Clinical Therapeutics/Volume ▮, Number ▮, 2018

Plasma Exchange for Neuromyelitis Optica Spectrum Disorders in Chinese Patients and Factors Predictive of Short-Term Outcome

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ABSTRACT

Purpose: The purposes of this article were to evaluate the short-term outcome of plasma exchange (PLEX) for neuromyelitis optica spectrum disorders (NMOSDs) in Chinese patients and to identify the factors predictive of a favorable response to therapy.

Methods: We retrospectively analyzed data from 29 Chinese patients with NMOSD. All patients received 2 to 7 sessions of PLEX every other day. Expanded Disability Status Scale (EDSS) scores were estimated at baseline, at relapse, and before and at follow-up after PLEX. Patients were assigned to 1 of 2 groups according to treatment responses of marked to moderate improvement and mild to no improvement.

Findings: Twenty-four of 29 patients (82.8%) showed functional improvement at 1 month after PLEX, 9 of whom experienced moderate to marked improvement. Early PLEX initiation and a lower baseline EDSS score were independent prognostic factors (both, $P < 0.05$). In addition, relapse symptoms of nonoptic neuritis and acute transverse myelitis plus circumventricular organs, seronegativity for aquaporin-4 antibodies, shorter initial therapy–PLEX interval, and no prior optic neuritis attacks were predictive factors significantly associated with a favorable response to treatment (all, $P < 0.05$). The delay time pre-PLEX was inversely correlated with reduction in EDSS score. The percentage reductions in EDSS score in groups receiving PLEX on days ≤15 and days 16 to 30 were significantly greater than those in the groups treated on days 31 to 60 and days 61 to 90 (all, $P < 0.05$). Most PLEX sessions were generally well tolerated.

Implications: PLEX is an effective therapy for NMOSD in the Chinese population, and early PLEX initiation was associated with a favorable response. We recommend an optimum PLEX time of 30 days from the time of disease onset. Further long-term prospective, multicenter studies that include a larger sample of patients with NMOSD treated with PLEX are necessary. (*Clin Ther*. 2018;▮:▮▮▮–▮▮▮)

Key words: Chinese, neuromyelitis optica spectrum disorders, outcome, plasma exchange, predictive factors, short-term.

INTRODUCTION

Neuromyelitis optica (NMO) is an autoimmune CNS-demyelinating disease with a defined autoantibody to aquaporin (AQP)-4 on the surface of astrocytes.[1,2] NMO has historically been considered a rare disease that selectively affects the optic nerves and spinal cord. The prevalence of NMO has increased yearly since the worldwide availability of the AQP4 antibody test (AQP4–immunoglobulin [Ig]G), including in China.[3] Moreover, NMO appears to be a multiorgan disorder [4,5] that is comorbid with other systemic autoimmune diseases.[6] Thus, the International Panel for NMO Diagnosis broadened the definition of NMO and provided a uniform nomenclature for NMO spectrum disorders (NMOSDs) in 2015.[7]

NMOSD relapses tend to be more severe compared with those in multiple sclerosis. Moreover, the disability care load of NMOSD is positively correlated with the number of relapses.[8] Most studies have focused on the prevention of relapses with the administration of various promising immunosuppressants, such as azathioprine and mycophenolate mofetil.[9,10] However,

Accepted for publication March 8, 2018.
https://doi.org/10.1016/j.clinthera.2018.03.007
0149-2918/$ - see front matter

acute-phase or relapse treatment should be considered as the foremost step in recovery. Unfortunately, in most countries, intravenous corticosteroids (IVCSs) are the only choice for NMOSD therapy because of their low cost and accessibility. Problems arise in patients who do not respond promptly to IVCS therapy. The recently emerging monoclonal antibody therapies, especially rituximab, have been recognized as first-line or rescue therapies for NMOSD[11,12]; however, the high cost of these treatments limits their clinical application. Due to the elimination of circulating pathogenic inflammatory mediators (antibodies, complement, and cytokines), plasma exchange (PLEX) has been shown to be a beneficial treatment of NMOSD.[13–16] However, the studies of PLEX in NMOSD have been conducted in Western or other Asian populations. China has one of the highest prevalences of NMOSD[3,17]; yet in China, data related to PLEX therapy for NMOSD remain obscure due to technical restrictions and an insufficient blood supply. To address this issue, we tested the efficacy of PLEX and identified the factors related to a favorable response to PLEX in Chinese patients with NMOSD.

PATIENTS AND METHODS

Patients

Twenty-nine Chinese patients (23 women) experiencing clinically and/or radiologically confirmed relapsing NMOSDs and who were hospitalized at the China-Japan Friendship Hospital (Beijing, China) between October 2010 (when the hospital's electronic medical system was officially launched) and July 2017 were consecutively enrolled. All of the patients received at least 2 sessions of PLEX treatment. None of the patients experienced evidence of new infection or other underlying acute medical conditions.

The 2006 revised neuromyelitis optica diagnostic criteria[18] and the 2015 International Consensus Diagnostic Criteria[7] were used to diagnose NMOSD. AQP4-IgG was analyzed by an independent medical inspection agency that used a cell-based assay (AQP4-IgG test kit; Euroimmun Co, Beijing, China). Serum specimens were collected during the acute phase in 28 cases. As another biomarker, anti–myelin oligodendrocyte glycoprotein antibodies were not recorded in the cases that exhibited seronegativity for AQP4-IgG. The following parameters were retrospectively recorded from the hospital's electronic medical system and were analyzed and compared among the subgroups: demographic data and clinical features, such as clinical course, relapse symptoms, severity, comorbidities (combined with thyroid dysfunction, xerophthalmia, and xerostomia), prior optic neuritis (ON) symptoms, prior number of relapses, AQP4-IgG status, imaging features, and adverse events.

The study protocol was approved by the institutional review board at China-Japan Friendship Hospital, and the need for informed consent was waived by the committee because of the retrospective nature of the study.

Treatment

Patients were considered candidates for PLEX if a limited response or deterioration in neurologic conditions was observed after an initial standard dose of IVCS (methylprednisolone or dexamethasone) or intravenous immunoglobulin (IVIg) treatment, or if severe disabling relapse (Expanded Disability Status Scale [EDSS][19] attack score of ≥6) was determined by at least 2 physicians on admission. All candidates received 2 to 7 sessions of PLEX every other day in the Neurology Department. One volume of plasma (~2-L plasma volume) was exchanged at each session. Fresh frozen plasma and human albumin solution were used as replacement liquid. Promethazine as an antiallergen and heparin as an anticoagulant were used separately before and after each session. The exchanged plasma volume was calculated based on each patient's sex, height, weight, and hematocrit level. Repeated blood analyses after PLEX included blood cell count, coagulation function, electrolyte level, and albumin/globulin concentration.

Clinical Evaluations

Neurologic functions (eg, visual acuity, motor and sensory function, walking ability, and sphincter function) were evaluated, and the EDSS score was obtained at baseline, relapse (attack), before PLEX (pre-PLEX) and after the last PLEX session, and at 1-month follow-up (residual). In order to avoid the effects of oral immunosuppressants or rehabilitation therapies on long-term neurologic improvement, the short-term outcome was evaluated after only 1 month of follow-up. An EDSS score of 0 indicated no neurologic impairment; 1.0 to 3.5, ambulatory status; 4.0 to 7.0, restrictions in mobility; 7.5 to 9.5,