



ANTI-INFLAMMATORY NEUROPHARMACOLOGY IN MULTIPLE SCLEROSIS: CURRENT DRUGS AND FUTURE DIRECTIONS

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Abstract

Background

Multiple Sclerosis is a chronic immune-mediated disorder of the central nervous system, driven primarily by neuroinflammation and oxidative injury. Despite significant advances in disease-modifying therapies, persistent inflammation and progressive neurodegeneration remain key challenges. The emerging field of anti-inflammatory neuropharmacology offers new strategies aimed at immune modulation, neuroprotection, and remyelination.

Objectives

This retrospective study aimed to evaluate the clinical, diagnostic, and imaging profiles of MS patients to identify patterns of neuroinflammatory activity and disability progression, and to relate these findings to current and emerging pharmacological interventions.

Methods

A record-based retrospective analysis was conducted on confirmed MS cases. Demographic, diagnostic, and neuroimaging data including Oligoclonal Bands, evoked potentials, and MRI lesion distributions were evaluated. Disability progression was measured using the Expanded Disability Status Scale (EDSS). Descriptive statistical analysis was performed using Microsoft Excel.

Results

Among 273 patients, females constituted 61.5% with a mean age of 38.4 ± 10.2 years. Oligoclonal Bands were positive in 59.3% of cases, and MRI showed predominant periventricular (68.5%) and cortical (54.2%) lesions. The mean EDSS increased from 1.4 ± 0.6 to 2.2 ± 0.8 , indicating gradual neurological decline.

Conclusion

The study highlights the central role of neuroinflammation in MS progression and underscores the importance of integrating biomarker-driven, neuroprotective, and regenerative pharmacological approaches for achieving sustained disease control and functional preservation.

Keywords: Multiple Sclerosis; Neuroinflammation; Anti-inflammatory Neuropharmacology; Neuroprotection; Disease-Modifying Therapies

1. Introduction

1.1 Background and Significance

Multiple Sclerosis (MS) is an immune-mediated, chronic condition of the central nervous system and causes demyelination, axonal damage and progressive neurological impairment. It is one of the most prevalent causes of long-term disability in young adults that lead to a wide range of sensory, motor, and cognitive deficits (Brambilla, 2019). The disease is noted by the presence of multifocal lesions of the white and grey matter which are due to a complicated interaction of genetic vulnerability, immune dysregulation and environmental stimulus.

The pathophysiological mechanism is based on the use of autoreactive T and B lymphocytes to infiltrate the central nervous system, where an inflammatory process is triggered that damages the myelin and neurons. Pro-inflammatory cytokines, chemokines, pro-inflammatory reactive oxygen species released by the activated microglia and astrocytes increase tissue damage and remyelination (Van Langelaar et al., 2020). In the long run, sustained inflammation facilitates axonal degeneration and glial scarring, which results in permanent neurological impairment.

Regardless of the widespread progress in the characterization of the disease, MS cannot be cured, and the neuroinflammation keeps becoming the cause of neurodegeneration. The emerging knowledge of immune-mediated processes has guided contemporary treatment to anti-inflammatory neuropharmacological approaches that strive to regulate immune functions, eliminate oxidative stress, and enhance neuroprotection (Nociti, 2020).

1.2 Review of Literature

1.2.1 Pathophysiological Mechanisms of Neuroinflammation

Microglia and astrocytes actively participate in the process of triggering and maintaining the inflammatory cascade in MS. Activated astrocytes secrete cytokines and chemokines that stimulate the activation of local immune responses and lead to gliosis (Brambilla, 2019). CCL2 and CXCL10 interactions also help recruit T and B lymphocytes into the central nervous system and increase the level of inflammation (Cui et al., 2020). T cells that are synergist in nature are the ones that directly damage the myelin sheath, B cells produce autoantibodies and incorporate antigens (Van Langelaar et al., 2020).

