular Health Study
CI	Cerebral infarction

CKD	Chronic kideny disease
CMRO	Cerebral metabolic rate of oxygen
CNS	Central nervous system
COX -2	Cyclo-oxygenase-2 inhibitors
CPP	Cerebral perfusion pressure
CT	Computed tomography
CVA	Cerebrovascular accident
CVD	Cerebrovascular disease
CVT	Cerebral venous thrombosis
DECODE	Diabetes epidemiology: collaborative analysis of diagnostic. criteria in Europe
DM	Diabetes mellitus
DVT	Deep venous thrombosis
EMS	Emergency medical services
Enos	Endothelial nitric oxide synthase
FBS	Fasting blood sugar
FFA	Free fatty acid
GABA	Gamma-aminobutyric acid
H	Hydrogen Ions
HbA1c	Haemoglobin A1c
HDL	High density lipoprotein
HE	Hepatic encephalopathy
HMG-CoA	The enzyme 3-hydroxy-3-methylglutaryl coenzyme A
HOPE-2	Heart Outcomes Prevention Evaluation
HPA	hypothalamus-pituitary-adrenal
HUS	Hemorrhagic uremic syndrome
ICH	Intracranial hemorrhage
ICP	Intracranial pressure
IL-6	Interleukin-6

INR	International normalized ratio
IV	Intravenous
LDL	Low-density lipoprotein
LDL-C	low-density lipoprotein cholesterol
LMWH	Low molecular weight heparinoid
LP(a)	Lipoprotein (a)
LPA	Lysophospholipid
MCAO	Middle cerebral aretery occlusion
MELAS	Mitochondrial encephalomyopathy, lactic acidosis, and stroke like episodes
MI	Myocardial infarction
MRFIT	The Multiple Risk Factor Intervention Trial
MRI	Magnetic resonance angiography
MTHFR	Methylene tetrahydrofolate reductase
NAD	Nicotinamide adenine dinucleotide
NCEP	National Cholesterol Education Program
NHLBI	The National Heart, Lung, and Blood Institute
NMDA	N-methyl-D-aspartic acid
nNOS	Neuronal nitric oxide synthase
NO	Nitric oxide
Nos	Nitric oxide synthase
NS	Nephrotic syndrome
OEF	Oxygen extraction fraction
OH	Orthrostatic Hypotension
PAF	Platelate activating factors
PAI-1	Plasminogen activator inhibitor 1

PBN	P-phenylN-tert-butyl nitrone
PCA	Posterior cerebral aretery
PCP	Phencyclidine
PCOS	Polycystic ovaries
PDAY	Pathobiological Determinants of Atherosclerosis in Youth
PDH E_1	Pyruvate-dehydrogenase E1-alfa deficiency
PEG-SOD	Superoxide dismutase attached to polyethylene glycol
pH_i	Intracellular pH
pH_o	Extracellular Ph
PKC	Protein kinase C
PMN	Polymorphonuclear leukocytes
propionyl-CoA	propionyl-coenzyme A
rCBF	Regional cerebral blood flow
ROS	reactive oxygen species
r-TPA	Recombinant tissue plasminogen activator
SAH	Subarachnoid hemorrhage
SIADH	Syndrome of inappropriate anti-diuretic hormone secretion .
SOD	Superoxide dismultase
SPECT	Single photon emission computerized tomography
SSRIs	Selective serotonin reuptake inhibitors
TBI	Traumatic brain injury
TG	Triglycerides
tHcy	Plasma homocysteine levels
TIA	Transient ischemic attack
TPA	Tissue plasminogen activator

TXA2	Thromboxane A_2
UE	Uremic encephalopathy
UKPDS	UK Prospective Diabetes Study
VISP	Vitamin Intervention for Stroke Prevention
XDH	Xanthine dehydrogenase
Xo	Xanthine oxidase

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Introduction

A stroke is a rapidly developing clinical symptoms and or signs of focal and at times 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).**

