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Efficacy and tolerance of Methylprednisolone in the treatment of multiple sclerosis relapses: the case study of Morocco

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ABSTRACT

Background: The objective of this study was to evaluate the clinical response and tolerability of intravenous Methylprednisolone in the management of acute relapses in patients with relapsing–remitting multiple sclerosis (RRMS) and progressive multiple sclerosis (PMS). These patients were followed for a period of two years in a real-world setting where access to alternative relapse treatments was limited.

Methods: Over a ten-year period, data were collected from 31 patients with multiple sclerosis (MS). This study focused on the management of relapses in relapsing– remitting and progressive MS using intravenous Methylprednisolone. All patients received Azathioprine as a background disease- modifying therapy and were followed for two years. Expanded Disability Status Scale (EDSS) scores and Annualised Relapse Rates (ARR) were recorded before treatment and during follow- up as descriptive longitudinal clinical indicators to assess the overall clinical course. Magnetic Resonance Imaging (MRI) data were also collected.

Results: The study included 31 patients treated with Methylprednisolone, including 17 with RRMS and 14 with PMS. During follow-up, a reduction in the ARR was observed in the RRMS group, decreasing from 2.88 to 0.29, and in the PMS group, from 2.64 to 0.29. Similarly, an improvement in the EDSS score was observed in the RRMS group, decreasing from 4.24 to 3.62, whereas relative stability was noted in the PMS group, with EDSS scores changing from 5.46 to 5.43.

Conclusion: This study confirms the established role of intravenous Methylprednisolone in the management of acute relapses of MS. In our real-world cohort, conducted in a resource-limited setting, relapse treatment was associated with a favorable short-term clinical course and good tolerability. However, Methylprednisolone should not be considered a disease-modifying therapy, and the long-term clinical evolution observed cannot be attributed solely to corticosteroid treatment.

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system characterized by the occurrence of neurological relapses and, over time, a possible progression of disability. The therapeutic management of MS generally relies on two complementary strategies: disease-modifying therapies aimed at reducing long-term inflammatory activity, and treatments intended to manage acute relapses. Among the latter, intravenous Methylprednisolone (IVMP), a glucocorticoid with strong anti- inflammatory properties, represents the standard treatment for the management of acute MS relapses.

Earlier MS research has indicated that methylprednisolone has potential advantages for patients with clinically isolated syndrome or RRMS [1, 2]. For instance, the US Food and Drug Administration (FDA) recommends intravenous methylprednisolone (IVMP), an anti-inflammatory glucocorticoid, for the treatment of MS relapses [3]. Similar to this, a large number of findings demonstrate that EDSS scores improvement clinically significantly in patients treated with IVMP frequently compared to baseline [4-8]. Additionally, it has been demonstrated that this therapy speeds up both the recovery [9] and the healing of relapses [10, 11]. By the same token, methylprednisolone has become a mainstay of relapse treatment. The first recommendation for patients with acute MS relapses is this treatment before any other treatments of interest, in a systematic review of the literature (SLR) [12]. This is the same real- life treatment regimen observed in patients undergoing an acute MS attack in the USA [13]. It is important to emphasize, however, that the primary objective of corticosteroid therapy in this context is to accelerate functional recovery rather than to alter the long-term natural course of the disease. Corticosteroids are therefore not considered disease- modifying therapies, and their effect on preventing future relapses or slowing disability progression has not been demonstrated.

Although studies have shown that IVMP is generally well tolerated, there are a few unfavorable effects that can occur despite how effective it is. But they were all minor and short-lived, with the most typical one being a metallic taste after ingesting the oral preparation [14]. Furthermore, a comprehensive systematic review and meta-analysis revealed that oral corticosteroids were strongly linked to insomnia [15]. Another unfavorable consequence was headaches.

