ARAŞTIRMA MAKALESİ/ORIGINAL RESEARCH

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Therapetic Plasmapheresis: A Retrospective Study; 12 Years of Single Center Experience

Terapötik Plazmaferez: Retrospektif Çalışma; 12 Yıllık Tek Merkez Deneyimi

Yusuf Hanazay[1], Sibel Gökçay Bek[2], Serkan Bakirdogen[3], Necmi Eren[2], Orkan Dervisoglu[2], Betul Kalender[2]
[1]Kocaeli Universitesi Tip Fakultesi, İç Hastalıkları Anabilim Dalı, Kocaeli, Türkiye
[2]Kocaeli Universitesi Tip Fakultesi, Nefroloji Anabilim Dali, Kocaeli, Türkiye
[3]18 Mayıs Universitesi Hastanesi, Çanakkale, Türkiye

ABSTRACT

INTRODUCTION: Therapeutic plasmapheresis has been used successfully in many systemic diseases for years.In this study, we aimed to examine the medical records of patients undergoing therapeutic plasmapheresis in our hospital and to evaluate the demographic characteristics,clinical and laboratory findings and treatment responses.

METHODS: Data of 268 patients treated with plasmapheresis between 2007 and 2019 in our hospital was analyzed. Demographic data (age, sex), plasmapheresis indications, number of sessions, use of immunosuppressive or intravenous immunoglobulin (IVIG), type of procedure, replacement fluid, response to treatment, laboratory values were analyzed.

RESULTS: TPE procedure was applied to 178 of 268 patients, DFPP procedure to 78, and lipid apheresis to 12. Of 178 patients who underwent TPE procedure, 92 were female (51.7%), 86 were male (48.3%), 38 of 78 patients who underwent the DFPP procedure were female (48.7%), 40 were male (51.3%), 5 of 12 patients who underwent lipid apheresis were female (41.7%), 7 male (58.3%). Hypotension in 23 (18.9%), allergic reaction in 5 (4.1%), fever in 1 (0.8%), and hypocalcemia in 1 (0.8%) and catheter-related problem 1(0.8%) were detected. The most common indications for TPE were TTP, HUS, ANCA-associated vasculitis, GBS and MG. Immunosuppressive was used in 107 patients (61.1%) and IVIG was used in 35 patients (20%) who underwent TPE. Albumin was used as a replacement fluid in 104 (62.3%) patients, and fresh frozen plasma (FFP) was used as a replacement fluid in 63 (37.7%).

DISCUSSION AND CONCLUSION: More studies are still needed on theraupetic plasmaphresis' role in diseases such as diabetic foot, ANCA-associated vasculitis.

Keywords: plasmapheresis, therapeutic plasma exchange, double filtration plasmapheresis

ÖZ

GİRİŞ ve AMAÇ: Terapötik plazmaferez yıllardır birçok sistemik hastalıkta başarıyla kullanılmaktadır. Bu çalışmada hastanemizde terapötik plazmaferez uygulanan hastaların tıbbi kayıtlarını inceleyerek demografik özellikleri, klinik ve laboratuvar bulguları ile tedavi yanıtlarını değerlendirdik.

YÖNTEM ve GEREÇLER: Ocak 2007 ile Aralık 2019 tarihleri arasında hastanemizde plazmaferez tedavisi gören 268 hastanın verileri analiz edildi. Demografik veriler (yaş, cinsiyet), plazmaferez endikasyonu, seans sayısı, immünosupresif ve ya intravenöz immünoglobulin (İVİG) kullanımı, işlem tipi, replasman sıvısı, tedaviye yanıt, işlem öncesi ve sonrası laboratuvar değerleri incelendi.

BULGULAR: 268 hastanın 178'ine terapötik plazma değişimi, 78'ine çift filtrasyon plazmaferez prosedürü ve 12'sine lipid aferez işlemi uygulandı. Terapötik plazma değişimi uygulanan 178 hastanın 92'si (%51,7) kadın, 86'sı erkekti (%48,3), çift filtrasyon plazmaferez işlemi uygulanan 78 hastanın 38'i kadın (%48,7), 40'ı erkek (%51,3), lipid aferezi yapılan 12 hastanın 5'i (%41,7) kadın, 7'si erkek (%58,3) idi.). 23 hastada (%18,9) hipotansiyon, 5 hastada (%4,1) alerjik reaksiyon, 1 hastada (%0,8) ateş, 1 hastada (%0,8) hipokalsemi ve 1 (0.8%) hastada katetere bağlı problem saptandı. 35 farklı hastalıkta 268 hastanın terapötik aferez ile tedavi edildiği belirlendi. Terapötik aferez için en yaygın tanılar TTP, HUS, ANCA ile ilişkili vaskülit, GBS ve MG idi. Terapötik plazma değişimi uygulanan 107 hastada (%61.1) immünosupresif, 35 hastada (%20) İVİG kullanıldı. Terapötik plazma değişimi Terapötik plazma değişimi uygulanan 104 (%62,3) hastada replasman sıvısı olarak albümin, 63 (%37,7) hastada replasman sıvısı olarak taze donmuş plazma (TDP) kullanıldı.

