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Original Article

Therapeutic Plasma Exchange for Treating Pediatric Neurological Diseases

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ABSTRACT

Objective: Therapeutic plasma exchange (TPE) is performed in various neurological, hematological, renal and autoimmune diseases. This study was conducted to determine the indications, efficacy, safety and complications of TPE in pediatric autoimmune neurological diseases.

Methods: In this study, patients who were hospitalized in the pediatric intensive care unit of a tertiary university hospital between January 2017 and December 2021 and underwent TPE due to neurological diseases were evaluated retrospectively.

Results: A total of 20 patients were included in the study. Their ages ranged from 6 to 237 months, with a mean age of 63.16±183.12 months. Neurological TPE indications of the patients were autoimmune encephalitis (50%, n=10), Guillain-Barre Syndrome (45%, n=9) and Acute Demyelinating Encephalomyelitis (6.7%, n=1), respectively. Catheter occlusion was observed in 2 (10%) patients, allergic reaction in 1 (5%) patient, and hypotension in 1 (5%) patient as complications of TPE. Muscle strength of patients with GBS was evaluated according to the Medical Research Council scale before transfer to the service. It was determined that the score increased from 0 to 1 in two patients, from 0 to 3 in three patients, and from 1 to 5 in four patients. In 9 of the patients diagnosed with encephalitis, regression of acute phase reactants and improvement in neurological evaluation were observed.

Conclusion: When TPE is applied with appropriate indications and by an experienced team in pediatric neurological diseases, treatment results can are satisfactory, its effectiveness increases and the complication rate decreases.

Keywords: Therapeutic plasma exchange, neurological disease, pediatrics

INTRODUCTION

Therapeutic plasma exchange (TPE) is a treatment method applied to eliminate pathogenic material or components that occur due to a disease and cause morbidity. It is applied to various neurological, hematological, renal and autoimmune diseases. The effectiveness of TPE is associated with the patient's changing plasma volume, the distribution of pathogenic material, and the rate of synthesis. The standard indications have been determined by the American Apheresis Association (ASFA) and are advisory and non-binding.[1] Autoimmune neurological diseases seen mainly in children; Guillain-Barré syndrome (GBS), acute disseminated encephalomyelitis (ADEM) and autoimmune encephalitis.

GBS is an acute, usually symmetrical and typically ascending paralysis disease caused by inflammation of peripheral nerves. Intravenous immunoglobulin (IVIG) is the first choice for treating pediatric patients. Plasma exchange is applied to eliminate

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circulating antibodies or other responsible factors.[2] Early (first 7 days) plasmapheresis significantly reduces morbidity (ASFA category I, grade 1A).

Acute disseminated encephalomyelitis is an inflammatory demyelinating disease of the central nervous system that affects children and young adults. Steroids are the main treatment option. In the absence of adequate response, treatment can be supported with IVIG and plasmapheresis (ASFA category II, grade 2C).[3]

The clinical manifestations of autoimmune encephalitis consist of a wide spectrum, such as seizures, movement disorders, behavioral and mood changes, psychosis, cognitive impairment, and autonomic dysfunction. The treatment includes steroids, IVIG and plasma exchange as first-line therapy (ASFA category I, grade 1C).[4]

This study was conducted to determine the indications, efficacy, safety and complications of TPE in pediatric autoimmune neurological diseases.

MATERIALS AND METHODS

A total of 20 children, 11 (55%) girls and 9 (45%) boys, who were hospitalized in the pediatric intensive care unit (PICU) between January 2017 and December 2021 and underwent TPE due to neurological diseases, were included in the study. IVIG was administered as the first treatment in all the patients, and steroid treatment was also applied in 60% of the patients. Plasma exchange was applied to patients whose clinical and laboratory parameters did not improve.

Plasma exchange was performed at the bedside with a PrismaFlex© (Gambro, Lund, Sweden) device. Fresh frozen plasma (FFP) was preferred as the replacement fluid (19 patients, 95%), and 5% human albumin was used in patients who had an allergic reaction to plasma (1 patient, 5%). It was aimed to replace 1-1.5 times the estimated plasma volume calculated. The formula 70 x weight (kg) x (1-Hct) was used for the estimated plasma volume. Anticoagulation was achieved with citrate or heparin, depending on the clinical condition of each patient. This study was approved by the University of Health Sciences Türkiye, Ümraniye Training and Research Hospital Clinical Research Ethics Committee (approval number: 08.10.2020/323).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc; Chicago, IL, USA) 21 package program. Normality was evaluated with Shapiro-Wilk tests and histogram plots. Data were expressed as mean, minimum, maximum, frequency, and percentage.

