Inflammatory Response in Acute Ischemic Stroke
Clinical, Laboratory, and Radiological Correlation

THESIS

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By

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﴿قالوا سبحانك لا علم لنا إلا ما علمتنا

إنك أنت العليم الحكيم﴾

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TO MY PARENTS

&

TO THE SOUL OF

MY GRANDMOTHER

ABSTRACT

Several studies described an association between acute ischemic stroke and elevated inflammatory markers. This study aimed at evaluating the relationship between inflammatory markers and pathogenesis of acute ischemic stroke, and whether they are correlated to the size of the infarction and severity of the stroke. Twenty patients as well as fifteen control subjects were submitted to history taking, general and neurological examinations, routine battery of investigations, measurements of C-reactive protein, fibrinogen, and IL-6. The results were correlated to both size of the infarction and severity of the stroke after three months. The inflammatory markers were higher in the stroke patients compared to the control group with a positive correlation to both size of the infarct and clinical outcome.

Key Words:
Stroke, CRP, Inflammation, Prognosis

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LIST OF ABBREVIATIONS

ADC	:	Apparent diffusion coefficient
AHA	:	American Heart Association
BBB	:	Blood brain barrier
CAM	:	Cell adhesion molecule
CCA	:	Common carotid artery
CDC	:	Centers for disease control and prevention
CNS	:	Central nervous system
CRP	:	C-reactive protein
CT	:	Computed tomography
CV	:	Cerebrovascular and cardiovascular
ECASS	:	European Cooperative Acute Stroke Study Group
GFAP	:	Glial fibrillary acidic protein
ICA	:	Internal carotid artery
ICAM	:	Intercellular cell adhesion molecules
IL-1	:	Interleukin-1
IL-10	:	Interleukin-10
IL-6	:	Interleukin-6
iNOS	:	Inducible nitric oxide synthase
MCA	:	Middle cerebral artery
MCA	:	Middle cerebral artery
MCP-1	:	Monocyte chemo-attractant protein-1
MIP-1α	:	Macrophage inflammatory protein-1α
MMPs	:	Matrix metalloproteinases
NO	:	Nitric oxide
PCA	:	Posterior cerebral artery
PCoA	:	Posterior communicating artery
PECAM	:	Platelet endothelial cell adhesion molecule
PWI	:	Diffusion weighted image
PWI	:	Perfusion weighted image
ROI	:	Region of interest
ROS	:	Reactive oxygen species
TCD	:	Transcranial Doppler
TGF	:	Transforming growth factor-β
TIAs	:	Transient ischemic attacks
TNF-α	:	Tumor necrosis factor-α
VCAM	:	Vascular cell adhesion molecule

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INTRODUCTION

INTRODUCTION

Stroke is one of the most frequent causes of death and disability worldwide, and has a significant clinical and socioeconomic impact. Although different mechanisms are involved in the pathogenesis of stroke, there is an increasing evidence showing that inflammation accounts for its progression, at least acutely **(Chamorro and Hallenbeck, 2006)**.

Inflammatory mediators contribute to stroke risk via various interrelated mechanisms **(Lindsberg and Grau, 2003)**. They also play an important role in the pathogenesis of ischemic stroke at different levels. First, inflammatory parameters such as C-reactive protein (CRP), fibrinogen, or leukocyte counts measured before ischemia are independent predictors of first or recurrent ischemic stroke **(Di Napoli et al., 2001)**. Second, brain ischemia elicits an inflammatory response with a rapid accumulation of granulocytes and later of mononuclear leukocytes around the infarct zone **(Garcia et al., 1994)**.

Elevation of the inflammatory parameters in the acute phase of ischemic stroke is a well-known phenomenon and may result from infectious complications or from the inflammatory reaction of the damaged brain tissue. Necrotic tissue is eliminated by cellular, humoral, and metabolic mechanisms, which are all part of the inflammatory reaction. It is noteworthy that inflammatory markers persist at an increased level after stroke and that such parameters assessed early after ischemia were shown to predict stroke outcome (**Kogure et al., 1996)**. Inflammation is among the targets of therapeutic interventions after stroke, thus knowledge on its time course is of great value.

AIM OF THE WORK

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The present study aimed at evaluating the role of inflammatory markers (CRP, Fibrinogen and IL-6) in the pathogenesis of acute ischemic stroke, and whether these inflammatory markers correlate to both the infarct size and the stroke severity. Moreover, this study also will assess the prognostic value of these inflammatory markers and the possibility of using them as predictors of the clinical outcome.

REVIEW OF LITERATURE

Chapter I

ACUTE CEREBROVASCULAR STROKE

Definition:

Stroke is an abrupt or ictal onset of focal or global neurological symptom caused by ischemia or hemorrhage within or around the brain resulting from diseases of the cerebral blood vessels **(Sacco, 1995)**.

Stroke is the most common life threatening neurological disease. In the United States and industrialized world, it is the third leading cause of death after heart diseases and tumors, besides; it is the most common cause of adult disability (**Li et al., 2002)**.

Pathophysiology and Types of Acute Cerebral Infarction:

Acute vascular occlusion is the central event in acute ischemic stroke precipitating the primary injury by limiting the flow of oxygen and glucose to a region of the brain **(Lewandowski and Barsan 2001)**. When blood supply is interrupted for 30 seconds, brain metabolism is altered. After 1 minute, neuronal function may cease. After 5 minutes, anoxia initiates a chain of events that may result in cerebral infarction; however, if oxygenated blood flow is restored quickly enough, the damage may be reversible **(Sacco, 2000)**.

Cerebral perfusion pressure in any arterial vascular territory is equal to difference between the mean arterial pressure and the venous back pressure **(Powers, 1991)**.

When perfusion pressure is reduced, reflex changes of the cerebro-vasculature occur to maintain the normal delivery of oxygen to the brain and consequently normal neurological function **(Barnett, 1992)**.