



Migraine Co morbidity in Patients with Multiple Sclerosis

Thesis

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LIST OF ABBREVIATIONS

BBB	Blood brain barrier
CAMERA	Cerebral Abnormalities in Migraine Epidemiological Risk Analysis study
CCL5	C-C motif ligand 5
CGRP	Calcitonin – gene related peptide
CIS	Clinically isolated syndrome
CNS	Central nervous system
CSD	Cortical spreading depression
DHE	Dihydroergotamine
ED	Emergency department
EDSS	Expanded Disability status Scale
HA	Headache
5-HT	5 Hydroxytryptamine
ICHD	International Classification Of Headache Disorders
IFN α	Interferone alpha
IFNβ	Interferone beta
IL-4	Interleukin-4
ICAM1	Intercellular adhesion molecule-1
MMP	Matrix metalloproteinases
MIDAS	Migraine Disability Assessment Scale
MOH	Medication over use headache
MRI	Magnetic Resonance Imaging
MS	Multiple Sclerosis
MSSS	Multiple Sclerosis Severity Scale

NCF	Nucleus Cuniforms
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B-cells
NO	Nitric oxide
NTZ	Natalizumab
PAG	Periaquidactal grey matter
PCP	Primary care providers
PET	Positron emission tomography
RRMS	Relapsing Remmiting Multiple Sclerosis
r CBF	Regional cerebral blood flow
RCT	Randomized controlled Trials
REMPT	Research Evaluating Migraine Prophylaxis Therapy
SPMS	Secondary Progressive Multiple Sclerosis
SNAE	Sustained freedom from pain with no adverse events
tDCS	Transcranial direct current stimulation
TMS	Transcranial magnetic stimulation
TN	Trigiminal neuralgia
TNC	Trigiminal Nucleus Caudalis
TNF	Tumor necrosis factor
TIA	Transient ischemic attack
TTH	Tension type headache
TGFβ	Tumor growth factor beta
WM	White matter
MWA	Multiple white matter abnormalities

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INTRODUCTION

Migraine is a chronic neurological disorder characterized by recurrent moderate to severe headache often in association with a number of autonomic nervous system symptoms. Typically the headache is unilateral, pulsating in nature, lasting from 4 to 72 hours, associated symptoms may include nausea, vomiting, photophobia, photophobia and the pain is generally aggravated by physical activity. Up to one-third of people with migraine headaches perceive an aura , a transient visual, sensory, language, or motor disturbance which signals that the headache will soon occur. Occasionally an aura can occur with little or no headache following it (***International classification of Headache disorders. 2013***).

Multiple Sclerosis (MS) symptoms at presentation vary individually and are unpredictable, although headache is not generally regarded as a symptom of MS, Migraine headache commonly affects patients with MS. Up to two-thirds of MS patients complain of headache , and the majority of MS patients with headache have migraine (***Gelfand and Goadsby., 2012***).

Several reports have documented that migraine headaches may occur during exacerbation of symptoms and may even herald

the onset of relapse in MS. Recently, it has been encountered that patients with MS, as diagnosed according to the 2010 revisions of the McDonald criteria, their initial presentation was worsening migraine headache, and after steroid therapy, the patients returned to the remission stage without obvious neurological sequel, and the headache improved significantly (**Tabby et al., 2013**).

There has been different hypothesis trying to explain the relation between migraine and MS.

It has been hypothesized that migraine may lead to multiple sclerosis via cortical spreading depression during migraine aura, increasing the permeability of the blood–brain barrier, thereby allowing circulating T cells to become sensitized to myelin . This is a testable hypothesis, though there are no strong data to support it. It has also been hypothesized that changes in cytokine expression during migraine attacks may predispose to autoimmune disease in the central nervous system (CNS) (**Kister and Apel., 2010**).

As migraine has been linked to changes in serotonin (5-HT) functions, the emergence of migraine headaches coincident with the onset of relapse implicates dysregulation of the 5-HT system in the pathophysiology of MS. This hypothesis is plausible

considering the evidence that MS patients are serotonergically depleted and that 5-HT is involved in maintaining the integrity of the blood brain barrier, disruption of which is believed to occur in the initial stages of exacerbation of MS symptoms. Furthermore, this hypothesis may have potential therapeutic implications in the treatment of exacerbations of MS and possibly in the prevention of relapse in the disease (**Sandyk and Awerbuch ., 1994**).

It also has been demonstrated the importance of Periaqueductal gray matter (PAGm) involvement in a patient presenting with acute worsening migraine headache as an initial manifestation of MS (**Joey et al ., 2005**).

As the PAG modulates pain via the descending system and exerts an antinociceptive effect to the peripheral afferent system. Several studies showed that patients having MS with a plaque located within the PAG region displayed a four-fold increase in migraine-like headaches (**Gee et al., 2005**).

The involvement of the PAG region may explain why some cases presented initially with worsening migraine headache without clinical response to conventional anti migraine medications (**Gee et al., 2005**).

The presence or worsening migraine as a symptom of MS could lead to diagnostic difficulties. Moreover, this symptom may be easily ignored in patients with a migraine history.

MS should be one of the differential diagnoses in young women showing a change in headache pattern or poor clinical drug response to headache treatment accompanied by episodes of focal neurological deficit. Failure to recognize MS may lead to inappropriate treatment and worse prognosis; therefore, early diagnosis in patients with MS is essential to improve their clinical outcomes and quality of life (*Guan – Yu et al., 2013*).

AIM OF THE WORK

- (1) Assessment of prevalence and severity of migraine in MS patients.
- (2) Assessment of the clinical and radiographic characteristics in MS patients with migraine.

CHAPTER 1

Migraine Headache

Introduction

Migraine is a very common chronic neurological disorder characterized by recurrent moderate to severe usually unilateral pulsating headache. (*The International Classification of Headache Disorders; 2013*).

It is twice more common in females than in males (*Le et al., 2011*), with female-to-male ratio from 2:1 at the age of 20 years to 3.3:1 at the age of 40 (*Lipton et al., 2001*).

Surprisingly migraine is more prevalent than Alzheimer's disease (patients aged ≥ 65 years), Parkinson's disease (patients aged ≥ 65 years), stroke, and multiple sclerosis combined (*Hirtz et al., 2007*). According to the global estimates migraine headache affects about 14.5% of the general population worldwide, with around 56 million people in Africa in a prevalence of 5.61 % (*Yohannes et al., 2014*), and was ranked as the third most prevalent disorder and seventh-highest specific cause of disability worldwide in the Global Burden of Disease Survey 2010 (*The International Classification of Headache Disorders., 2013*).