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ORIGINAL ARTICLE

Early Spinal Cord Pseudoatrophy in Multiple Sclerosis and their Treatment Through Interferon Beta

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ABSTRACT

Background: Multiple sclerosis (MS) frequently affects spinal cord (SC), resulting in motor, sensory, and autonomic impairment. Many pathological problems, including demyelination and neuroaxonal loss, are examined in vivo with MRI in MS.

Objectives: This research was performed for confirming effects of early SC pseudoatrophy (PA) in MS treated using interferon beta on SC in early IFN therapy.

Methods: PA was diagnosed using MRI and patients were classified based on McDonald's 2010 criteria into 05 categories of clinical attacks. They were treated using IFN-1a 44 g, beginning after FCDE, administered thrice or once weekly for 2 years and their EDSS scores were baseline evaluated.

Results: Kurtzke EDSS scoring system was implied to determine the disability of MS. After treating for 02 years, the Group A patients was scored 1.0 and Group B 1.5. The MS disability in SC was significantly reduced in both treatment groups, though, significantly enhanced domino effects ($p<0.05$) were observed in treatment group A administered with three doses weekly (51.41%) followed by single weekly (48.51%); and EDSS scores were significantly declined ($p<0.05$) from 2.5 to 1.0 and 1.5 respectively.

Conclusion: It was evidenced that PA affected the SC and caused significant spinal lesions. PA of SC was utilized as biomarker to monitor therapeutic impacts in MS. The PA in MS-affected individuals was significantly treated in early arena and disability of MS of SC was significantly declined with interferons.

Keywords: Interferons; McDonald's scoring; Pseudoatrophy; Sclerosis.

INTRODUCTION

Spinal cord atrophy, in addition to brain shrinkage, has drawn more attention recently as a factor connected to clinical impairment. Several studies have highlighted the importance of spinal cord volumetry as clinical impairment marker and disease propagation. Atrophy rates of SC volumetry are higher than those shown for brain atrophy [1]. MS is a continual inflammatory neurodegenerative and demyelinating disorder of SC with probable frequency of >0.9 (Millions) cases in US in 2020. MS symptoms often manifest in people between the ages of 20 and 50 and include tiredness, tremor, decreased mobility, depression, sensory loss, visual impairment, deformities in genitourinary area, ataxia, motor weakness, cognitive impairment and pain. These symptoms negatively affect the quality of life [2-5].

Progressive forms of MS are characterized clinically by governing neurological disabilities, irrespective of relapses. They presented being the initial disease itinerary or post preliminary relapsing segment. With emergence of effectual medications for relapsing-remitting MS over the previous two decades, momentous progress was made in devising strategies for MS treatment. Even though inflammation is prominent and considered as crucial inflammatory lesions of RRMS, but fundamental pathology in disease propagation is still idiopathic, rendering therapeutic development as tremendous confrontation [6-8].

Early therapy (ET) utilizing interferon, oral teriflunomide, glatiramer acetate or per-os cladribine has been proven to curtail the incidence of rising MS in patients with a first clinical demyelinating event (FCDE). ET using IFN -1a 44 g, beginning post-FCDE and administered subcutaneously thrice weekly or once weekly for 2 years had delayed conversion to McDonald MS (2005 criteria) and CDMS relative to placebo. Moreover, regular treatment (tiw vs qw) scrutinized progression of McDonald's sclerosis [9-10].

Hence, our investigation aimed to confirm impacts of early SC pseudoatrophy in MS treated with interferon beta pseudoatrophy on the spinal cord in subjects receiving early interferon-beta therapy.

MATERIAL AND METHODS

The study was conducted from January 2019 to April 2022 and 247 patients have been recruited for this prospective and longitudinal, MS Cohort Study in Islamabad, Pakistan. As per study design, DMT-naive persons were included in this trial. All patients fulfilled the McDonald 2010 criteria for CIS or early definite relapsing-remitting MS (RRMS) within six months previous to inclusion [11-12]. If a patient's authentic MRI data was missing or insufficient value, they were removed from the current analysis.

Patients were treated using IFN -1a 44 g, beginning after FCDE and administered (S/C) thrice or once weekly for 2 years. Data pertaining to protection cum efficacy was gathered every three months until conversion, and then every six months thereafter. The EDSS scores and CDMS evaluations were obtained at baseline (month 24) and every six months thereafter (Table 1). MRI was performed quarterly during study phase on baseline extension, and subsequently at last treatment visits of patients.