TARTIŞMA ve SONUÇ: Terapötik aferezin diyabetik ayak, ANCA ilişkili vaskülit gibi hastalıklardaki rolü ile ilgili daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: plazmaferez, terapötik plazmaferez, çift filtrasyon plazmaferez

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Correspondence: Sibel Gökçay Bek, Kocaeli Universitesi Tıp Fakultesi, Nefroloji Anabilim Dali, Kocaeli, Türkiye
E-mail: beksibel@gmail.com
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INTRODUCTION

The aim of therapeutic plasmapheresis is to reduce the damage caused by the pathological process to the organism by reducing plasma components known to be effective in the etiopathogenesis of various diseases or to reverse this damage to a certain degree. Examples are various proteins, cryoglobulins, immunocomplexes, lipoproteins, autoantibodies, alloantibodies, and toxins found in plasma that may be responsible for disease pathogenesis and are considered harmful to patients (1). Therapeutic plasmapheresis has been used successfully in many systemic diseases for years (thrombotic thrombocytopenic purpura, myasthenia gravis, familial hypercholesterolemia, etc.) and has provided a significant reduction in mortality and morbidity (2). In this study, we aimed to retrospectively examine the medical records of patients undergoing therapeutic plasmapheresis in our hospital and to evaluate the demographic characteristics, clinical and laboratory findings and treatment responses.

MATERIAL and METHODS

We analyzed data from 268 patients treated with plasmapheresis between January 2007 and December 2019 in our hospital. This study was accepted by University Ethical Committee with the document number KOU-GOKAEK-2019/328. The data were obtained by retrospectively examining the hospital information record system and apheresis unit file records. The inclusion criteria included all of the plasmapheresis done for adult patients who are older than 18 years old. The indications were evaluated and planned by nephrology, hematology, endocrinology, dermatology, hepatology and neurology according to the disease treated. Demographic data (age, sex), plasmapheresis indication, number of sessions, use of immunosuppressive or intravenous immunoglobulin (IVIG), type of procedure, replacement fluid, response to treatment, and laboratory values before and after the procedure were analyzed.

Fresenius multiFiltrate 4008S (Fresenius Medical Care Deutschland GmbH, Hamburg, Germany) and Plasauto EZ Asahi (Asahi Kasei Kuraray Medical Co, Tokyo, Japan) devices were used for plasmapheresis procedures. Hemodynamic parameters were followed throughout the procedure. For the calculation of replacement fluid volume, plasma volume (The formula L) = weight × 0.065 × (1 - hematocrit) was used. Fresh frozen plasma and 20% human albumin (isotonic saline diluted to 5% albumin) were used as replacement fluid. Antihistamines and intravenous calcium replacement were not routinely applied as premedication in our center, they were applied in case of symptoms. Heparin was preferred in all procedures requiring anticoagulation

The indications of therapeutic plasma exchange (TPE) were principally based on the relevant guideline of the American Society for Apheresis (ASFA) (3). The response to treatment was graded as complete (CR), partial (PR), or none (NR). Resolution of all the pathological clinical and laboratory findings following an adequate number of TPE was defined as a complete response. Patients with no improvement in clinical and laboratory findings after TPE sessions were identified as non-responders. The partial response includes clinical and laboratory results not fitting into both of the aforementioned categories.

Continuous variables were expressed as means± SD, and categorical variables were expressed as proportions. Differences in continuous variables were evaluated using a t-test. Categorical variables were compared using the chi-square test. The p-values less than 0.05 were considered significant. Statistical analyses were performed using SPSS version 25.0 for Windows software (International Business Machines, Armonk, NY).