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

Stroke is the third leading cause of death in the United States following cardiac disease and cancer related deaths. Approximately 29% of patients die within one year following stroke. These percentage rises in patients older than 65 years **(Adams et al., 2005) .**

The brain is the most metabolically active tissue in the body . While representing only 2% of the body's mass, it requires 15-20% of the total resting cardiac output to provide the necessary glucose and oxygen for its metabolism **(Marler et al.,1997).**

Ischemic stroke results from events that limit or stop blood flow , such as embolism , thrombosis in situ , or relative hypo perfusion. As blood flow decrease , neuron cease functioning , and irreversible neuronal ischemia and injury begin at blood flow rate of less than 18ml/min **(Schneider et al., 2004) .**

Metabolic neurological disorder include a wide variety of conditions. Imbalance in key metabolism constituents , include gases , electrolytes, vitamins and hormones can produce dramatic systemic and neurological consequences leading to stroke **(Dejong et al., 2005) .**

Inherited metabolic syndromes associated with an increase occurrence of stroke include MELAS syndromes , pseudoxathoma elasticum, Fabry`s disease . homocystinuria , and sulfate oxidase deficiency. Although these disorder are relatively uncommon they are typically more symptomatic in patient younger than 40 years **(Dawid , 1997) .**

Smoking represents a significant and modifiable risk factor . It has been demonstrated that current smokers who smoke 20 or more cigarettes per day have an associated increase of stroke risk approximately 2 – 4 times that of a nonsmoker **(Brown et al.,2004) .**

Ischemic and hemorrhagic stroke and stroke of undetermined origin may be related to alcohol intake .Both mortality and morbidity from ischemic infarction seem to be increased among heavy drinker as well as the risk of stroke recurrences **(Gdovinova ., 2002) .**

Multiple illicit drugs, including heroin, amphetamine, cocaine, sympathomimetics such as phenylpropanolamine, ephedrine and pseudoephedrine, phencyclidine, lysergic acid diethylamide, marijuana, and alcohol, have been associated with stroke **(Kernan et al.,2000).**

Abnormalities in blood cell constituents and plasma proteins may result in a hypocoagulable or hypercoagulable state with corresponding abnormalities In blood viscosity and stasis , which predispose the patient to cerebral ischemia or cerebral hemorrhage **(Dawid , 1997).**

Preexisting hyperglycemia is found commonly in patients presenting with acute stroke, and hypoglycemia may present with focal symptoms mimicking acute stroke. Diabetes mellitus increases the risk for all types of stroke **(Aslan ,1997).**

Diabetes is strongly linked with high blood pressure and, although diabetes is a treatable condition, yet it increases a person's risk for stroke **(Dejong et al., 2005) .**

Both hyperthyroidism and hypothyroidism can contribute to a cardioembolic source for stroke **(Gaede et al ., 2003).** Hyperparathyroidism and hypopituitarism may have an increased risk of stroke **(Parsons et al ., 2002).**

Metabolic problems are a rare cause of pediatric stroke may give rise to strokes in young adults. Homocystinuria and Fabry`s disease cause vascular occlusion; other metabolic disorders do not cause vascular insufficiency and are more properly termed strokelike episodes . Metabolic strokes can be caused by organic acidurias, mitochondrial abnormalities, lysosomal disorders, and urea cycle defects **(DeGraba et al ., 1995).**

The metabolic disturbance that occur with organ failure may be accompanied by pronounced neurological abnormalities as in cardio respiratory arrest and hepatic encephalopathy . A severe metabolic encephalopathy may also develop with systemic infection , sepsis, burn , and multiple organ failure causing transient focal neurological deficit mimicking a TIA , and even stroke **(Dejong et al ., 2005)** .

Metabolic disorders should be excluded in all patients with a diagnosis of suspected stroke, especially if the presentation is associated with a confusional state or focal seizures. The conventional symptoms and signs of the metabolic disorders may be minimal or absent. The relative rarity of these disorders among patients with suspected stroke is overshadowed by the importance of early recognition and treatment, in order to minimize morbidity and mortality **(Berkovic et al.,2002) .**