RESULTS

The ages of the patients ranged from 6 to 237 months, with a mean age of 63.16±183.12 months. Neurological TPE indications of the patients were autoimmune encephalitis (50%, n=10) GBS (45%, n=9) and Acute Demyelinating Encephalomyelitis (6.7%, n=1), respectively. An average of 4 sessions of TPE (minimum 2, maximum 9 sessions) was applied to the patients. 45% of the patients were followed up with invasive mechanical ventilation and 15% with non-invasive mechanical ventilation. TPE was performed by inserting a double lumen central venous temporary hemodialysis catheter. The internal jugular vein (60%, n=12), femoral vein (35%, n=7) and subclavian vein (5%, n=1) were used for venous access, respectively.

The mean Pediatric Risk of Mortality Score III (PRISM III) score of the patients was calculated as 16.95±9.90. The clinical and demographic data of the patients are summarized in Table 1.

Unfractionated heparin was used mostly in anticoagulant treatment (90%, n=18). The Citrate was preferred (10%, n=2) in patients who underwent TPE with continuous renal replacement therapy. Catheter occlusion was observed in 2 (10%) patients, allergic reaction in 1 (5%) patient, and hypotension in 1 (5%) patient as complications of TPE.

Muscle strength of patients with GBS was evaluated according to the Medical Research Council scale[5] before transfer to the service. It was determined that the score increased from 0 to 1 in two patients, from 0 to 3 in three patients, and from 1 to 5 in four patients. While acute phase reactants regressed and neurological evaluation improved in 9 of the patients diagnosed with encephalitis, one patient died from septic shock. One patient

Table 1. Clinical and demographic data of the patients

		Min.-Max.	Mean ± SD
Age (mounts)		6-237	63.16±183.12
PRISM III score		0-40	16.95±9.90
Total number of sessions		2-9	4.66±2.61
Days in PICU		2-109	23.61±20.45
		n (15)	%
Gender	Female	11	55%
	Male	9	45%
Mechanic ventilaion (MV)	None	8	40%
	IMV*	9	45%
	NIMV**	3	15%
Neurological disease			ASFA indication
Autoimmune encephalitis	10 (50%)		I/1C
Guillain-Barre syndrome	9 (45%)		I/1A
Acute demyelinating encephalomyelitis	1 (5%)		II/2C

*IMV: Invasive mechanical ventilation, **NIMV: Non-invasive mechanical ventilation, Min.: Minimum, Max.: Maximum, SD: Standard deviation, ASFA: American apheresis association, PICU: Pediatric Intensive Care Unit

was transferred by tracheotomy and the other patients were transferred by spontaneous breathing. The mortality rate was 5% in neurological patients who underwent TPE.

DISCUSSION

TPE is successfully applied in various pediatric neuroimmunological diseases, often acute and chronic inflammatory polyneuropathy, acquired demyelinating diseases of the central nervous system, autoimmune encephalitis, paraneoplastic syndromes, and inflammatory vascular diseases of the central nervous system.[6-10]

Özkale et al.[11] reported that the most common indication in 22 pediatric patients who underwent 135 sessions of TPE was inflammatory neuropathy, followed by acquired demyelinating disease, autoimmune encephalitis, and paraneoplastic limbic encephalitis, respectively. In a study published in 2019, in which 58 pediatric patients who underwent TPE due for neurological diseases were evaluated retrospectively, it was reported that 36% of the patients were treated with category I, 27% with category II and 12% with category III according to ASFA criteria (11th). It was stated that before the TPE application, 90% of the patients were given anti-inflammatory/immunomodulator treatments consisting of steroids and 78% IVIG treatment, and the average time between the onset of the disease and the application of TPE was 25.5 days.[12] In our study, TPE was applied to 10 patients with a diagnosis of autoimmune encephalitis, 9 patients with a diagnosis of GBS, and 1 patient with a diagnosis of ADEM. Of these patients, 19 were in the ASFA I category and 1 in the ASFA II category. Two of the patients diagnosed with autoimmune encephalitis had received IVIG, 2 steroids, and 6 IVIG + steroids treatment before TPE application.

Previous studies have showed that response rates with TPE in autoimmune encephalitis range from 47% to 85%.[11,12] All the 5 patients treated with TPE in this study showed mild improvement with a median one point improvement in mRS score. IVIG had been administered before TPE in all patients with autoimmune encephalitis, and indications were dominated by intractable epileptic seizures. Moreover, previous studies have demonstrated that time to TPE seems to be one of the most critical factors for a sufficient response.[13,14]

It has been reported that patients with peripheral nervous system disease respond better to TPE treatment than those with central nervous system disease. Savransky et al.[15] reported that in their study involving 65 pediatric patients who underwent TPE, they observed significant neurological improvement at the end of TPE in 72% of the cases and at 6-month follow-up in 88.5% of them. The authors reported that they did not detect a relationship between the onset of TPE and clinical improvement, unlike studies suggesting that early TPE application within the first 15 days after the onset of the neurological attack is a predictor of 6-month recovery. We also observed that a significant neurological improvement was achieved in the muscle strength evaluation of our patients.