The oxidative stress additionally increases neuroinflammation, thereby turning it self-promoting and accelerating the progression of axonal degeneration and neuronal death (Padureanu et al., 2019). The development of reactive oxygen species and deterioration of mitochondrial activity are the factors that precondition this process (Pegoretti et al., 2020). The cholinergic system activity has also been linked to the dysregulated inflammatory signalling, and neurochemical pathway is also significant in MS pathophysiology (Gatta et al., 2020). Neuroimaging, like sodium MRI, has been used to study the cellular kinetic and temporal processes of inflammation and demyelination (Huhn et al., 2019). Glial activation facilitates the unremitting development of chronic illnesses because it leads to the invasion of the immune cells to the brain, and the impairment of the blood-brain barrier (Kaur et al., 2019; Sulhan et al., 2020).

1.2.2 Current Pharmacological Approaches in MS Management

Over the past two decades, there is a shift in the treatment of MS where disease-modifying therapies (DMTs) are brought out. These are the agents that target the immune pathways in an attempt of reducing the rate of relapses and their frequency and reducing the rate of progression. Interferon-2 and Glatiramer acetate were the original DMTs and proved to control the cytokine patterns and reduce relapses (Ganji et al., 2020). Subsequently, the development of oral S1P receptor inhibitors, including Fingolimod and Siponimod, was made, that is, these agents prevent the exit of lymphocytes and inhibit the invasion of CNS (Bordet et al., 2020).

S1P modulators have also recently been demonstrated to be permissive to the survival of oligodendrocytes and their remyelination and immunomodulatory and neuroprotective (Roggeri et al., 2020). Dimethyl fumarate induces two actions i.e., the activation of the Nrf2 antioxidant pathway and inhibition of cytokine release (Saidu et al., 2019). Ocrelizumab is a CD20-targeting monoclonal antibody with a high level of efficacy in relapsing and progressive MS, which advocates the pathogenicity of B cells (Myhr et al., 2019).

These therapies are long-term, which is backed by real-life studies (Krysko et al., 2020), yet such concerns as the possibility of infection and malignancy have been reported (Carbone et al., 2020). Consequently, the treatment regimens should be optimised against the efficacy and long-term patient tolerability.

1.2.3 Emerging Anti-inflammatory and Neuroprotective Strategies

Recent studies are placing more importance on therapies that are able to not only suppress inflammation but also promote neuroprotection and remyelination. The anti-inflammatory agents have the potential to mitigate the loss of neurons by inhibiting the activation and oxidative damage of microglia (Nzogang and Donkeng, 2020). Curcumin, resveratrol and flavonoids are natural compounds, which have been demonstrated to have the ability to decrease pro-inflammatory cytokines and improve neuronal resilience (Rehman et al., 2019). The development of neuroimaging allows quantifying inflammation and the response to treatment with greater precision (Tommasin et al., 2019).

Current studies aim at the second generation of drugs which combine anti-inflammatory, neuroprotective and remyelinating actions. Those targets that concern mitochondrial metabolism and glial signaling hold particularly high promise (Villoslada and Steinman, 2020). Thorough examination of the literature highlights the importance of multifaceted therapeutic methods in the long-term disease control and neuroprotection (Shamaa et al., 2020).

1.3 Research Gap

Although there is marked improvement in comprehending MS immunopathology and the development of specific therapeutic agents, it has considerable limitations in bridging its real-life clinical indicators of neuroinflammation with pharmacologic processes. Majority of the previous studies simply considered clinical outcomes or molecular pathways but not a combination of neuroimaging, cerebrospinal fluid biomarkers and disability measures to reflect the spectrum of inflammatory activity. Moreover, many studies of the pharmacological effectiveness are considered within the scope of a short-term immunological effect, although fewer studies have been conducted in a systematic manner to clarify the relationship between chronic inflammation and the development of long-term disability, as well as to understand how these trends are applied to inform the evolution of neuroprotective therapy (Pegoretti et al., 2020). Thus, a systematic retrospective analysis is justified in order to address this gap and match clinical indicators with anti-inflammatory neuropharmacological interventions.

1.4 Rationale and Objectives

Although several pharmacological interventions have improved disease outcomes in MS, persistent inflammation and neurodegeneration remain key challenges. Understanding the real-world distribution of inflammatory markers, lesion burden, and disability progression is critical for optimizing therapeutic strategies and identifying unmet clinical needs.