Additionally, IVMP is a relapse treatment option for MS that has been authorized by the FDA and other drug regulatory agencies and has demonstrated to be a highly successful relapse treatment choice [6-8]. Hence, IVMP is a viable option as the initial course of treatment for acute MS relapses in patients who are eligible, considering the evidence base and reduced cost of corticosteroids, and also may be advantageous in low-income communities.

Accordingly, the aim of the present study was to evaluate the clinical response and tolerability of intravenous Methylprednisolone used for relapse management in patients with relapsing–remitting or progressive multiple sclerosis during a two- year follow- up period in a real- world clinical setting.

METHODS

Study design

This study focuses on the management of multiple sclerosis relapses with methylprednisolone. It is a retrospective cohort study designed to describe the clinical response and tolerability of methylprednisolone administered for relapse treatment in Moroccan patients with relapsing–remitting or progressive multiple sclerosis in a real-world clinical setting.

Study population

The study population included 31 patients with relapsing– remitting or progressive multiple sclerosis who experienced neurological relapses treated with Methylprednisolone. All patients were from the Kenitra region (Morocco) and were managed at El- Idrissi Hospital in Kenitra, a university hospital center, between July 2009 and July 2019.

Study inclusion and exclusion criteria

To be included in this study, patients were required to present with a neurological relapse of

multiple sclerosis requiring treatment with Methylprednisolone and to have a diagnosis of relapsing– remitting or clinically established progressive multiple sclerosis, according to the diagnostic criteria of McDonald 2001 [16] and Poser et al. [17].

Patients who received relapse treatment other than Methylprednisolone, those with a contraindication to this therapy, and those with another significant medical condition likely to influence the clinical course were excluded from the study.

A comprehensive neurological examination was performed in all patients. Laboratory investigations, including standard urinalysis, thyroid-stimulating hormone measurement, blood biochemical testing, and complete blood count, were also conducted. Bone mineral density at the lumbar spine was measured. Blood pressure and heart rate were monitored before and after each administration of Methylprednisolone.

Evaluation by EDSS score and ARR

The mean Expanded Disability Status Scale (EDSS) score and the annualised relapse rate (ARR) were recorded at baseline and during the two- year observation period in patients with relapsing– remitting multiple sclerosis. The same parameters were also collected in patients with progressive multiple sclerosis.

The EDSS score measured before the administration of Methylprednisolone during the relapse was considered the baseline value. At each follow- up visit, a neurological evaluation was performed and the EDSS score was assessed in order to document the clinical course over time.

Data on relapses occurring during the observation period were recorded to calculate the annualised relapse rate (ARR), defined as the mean number of relapses per patient per year during the follow-up period.

These parameters were used as descriptive clinical indicators to characterize the clinical course of the patients during follow- up, without the intention of demonstrating a disease- modifying effect attributable to relapse treatment.

Characteristics studied

Data were obtained from the multiple sclerosis registry maintained by the neurologist and from the patients' hospital medical records. Baseline characteristics were collected, including sex, age at disease onset, age at the time of clinical management, and the duration of disease progression prior to relapse management with Methylprednisolone.

Information related to clinical follow-up was also collected, including the duration of follow-up, the occurrence of potential treatment- related adverse events, as well as Expanded Disability Status Scale (EDSS) scores and annualised relapse rates (ARR) recorded at baseline and during the observation period.

Available magnetic resonance imaging (MRI) data were also retrieved from the medical records using the same procedure.

Data resource and measurement

Data collection tool

Data were collected using a standardized data collection form developed for the study. This tool was used to obtain demographic and clinical information on patients with multiple sclerosis managed at the University Hospital of Kenitra (Morocco) between July 2009 and July 2019, based on the multiple sclerosis registry and the patients' hospital medical records.

Data collection

Demographic data collected included patient sex, age at disease onset, age at the time of clinical management, and the duration of disease progression prior to relapse management with Methylprednisolone.