Yıldırım et al.[16] reported in 2021 that; TPE was found to be more effective on GBS, autoimmune encephalitis and myasthenia gravis, less effective on ADEM and febrile infection-related epilepsy syndrome. There was no correlation between improvement with TPE and clinical parameters, including age, sex, diagnosis, disease duration before TPE, presence of intubation, and length of stay in the intensive care unit and hospital.[16]

CONCLUSION

When TPE is applied with appropriate indications by an experienced team in pediatric neurological diseases, treatment results can be satisfactory, its effectiveness increases and the complication rate decrease.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Türkiye, Ümraniye Training and Research Hospital Clinical Research Ethics Committee (approval number: 08.10.2020/323).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.A., S.E., Design: G.A., S.E., H.İ., Data Collection or Processing: H.Y., H.C.T., H.İ., Analysis or Interpretation: H.Y., H.C.T., B.K., Literature Search: G.A., S.E., H.C.T., H.İ., B.K., Writing: G.A., S.E., B.K.

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References

1. Padmanabhan A, Connelly-Smith L, Aqui N, et al. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the Writing Committee of the American Society for Apheresis: the eighth special issue. J Clin Apher. 2019;34:171-354.
2. Hughs RA, Chevret S, Annane D. Plasma exchange for Guillain-Barré syndrome. Cochrane Database Syst Rev. 2017;2:CD001798.
3. Borras-Novell C, García Rey E, Perez Baena LF, Garcia IJ, Cahiz DC, Cambra F. Therapeutic plasma exchange in acute disseminated encephalomyelitis in children. J Clin Apher. 2015;30:335-39.
4. Stingle C, Cardinale K, Van Mater H. An Update on the Treatment of Pediatric Autoimmune Encephalitis. Curr Treat Options Rheumatol. 2018;4:14-28.
5. Hermans G, Clerckx B, Vanhullebusch T, et al. Interobserver agreement of Medical Research Council sum-score and handgrip strength in the intensive care unit. Muscle Nerve. 2012;45:18-25.
6. Korinthenberg R, Trollmann R, Felderhoff-Muser U, et al. Diagnosisi and treatment of Guillain-Barre Syndrome in childhood and adolescence: An evidence-and consensus-based guidline. Eur J Paediatr Neurol. 2020;25:5-16.
7. Wang CX. Assessment and management of acute disseminated encephalomyelitis in the pediatric patient. Paediatr Drugs. 2021;23:213-21.
8. Ipe TS, Meyer EK, Sanford KW, Joshi SK, Wong ECC, Raval JS. Use of therapeutic plasma exchange for pediatric neurological diseases. Clin Apher. 2021;36:161-76.

9. Naik A, Prakash S, Ray GK, Mukherjee S. Variable response to therapeutic plasma exchange in pediatric anti-NMDA receptor encephalitis. Transfus Clin Biol. 2021;28:287-90.
10. Suppiej A, Nosadini M, Zuliani L, et al. Plasma exchange in pediatric anti-NMDAR encephalitis: A systematic review. Brain Dev. 2016;38:613-22.
11. Özkale M, Erol I, Özkale Y, Kozanoğlu İ. Oveview of therapeutic plasma Exchange in pediatric neurology:a single center experience. Acta Neurol Belg. 2018;118:451-58.
12. Eyre M, Hacohen Y, Lamb K, et al. Utility and safety of plasma exchange in paediatric neuroimmune disorders. Dev Med Child Neurol. 2019;61:540-46.
13. Suppiej IA, Nosadini M, Zuliani L, et al. Plasma exchange in pediatric anti-NMDAR encephalitis: a systematic review. Brain Dev. 2016;38:613-22.
14. Nosadini M, Mohammad SS, Ramanathan S, Brilot F, Dale RC. Immune therapy in autoimmune encephalitis: a systematic review. Expert Rev Neurother. 2015;15:1391-419.
15. Savransky A, Rubstein A, Rios MH, et al. Prognostic indicators of improvement with therapeutic plasma exchange in pediatric demyelination. Neurology. 2019;93:E2065-E2073.
16. Yıldırım M, Bektaş OÖ, Botan E, et al. Therapeutic plasma exchange in clinical pediatric neurology practice: Experience from a tertiary referral hospital. Clin Neurol Neurosurg. 2021;207:106823.