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Beneficial effect of plasma exchange in acute attack of neuromyelitis optica spectrum disorders

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ABSTRACT

Background: Plasma exchange (PLEX) is routinely performed in neuromyelitis optica spectrum disorders (NMOSD) patients with an acute attack who do not respond to corticosteroids treatment.
Objective: To compare treatment outcomes in NMOSD patients with an acute attack between the two groups.
Methods: We retrospectively studied 67 attacks from 52 NMOSD patients. Outcome measurements using Expanded Disability Status Scale (EDSS), modified Rankin Scale (mRS) were compared.
Results: There were 23 IVMP responders, 16 IVMP non-responders refusing PLEX, 12 IVMP non-responders/PLEX responders, and 16 IVMP/PLEX non-responders. The IVMP-responders showed faster improvement since the time of discharge but seemed to have less treatment benefit over time. However, IVMP non-responders/PLEX responders showed continuous and maximum improvement at 6 months (ΔEDSS from nadir: 1 for IVMP-responders vs 0.5 for IVMP non-responders without PLEX vs 2.75 IVMP non-responders/PLEX-responders vs 0.5 IVMP/PLEX non-responders; $p = 0.49$) and had comparable outcomes to the IVMP-responders (nadir EDSS 8.0 to 5.25 [ΔEDSS = 2.75] vs nadir EDSS 6.5 to 5.0; [ΔEDSS = 1.5], respectively).
Conclusion: Add - on PLEX treatment in NMOSD patients with an acute attack should be considered in those not responding to IVMP alone.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disease of the CNS, which is caused by the aquaporin − 4 (AQP4) antibody binding to astrocytic foot processes, resulting in astrocyte injury and finally to oligodendrocyte damage, demyelination, and neuronal loss (Wingerchuk et al., 1999; Pittock et al., 2006). Because disability in NMOSD is attack-related, treatment should be started as early as possible to retain functional capacities (Sato et al., 2012).

High-dose intravenous methylprednisolone (IVMP) 1 g daily for 3–7 consecutive days is often the recommended first treatment for an acute attack in NMOSD while plasma exchange (PLEX) is routinely performed in NMOSD patients who do not respond to treatment with high-dose corticosteroids (Sellner et al., 2010). Recent studies have suggested PLEX may also be used as the first-line therapy, especially in NMOSD with high cervical myelitis/brainstem involvement with respiratory compromise (Collongues and Seze, 2011).

Given that previous retrospective studies have demonstrated favorable clinical outcomes in NMOSD patients in the therapeutic arms treated with add-on PLEX compared with those receiving IVMP alone (Cortese et al., 2011; Kim et al., 2013), we aimed to compare clinical outcomes in NMOSD patients with an acute attack between IVMP treatment alone and IVMP treatment with add - on PLEX.

2. Materials and methods

2.1. Patient eligibility criteria and treatment protocol

We retrospectively reviewed the medical records of NMOSD patients who were admitted at Siriraj Hospital between 2009 and 2016 with an acute attack within 30 days of clinical onset. Eligibility criteria were (1) age 18 years or older, (2) meeting the NMOSD 2015 diagnostic criteria (Wingerchuk et al., 2015), (3) having at least 6 months of follow-up

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Table 1
Baseline characteristics of the 67 attacks in 52 NMOSD patients.

Characteristics	IVMP-responders (n = 23)	IVMP non-responders without PLEX (n = 16)	IVMP non-responders/ PLEX responders (n = 12)	IVMP/PLEX non-responders (n = 16)	P-value
Age at attack: years; mean (SD)	42.7 (12.8)	44.3 (10.5)	41.8 (9.72)	46.0 (16.9)	0.814
18 to < 50 years; n (%)	15 (65.2)	11 (68.3)	9 (75.0)	10 (62.3)	
≥ 50years; n (%)	8 (34.8)	5 (31.3)	3 (25.0)	6 (37.5)	
Female; n (%)	23 (38.4)	15 (23.1)	12 (18.5)	15 (23.1)	0.542
Concomitant diseases; n (%)					
Diabetes mellitus	1 (4.30)	0 (0.00)	0 (0.00)	1 (6.30)	1.000
Hypertension	1 (4.30)	2 (12.5)	0 (0.00)	2 (12.5)	0.476
Dyslipidemia	0 (0.00)	0 (0.00)	2 (12.5)	1 (6.30)	0.281
Malignancy	1 (4.30);DLBCL	1 (6.30);CA Cervix	0 (0.00)	0 (0.00)	1.000
Autoimmune diseases	1 (4.30); SLE	0 (0.00)	0 (0.00)	0 (0.00)	1.000
AQP4-Ab positive; n (%)	23 (100)	14 (87.5)	11 (91.7)	15 (93.8)	0.278
Disease duration: months; median (min-max)	56.7 (0–210)	54 (0–201)	74.6 (0–229)	51.7 (0–209)	0.928
Receiving immunosuppressant; n (%)	13 (56.5)	7 (43.8)	8 (66.7)	10 (62.5)	0.668
Azathioprine	12 (52.0)	6 (37.5)	5 (41.7)	8 (50.0)	
Mycophenolate	0 (0.00)	1 (6.25)	2 (16.7)	1 (6.30)	
Others	1 (4.30)		1 (8.30)	1 (6.30)	
Location of the attacks; n (%)					0.261
Spinal cord	14 (60.9)	8 (50.0)	8 (66.7)	8 (50.0)	
Optic nerve	4 (17.4)	5 (31.3)	0 (0.00)	4 (25.0)	
Brain	3 (13.0)	1 (6.25)	0 (0.00)	0 (0.0)	
Multifocal involvement	2 (8.70)	2 (12.5)	4. (3.33)	4 (25.0)	
Number of prior attacks; median (min - max)	3.5 (1–14)	3 (1–18)	3.5 (1–16)	2.5 (1–15)	0.968
Interval from attack onset to first day of IVMP treatment-days; median (min-max)	6 (0–25)	10.5 (0–21)	6 (1–26)	5 (0–25)	0.539
Interval from attack onset to first day of PLEX-days; median (min-max)	NA	NA	13 (3–29)	12 (7–34)	0.889