Clinical data included Expanded Disability Status Scale (EDSS) scores and annualised relapse rates (ARR) recorded at baseline and during the observation period, as well as available magnetic resonance imaging (MRI) data.

Information was obtained using a standardized data collection form based on the multiple sclerosis registry and the patients' hospital medical records, in collaboration with the neurologist responsible for patient follow-up.

All demographic and clinical data were entered into a secure electronic database stored on a password-protected computer.

Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software. Quantitative variables were described as means, ± standard deviations or medians, depending on the distribution of the data. Qualitative variables were presented as frequencies and percentages.

Comparative analyses were conducted to examine changes in Expanded Disability Status Scale (EDSS) scores and annualised relapse rates (ARR) recorded at baseline and during the observation period in patients with relapsing–remitting and progressive multiple sclerosis.

Statistical comparisons were performed using the Student's t- test or analysis of variance (ANOVA) for quantitative variables, and the chi-square test or Pearson correlation coefficient to assess associations between variables. A $p < 0.05$ was considered statistically significant.

Ethical considerations

This study was approved by the Ethics Committee of the Provincial Health Service (reference No. 4361, October 21, 2019).

The study was conducted in accordance with the ethical principles governing biomedical research and with regulations concerning the confidentiality of medical data. Clinical information was extracted from medical records and the multiple sclerosis registry with strict respect for patient anonymity.

All necessary measures were implemented to ensure the protection of patient privacy and the confidentiality of personal data.

RESULTS

Demographic analysis of MS patients

In this retrospective cohort, a total of 31 patients with multiple sclerosis who experienced neurological relapses managed with Methylprednisolone were included in the analysis. Among them, 17 patients (55%) had relapsing–remitting multiple sclerosis (RRMS), whereas 14 patients (45%) had progressive multiple sclerosis (PMS).

Among the patients with RRMS, 11 were women and 6 were men. The mean disease duration prior to relapse management with Methylprednisolone was 4.94 years (range: 0–10 years). The mean age at the time of relapse management was 34.53 ± 6.71 years (range: 25– 45 years), while the mean age at disease onset was 29.59 ± 7.73 years (range: 20–44 years). The duration of clinical follow-up in this group was two years (Table 1).

Among the 14 patients with progressive multiple sclerosis, 12 were women and 2 were men. The mean disease duration prior to relapse management was 3.57 years (range: 1– 10 years).

The mean age at the time of relapse management was 43.71 ± 4.12 years (range: 39–52 years), while the mean age at disease onset was 40.14 ± 4.45 years (range: 35–51 years). The duration of clinical follow-up in this group was also two years (Table 1).

Clinical analysis of MS patients

EDSS score

In the group of patients with relapsing– remitting multiple sclerosis (RRMS), comprising 17 patients (55% of the cohort), Expanded Disability Status Scale (EDSS) scores were recorded at baseline and during the two-year observation period. The mean EDSS score was 4.24 at baseline and 3.62 during follow-up.

In the group of patients with progressive multiple sclerosis (PMS), which included 14 patients (45% of the cohort), the same parameters were assessed. In this group, the mean EDSS score was 5.46 at baseline and 5.43 during the observation period.

These results describe the evolution of EDSS scores observed during follow- up in the two patient groups (Table 1).

Statistical analysis did not reveal a significant difference in mean EDSS scores at baseline between patients with relapsing– remitting multiple sclerosis (RRMS) and those with progressive multiple sclerosis (PMS) (p = 0.08).

However, a statistically significant difference was observed in mean EDSS scores between the two groups during follow-up (p = 0.03) (Figure 1.a).

The ARR

Among patients with relapsing– remitting multiple sclerosis (RRMS), the mean annualised relapse rate (ARR) during the year preceding the start of follow- up was 2.88. During the observation period, the mean ARR recorded in this group was 0.29.

Among patients with progressive multiple sclerosis (PMS), the mean ARR during the year preceding the start of follow- up was 2.64. During the observation period, the mean ARR recorded in this group was also 0.29.

