RECENT METHODS IN INVESTIGATING PATIENTS WITH MIGRAINE

THESIS

SUBMITTED FOR PARTIAL FULFILLMENT OF

M.D. DEGREE IN NEUROLOGY

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1991

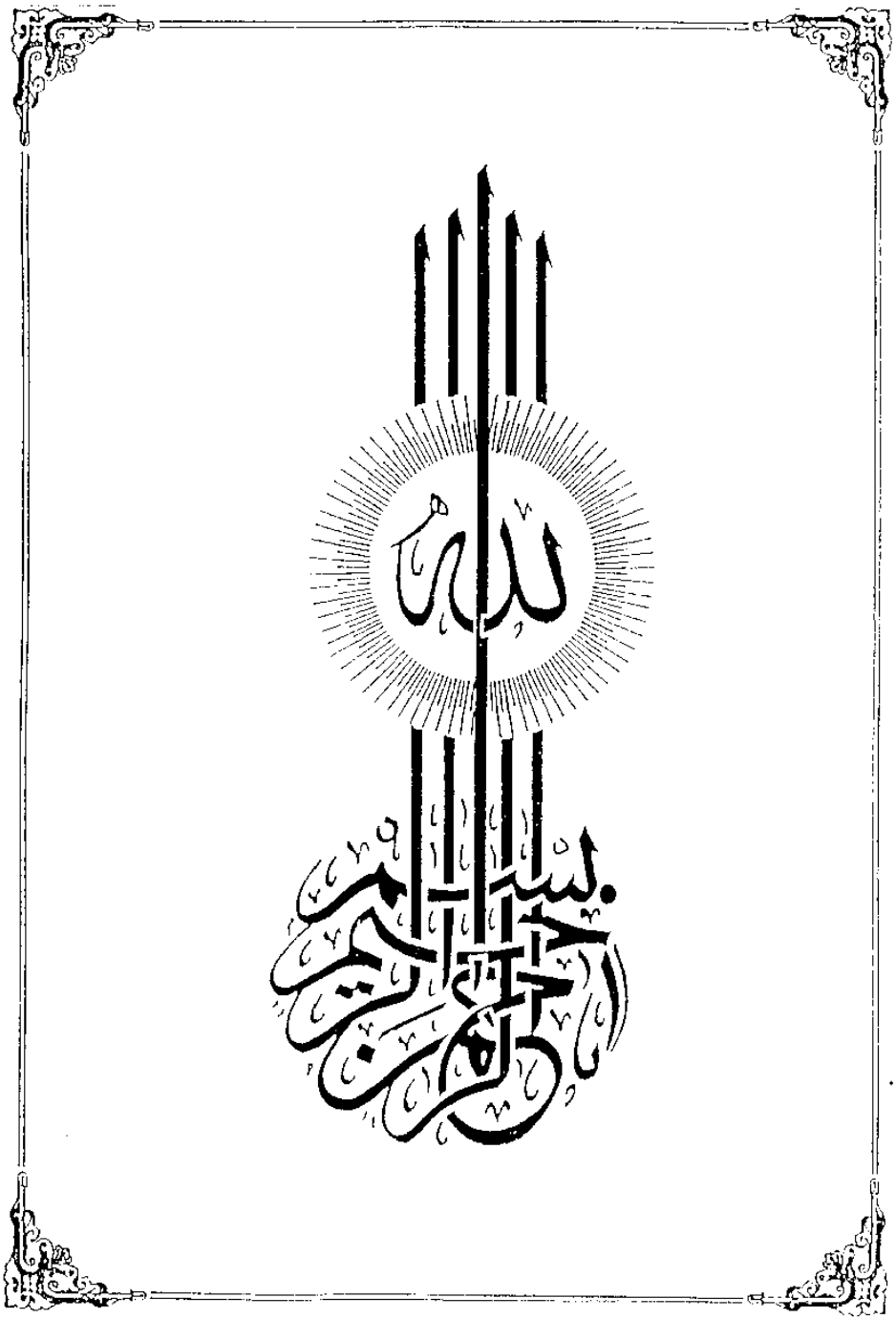
ACKNOWLEDGEMENT

I would like to express my deepest gratitude to **PROF. DR. M. MOUSTAFA** and **PROF. DR. E. FADLY** for giving me the honour of supervising this work which could not have been accomplished without their guidance and help.