RESULTS

The therapeutic plasma exchange (TPE) procedure was applied to 178 of 268 patients, the double filtration plasmapheresis (DFPP) procedure to 78, and lipid apheresis to 12. Of 178 patients who underwent TPE procedure, 92 were female (51.7%), 86 were male (48.3%), 38 of 78 patients who underwent the DFPP procedure were female (48.7%), 40 were male (51.3%), 5 of 12 patients who underwent lipid apheresis were female (41.7%), 7 male (58.3%). The mean age of those who underwent TPE was 47±16.6, the mean age of those who underwent DFPP was 49.5±17, and the mean age of those who underwent lipid apheresis was 44±15. 1549 sessions of TPE (70%), 600 sessions of DFPP (27%), and 55 sessions of lipid apheresis (3%) were applied. Of 235 patients whose viral serology information was available, 3 of them were positive for hepatitis B (1.2%) and 2 for hepatitis C positive (0.8%). Human immunodeficiency virus(HIV), hepatitis B, and hepatitis C were negative in 230 patients (98%). No complications were observed in 91 of 122 patients (74.6%) during the therapeutic apheresis procedure. Hypotension in 23 patients (18.9%), allergic reaction in five patients (4.1%), fever in one patient (0.8%), and hypocalcemia in one patient (0.8%) and catheter-related complication (0.8%) in one patient were detected (Table 1).

Table 1- Complications During All Treatment Sessions

Complications	Number of patients(n)	Percent %
None	91	74,6
Hypotension	23	18,9
Allergic reaction	5	4,1
Fever	1	0,8
Hypocalcemia	1	0,8
Catheter-related problem	1	0,8
Total	122	100

The diseases in which therapeutic apheresis was applied, the number of sessions and treatment responses are shown in Table 2. It was determined that 268 patients were treated with therapeutic apheresis in 35 different diseases. Patients were divided into four subgroups according to their diagnosis: Hematology, nephrology-rheumatology, neurology and other. Nephrology-rheumatology and neurology groups constituted the largest subgroups. The most common diagnoses for therapeutic apheresis were thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), ANCA-associated vasculitis, Guillain-Barre Syndrome (GBS) and myasthenia gravis (MG). Immunosuppressive was used in 107 patients (61.1%) and intravenous immuneglobulin (IVIG) was used in 35 patients (20%) who underwent TPE. No additional treatment was used in 33 patients (18.9%).Immunosuppressive was used in 30 patients(38,5%) and IVIG was used in 16 patients(20.5%) who underwent DFPP. In 32 patients (41%) no medication was used as an adjunctive treatment. Immunosuppressive agents were used in 24 (92.3%) of TTP patients, IVIG was used in 20 (66.7%) of GBS patients, ımmunosuppressive agents were used in 19 (73%) of ANCA- associated vasculitis patients, IVIG was used in 11 (57.9%) of MG patients. Albumin was used as a replacement fluid in 104 (62.3%) patients, and fresh frozen plasma (FFP) was used as a replacement fluid in 63 (37.7%) patients who underwent TPE. FFP was used as a replacement fluid in all TTP patients.FFP was used as a replacement fluid in 72% and albumin was used in 27.8% of the patients with HUS. Albumin was used in 81% and FFP was used in 19% of the patients with ANCA- associated vasculitis. Albumin was used in 91.7% and FFP was used in 8.3% of the patients with MG. Albumin was used in 80% and FFP was used in 20% of the patients with GBS. During their hospital stay, 22 patients (8.2%) died as a result of various morbidities, complications, or unresponsiveness to treatment. There was no patient who died during the plasmapheresis procedure. The mortality rate in TTP was % 15.4, 5% in HUS, 11.5% in ANCA- associated vasculitides, and 10.3% in GBS. No patient died with the diagnosis of MG. The changes in laboratory values before and after the TPE procedure are shown in Table 3. The change in laboratory values before and after the DFPP procedure is shown in Table 4. A significant increase in Hgb(p=0.002), Hct(p=0.001), platelet (p<0.001) values was found after the procedure in patients who underwent therapeutic plasmapheresis due to TTP. LDH(p=0.001), T.bil(p=0.001), I.bil(p=0.001), creatinine (p=0.019) values were found to decrease significantly after plasmapheresis in patients with TTP. In patients who underwent therapeutic plasmapheresis for HUS, there was a significant increase in Plt(p=0.001) after the procedure. LDH(p<0.001),T.bil(p<0.001),I.bil(p=0.001), creatinine(p<0.001)) values decreased significantly after the procedure in patients with HUS. A significant decrease was found in LDH (p<0.001), Plt(p=0.001), creatinine (p=0.001) values after the procedure in patients who underwent therapeutic plasmapheresis due to ANCA-associated vasculitis. There was no significant change in Hgb, Hct, Plt, Ldh, total and indirect bilirubine, creatinine values after the procedure in patients who underwent therapeutic plasmapheresis for MG and GBS. When the seasonal distribution of therapeutic plasmapheresis procedures was evaluated, it was determined that 84 patients (31.3%) were treated in winter, 66 patients (24.6%) in autumn, 61 patients (24.6%) in summer, 57 patients (21.3%) in spring.