The present study was designed to:

1. Analyze clinical and neuroimaging indicators to characterize patterns of neuroinflammatory progression in MS;
2. Evaluate the extent of disability progression using the Expanded Disability Status Scale (EDSS); and
3. Relate these findings to current and emerging anti-inflammatory neuropharmacological approaches to identify future directions for therapeutic development.

2. Materials and Methods

2.1 Study Design

The study was conducted in the form of a retrospective, observational, and record-based research that was supposed to assess the clinical and neuroimaging features of patients diagnosed with Multiple Sclerosis (MS). It was aimed at determining the trends of neuroinflammatory progression and disability rates through the analysis of medical records that were already in place. This design enabled the behaviour of diseases to be assessed in a real-world setting without direct interventions or alteration of treatment programs on patients.

2.2 Data Source

The authors used secondary clinical data that was obtained through the knowledge of available medical files of Multiple Sclerosis patients. Each record had complete demographic, clinical, diagnostic, and neuroimaging information with reference to the study objectives. The demographic variables were age, sex and the years of formal education. Clinical data consisted of the Expanded Disability Status Scale (EDSS) scores at baseline and at follow-up stages as a measure of the level of neurological disability. Diagnostic indicators were that there are the Oligoclonal Bands, neurophysiological tests that were performed on them, the Lower Limb Somatosensory Evoked Potentials (LLSSEP), Upper Limb Somatosensory Evoked Potentials (ULSSEP), Visual Evoked Potentials (VEP), and Brainstem Auditory Evoked Potentials (BAEP). Neuroimaging data was Magnetic Resonance Imaging (MRI) results of lesion localization in periventricular, cortical, infratentorial, and spinal cord areas, which were imperative in terms of the anatomical location of the inflammatory demyelination.

2.3 Inclusion and Exclusion Criteria

To provide validity and completeness of the analysed data, all patient records were filtered against predetermined inclusion and exclusion criteria. The inclusion criteria were those with clinically confirmed Multiple Sclerosis, which met the revised McDonald diagnostic criteria, and had complete demographic, MRI, and EDSS data. Data were filtered out when the records did not include the necessary clinical or imaging information or when the patient had co-morbid autoimmune, metabolic or neurological conditions that could confound the process of measuring disability or neuroinflammatory process. This sampling methodology also guaranteed the utilization of high quality and comprehensive records which reduced the possible sources of bias as well as ensuring the retrospective analysis was accurate.

2.4 Parameters Analysed

The variables that were analyzed within this research were grouped in four major areas namely demographic, clinical, diagnostic, and imaging. Age and gender were the demographic parameters that were used to set the parameters of the study population. The level of disability progression was measured with clinical parameters, where the initial and final EDSS scores were considered. Diagnostic signs like Oligoclonal Bands and evoked potential findings (LLSSEP, ULSSEP, VEP and BAEP) were viewed as a sign of neurophysiological involvement and inflammatory process. The imaging parameters based on MRI results reported the distribution of lesions in various regions of the brain and the spinal cord that provided a clue on the spatial distribution of neuroinflammatory damage.

2.5 Data Analysis

Microsoft Excel was used in arranging and analysing the data. The data were summarized using the tools of descriptive statistics, that is, calculating means, percentages, frequency distributions. The analysis underpinned a descriptive methodology, that is, determining apparent trends and associations between clinical, diagnostic, and imaging variables, but not conducting inferential statistical analysis.

Such a methodology guaranteed clarity and transparency in addition to reproducibility without making the methodology too complex to suit retrospective clinical research.

2.6 Ethical Considerations

The analysis was done using all anonymized patient information to enforce confidentiality. The protocol used in the study was approved by the Institutional Ethics Committee. Since it was an analysis of secondary data with no personal contact with the patients, the need of an individual informed consent was eliminated. The study met the ethical standards presented in the Declaration of Helsinki, where the privacy, integrity, and proper management of clinical data were respected.

