بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

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MONA MAGHRABY

Predication of Response to Disease Modifying Therapy in Multiple Sclerosis.

Thesis

Submitted for Partial Fulfillment of Master Degree in Neuropsychiatry

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List of Abbreviation

Abbr.	Full term
APC	Antigen presenting cell
BAFF	B-cell activating factor
BBB	Blood brain barrier
CIS	Clinically isolated syndrome
CNS	Central Nervous System
CO	Carbon monoxide
CSF	Cerebrospinal fluid
CYC	Cyclophosphamide
DMF	Dimethyl fumarate
DMT	Disease-modifying therapies
EBV	Epstein Barr virus
EDSS	Expanded Disability Status Scale
FasL	Fas-ligand
GA	Glatiramer acetate
HLA	Human leukocyte antigen
IFN	Interferon
IFNγ	Interferon gamma
IL	Interleukin
IMSGC	International MS Genetics Consortium
JCV	John Cunningham virus
MBP	Myelin basic protein
MHC	Major histocompatibility complex
MRI	Magnetic resonance imaging
MS	Multiple Sclerosis
MSCs	Mesenchymal stem cells
NO	Nitric oxide

OCB	Oligoclonal band
PML	Progressive multifocal leucoencephalopathy
PPMS	Primary progressive multiple sclerosis
PRMS	Progressive relapsing multiple sclerosis
RRMS	Relapsing remitting multiple sclerosis
S1P	Sphingosine 1-phosphate
SC	Sub cutaneous
SPMS	Secondary progressive multiple sclerosis
TGF-β	Transforming growth factor beta
Th	T helper
TNF-α	Tumor Necrosis factor alpha
Treg	T regulatory
VD	Vitamin D

ABSTRACT

Background: Multiple sclerosis is an idiopathic inflammatory disease of the central nervous system and the second most common cause of disability in young adults. Choosing an effective treatment is crucial to preventing disability.

Aim of the Work: to identify predictors of DMT after one year of treatment.

Patients and Methods: In this retrospective study 150 patients with confirmed diagnosis of relapsing remittent MS was recruited from the MS unit at the Neurology departments from both Ain Shams University and Cairo University Students hospital. All of the study population were receiving either interferons or fingolimod. Modified Rio score was used to classify patient to responders and non responders.

Results: In this study 128 patients were found responders and 22 were found non responders. There was a significant difference between responders and non-responders regarding age of the participants. The age was significantly older in responders compared to non-responders (mean of 32.37±7.248 versus 28.55±5.361 years respectively; P = 0.019). Gender was not a significant predictor of response to therapy. As regard the EDSS at the time of enrollment, it was significantly higher in non-responders [median (IQR) of 2 (1-3)] compared to responders [median (IQR) of 1 (0 – 2.5)] (P = 0.029). Both total number of relapses throughout the course of disease and number of relapses in the last year were significantly higher in non-responders compared to responders (P < 0.001). All of the studies MRI parameters including number of T2 lesions, black holes, current enhancing lesions, along with spinal lesions had no significant correlation with response to therapy. After performing regression analysis, modified Rio score was a significant predictor for response to DMT (P=0.001). The longer the duration of therapy with DMT was predictive for response to DMT (P=0.032). Also the compliance to medications (P=0.005), and the lower total number of relapses throughout the course of disease (P=0.004) were significant predictors for response to DMT among the study population.

Conclusion: In this study modified Rio score, the longer the duration of therapy with DMT, the compliance to medications, and the lower total number of relapses throughout the course of disease were found to be a significant predictors for response to DMT among the study population.

INTRODUCTION

Multiple Sclerosis (MS) is a chronic inflammatory disease of the Central Nervous System (CNS) leading to demyelination and diffuse neurodegeneration in both brain and spinal cord ***(Correale et al., 2019)***

MS is the most common progressive neurologic disease of young adults worldwide ***(Wallin et al., 2019)***

MS diagnosis based on McDonald's diagnostic criteria, which link clinical manifestation with characteristic lesions demonstrated by magnetic resonance imaging (MRI),cerebrospinal fluid (CSF) analysis, and visual evoked potentials ***(Kamińska et al., 2017).***

Subtypes of MS are considered important not only for prognosis but also for treatment decisions and include: relapsing remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), and progressive relapsing MS (PRMS). ***(Ghasemi et al., 2017)***

Approximately 87% of patients present with RRMS, Which characterized by acute attacks (relapses) followed by partial or full recovery (remission) ***(Loma & Heyman ,2011)***

MS patients will require treatment with disease-modifying therapies (DMT) for rest of their lives after diagnosis (***Compston et al., 2008).***

The primary aim of treatment is to reduce disease activity to optimize neurologic reserve, cognition, and physical function ***(Giovannoni et al., 2016)***

Numerous disease-modifying therapies exist that reduce relapses, reduce MRI activity, and delay disability, especially when initiated early in the disease when the inflammatory component of the disease is strongest ***(Jones, 2016).***

The interferon (IFN) have been shown to reduce relapse rates and new MRI activity; they also delay disability progression as measured by the Expanded Disability Status Scale (EDSS) ***(Calabresi et al., 2014).***

Oral fingolimod a sphingosine 1-phosphate (S1P) receptor agonist, is the first oral agent and the first in a novel class of DMTs to be approved for use in the US for the treatment of relapsing forms of MS a valuable emerging option for the treatment of adult patients with relapsing forms of MS ***(Scott, 2011).***

It is important to monitor treatment efficacy, as breakthrough disease can lead to irreversible neurologic disability, and transitioning into a progressive form of MS may close the therapeutic window of opportunity for the disease modifying therapies (***Rae-Grant et al., 2015) .***

A baseline brain MRI should be performed with the initiation of a new disease-modifying therapy and a follow-up brain MRI to assess treatment response should be performed 6 months after starting a new disease-modifying therapy (and then every 6 months to 2 years) (***Trabouslee et al., 2015) .***

Both clinical and MRI measures have proven useful in detecting disease activity and progression in patients with RRMS who are treated with DMT, and these two measures have been used in combination, to assess treatment response ***(Sormani et al., 2013)***

AIM OF THE WORK

The aim of this study is to identify clinical and radiological predictors of response to disease modifying therapies in patients with relapsing remittent multiple sclerosis after one year of therapy.