These findings describe the ARR values observed prior to the start of follow-up and during the observation period in the two patient groups (Table 1).

Figure 1: b. Changes in the annualised relapse rate (ARR) during the follow-up period.

Statistical analysis comparing patients with relapsing–remitting multiple sclerosis (RRMS) and those with progressive multiple sclerosis (PMS) did not reveal a significant difference in mean ARR at the beginning of follow-up (p = 0.137).

Similarly, no statistically significant difference in mean ARR was observed between the two groups during the follow-up period (p = 0.115) (Figure 1.b).

MRI

In patients with relapsing– remitting multiple sclerosis (RRMS) and progressive multiple sclerosis (PMS), the available magnetic resonance imaging (MRI) examinations showed demyelinating lesions consistent with the diagnosis of multiple sclerosis, particularly in brain regions typically involved in this disease.

Analysis of disability in MS patients

Among patients with relapsing–remitting multiple sclerosis (RRMS), worsening of disability was observed in 11.8% of patients during the follow-up period. The remaining patients showed either an improvement in disability score or ongoing clinical activity.

In patients with progressive multiple sclerosis (PMS), worsening of disability was observed in 28.6% of patients. The other patients exhibited an improvement in disability score, a stable clinical course, or advanced functional dependency, including patients who were bedridden (Figure 2).

During the follow- up period, 82.4% (14/17) of patients with relapsing– remitting multiple sclerosis (RRMS) showed an improvement in disability score, whereas 57.1% (8/14) of patients with progressive multiple sclerosis (PMS) also exhibited an improvement in disability score. These observations are illustrated in Figures 2, 3, and 4.

Withdrawals

None of the patients discontinued intravenous Methylprednisolone during the study period, due to its good tolerability and the absence of significant adverse effects.

No deaths were reported among the patients throughout the observation period.

Tolerance and safety

No adverse events (AEs) were reported during the treatment period.

Intravenous Methylprednisolone was well tolerated by all patients, and no contraindications were identified.