3. Results

3.1 Demographic Characteristics

The patient records analysed amounted to 273. Table 1 provides the demographic profile of the study population. The average of the ages of the subjects was 38.41 ± 10.2 , whose range was 18-65. There were 61.5% females and 38.5% males, and this indicates the proven female predisposition in Multiple Sclerosis. Most of the participants had also reached 10-15 years of formal education and therefore the level of education was moderate among the group members.

Table 1. Demographic characteristics of the study population

Parameter	Category	Frequency (n = 273)	Percentage (%)
Gender	Male	105	38.5
	Female	168	61.5
Age (years)	18–30	72	26.4
	31–45	128	46.9
	46–65	73	26.7
Schooling (years)	<10	56	20.5
	10–15	142	52.0
	>15	75	27.5

Figure 1 depicts the age and gender distribution, showing the predominance of females in the 31–45-year age group, consistent with known epidemiological trends.

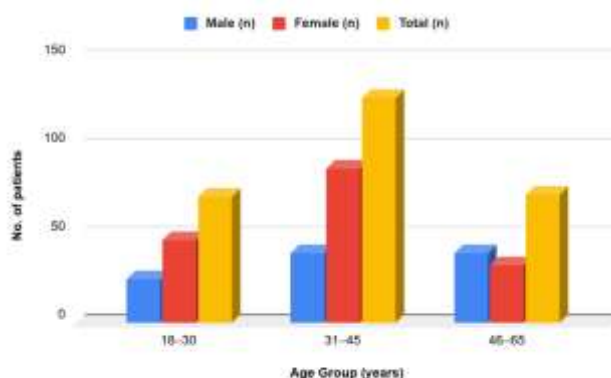


Figure 1. Age and gender distribution of the study population

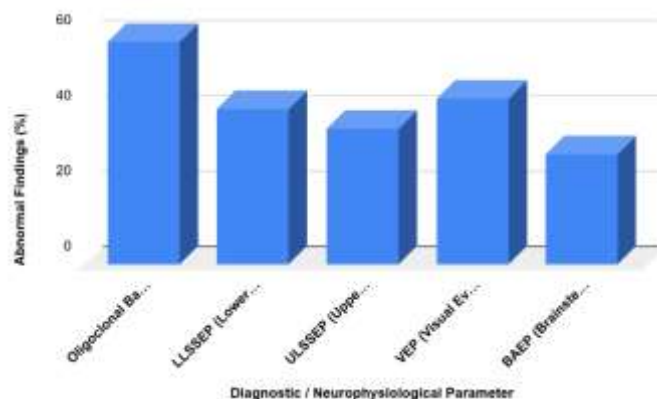
3.2 Diagnostic and Neurophysiological Findings

Diagnostic assessment showed that the rate of inflammatory activity was high among the participants. Table 2 indicates that 59.3 percent of the patients had positive results of Oligoclonal Bands indicating that there was active inflammation within the intrathecal region. Neurophysiological evaluation showed LLSSEP, ULSSEP, VEP and BAAP abnormalities in 41.4 percent, 36.2 percent, 44.3 percent, and 29.3 percent, respectively, with these being demonstrations of diffuse neural pathway involvement that is typical of demyelination.

Table 2. Distribution of diagnostic and neurophysiological findings

Diagnostic Parameter	Normal (%)	Abnormal (%)
Oligoclonal Bands	40.7	59.3
LLSSEP	58.6	41.4
ULSSEP	63.8	36.2
VEP	55.7	44.3
BAEP	70.7	29.3

The pattern of neurophysiological abnormalities and Oligoclonal Band positivity observed in Table 2 indicates widespread neuroinflammatory involvement. Figure 2 further illustrates this pattern, emphasizing the predominance of inflammatory demyelination affecting multiple functional pathways.