Throughout the initial trial, Expanded Disability Status Scale (EDSS) scores were examined each six months [13]. Early spinal cord pseudoatrophy in MS treatment through IFN beta was studied by means of MRI as mentioned in Fisher et al. [13].

Table 1: Group allocation of the treatments in multiple sclerosis patients

S. No	Group	No. of patients	Treatment	Dose	Route
1	A	127	IFN -1a 44 g	Thrice weekly	Subcutaneous
2	B	120	IFN -1a 44 g	Once weekly	Subcutaneous

Each research year's atrophy rates were predicted as percentage change in fractional volumes. Patients were categorized as progressors (defined as a 1.0-point increase in EDSS score confirmed at 6 months) or nonprogressors ("stable patients"). The data evaluation was done to assess therapeutic impacts on atrophy, first-year differences in GM and WM atrophy, and changes in atrophy rates based on disease progression status. Using One-way ANOVA including Tukey HSD, differences depending on treatment, disability progression status and study year, was analyzed.

The institution granted the ethical approval to conduct this therapeutic trial and informed written consent was also received from the study population, under the supervision of the Director of Neurosurgery.

RESULTS

This prospective research was conducted in Islamabad from January 2019-April 2022 and 247 patients were incorporated. Patients' demographics and contacts were duly noted on pre-designed approved questionnaire by Institute of Neurosurgery. Most of the patients had an age over 45 years (51.82%; 128/247), followed by 19-45 years (30.76%; 76/247) and less than 18 years (17.40%; 43/247). Males were affected the most (63.56%; 157/247) than females (36.43%). 70.04% of patients were educated and 29.95% were illiterate, while 52.22% were from rural areas and 47.77% were from urban regions (Table 2).

The MS patients were diagnosed by means of McDonald's 2010 criteria and were classified into 05 classes accordingly, based on the number of clinical attacks, with a number of lesions seen via MRI in SC accompanied with clinical record. Significantly large study population pertained to category 1 (27.53%; 68 patients), subsequently category 2 (23.07%; 57), class 4 (20.64%; 51), class 3 (17.0%; 42), while least number of patients were found in category 5 (11.74%; 29 patients) (Figure 1).

Table 2: Demographic features of patients with SC pseudoatrophy

S. No	Demographic feature	Number of patients (n)	Frequency (%)
1	Age (Years)		
	<18 years	43	17.40
	19-45	76	30.76
	>45	128	51.82
2	Sex		
	Male	157	63.56
	Female	90	36.43
3	Education		
	Literate	173	70.04
	Illiterate	74	29.95
4	Locale		
	Rural	129	52.22
	Urban	118	47.77