Figures

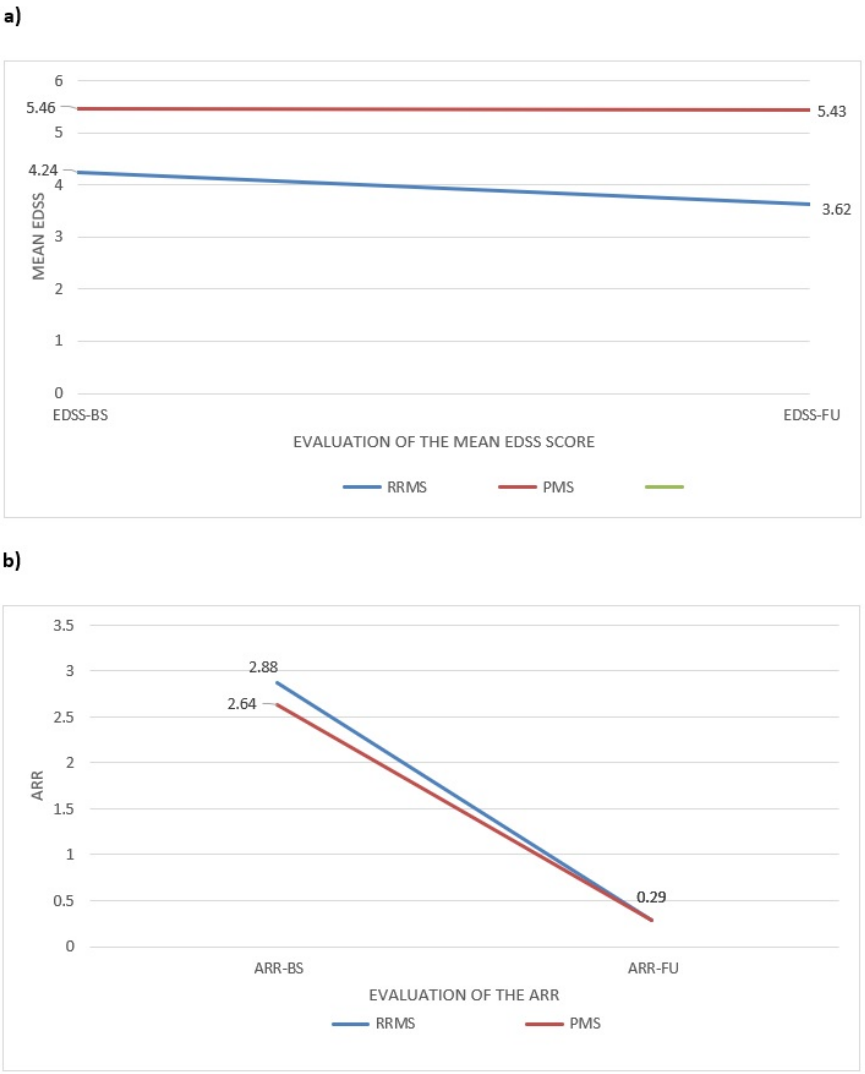

Figure 1: (a) The figure presents the mean Expanded Disability Status Scale (EDSS) scores measured at baseline (EDSS-BS) and during follow-up (EDSS-FU) in patients with relapsing–remitting multiple sclerosis (RRMS) and progressive multiple sclerosis (PMS). (b) The figure presents the mean annualised relapse rate (ARR) measured at baseline (ARR-BS) and during the observation period (ARR-FU) in patients with relapsing–remitting multiple sclerosis (RRMS) and progressive multiple sclerosis (PMS).

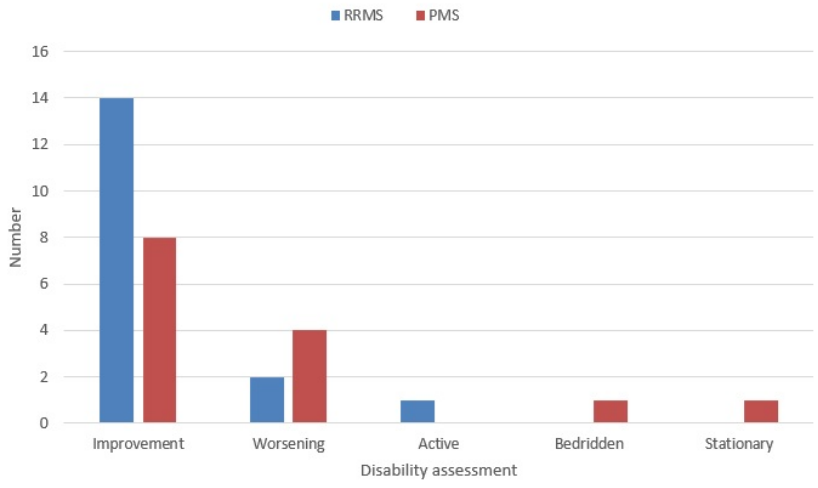

Figure 2: Changes in disability during the follow-up period in patients with relapsing–remitting multiple sclerosis (RRMS) and progressive multiple sclerosis (PMS). In patients with relapsing–remitting multiple sclerosis (RRMS), 11.8% showed worsening of disability, whereas 82.4% showed improvement during follow-up. In patients with progressive multiple sclerosis (PMS), 28.6% showed worsening, whereas 57.1% showed improvement.