Table 2-Primary Diseases and Treatment Responses

Primary Disease	**Number of patients**	**Number of sessions**	**Treatment Response**		
			NR	**PR**	**CR**
HEMATOLOGY	61	740			
TTP	26	356	4	5	17
HUS	20	271	2	10	8
Multiple Myeloma	9	50	5	3	1
ABO incompatibility	2	43	0	0	2
HELLP Syndrome	2	13	0	0	2
Autoimmune hemolytic anemia	1	2	0	1	0
Waldenstrom Macroglobulinemia	1	5	0	1	0
NEPHROLOGY-RHEUMATOLOGY	86	729			

ANCA-associated vasculitis	26	247	5	19	2
Crescentic Glomerulonephritis	17	148	8	6	3
Systemic Lupus Erythematosus	8	82	2	6	0
FSGS	7	50	1	3	3
Recurrent FSGS	7	56	3	4	0
Membranoproliferative glomerulonephritis	4	28	0	3	1
Acute renal allograft rejection	4	28	1	2	1
Chronic Transplant Nephropathy	4	16	1	3	0
Anti GBM disease	4	36	2	2	0
Henoch Schonlein Purpura	2	13	0	2	0
Minimal Change Disease	1	7	0	0	1
Membranous Glomerulonephritis	1	9	0	1	0
Poststreptococcal Glomerulonephritis	1	9	0	0	1
NEUROLOGY	80	450			
GBS	30	159	9	13	8
MG	19	104	1	15	3
Transverse Myelitis	10	60	3	7	0
NMO	8	52	0	8	0
Polyneuropathy	6	27	4	2	0
Multiple Sclerosis	5	36	1	4	0
Autoimmune Encephalitis	2	12	1	1	0
OTHERS	41	285			
Diabetic Foot	18	154	17	1	0
Hyperlipidemia	12	55	0	0	12
Pemfigus Vulgaris	4	30	3	1	0
Drug Eruption	3	15	1	2	0
Necrobiosis Lipoidica	1	14	0	1	0
Sudden Hearing Loss	1	12	0	1	0
Crohn's Disease	1	3	0	1	0
Thyrotoxicosis	1	2	0	1	0

Thrombocytopenic Purpura(TTP), Hemolytic Uremic Syndrome (HUS), Neuromyelitis Optica (NMO), Focal segmental glomerulosclerosis (FSGS) , Guillain-Barré Syndrome (GBS), Myastenia Gravis (MG)

Table 3- Evaluation of Laboratory Values before and After TPE

	n	Before(Mean±SD)	After(Mean±SD)	p
WBC(10^3/µL)	165	11,1±5,6	10,5±6,07	0,228
Neu(10^3/µL)	167	8,76±5,27	8,1±5,34	0,143
Hgb(g/dl)	168	10,3±2,66	10,3±2	0,836
Hct	168	30,5±8,11	30,7±6,1	0,720
Plt(10^3/µL)	168	199,2±129,6	200,2±89,3	0,920
Cre(mg/dl)	174	2,56±2,45	1,72±1,63	<0,001
LDH(U/L)	125	560±586	307±375	<0,001
ALT(U/L)	163	30,2±29,4	27,5±46,3	0,510
AST(U/L)	160	30±35,7	24±22,6	0,016
ALP(U/L)	108	82,2±67,3	66,6±58,9	0,024
T.Bil(mg/dl)	111	1,68±3,92	0,78±0,83	0,012
I.Bil(mg/dl)	110	0,93±1,3	0,49±0,42	0,001
Na(mEq/L)	166	137,5±5,5	138,6±4,2	0,009
K(mEq/L)	173	4,04±0,68	4,03±0,56	0,827
Ca(mg/dl)	173	8,82±0,66	8,84±0,61	0,664
Cl(mEq/L)	157	102,78±5,96	103,35±5,41	0,249
CRP(mg/L)	162	47,54±60,56	18,33±35,67	<0,001