**Figure 2. Distribution of diagnostic and neurophysiological abnormalities**

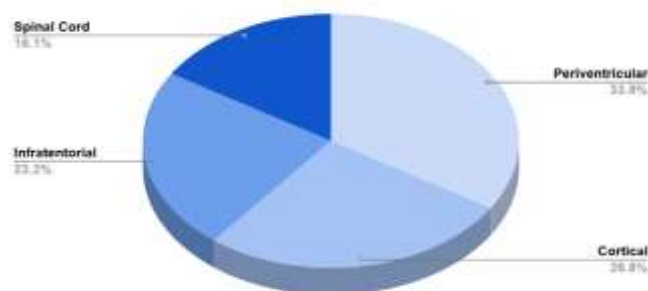
3.3 MRI Lesion Distribution

Magnetic Resonance Imaging (MRI) revealed that the lesions were more apparent in the periventricular, (68.5 %) and cortical (54.2 %) regions, followed by infratentorial (46.9 %) and spinal cord (32.6 percent) regions. The presence of periventricular lesions is predominant which correlates with the typical radiological appearance of MS. Table 3 gives a description of lesions as they appear in anatomical locations.

Table 3. Distribution of MRI lesions in patients with Multiple Sclerosis

MRI Location	Lesion Present (n)	Percentage (%)
Periventricular	187	68.5
Cortical	148	54.2
Infratentorial	128	46.9
Spinal Cord	89	32.6

Figure 3 provides a visual summary of MRI lesion distribution, highlighting the relative dominance of periventricular and cortical regions.

**Figure 3. MRI lesion distribution in different anatomical regions**

3.4 Disability Progression (EDSS Analysis)

The Expanded Disability Status Scale (EDSS) was used to determine the degree of disability of the patients in the first and the last clinical assessment. Table 4 presents the summarization of the results. The SDSS, mean, and Standard Deviation of the EDSS at the start of the study were 1.4 ± 0.6 and 2.2 ± 0.8 respectively, indicating a slow process of the occurrence of neurological impairment. First, there were 63.0 percent of patients with mild disability (EDSS 0-2.5), 27.1 percent with moderate disability (3.0-5.5), and 9.9 percent severe disability (6.0 or above). The mild cases dropped at follow-up to 43.2% and moderate and severe cases increased to 37.0 and 19.8, respectively (Table 4).

Table 4. Comparison of Initial and Final EDSS Scores

EDSS Category	Initial (n, %)	Final (n, %)
Mild (≤ 2.5)	172 (63.0 %)	118 (43.2 %)
Moderate (3.0–5.5)	74 (27.1 %)	101 (37.0 %)
Severe (≥ 6.0)	27 (9.9 %)	54 (19.8 %)
Mean $\pm$ SD	1.4 ± 0.6	2.2 ± 0.8

3.5 Correlation Between MRI Findings and Disability Status

Edema combined periventricular lesions and lesions combined with lesions of the spinal cord exhibited higher scores in EDSS than those with in the isolated cortical lesions and infratentorial lesions. The observation indicates that the distribution of lesions plays an important role in determining the level of disability. Although the inferential statistics was not done, the descriptive trends showed that the involvement of multiregional lesions was associated with more severe neurodegeneration, which supported the idea of the neurodegeneration occurring in MS due to inflammation.

4. Discussion

This retrospective study contributes to the role that neuroinflammation plays in Multiple Sclerosis (MS) pathophysiology and progression. The observed demographic profile consisting of a large proportion of females and the highest incidence in the age group of 31-45 years reflects previously developed epidemiological trends. The above trend of general Oligoclonal Band (OCB) positivity, and neurophysiological abnormalities in the VEP, SSEP and BAEP studies, denote diffuse demyelinating activity throughout the numerous neural pathways. These findings are consistent with the earlier findings indicating that OCBs contribute to the diagnostic specificity of MRI criteria and predictive biomarker of disease conversion and progression (Makhani et al., 2019).

The periventricular and cortical areas were the most frequently affected by the findings of Magnetic Resonance Imaging (MRI) in this study, which is also in line with the classical radiologic presentation of MS. The presence of coexistence between the lesions of the periventricles and spinal cord were associated with an increase in the EDSS score, which implied that the location of lesions has a direct correlation with the extent of disability. The same correlations have been emphasized in earlier literature, in which combined lesion patterns associated with more inflammatory demyelination aggression and more neuroaxonal loss (Duarte-Delgado et al., 2019). Disruption of the blood-brain barrier (BBB) in clinical and experimental models is a key stimulus in the pathogenesis of the infiltration of the leukocytes, cytokine release and the following neuronal damage.

