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RESEARCH ARTICLE

Evaluation of Response to Relapse Treatment in Multiple Sclerosis According to Relapse Characteristics

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Abstract

Objective: Relapses in patients with multiple sclerosis (MS) were evaluated based on symptom characteristics, treatment response, and recovery rates. These factors were evaluated before and after relapse treatment, as well as at the first- and sixth-months following treatment.

Materials and Methods: Patient's physical status was evaluated using the Expanded Disability Status scale (EDSS). Based on the characteristics of their relapses, patients were categorized as either monosymptomatic or polysymptomatic. Treatment response was then analyzed according to these groupings.

Results: The study included 59 MS patients, with a mean age of 33.69±8.28 years (46 females, 13 males). Based on relapse symptom characteristics, 27.1% of patients had polysymptomatic relapses, while 72.9% were monosymptomatic. A total of 23 patients experienced monosymptomatic relapses. Regarding specific relapse symptoms, 66.1% presented with sensory symptoms, 47.5% with motor symptoms, 32.2% with optic neuritis (ON), 6.8% with cerebellar signs, 35.6% with brainstem involvement, and 13.6% with sphincter symptoms. Significant improvement following treatment was observed in patients with brainstem involvement and in the ON group (p=0.04 and p=0.039, respectively). However, no significant difference in EDSS scores was noted at 1 and 6 months posttreatment (p=0.068 and p=0.194, respectively). In the sensory involvement group, the mean EDSS score was 2.65±1.24 before treatment, 2.05±0.76 after treatment, 1.85±0.81 at 1 month, and 1.55±0.98 at 6 months, indicating significant improvement (p=0.04 and p=0.041, respectively).

Conclusion: Both ON and sensory involvement were associated with favorable prognosis. While significant improvement n EDSS was noted in the ON group before and after treatment, this improvement was not sustained at the first and sixth months. In contrast, patients with sensory involvement demonstrated continuous and significant improvement across all time points-before treatment, after treatment, and at 1 and 6 months. These findings highlight the importance of addressing sensory relapses and their potential for sustained recovery.

Keywords: Expanded disability status scale (EDSS), multiple sclerosis, relapses

Introduction

Multiple sclerosis (MS) is a demyelinating and neurodegenerative disorder that impacts various functional systems within the central nervous system. Common symptoms include blurred vision, double vision, limb weakness, sensory loss, imbalance, and disturbances in bowel and bladder function (1,2). A neurological symptom lasting more than 24 hours in the absence of fever, infection, or stress is defined as a relapse, with at least 30 days required between separate relapse episodes. Relapses are linked to functional decline and reduced quality of life. If symptoms persist following a relapse, this may contribute to cumulative disability, referred to as relapse-associated worsening (RAW) (3,4). Proper management of relapses is important to prevent long-term disability (1,2). In cases of moderate to severe relapse, intravenous methylprednisolone at 1 g/day is typically administered for 5-10 days. If the response to corticosteroids is inadequate, plasmapheresis may be considered. Early detection of even mild neurological deterioration is critical for prompt and effective treatment (5).

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Poor prognostic indicators in MS include male sex, smoking, obesity, low vitamin D levels, African descent, early age at disease onset, and rapid disease progression. Moreover, factors such as brain volume loss, relapse frequency, presence of new T2 lesions, and contrast-enhancing lesions are important predictors of disability within 5 years. Clinically, sphincter dysfunction, pyramidal and cerebellar involvement, early cognitive impairment, brainstem symptoms, and a high Expanded Disability Status scale (EDSS) score at the first relapse are associated with worse outcomes (5).

Studies have shown that relapse recovery tends to be more favorable in younger patients, those receiving disease-modifying therapies, individuals with longer disease duration, and those without bowel or bladder involvement. The EDSS is a commonly used tool to assess disease progression in MS by evaluating central nervous system functions, including pyramidal, cerebellar, brainstem, sensory, sphincter, visual, and cerebral domains. The EDSS uses a scale from 0 to 10: scores from 0 to 4 reflect neurological deficits, scores from 4 to 6 primarily assess walking ability, and scores from 6 to 10 focus on ambulatory function. During relapses, EDSS scores typically increase depending on the symptoms and areas affected in the central nervous system. Following appropriate treatment, partial, complete, or near-complete improvements in EDSS scores may occur in treatment-responsive relapses. The initial and predominant pathophysiological mechanism in MS involves disruption of the blood-brain barrier, leading to immune-mediated damage to myelin and axons in both white and gray matter. In addition, intrathecal immune activation involving various glial and immune cells has recently been recognized as a complex and significant contributor to disease progression. Therefore, initiating effective treatment at the earliest possible stage is considered important for long-term outcomes (1).

This study aimed to evaluate the response to relapse treatment based on symptom characteristics and to compare EDSS changes before and after treatment, as well as at the first and sixth months following treatment.

Materials and Methods

Study Population

This study included patients diagnosed with MS who were followed at the Neurology Clinic of Samsun University and received treatment for MS relapses between January 2023 and June 2024. Demographic data of the patients were recorded. Relapse characteristics and severity were evaluated using the EDSS. Based on relapse presentation, patients were categorized as either monosymptomatic or polysymptomatic.