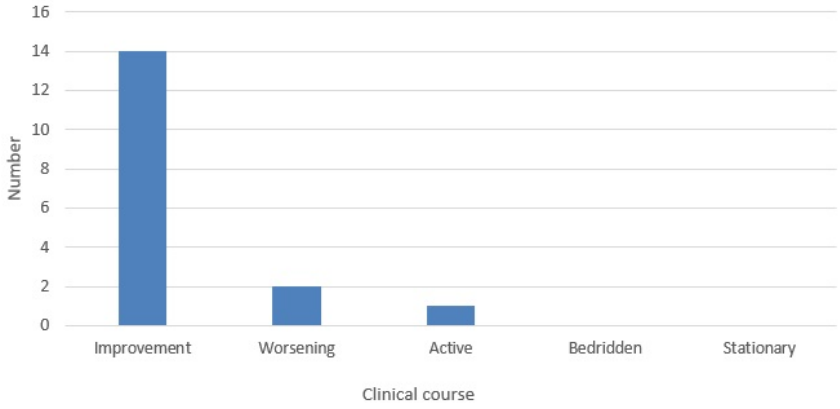

Figure 3: Changes in disability during the follow-up period in patients with relapsing–remitting multiple sclerosis (RRMS). In patients with relapsing–remitting multiple sclerosis (RRMS), 11.8% (2/17) showed disability worsening, 82.4% (14/17) showed improvement, and 5.8% (1/17) showed persistent clinical activity.

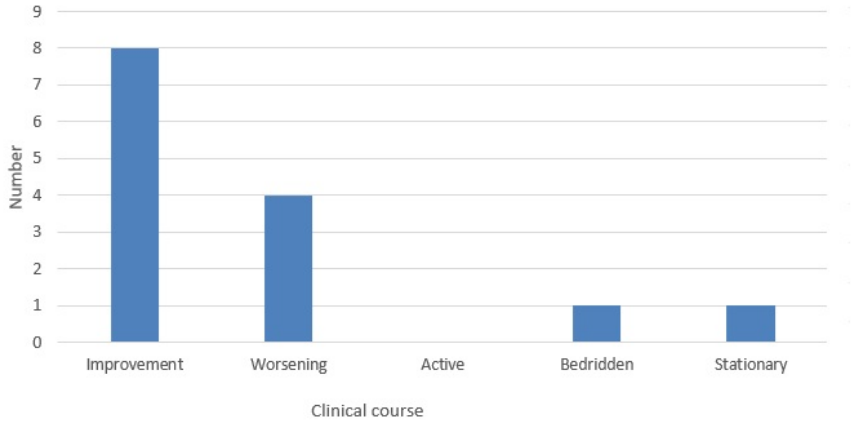

Figure 4: Changes in disability during the follow-up period in patients with progressive multiple sclerosis (PMS). In patients with progressive multiple sclerosis (PMS), 28.6% (4/14) showed disability worsening, 57.1% (8/14) showed improvement, 7.1% (1/14) were bedridden, and 7.1% (1/14) remained stable.

Tables

Characteristics	RRMS	PMS
Number	17	14
Frequency (%)	55	45
Gender (male/female)	6/11	2/12
Mean age at disease onset	29.59 ±7.73	40.14 ±4.452
Range of the mean age at disease onset	20-44	35-51
Mean age at start of treatment	34.53 ±6.719	43.71 ±4.122
Range of the mean age at the start of treatment	25-45	39-52
Mean disease duration (year)	4.94	3.57
Range of the duration of the disease	0-10	1-10
Treatment duration (year)	2	2
Baseline mean EDSS	4.24 ±1.427	5.46 ±0.82
Range of baseline EDSS	2-6	3-7
Final mean EDSS	3.62 ±1.816	5.43 ±1.141
Range of the final EDSS	1-7	3-7
Basic mean ARR	2.88 ±0.857	2.64 ±0.633
Final mean ARR	0.29 ±0.686	0.29 ±0.611

Table 1: Baseline characteristics of patients with multiple sclerosis included in the study. This table summarizes the demographic and clinical characteristics of the cohort of Moroccan patients with relapsing–remitting multiple sclerosis (RRMS) and progressive multiple sclerosis (PMS).