I am also indebted to my supervisor **PROF. DR. T. HAMSA** his sincere help go beyond every evaluation.

Thanks are also due **PROF. DR. SAMIHA ABD ELMONIM** for her invaluable aids for **PROF. DR. AMIRA AHMED** for her support and guidance.

Last but not the least I would like to thank all my collegues in the neuropsychiatric department for their involuable co-operation.



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LIST OF ABBREVIATIONS

ADP	Adenosine diphosphate
ATIII	Antithrombin III
ATP	Adenosine triphosphate.
BAEP	Brain stem auditory evoked potentials.
BEAM	Brain electrical activity mapping.
C1	Complement component 1.
C4	Complement component 4.
cAPM	Cyclic adenosine monophosphate.
CBF	Cerebral blood flow.
CME	Computed mapping of electroencephalograpy.
CMI	Circulatig platelet microaggregate index.
CNS	Central nervous system.
C.N.V.	Contingent negative variation.
CSF	Cerbrospinal fluid.
CT scan	Computerized tomography brain scan.
DBH	Dopamine B-hydroxylase enzyme.
EC	External carotid.
EEG	Electroencephalography.
EIA	Enzyme immunoassay.
ENG	Electronystagmography.
FAA	Free fatty acid.
FVEP	Flash visual evoked potentials.
H1,H2	Histamine receptor type I,II.
5-HIAA	5-Hydroxy indole acetic acid.

5HT	Serotonin
IC.	Internal carotid artery
IgE	Immunoglobulin type E
IPL	Interpeak latencies
6-Keto PG F1α	Prostacyclin metabolite
L.C.	Locus ceruleus
L.K.	Leukotrines
Mag GAR	Magnetic Goat anti-Rabbit IgG
MAO	Monoamine oxidase enzyme
N120	Negative wave after 120 msec latency
NRM	Nucleus raphe magnus
OD	Optical density.
P100	Positive wave after 100 msec latency
PAG	Periaqueductal grey matter.
PET	Positron emission tomography
PG	Picogram.
PGI2	Prostacyclin
PGs	Prostaglandins
PNPP	Paranitrophenyl phosphate substrate.
PRVEP	Pattern Reversal visual evoked potentials
PST	Phenol sulphate transferase
$S_{1,2}$	Serotonin receptor I,II
S.D.	Spreading depression
SPM	Significant probability mapping
TXA2	Thromboxan A2.
VMA	Vanilyl mandilic acid.
^{133}Xe	Radioactive Xenon - 133

INTRODUCTION

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Migraine is a paroxysmal disorder characterized in its fully developed form by visual and/or other sensory phenomena in an aura associated with or followed by unilateral headache and vomiting. While this definition is satisfactory for classical migraine, there are many patients who never experience an aura and in whom the headache is always bilateral. The single most characteristic and constant feature is that migraine is a paroxysmal disorder, i.e. the throbbing headache occurs in attacks separated by intervals of freedom.

The most plausible hypothetical explanation of migraine is that it is due to arterial spasm followed by dilatation. Focal EEG changes have been observed in the opposite cerebral cortex consistent with cerebral ischaemia. CBF studies showed that, the decreased blood flow during the aura is bilateral and is usually most marked in that area of the brain clinically relevant to the aura. In addition CT scan showed evidence of focal brain oedema during migraine attack *[Cala and Mastalgia, 1976]*.

It is recognized that these vascular phenomena were themselves probably secondary to humoral and / or neurogenic factors [Edmeas, 1987].

In the last two decades, there is much interest in the possible role of vaso-active agents in the development of migraine symptoms. Studies have largely been focused on amines such as noradrenaline, adrenaline, serotonin, tyramine and histamine.