Data Collection

EDSS scores prior to treatment, immediately after treatment, and at the first- and sixth-months posttreatment were retrieved from patient records and the hospital database. Relapses were classified into sensory, motor, brainstem involvement, and optic neuritis (ON) groups based on presenting symptoms. EDSS scores for each group were compared across the pretreatment, posttreatment, first month, and sixth month time points.

Ethics Approval

The study received approval from the Samsun University Non-interventional Clinical Research Ethics Committee (decision no.: 2025/6/20, date: 19.03.2025). Written informed consent was obtained from all patients who agreed to participate.

Statistical Analysis

The collected data were coded and analyzed using the SPSS software package (Version 22.0, SPSS Inc., Chicago, IL, USA). Continuous variables with a normal distribution were presented as mean ± standard deviation, while non-normally distributed continuous variables were expressed as median (minimum-maximum). Categorical variables were reported as number and percentage. The Kolmogorov–Smirnov test was used to assess the normality of continuous variables. A p-value of <0.05 was considered significant in all analyses.

Results

A total of 59 patients diagnosed with MS were included in the study, with a mean age of 33.69±8.28 years and an average disease duration of 3.16±4.48. The study population consisted of 46 females and 13 males. Based on relapse symptom characteristics, 27.1% of the patients were classified as polysymptomatic and 72.9% as monosymptomatic. The distribution of relapse symptoms was as follows: sensory symptoms in 66.1%, motor involvement in 47.5%, ON in 32.2%, cerebellar signs in 6.8%, brainstem involvement in 35.6%, and sphincter dysfunction in 13.6% (Figure 1). In addition, 66.1% of patients demonstrated poor prognostic indicators, including sphincter involvement, motor symptoms at onset, and brainstem or cerebellar findings. In patients with sensory involvement, the mean EDSS score was 2.65±1.24 before

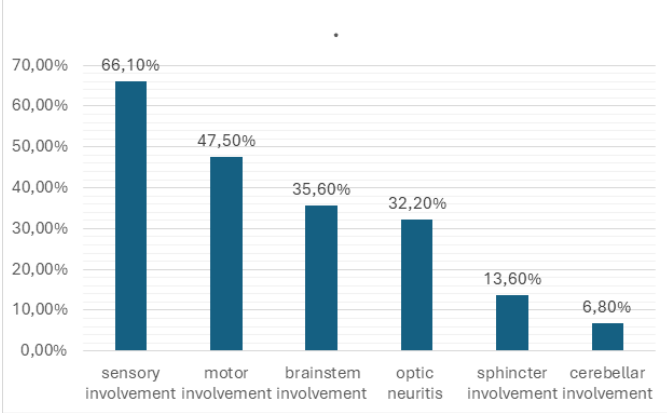

Figure 1. Distribution of relapse symptoms in the study group

treatment, 2.05±0.76 after treatment, 1.85±0.81 at the first month, and 1.55±0.98 at the sixth month, showing significant improvement over time (p=0.04 and p=0.041, respectively). This improvement persisted across both follow-up periods. In contrast, among patients without sensory involvement, the mean EDSS was 1.34±0.58 after treatment, 1.42±0.53 at 1 month, and 1.76±0.43 at 6 months, with a continued increase in EDSS at the sixth month, indicating ongoing deterioration (p=0.04 and p=0.045, respectively) (Table 1). In the ON group, the mean EDSS was 2.21±0.56 before treatment, 1.28±0.75 after treatment, 1.42±0.34 at the first month, and 1.92±0.44 in the sixth month (p=0.589 and p=0.068, respectively). These results indicate that although some improvement was noted immediately after treatment, no statistically significant change was observed at the first- or sixth-month. In patients without ON, the mean EDSS was 2.46±1.10 before treatment, 1.81±0.70 after treatment, 1.68±0.79 at the first month, and 1.56±0.79 at the sixth month, showing continued improvement over time (p=0.398 and p=0.49, respectively) (Table 2). Among patients with brainstem involvement, the mean EDSS was 2.35±0.89 before treatment, 1.50±0.40 after treatment, and 1.42±0.67 at the first month. Although there was a reduction in EDSS from posttreatment to the first month, the change was not statistically significant. By the sixth month, the mean EDSS had increased to 1.71±0.48, indicating no sustained improvement (p=0.854 and p=0.194, respectively). In the group without brainstem findings, the mean EDSS was 2.40±1.02 before treatment, 1.71±0.85,1 after treatment, 1.68±0.70 at the first month, and 1.65±0.81 at the sixth month. Although the EDSS score showed a slight decrease over time, no statistically significant improvement was observed (p=0.776 and p=0.80, respectively) (Table 3).