WBC:white blood cell, Neu:neutrophil, Hgb:Hemoglobin, Hct:Hematocrit, Plt:Platelets, Cre:creatinine, LDH: Lactate Dehydrogenase, ALT:Alanine Transaminase, AST:Aspartat Transaminase, ALP:Alkaline Phosphatase, T.Bil:Total Bilirubin, İ.Bil:Indirect Bilirubin, Na:Sodium, Cl:chlorine, Ca:Calcium, K:Potassium, CRP: C reactive protein

Table 4- Evaluation of Laboratory Values before and after DFPP

	n	Before(Mean±SD)	After(Mean±SD)	p
WBC(10^3/µL)	75	9,9±6,3	10,9±6,1	0,298
Neu(10^3/µL)	75	7,6±5,8	8,3±5,3	0,424
Hgb(g/dl)	76	10,7±2,2	10,9±2	0,341
Hct	76	31,9±7,1	32,2±6,3	0,675
Plt(10^3/µL)	75	267,2±125,1	260,8±120,5	0,642
Cre(mg/dl)	77	2,26±2,3	1,91±1,91	0,094
LDH(U/L)	44	373,7±363,4	323,5±359,2	0,459
ALT(U/L)	66	30,1±32,3	31,2±33,5	0,828
AST(U/L)	66	23,7±21	27,2±32,7	0,422
ALP(U/L)	41	91,5±64	77,1±102,3	0,389
T.Bil(mg/dl)	35	0,72±0,51	0,54±0,35	0,016
I.Bil(mg/dl)	35	0,42±0,32	0,26±0,15	0,002
Na(mEq/L)	75	136,6±4,9	137±4,3	0,580
K(mEq/L)	77	4,1±0,71	4,3±0,61	0,182
Ca(mEq/L)	76	8,9±0,64	8,7±0,53	0,004
Cl(mEq/L)	65	105,5±5,6	106,1±4,5	0,413
CRP(mg/L)	69	42,4±47,5	22,7±32,2	0,003

WBC: white blood cell, Neu:neutrophil, Hgb:Hemoglobin, Hct:Hematocrit, Plt:Platelets, Cre:creatinine, LDH:Lactate Dehydrogenase, ALT:Alanine Transaminase, AST:Aspartat Transaminase, ALP:Alkaline Phosphatase, T.Bil:Total Bilirubin, İ.Bil:Indirect Bilirubin, Na:Sodium, Cl:chlorine, Ca:Calcium, K:Potassium, CRP: C reactive protein

DISCUSSION

Therapeutic plasmapheresis is a treatment modality that has been used successfully for more than 40 years, with proven effectiveness in suppressing exacerbations in life-threatening acute conditions of diseases where cytotoxic treatment and/or conventional treatments are not fast effective which saves time for the patient and the physician (2,4).

In a study examining the apheresis data of 15651 patients, it was reported that 42% of all patients were women, and TPE was the most applied procedure among 104000 procedures, with a rate of 28% (5). In a study in which 845 therapeutic apheresis procedures applied to 114 patients were examined, it was reported that the most applied procedure was TPE (92%) which was applied 778 times, followed by fewer platelet apheresis, DFPP, and leukocyte apheresis procedures (6). In our study, the TPE procedure was the most frequently applied procedure type. The DFPP was the second most frequently applied procedure. The reason for the higher frequency of DFPP procedures compared to other clinics seems to be that it is especially preferred by our clinicians in different indications (diabetic foot, GBS, FSGS, etc.)

The prevalence of hepatitis B has been reported to be between 2-7% and the prevalence of hepatitis C has been reported to be between 1-2.5% in our country (7). The fact that our hepatitis B prevalence was lower than the literature may be related to our low sample number, while our hepatitis C prevalence was found to be

compatible with the national prevalence.

In a study, the complication rate in therapeutic apheresis procedures was reported to be between 5-12%. Among the complications, hypocalcemia was reported to be the most common with 1.5-9%, hypotension was the second with 0.4-4.2%, and urticaria and anaphylactic reactions were less frequent (8). No complications were observed in 91 of our 122 patients. The most common complication was hypotension observed in 23 patients .Allergic reactions were observed in 4 patients . Hypocalcemia was observed in 1 patient . The low rate of hypocalcemia seems to be related to not using citrate as an anticoagulant. We did not have any patients who died during the apheresis procedure.