DISCUSSION

Multiple sclerosis (MS) is a chronic immune- mediated disease involving both genetic and environmental factors. In the clinical course of the disease, the occurrence of relapses represents an important aspect of disease activity. A relapse is generally defined as the appearance or worsening of neurological symptoms lasting more than 24 hours, in the absence of another identifiable cause, and occurring at least 30 days after a previous episode [18, 19]. Such episodes may be associated with functional impairment and a reduction in patients' quality of life.

The management of relapses therefore represents an important component of the clinical care of individuals with MS. Corticosteroids are commonly used in this context because they may contribute to a faster functional recovery during acute relapses, although their effect on the long-term course of the disease appears limited [20, 21]. In addition, the occurrence of relapses may negatively affect patients' psychological well- being, highlighting the importance of appropriate symptomatic management.

Several studies have reported that corticosteroid administration, most often via the intravenous route, is associated with a more rapid clinical recovery following a relapse [22]. Other studies have also suggested that orally administered corticosteroids may provide comparable outcomes to intravenous corticosteroids in the management of MS relapses [15, 22-24]. Among these treatments, methylprednisolone and prednisone are widely used in clinical practice for the management of MS relapses.

In this cohort, a lower annualised relapse rate (ARR) was observed during the follow-up period compared with the period preceding methylprednisolone administration. This finding is presented descriptively and reflects the clinical course of the patients during the observation period. In addition, intravenous methylprednisolone was generally well tolerated in this patient population, with no major adverse events reported during the treatment period.

The Disability Status Scale (DSS), which primarily assesses neurological function and walking ability, has been widely used to evaluate and monitor the progression of disability over time [25]. This scale has undergone several revisions in order to better reflect levels of disability observed in clinical practice and was subsequently expanded into the Expanded Disability Status Scale

(EDSS) [26]. According to commonly accepted criteria, in patients with an EDSS score ≤ 5.5, an increase of at least 1 point is considered clinically meaningful, whereas in patients with an EDSS score > 5.5, an increase of 0.5 point may be interpreted as clinically significant worsening [27].

In our cohort, EDSS scores measured during follow- up were used to describe changes in disability status among the included patients. In individuals with relapsing– remitting multiple sclerosis (RRMS), the mean EDSS score changed from 4.24 at the beginning of follow-up to 3.62 after two years of observation. Among patients with progressive multiple sclerosis (PMS), the mean EDSS score changed from 5.46 to 5.43 during the same period. These findings describe the evolution of EDSS scores during follow-up within the studied cohort.

Previous studies have also reported the use of Methylprednisolone, either alone or in combination with other therapies, in the management of multiple sclerosis relapses, with variations in EDSS scores observed during follow-up [28, 29]. The patterns observed in our study appear broadly consistent with those reported in the literature, while remaining descriptive of the clinical course within this cohort.

As noted previously, corticosteroids are commonly used in the management of multiple sclerosis relapses, mainly because of their anti- inflammatory properties. Several biological mechanisms have been proposed to explain their effects at the molecular level, including reduced expression of adhesion molecules, inhibition of leukocyte migration across the blood–brain barrier, and modulation of cytokine production and lymphocyte populations [30, 31]. Glucocorticoids have also been associated with increased production of anti- inflammatory cytokines such as interleukin-4 (IL-4) and transforming growth factor- β, as well as reduced levels of pro- inflammatory mediators including interferon- γ, tumor necrosis factor- α, IL-2, and IL-12 [30].

However, corticosteroid administration may also be associated with a range of adverse effects, varying from mild manifestations to more severe complications. Reported effects include weight gain, edema, sleep and mood disturbances, myopathy, cataracts, osteoporosis, hypertension, glucose intolerance, gastrointestinal disorders, pancreatitis, and avascular necrosis [31]. In the context of intravenous methylprednisolone (IVMP), several studies have nevertheless reported an overall acceptable safety profile, with most adverse events being transient and of mild intensity, such as insomnia, headache, or a metallic taste [14].