Discussion

Corticosteroids are commonly used to manage MS relapses. Evaluating relapse severity using EDSS is critical, and if the EDSS score increases by 1 point or more, treatment is strongly advised. However, mild relapses-particularly sensory relapses-with less than 1 point increase in EDSS may not require immediate treatment; these patients should be re-evaluated within 2 weeks. If an increase in EDSS is observed during this period, treatment should then be initiated (6). According to a study on managing severe relapses in MS, not all relapses necessitate treatment. Instead, therapy should be prioritized for relapses that result in functional impairment or disability, in order to

Table 1. EDSS scores of patients with and without sensory involvement (excluding poor prognostic factors)

	Sensory relapses		Relapses without sensory involvement	
EDSS before treatment	2.65±1.24	p=0.041	2.19±0.66	p=0.005
EDSS after treatment	2.05±0.76		1.34±0.59	
EDSS in 1st month of treatment	1.85±0.81	p=0.04	1.42±0.53	p=0.04
EDSS in 6th months of treatment	1.55±0.98	p=0.23	1.76±0.43	p=0.045

EDSS: Expanded Disability Status scale

Table 2. EDSS scores of patients with and without optic neuritis (excluding poor prognostic factors)

	Optic neuritis relapses		Relapses without optic neuritis	
EDSS before treatment	2.21±0.56	p=0.039	2.46±1.10	p=0.006
EDSS after treatment	1.28±0.75		1.81±0.70	
EDSS in 1st month of treatment	1.42±0.34	p=0.589	1.68±0.79	p=0.398
EDSS in 6th months of treatment	1.92±0.44	p=0.068	1.56±0.79	p=0.49

EDSS: Expanded Disability Status scale

Table 3. EDSS scores of patients with and without brainstem involvement (excluding poor prognostic factors)

	Relapses without brainstem involvement		Relapses without brainstem involvement	
EDSS before treatment	2.35±0.89	p=0.04	2.46±1.10	p=0.005
EDSS after treatment	1.50±0.40		1.81±0.70	
EDSS in 1st month of treatment	1.42±0.67	p=0.854	1.68±0.79	p=0.776
EDSS in 6th months of treatment	1.71±0.48	p=0.194	1.56±0.79	p=0.09

EDSS: Expanded Disability Status scale

restore function and limit lasting disability (7). In contrast to this approach, there is an argument that every relapse should be treated promptly, emphasizing the importance of early and effective inflammation control. RAW has been shown to occur from the early stages of the disease and contributes to permanent disability and transition to the progressive phase (3,8). Additionally, RAW has been linked to the number of relapses experienced early in the course of relapsing-remitting MS (3,4). Failure to effectively manage a relapse is directly associated with RAW and is is a primary factor in the accumulation of disability. In our study, patients with sensory symptoms showed continued improvement after treatment, as well as at the first and sixth months. This highlights the importance of treating sensory relapses and supporting sustained recovery. However, one limitation of our study is the lack of untreated patients for comparison. Nonetheless, it is noteworthy that these patients showed benefits from relapse treatment. While RAW is a key contributor to disability in pediatric MS, progressive, irreversible disability (PIRA) is a major factor in adult-onset MS, a finding supported by several studies (9-13). In addition, while a significant improvement in EDSS was observed in the ON group before and after treatment, no significant difference was found at the first and sixth months.

A study found that patients who experienced RAW and PIRA reached a significant disability milestone simultaneously. However, the progression was faster in the PIRA group. The more rapid disability development in the PIRA group suggests that these patients require more urgent treatment interventions. Additionally, there is evidence that relapses contribute to long-term disability in the early stages of MS (14). It has been confirmed that relapses contribute to long-term disability early in the disease, although PIRA remains the primary factor in cumulative disability (2). While PIRA is recognized as the leading cause of cumulative disability, it is crucial to emphasize the importance of treating relapses. Timely management of relapses is essential to prevent long-term disability and enhance quality of life. Untreated relapses can lead to permanent nervous systems damage, resulting in irreversible disability beyond temporary flare-ups (15). Effective relapse treatment helps reduce disability and slows disease progression (16). Consequently, early diagnosis and treatment strategies are vital for improving the quality of life in MS patients.

Study Limitations

The limitations of this study its retrospective design, single-center setting, and small sample size. A multicenter prospective study with a larger patient population could provide more robust insights.

Conclusion

In conclusion, this study emphasizes the importance of actively treating all MS relapses, regardless of their initial symptoms. Our results show that patients with sensory relapses, in particular, benefit from timely and appropriate treatment, with lasting improvements in EDSS scores observed up to 6 months after the relapse. Despite being limited by its retrospective and single-center nature, this study adds to the growing body of evidence suggesting that early intervention during relapses can positively impact long-term neurological outcomes and help reduce RAW.

Ethics

Ethics Committee Approval: The study received approval from the Samsun University Non-interventional Clinical Research Ethics Committee (decision no.: 2025/6/20, date: 19.03.2025).

Informed Consent: Written informed consent was obtained from all patients who agreed to participate.

Footnotes

Authorship Contributions

Design: H.D., S.C., Data Collection or Processing: H.D., S.C., Analysis or Interpretation: H.D., S.C., Literature Search: H.D., S.C., Writing: H.D., S.C.

Conflict of Interest: No conflict of interest was declared by the authors.

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