In a study by the Canadian Apheresis Group, the most common indications for therapeutic apheresis procedures were TTP (38.8%), MG (14.4%), and GBS (6.2%), respectively.(9) In another study conducted in France, the most common indications for therapeutic plasmapheresis procedures were MG, GBS, TTP, and HUS, respectively.(10) Our most common therapeutic apheresis indications were GBS, TTP, ANCA-associated vasculitis, HUS, MG, diabetic foot, crescentic glomerulonephritis. Our indications were mostly hematological and neurological indications. The indications reported in the study were in accordance with the literature.

In acute diseases such as TTP and GBS, plasma exchange is recommended until the patient's clinic improves and laboratory values return to normal (2). Our indications with the high number of sessions were TTP, HUS, ANCA-associated vasculitis, and crescentic glomerulonephritis, GBS, and MG. Patients diagnosed with TTP and GBS were initially taken to plasmapheresis every day, and then every other day plasmapheresis was applied according to clinical response and laboratory values.

In the treatment of TTP and HUS, plasma exchange with FFP or cryosupernatant is recommended (11). The preferred replacement fluid in all of our TTP patients was FFP. FFP was preferred in HUS patients. In a randomized controlled study conducted with 110 GBS patients in France, the patients were divided into 2 groups those treated with FFP and those treated with albumin, although there was no significant difference in treatment response in both groups, albumin was found to have a lower side-effect profile;therefore, it has been suggested that albumin should be preferred primarily for plasma exchange in GBS (12).

While mortality rates in TTP were almost 100% until the 1960s, significant improvement in mortality rates was observed with the use of corticosteroids, plasma infusion, and plasma exchange in the treatment, and mortality rates decreased to 10-20%; however, mortality rates are still high (11). Our mortality rate was found to be 15.4% in TTP patients. It is recommended to use rituximab in patients who do not respond to therapeutic plasma exchange with FFP in the treatment of TTP (13). Complete response or partial response was obtained in 22 of our 26 patients with TTP (84.6%), and rituximab was used in 4 patients (15.4%) without response. Although mortality rates in GBS are reported to be between 4-7%, it has been reported that the mortality rate in the acute phase is up to 20%.(14,15) Our mortality rate in GBS was found to be 10.3%.

A total of 247 sessions of plasmapheresis were applied to 26 patients with ANCA-associated vasculitis. Therapeutic plasma exchange was applied to 22 patients, DFPP was applied to 4 patients. Albumin was used as a replacement fluid in 18 patients, and FFP was used in 4 patients who underwent TPE for ANCA-associated vasculitides. In ANCA-associated vasculitis, primarily albumin is recommended as a replacement fluid, and if there is diffuse alveolar hemorrhage, the use of FFP is recommended (3). In the PEXIVAS study, it was revealed that plasma exchange did not have an additional benefit in the development of all-cause mortality or end-stage renal disease, and low-dose corticosteroid therapy was similarly effective in controlling the disease. In the MEPEX study, it was shown that although therapeutic plasmapheresis did not benefit survival, it improved renal function within 3-12 months following treatment (16,17). When the pre-and post-procedure creatinine values of our patients who underwent plasmapheresis for ANCA-positive vasculitis were compared, the mean creatinine was 5±2.7 before the procedure, and 3.1±2 after the procedure, and it was observed that there was a significant decrease in creatinine after the procedure. Although studies show that immunosuppressive drugs are successful in the remission of the disease in severe-onset systemic involvement, more randomized controlled studies are needed on plasmapheresis treatment in ANCA-associated vasculitis.

Plasmapheresis in MG is recommended at category I evidence level for acute myasthenic crisis and category II for long-term therapy (3). It has been stated that plasmapheresis may be as effective as IVIG therapy in severe MG (18). In another study, the effectiveness of IVIG and plasmapheresis were compared and it was found that there was no statistical difference between the two treatment methods. However, it was stated that patients who received plasmapheresis and IVIG together showed improvement after one week, while patients who received only IVIG showed improvement after four weeks (19). It was determined that IVIG was used in the treatment of 11 of our 19 patients who underwent plasmapheresis for MG. Therapeutic plasmapheresis in GBS is recommended by ASFA at category I (3). In a randomized controlled study in which 383 adult patients compared TPE alone, IVIG alone, and IVIG followed by TPE treatments in GBS, no difference was found in the

treatment response in the 3 groups (20). In a study conducted in India, plasmapheresis was found to be more effective and cost-effective than IVIG (21). A total of 159 sessions of plasmapheresis were applied to 30 patients due to GBS. IVIG was used in 20 of 30 patients . In our hospital, IVIG treatment was generally used before plasmapheresis treatment. Which treatment modality will be applied in GBS and MG should be evaluated on a case-by-case basis.