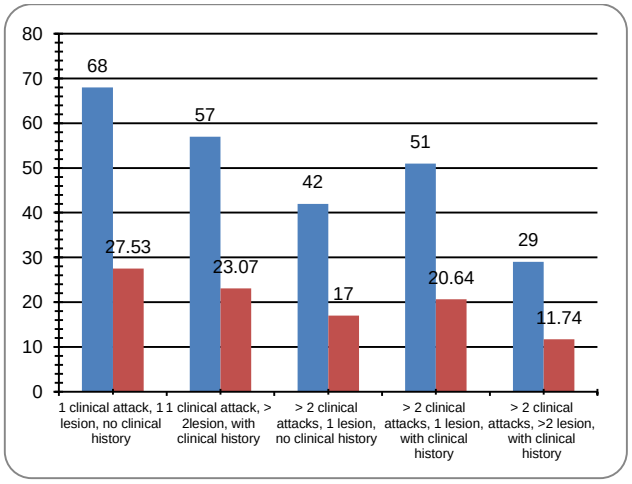

Figure 1: Diagnosis of MS patients using McDonald's 2010 criteria

The status of pertaining to MS disability was evaluated in participants using Kurtzke EDSS scores. All patients with an EDSS score of 2.5 in the early pseudoatrophy stage of the spinal cord in MS patients were selected and treated with interferons, according to the findings of our study. Normal persons have an EDSS score of 0, 1.0 for no disability but minimal signs in one Functional system (FS) score, 1.5 again with no disability but more than one FS score, 2.0 has a minimal disability and with grade 2 FS and EDSS 2.5 meant minimal disability in 2 grade 2 FS scoring system. In our research, all the patients were selected with an EDSS score of 2.5 and subsequently were treated with IFN. After 02 years therapy, EDSS scores were evaluated and it was seen that patients in Group A had EDSS 1.0 and Group B had EDSS 1.5 post-treatment regimen (Table 3). Following two years of treatment, EDSS scores were assessed and it was determined that Group A patients had EDSS levels of 1.0 and Group B patients had EDSS scores of 1.5. The disability of MS of the spinal cord was significantly reduced in both treatment groups administered interferons; however, significantly better results were observed in treatment group A administered three doses weekly (51.41%) followed by one dose weekly (48.51%); and EDSS attainment was significantly reduced from 2.5 to 1.0 and 1.5 respectively.

Table 3: Kurtzke Expanded Disability Status Scale (EDSS) of MS patients

S. No	Group A (Median)		Group B (Median)		χ^2	p-value
	Before treatment	After treatment	Before treatment	After treatment		
1	2.5	1.0	2.5	1.5	0.328	0.566

DISCUSSION

In 1993, US Food and Drug Administration approved recombinant interferon as first disease-modifying remedy for MS ailment of SC. Clinical trials and real-world observational surveys established efficacy of IFN therapy since then. Similarly, our research findings revealed that all patients were selected with an EDSS score of 2.5 by early pseudoatrophy stage of SC of MS-affected individuals and subsequently were treated with interferons. After treatment of 02 years, EDSS scores were evaluated and it was seen that patients in Group A had EDSS 1.0 and Group B had EDSS 1.5 post-treatment regimen. The disability of MS of SC was drastically curtailed in both treatment groups treated through IFN, however, remarkable results were visible in group A treated utilizing three weekly dosage (51.41%) followed by single weekly dosage (48.58%) and EDSS figure was significantly curtailed from 2.5 to 1.0 and 1.5 respectively.

Comparable to our research where MRI demonstrated that therapy with IFN -1a decreased gadolinium-enhancing lesions, T2 and grey matter atrophy compared to placebo. Following the release of intramuscular IFN -1a, array of profound-efficacy medications for MS were approved; however, the benefits of these therapies were weighed against elevated risk of adverse impacts associated to long-term usage. Antiviral features of IFNs also designated therapeutic scenario for IFNs in lowering the risk of other viral infections too [2, 14, 15]. Individuals treated utilizing interferon-beta revealed inclined annual incidence brain volume and cervical cord area alterations in 1st year post-initiation therapeutics, although atrophy rates alleviated at substantially similar level in subsequent year compared to placebo. During 1st year of interferon-beta treatment, findings indicated that pseudoatrophy occurred in brain cum SC [1].

It was demonstrated that progressing MS and RRMS patients had opposing effects on SC volume. They illustrated the drift towards larger cervical cord volumes in RRMS patients exclusively, which they interpreted as expansions owing to inflammation or edema that would disguise real atrophy [16-17]. SC atrophy appeared to be more pronounced than brain atrophy, indicating higher susceptibility towards pathogenic alterations in MS, as evidenced through a significantly deteriorated SC. However, SC atrophy was characterized by a significant degree of inter-individual heterogeneity, for both minute physical elements and confounding impacts like pulsation and motion anomalies during MRI scanning. These effects contributed not only to the inter-individual variability of MUCCA but also to the intra-individual variability between multiple MRI sessions. In addition, MUCCA quantification based on brain MRI was prone to geometrical picture distortions since the upper cervical cord is placed off-center of sagittal images, close to peripheral field view [18-19].

In keeping with a previous study, we observed significantly less GM atrophy was observed but no WM atrophy with IM IFN beta-1a compared to placebo. These results implied that GMF

change was more significant than WMF as a predictor for tissue loss [13, 20].

CONCLUSION

Overall, findings of our research endowed with evidence that PA affected SC and rendered significant lesions in SC diagnosed vide MRI. Spinal cord PA was implied as a biomarker for monitoring treatment effects in MS. The PA in MS-affected patients could significantly be treated in early phases and to diminish the disability of MS of SC in both the treatment groups treated with interferons, however, significantly profound results were seen in patients treated with three weekly doses of IF (51.41%) followed by one dose weekly (48.58%) and EDSS scores were significantly abridged from 2.5 to 1.0 and 1.5 respectively.

Conflict of Interest: None

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