Abbreviations: IVMP, intravenous methylprednisolone; NMOSD, neuromyelitis optica disorder; AQP4-Ab, aquaporin − 4 antibody; PLEX, plasma exchange; DLBCL, diffuse large B-cell lymphoma; SLE, systemic lupus erythrematosus; CA cervix, cervical cancer; NA, not applicable.

after the treatment, and (4) having had no relapse at least 90 days prior to the acute attack (Wingerchuk et al., 2015)

The patients were treated with IVMP 1 g daily for 5 consecutive days for acute optic neuritis (ON) or acute myelitis or brain/brainstem attack, followed by tapering off with oral prednisolone within 2 weeks (Beck and Cleary, 1993; Scott et al., 2011; Wingerchuk and Weinshenker, 2008). If a patient was not responding, they then had 1 l of total plasma volume exchanged for a similar volume of 5% albumin on alternate days for 5 sessions (Schwartz et al., 2016).

2.2. Definition of non-responder

The responses were assessed at day 7 after the initiation of IVMP treatment. A non-responder was defined as any of the following:

1) For a transverse myelitis (TM) attack, a non-responder was defined as having no improvement of at least 1 grade of MRC Scale for Muscle Strength (Medical Research Council, 1981).
2) For an ON attack, a non-responder was defined as having no improvement in visual acuity ≥ 2 lines of the near chart vision with a baseline visual acuity ≥ 0.025 or 1 step better if the baseline visual acuity was worse than counting fingers (Lange et al., 2009).
3) For attacks at other locations, a non-responder was defined as having no clinical improvement or worsening symptoms as evaluated by the clinicians.

For those proceeding to have PLEX, we assessed the response after completing the fifth session of PLEX.

2.3. Outcome measurements

We recorded clinical parameters at several time points, namely the admission date, discharge date, as well as at 1-, 3- and 6-month follow-up visits. Clinical parameters recorded included the number of attacks, time to the next attack, Extended Disability Status Score (EDSS) (Kurtzke, 1983), change in EDSS over time, and PLEX-related adverse events. Baseline EDSS was defined as a confirmed EDSS at least 3 months prior to the acute attack. Change in EDSS over time was calculated intraindividually in patients at different time points.

2.3.1. Standard protocol approvals registrations, and patient consents

This study was approved by Siriraj Institutional Review Board, 541/2559 (EC1). All patients provided written informed consent.

2.3.2. Statistical analysis

We used SPSS version 18 for the analyses. Categorical variables were compared using the Chi-squared test or Fisher's exact test. Continuous variables were compared using the t-test or Mann-Whitney *U* test. Predictive factors of response were determined by logistic regression analysis. Significance was considered to be $P < 0.05$. Percentage values were rounded.

3. Results

3.1. Demographic data

A total of 67 attacks occurred in 52 NMOSD patients (3 attacks in 3 patients, 2 in 9 patients, and 1 in 40 patients). The mean number of attacks was 1.29 ± 0.57 attacks per patient. There were 50 female (96.2%) and 2 male (3.8%) with the mean age at the time of the attack of 43.7 ± 12.8 years. The majority of patients had spinal cord attack (56.7%), followed by optic nerve (19.4%) and brain or brainstem involvement (5%). Almost all of the cases had anti AQP4-IgG in the serum (92.3%).

Thirty-nine attacks were treated with IVMP alone including 23 IVMP-responders and 16 IVMP non-responders who refused PLEX (IVMP non-responders/no PLEX). The other 28 attacks were IVMP non-responders who had PLEX, 12 IVMP non-responders who were PLEX responders (IVMP non-responders/PLEX responders), as well as 16 IVMP and PLEX non-responders (IVMP/PLEX non-responders). There were no significant differences between treatment groups in baseline characteristics (Table 1).