Although rheopheresis and lipid apheresis are recommended in the treatment of diabetic foot, clinics performing DFPP have also been reported (22,23). In the study performed by 8 patients with type 2 diabetes, rheopheresis was applied in addition to classical wound care for diabetic foot, significant wound healing was found in 4 patients, partial wound healing was found in 2 patients and prolongation in the time to amputation, and no response was obtained in 2 patients (23). In another study conducted with diabetic foot patients, a significant improvement was observed in wound healing after 4-5 sessions of plasmapheresis in 19 patients. It was stated that this may be related to the removal of molecules such as LDL cholesterol, fibrinogen, fibronectin, and vWF from the blood as a result of plasmapheresis. It has been stated that plasmapheresis can be applied to narrow the amputation margin (24). In our center, 17 of 18 patients (94.4%) who underwent DFPP due to diabetic foot syndrome did not respond to the treatment and the patients underwent amputation within 6-12 months following the procedure. The reason for our patients to undergo amputation may be related to their late admission and uncontrolled diabetes. Although our study is retrospective, it may guide the plasmapheresis efficiency in the treatment of diabetic foot. Randomized controlled studies are still needed on the efficacy of plasmapheresis in the treatment of diabetic foot.

It has been reported that there may be an increase in autoimmune disease exacerbations in winter and autumn due to various factors (viral infections, low vitamin D) (25). In a retrospective cohort study of GBS patients, the incidence of GBS was 14% higher in winter than in summer (26). Considering the seasonal distribution of the number of patients who underwent therapeutic plasmapheresis, it was determined that more patients were treated in the winter and autumn seasons.

Conclusion

Therapeutic apheresis plays an important, safe and effective adjuvant treatment for several diseases with lesser complication rates and better mortality and morbidity outcomes.

Ethics Committee Approval: This study was approved by University Ethical Committee with the document number of KOU-GOKAEK-2019/328.

Authors' contributions:

Sibel Gokcay Bek: Data collection, Research idea and study design, data acquisition, data analysis/interpretation, statistical analysis, supervision or mentorship ; Serkan Bakırdogen: Research idea and study design, data acquisition, data analysis/interpretation, statistical analysis; Necmi Eren: Data acquisition, data analysis/interpretation; Yusuf Hanazay: Data collection, Research idea and study design, data acquisition, data analysis/interpretation, statistical analysis; Erkan Dervişoğlu: Data acquisition; Betul Kalender Gonullu: Supervision or mentorship

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REFERENCES

1.McLeod B. Rationales for therapeutic apheresis. Hematology. 2005 Sep;10(sup1):203.

2. Szczepiorkowski ZM, Winters JL, Bandarenko N, Kim HC, Linenberger ML, Marques MB, et al. Guidelines on the use of therapeutic apheresis in clinical practice--evidence-based approach from the Apheresis Applications Committee of the American Society for Apheresis. J Clin Apheresis. 2010;25(3):83–177.

3.Padmanabhan A, Connelly-Smith L, Aqui N, Balogun RA, Klingel R, Meyer E, 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 Apheresis. 2019 Jun;34(3):171–354.

4.Ward DM. Conventional apheresis therapies: a review. J Clin Apheresis. 2011;26(5):230.

5.Stegmayr B, Newman E, Witt V, Derfler K, Leitner G, Eloot S, et al. Using the World Apheresis Association Registry Helps to Improve the Treatment Quality of Therapeutic Apheresis. Transfus Med Hemotherapy. 2021 Jan 5;1–6.

6.Kadikoylu G, Yavasoglu I, Ozkul A, Akyol A, Yukselen V, Guney E, et al. The single center registry for therapeutic apheresis in Turkey: 11-year activity. Transfus Apher Sci. 2012 Aug;47(1):61–5.

7.Te HS, Jensen DM. Epidemiology of Hepatitis B and C Viruses: A Global Overview. Clin Liver Dis. 2010 Feb;14(1):1–21.

8.Mokrzycki MH, Kaplan AA. Therapeutic Plasma Exchange: Complications and Management. Am J Kidney Dis. 1994 Jun 1;23(6):817–27.