Prostaglandins are a group of long chain fatty acids that have caused so much confusion in the biochemical background of many medical problems and the area of headache research has not been spared. Their vasoactive and platelet effective properties have made them prime suspects for a principle role in the chain of events involved in the production of migraine *[Dexter, 1987]*.

The injection of prostaglandin E (PGE) has been reported by *Carlson et al. (1968)* to produce migrainous attacks. Proslaglandin inhibiting drugs such as aspirin and indomethacin can block the synthesis of thromboxan from arachidonic acid thus blocking a major pathway for inducing platelet aggregation and release reaction. These drugs are also useful in aborting migraine attack . While the exact role played by prostaglandins in migraine headache has not been fully elucidated, it appears quite possible that prostaglandin matabolism may be involved in the migraine process and in the production of stroke as a sequela of severe migraine headache.

Plasma coagulability and platlet aggregation increased during migraine paroxysms. Patients with complicated migraine showed increased thrombus generation, decreased antithrombin III, increased fibrinogen degradation products and platelet hyperaggregability *[Kalendovsky and Austin, 1975]*.

Lance, (1987) proposed a recent hypothesis to explaine the pathogenesis of migraine. According to this hypothesis the brain is the site of pathology in migraine and the vascular and humoral phenomena are secondary events.

All the above considerations guide us to study the subject of migraine from 3 points :

(i) The difference between the types of migraine and whether the available classification is satisfactory as regards treatment.

(ii) The humoral factors and their role in management.

(iii) The long suspected relationship between migraine and cerbrovascular accident.

AIM OF THE WORK

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i) To study the level of biochemical agents and platelet aggregation in migrainous patients and its correlation to the clinical presentation (Type of migraine, frequency, duration of the attack, age of the patients), in order to build up the drug prophylactic therapy on the basis of these biochemical changes.

ii) Correlation of these biochemical changes to electrophysiological changes in order to differentiate the different clinical pictures electrophysiologically if possible.

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE OF MIGRAINE

Migraine was the first headache syndrome to be differentiated probably because of its sometimes dramatic features of blinding headaches and vomiting. Migraine has been mentioned in the ancient Egyption medicine. The main source of information about ancient Egyptian medicine is the Ebers Papyrus said to have been found between the legs of a mummy in the necropolis of Thebes. It has been estimated that the Ebers Papyrus which mentions migraine, neuralgia and shooting head pains, was written or transcribed from earlier medical documents in approximately 1550 B.C. The papyrus is obviously based on earlier writings since one prescription was written for King Usphias who reigned in 3700 B.c. In these days, an advice was given to the headache sufferer, a clay crocodile was firmly bound to the head of the patient with herbs being placed in the mouth of the crocodile *[Major, 1930]*. Aretaeus has given clear description of the disorder. He reported as heterocrania, a paroxysmal headache disorder that occured on one side of the head, recurred at regular intervals, was associated with vomiting and photophobia and was ameliorated by dark surroundings *[Pearce, 1975]*. About 50 years later, Galen (141-201 A.D.) focusing upon unilateral localization introduced the term hemicrania which was later translated into migraine *[Pearce, 1975]*.

Galen conjecture that migraine was caused by dispatch of noxious vapours and fluid from extracerebral organs, especially the gall bladder, was widely accepted and inhibited medical thinking about migraine for some 1400 years *[Lance, 1982]*.

During the 17th century scientific thoughts began once more with a debate as to whether migraine was primarily vascular or neurogenic *[Schiller, 1975]*.

Modern approaches to migraine probably began with the publication of Liveing on migraine in 1873). Liveing believed that the analogy of migraine to epilepsy was obvious and the clinically apparent circulatory phenomena were secondary to the CNS discharge or nerve storm. These views were shared by John Huling Jackson and William Richard Gower *[Raskin, 1988]*.

Attention was focused upon the vascular feature in 1952 when Rothlin recommended parenrtal ergotamine for the treatment of migraine *[Rothlin, 1955]*. At first, it was believed to be effective because of its sympathetic blocking action. *Graham and Wolf (1938)* showed that administration of this drug reduced the amplitude of the pulsation of the temporal artery in patients with headache and that this effect was associated with a decrease in head pain. However,