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ORIGINAL ARTICLE

Therapeutic Plasma Exchange in Patients with Neurologic Disorders: Review of 63 Cases

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Abstract Therapeutic plasma exchange (TPE) is a procedure that reduces circulating autoantibodies of the patients. TPE is commonly used in neurological disorders where autoimmunity plays a major role. We report our experience with regard to the indications, adverse events and outcomes of plasma exchange in neurological disorders. Sixty-three patients were included to this retrospective study. Median age was 48 years (range 1–85), there was a predominance of males. Neurological indications included Guillain-Barrè syndrome ($n = 22$), myasthenia gravis ($n = 21$), chronic inflammatory demyelinating polyneuropathy ($n = 7$), polymyositis ($n = 3$), multifocal motor neuropathy ($n = 2$), acute disseminated encephalomyelitis ($n = 2$), neuromyelitis optica ($n = 2$), multiple sclerosis ($n = 2$), limbic encephalitis ($n = 1$) and transverse myelitis ($n = 1$). TPE was frontline therapy in 57 % of the patients ($n = 36$). Total number of TPE sessions was 517; median number of sessions per patient was 8 (range 1–66). TPE was done through a central venous access in 97 % and through a peripheral venous access in 3 % of the patients. Human albumin was used as replacement fluid in 49 %, hydroxyethyl starch (HES) in 49 % and fresh frozen plasma in 2 % of the cases. Adverse reactions were recorded in 60 % of the patients. Total ratio of complications in 517 TPE procedures was 10.8 % and these were mild and manageable such as allergic reactions and hypotension. Overall response rate was 81 %. Interestingly, complication and response rates were similar in both HES and human albumin groups. We conclude that TPE is an effective treatment in neurologic diseases in which autoimmunity plays an important role in the pathogenesis and HES can be used instead of albumin as replacement fluid in these disorders, since it is cost-effective, has similar efficacy and complication rates.

Keywords Therapeutic plasma exchange · Guillain-Barrè syndrome · Myasthenia gravis · Demyelinating disease · Polyneuropathy

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Introduction

Therapeutic plasma exchange (TPE) is a procedure that reduces the amount of circulating autoantibodies, alloantibodies, immune complexes and monoclonal proteins by centrifugation and replacement of patient's plasma [1–3]. This mechanism allows the use of TPE in the treatment of neurologic disorders in which autoimmunity plays a major

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role [1]. It is a standard treatment for Guillain-Barrè syndrome (GBS) and myasthenia gravis (MG), moreover in some other neurologic disorders, TPE has increasingly been mentioned as a possible treatment choice [4–14]. However there is limited experience of TPE in some relatively uncommon neurologic disorders.

This retrospective study was performed as an analysis of our experience with regard to the indications, adverse events and outcomes of plasma exchange in neurological disorders, including the relatively uncommonly diagnosed ones, and here we review the medical records of our patients with neurological disorders requiring plasma exchange.

Materials and Methods

The medical records of 63 patients with neurological diseases who had been treated by TPE between March 2002 and June 2014 at Mersin University Medical Faculty Hospital, Neurology Department were analyzed for the demographic details of the patients (age, gender), indications for TPE, results of treatment and complications of the procedure. We also collected clinical histories of the patients including drug intakes and treatments (therapeutic plasma exchange as front/second line treatment, adjuvant agents, i.e., corticosteroid, intravenous immunoglobulin [IVIG], pyridostigmine and immunosuppressive drugs). The local ethics committee approved this retrospective analysis.

Continuous flow cell separators Fresenius Com.Tec and Spectra Optia instruments were used for TPE. Therapeutic plasma exchange was performed every other day for most of the patients and a total 1–1.5 volume of plasma was exchanged for each cycle depending on patients' heights, weights, genders and hematocrit values. Fresh frozen plasma (FFP), 5 % solution of human albumin or hydroxyethyl starch (HES) was used as volume replacement fluid and acid citrate-dextrose solution A was used as anticoagulant during procedure. Patients underwent TPE by using a 16 G backeye access needle in an antecubital fossa vein; a 20 G venous cannula was placed in the opposite arm for the return line. Central venous catheters preferably 12 F double-lumen dialysis catheters inserted through the jugular or subclavian vein were used in patients with an inadequate peripheral venous access (PVA). All procedures were performed by senior apheresis technicians. Vital signs were monitored at the beginning and at the end of each procedure, and patients were monitored for adverse events during all procedures. Written informed consent was obtained from all patients after the procedural risks were explained in detail before each procedure.

For the outcomes of TPE, the severity of abnormal findings in neurological examination at the end of TPE was compared with the symptoms before the beginning of the procedure. If the neurological deficit of the patients improved completely, this was accepted as "complete response (CR)". If there was some response, but the neurological deficit did not disappear completely after TPE, it was accepted as "partial response (PR)" and if there was not any response after TPE, it was classified as "no response (NR)".

Statistics

Categorical variables were summarized with frequency and percent. Chi square or Fisher-Freeman Exact tests were used for comparing response rates between human albumin or hydroxyethyl starch solutions and different instruments, and exact p values provided with Monte Carlo simulations. Statistical analyses were done by PASW v.18 statistical package and p values <0.05 were evaluated statistically significant.