Some gastrointestinal manifestations, including corticosteroid- associated gastritis, have been suggested to result primarily from systemic mechanisms rather than from direct irritation of the gastric mucosa [32]. In addition, several clinical trials have evaluated the use of high-dose oral corticosteroids in the management of MS relapses [6, 7, 24, 33, 34]. A systematic review and meta-analysis reported that insomnia was among the most frequently observed adverse events following oral corticosteroid administration, although these events were generally mild and temporary [15].

Overall, these findings from the literature describe the patterns of use and the safety profile of corticosteroids in the management of multiple sclerosis relapses.

In individuals with multiple sclerosis, the occurrence of relapses represents an important aspect of the clinical course of the disease. On average, a patient may experience a relapse approximately every two years, although the frequency and severity of these episodes can vary substantially between individuals. Some relapses may be relatively mild, whereas others may lead to more pronounced functional impairment and require hospitalization and supportive medical care [35].

The occurrence of relapses may also be associated with a substantial increase in healthcare-related costs for both patients and healthcare systems. In the United States, for example, the cost of care has been reported to increase by more than six fold during a relapse episode, whether managed in an outpatient setting or requiring hospitalization [36].

Intravenous methylprednisolone (IVMP) is widely used in the management of acute multiple sclerosis relapses in eligible patients, based on the available clinical evidence and its established use in clinical practice. High-dose oral corticosteroids have also been investigated

as a potential alternative approach for the management of relapse episodes.

In this context, oral corticosteroid administration may offer certain practical advantages, including greater convenience and accessibility for patients. However, comparative evaluation of oral and intravenous corticosteroid regimens requires well-designed studies in order to better characterize their patterns of use, tolerability, and clinical outcomes [22].

The findings of this study confirm the established role of intravenous Methylprednisolone in the management of acute relapses of multiple sclerosis. In our cohort of Moroccan patients, the clinical course observed during follow-up showed a reduction in the annualised relapse rate (ARR) in both the relapsing–remitting and progressive MS groups. In addition, an improvement in Expanded Disability Status Scale (EDSS) scores was observed among patients with relapsing– remitting multiple sclerosis, while relative stability was noted among those with progressive forms of the disease.

However, these observations should be interpreted with caution. Methylprednisolone represents a symptomatic treatment for relapses primarily aimed at accelerating clinical recovery and should not be considered a disease-modifying therapy. The clinical evolution observed during follow-up may be influenced by several factors, including post-relapse recovery, the natural fluctuations of the disease, as well as the effect of background therapy with Azathioprine administered to the patients.

Nevertheless, in resource-limited settings where access to alternative therapeutic options may be restricted, Methylprednisolone remains an essential option for the management of acute MS relapses. Its short-term clinical effectiveness, generally favorable tolerability profile, and relatively affordable cost contribute to its widespread use in clinical practice. These findings therefore provide real-world evidence regarding the use of Methylprednisolone in relapse management and highlight the importance of continued research aimed at optimizing therapeutic strategies across different healthcare resource settings.

CONFLICT OF INTEREST

There is no conflict of interest disclosed by the authors in the publication of this manuscript.

AUTHOR CONTRIBUTIONS

Mirhani Ali: conceptualized and designed the manuscript, designed and developed the questionnaire, wrote the manuscript, analyzed and interpreted the data, supervised the manuscript, and contributed to its editing and revisions.

Auajjar Nabila: contributed to the formatting, content, finalization, and overall proofreading of the manuscript.

The responsibility of Slimani Chouki was to administer the questionnaire at the university hospital, facilitate access to patient records, and coordinate the study at the hospital.

Attarassi Benaissa: critically reviewed and revised the manuscript, ensuring scientific accuracy and consistency.

The final version of the manuscript was reviewed, edited, read, and approved by all authors for submission.

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