The progressive rise of EDSS scores in follow-up examinations in the current analysis is evidence of the cumulative risk of chronic inflammation on long-term disability. Even minor increases in the EDSS even though the mean progression was moderate, there was neuroaxonal loss over time. This tendency is similar to the results of real-world cohort studies that suggest that the accumulation of clinical disabilities can persist even in the case of seemingly controlled acute relapses (Cohen et al., 2020). This evidence informs the idea that subclinical inflammatory activity does not stop at the stage of relapse suppression, which confirms the necessity of immune modulating and neuroprotecting therapies.

New evidence shows the significance of biomarker-based therapy to inform personalized treatment. The circulation of cytokines, the presence of neurofilament light chain, and high-quality imaging measures can be used to predict the response to therapy and disease progression (Breiteneder et al., 2020). These markers can be included in the clinical decision-making frameworks to enable the early detection of patients that have a high risk of rapid progression and enhance the assessment of anti-inflammatory drug effectiveness.

The findings also focus on the role of nutritional and metabolic interventions in regulating the level of inflammation. There is evidence that inflammatory cytokines could be diminished by omega-3 fatty acid supplementation, which also had a modest effect on EDSS outcomes in MS, which is an additional possible therapeutic option (Sedighiyan et al., 2019). Even though the nutritional interventions cannot stop the disease progression independently, they have a synergetic effect when combined with disease-modifying therapies and can increase the overall neuroprotective abilities.

In addition, regenerative neuropharmacology is promising with development of promising avenues to remyelination and axonal repair. According to the experimental evidence, cell-based transplantation strategies have the potential to induce oligodendrocyte differentiation, remyelinate, and enhance functional recovery in demyelinating models (Mangale et al., 2019). These results are consistent with the overall therapeutic objective that is related to the combination of anti-inflammatory and regenerative approaches to obtain long-term neurological maintenance.

Together, the results of this paper add to the cumulating body of literature that MS is an evolving spectrum of inflammatory and neurodegenerative events. The demonstrated association between the distribution of lesions and the disability progression provides the clinical significance of the neuroimaging markers as the surrogate measure of disease activity. The combination of biomarkers, nutritional regulation, and new neuroprotective interventions into an individualized treatment paradigm can be the best strategy in the future. Further studies especially retrospective studies that correlate clinical, imaging, and pharmacological information will play an important role in tightening the antipharmacological neuropharmacology procedures and improving the precision of Multiple Sclerosis management.

5. Conclusion

This present study has revealed the significance of neuroinflammation as one of the most important factors on the disease activity and progression in Multiple Sclerosis. The apparent diffuseness of the demyelinating lesion over the lesion site is validated by the high incidence of Oligoclonal Band positivity and neurophysiological defects of the different sensory and motor pathways. The radiological equivalents of inflammation-induced neurodegeneration manifested in the fact that the MRI reveals the prevalent patterns of periventricular and cortical damages, which is supported by the rising of the EDSS scores indicating the load of disability imposed by the chronic inflammatory damage. All these observations keep supporting the fact that neuroinflammation persists even in the clinically stable phases, which makes it important to introduce therapeutic interventions, which do not only address management of relapses, but also the processes of immune dysregulation and neuronal protection. Biomarker-based diagnostics and neuroimaging development and introducing the adjunctive nutritional and neuroprotective interventions will bring a beneficial change in the process of a therapeutic approach customization. Moreover, the new potential of regenerative and cell-based therapies is providing a new horizon of reversing the process of demyelination and repair of neuronal integrity. Overall, the anti-inflammatory, neuroprotective, and regenerative paradigm is essential to the practice of the multifaceted neuropharmacological approach in Multiple Sclerosis patients to achieve long-term disease stabilization and improve their lives.

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