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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/18857
DOI URL: http://dx.doi.org/10.21474/IJAR01/18857

RESEARCH ARTICLE

UNLOCKING HOPE: OVERCOMING THERAPEUTIC CHALLENGES IN PROGRESSIVE MULTIPLE SCLEROSIS

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Manuscript Info

Manuscript History
Received: 10 April 2024
Final Accepted: 14 May 2024
Published: June 2024

Abstract

Progressive forms of multiple sclerosis (MS) present significant therapeutic challenges, underscoring the pressing need for effective treatments in this domain. While relapsing-remitting MS (RRMS) transitions to secondary progressive MS (SPMS) for many patients, others experience primary progressive MS (PPMS) from the disease's onset. Despite similarities in pathophysiology and clinical progression between SPMS and PPMS, treatment options remain limited. The recent approval of ocrelizumab for PPMS marks a notable advancement, though its efficacy is modest. This retrospective study, conducted at the Neurology Department of Mohammed VI University Hospital, evaluates the tolerance and therapeutic efficacy of various treatments in progressive MS. Nineteen patient records spanning six years were analyzed, with therapeutic interventions including Fingolimod, Rituximab, cyclophosphamide-solumedrol, and ocrelizumab. Assessments utilizing the Expanded Disability Status Scale (EDSS) revealed stabilization or improvement in 15.7% of secondary progressive MS and 21% of primary progressive MS patients after 12 months of treatment. The duration of the progressive phase emerged as a key predictor of therapeutic response. Despite the approval of ocrelizumab in Morocco for PPMS, its utilization remains limited, suggesting the need for targeted studies focusing on early-stage clinical progression. Overall, this study underscores the unmet need for effective treatments in progressive MS and highlights ongoing research efforts aimed at addressing this challenge.

Introduction:-

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system. The majority of MS patients have relapsing-remitting multiple sclerosis (RRMS), and over time, many transition to secondary progressive MS

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(SPMS). Some patients develop progressive neurological impairment from the onset and are classified as having primary progressive MS (PPMS) [1]. The pathophysiology, mechanisms, and clinical progression of SPMS and PPMS are very similar. However, treatments for progressive MS, encompassing both PPMS and SPMS, have been limited, highlighting an unmet need in the field [2]. The recent regulatory approval of ocrelizumab for the treatment of PPMS represents a significant advancement in this regard, though its impact is modest [3]. This study will focus on the tolerance and therapeutic efficacy in progressive MS at the Neurology Department of the Mohammed Vl University Hospital.

Materiels and Methods:-

This study involves a retrospective analysis of 19 patient records diagnosed with progressive MS over a six-year period (from January 2014 to December 2019). Nine patients had primary progressive MS, and nine had secondary progressive MS. Of these patients, nine were treated with Fingolimod, seven with Rituximab, two with monthly double boluses of cyclophosphamide-solumedrol, and one with ocrelizumab. The therapeutic indications were based on the type of disease, previous disease-modifying treatments received, and the benefit-risk assessment.

We used the Expanded Disability Status Scale (EDSS) as the efficacy evaluation criterion at the start of treatment, at 6 months, and at one year of treatment. Additionally, we assessed both clinical and biological tolerance.

Results:-

One of the nine patients treated with Fingolimod experienced significant adverse effects (bradycardia, severe leukopenia), which did not necessitate discontinuation of treatment. After 12 months of treatment, 15.7% of patients with secondary progressive MS and 21% of patients with primary progressive MS were stabilized or improved. The response rate and the extent of the response did not differ between the two groups (primary and secondary).

The only predictive factor for a favorable therapeutic response was the duration of the progressive phase. This duration was 3 years for patients who showed improvement, compared to 4.7 years for other patients. We also observed that patients who had a poor response after 6 months of treatment were also poor responders after 12 months.

Discussion:-

Our results warrant confirmation through a randomized, double-blind, placebo-controlled study. However, we emphasize the good tolerance of the different therapeutic options for progressive forms of MS. Additionally, it appears that a favorable treatment response is not dependent on the type of disease progression but is correlated with the duration of the progressive phase [3]. Despite the availability of ocrelizumab in Morocco as an approved treatment for primary progressive forms, few patients benefit from it [4]. We suggest conducting a targeted study on this form, focusing on patients with clinical progression at the earliest possible stage of the disease.

Conclusion:-

The treatment of progressive MS represents an unmet need in the management of the disease. Ongoing research is focused on therapeutics with neuroreparative, remyelinating, neuroprotective, and anti-inflammatory potential in this context.

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