9.Clark WF, Rock GA, Buskard N, Shumak KH, LeBlond P, Anderson D, et al. Therapeutic plasma exchange: an update from the Canadian Apheresis Group. Ann Intern Med. 1999 Sep 21;131(6):453–62.

10.Korach J-M, Petitpas D, Paris B, Bourgeade F, Passerat V, Berger P, et al. Plasma exchange in France: Epidemiology 2001. Transfus Apher Sci Off J World Apher Assoc Off J Eur Soc Haemapheresis. 2003

Oct;29(2):153–7.
11.George JN. How I treat patients with thrombotic thrombocytopenic purpura-hemolytic uremic syndrome. Blood. 2000 Aug 15;96(4):1223–9.
12.French Cooperative Group on Plasma Exchange in Guillain-Barré syndrome Efficiency of plasma exchange in Guillain-Barré syndrome: role of replacement fluids. Ann Neurol. 1987 Dec;22(6):753–61.
13.Joly BS, Coppo P, Veyradier A. Thrombotic thrombocytopenic purpura. Blood. 2017 25;129(21):2836–46.
14.Alshekhlee A, Hussain Z, Sultan B, Katirji B. Guillain-Barre syndrome - Incidence and mortality rates in US hospitals. Neurology. 2008 May 1;70:1608–13.
15. Berg B van den, Bunschoten C, Doorn PA van, Jacobs BC. Mortality in Guillain-Barré syndrome. Neurology. 2013 Apr 30;80(18):1650–4.
16.Jayne DRW, Gaskin G, Rasmussen N, Abramowicz D, Ferrario F, Guillevin L, et al. Randomized Trial of Plasma Exchange or High-Dosage Methylprednisolone as Adjunctive Therapy for Severe Renal Vasculitis. J Am Soc Nephrol. 2007 Jul 1;18(7):2180–8.
17.Walsh M, Merkel PA, Peh CA, Szpirt W, Guillevin L, Pusey CD, et al. Plasma exchange and glucocorticoid dosing in the treatment of anti-neutrophil cytoplasm antibody associated vasculitis (PEXIVAS): protocol for a randomized controlled trial. Trials. 2013 Mar 14;14(1):73.
18. Gajdos P, Chevret S, Clair B, Tranchant C, Chastang C. Clinical trial of plasma exchange and high-dose intravenous immunoglobulin in myasthenia gravis. Myasthenia Gravis Clinical Study Group. Ann Neurol. 1997 Jun;41(6):789–96.
19.Rønager J, Ravnborg M, Hermansen I, Vorstrup S. Immunoglobulin treatment versus plasma exchange in patients with chronic moderate to severe myasthenia gravis. Artif Organs. 2001 Dec;25(12):967–73.
20.Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome. Lancet Lond Engl. 1997 Jan 25;349(9047):225–30.
21. Cost-minimization analysis in the Indian subcontinent for treating Guillain Barre Syndrome patients with therapeutic plasma exchange as compared to intravenous immunoglobulin - Maheshwari - 2018 - Journal of Clinical Apheresis - Wiley Online Library [Internet]. [cited 2021 Feb 19]. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/jca.21646
22.Lumlertgul D, Suteeka Y, Tumpong S, Bunnachak D, Boonkaew S. Double Filtration Plasmapheresis in Different Diseases in Thailand. Ther Apher Dial. 2013;17(1):99–116.
23. Klingel R, Mumme C, Fassbender T, Himmelsbach F, Altes U, Lotz J, et al. Rheopheresis in patients with ischemic diabetic foot syndrome: results of an open label prospective pilot trial. Ther Apher Dial Off Peer-Rev J Int Soc Apher Jpn Soc Apher Jpn Soc Dial Ther. 2003 Aug;7(4):444–55.
24.Voinov VA. Plasmapheresis in Diabetic Foot Syndrome Treatment. Recent Res Endocrinol Metab Disord. 2021 Jan 12;3(1):1–6.
25. Ogura T, Kameda H. Autoimmune diseases and seasonal variations. Nihon Rinsho Meneki Gakkai Kaishi. 2014;37(1):25–32.
26. Webb AJS, Brain SAE, Wood R, Rinaldi S, Turner MR. Seasonal variation in Guillain-Barré syndrome: a systematic review, meta-analysis and Oxfordshire cohort study. J Neurol Neurosurg Psychiatry. 2015 Nov;86(11):1196–201.