Results

Sixty-three patients were included into this study. Of the 63 patients, 37 (59 %) were men and 26 (41 %) were women with a median age 48 years (range 1–85) (Table 1). Seventy-nine percent of the cases were in category I, 11 % were in category II, 2 % were in category III and 8 % were in category IV according to the American Society for Apheresis (ASFA) 2010 guidelines [15]. The diagnosis was GBS in 35 % (n: 22), MG in 33.2 % (n: 21), chronic inflammatory demyelinating polyneuropathy (CIDP) in 11.1 % (n: 7), polymyositis in 4.7 % (n: 3), multifocal motor neuropathy (MMN) in 3.2 % (n: 2), acute disseminated encephalomyelitis (ADEM) in 3.2 % (n: 2), neuromyelitis optica (NMO) in 3.2 % (n: 2), multiple sclerosis (MS) in 3.2 % (n: 2), limbic encephalitis (LE) in 1.6 % (n: 1), transverse myelitis (TM) in 1.6 % (n: 1) of the cases (Table 1). TPE was frontline therapy in 57 % of the patients (n: 36), while 43 % of the cases (n: 27) were treated with corticosteroid (n: 26), pyridostigmine (n: 14), azathioprine (n: 7) and/or IVIG (n: 4) prior to TPE. Total number of TPE sessions was 517. The number and frequency of TPE procedure depended upon the clinical scenario; some patients required long term maintenance TPE. Median number of TPE sessions per patient was 8 in the current study and ranged between 1 and 66. Only 1 session was performed in a patient in myasthenic crisis and in a patient with GBS since they died. The patient in whom 66 sessions of TPE was done was a myasthenic patient with a follow-up of 12 years. The procedure was done through a

Table 1 Demographic details of the patients and indications, results of therapeutic plasma exchange

	GBS (22)	MG (21)	CIDP (7)	Polymyositis (3)	MMN (2)	ADEM (2)	NMO (2)	MS (2)	Limbic encephalitis (1)	TM (1)	Total (63)
Age (median)	47.5	50.6	51	55.6	40.5	45	50.5	35	40	19	48
Sex (M/F)	11/11	10/11	6/1	2/1	2/0	1/1	2/0	1/1	1/0	1/0	37/26
TPE as front line therapy (n)	21 (58.3 %)	6 (16.6 %)	4 (11.1 %)	3 (8.6 %)	0	0	0	1 (2.7 %)	0	1 (2.7 %)	36 (57 %)
TPE as second line therapy (n)	1 (3.7 %)	15 (55.6 %)	3 (11.1 %)	–	2 (7.4 %)	2 (7.4 %)	2 (7.4 %)	1 (3.7 %)	1 (3.7 %)	–	27 (43 %)
Total TPE sessions (n)	101 (19.6 %)	247 (47.8 %)	95 (18.4 %)	30 (5.8 %)	10 (1.9 %)	7 (1.4 %)	7 (1.4 %)	10 (1.9 %)	5 (0.9 %)	5 (0.9 %)	517
Median TPE sessions (n)	5	12	14	10	5	4	4	5	5	5	8
Treatment prior TPE (n)											
Steroid	1 (3.8 %)	15 (57.8 %)	2 (7.7 %)	–	2 (7.7 %)	2 (7.7 %)	2 (7.7 %)	1 (3.8 %)	1 (3.8 %)	–	26
IVIG	1 (25 %)	1 (25 %)	2 (50 %)	–	–	–	–	–	–	–	4
Other	–	21 (100 %)	–	–	–	–	–	–	–	–	21
Replacement fluid (n)											
Albumin	9 (29 %)	11 (35.6 %)	5 (16.2 %)	2 (6.4 %)	1 (3.2 %)	1 (3.2 %)	–	2 (6.4 %)	–	–	31 (49 %)
FFP	3 (60 %)	–	2 (40 %)	–	–	–	–	–	–	–	5 (2 %)
HES	12 (38.7 %)	10 (32.3 %)	2 (6.5 %)	1 (3.2 %)	1 (3.2 %)	1 (3.2 %)	2 (6.5 %)	–	1 (3.2 %)	1 (3.2 %)	31 (49 %)
Response (n)											
CR	4 (18.2 %)	17 (77.3 %)	0	0	0	0	0	0	0	1 (4.5 %)	22 (35 %)
PR	14 (48.3 %)	2 (6.9 %)	6 (20.7 %)	3 (10.4 %)	1 (3.4 %)	0	1 (3.4 %)	2 (6.9 %)	0	0	29 (46 %)
NR	4 (33.4 %)	2 (16.7 %)	1 (8.3 %)	0	1 (8.3 %)	2 (16.7 %)	1 (8.3 %)	0	1 (8.3 %)	0	12 (19 %)

GBS Guillain-Barrè syndrome, *MG* myasthenia gravis, *CIDP* inflammatory demyelinating polyneuropathy, *MMN* multifocal motor neuropathy, *ADEM* acute disseminated encephalomyelitis, *NMO* neuromyelitis optica, *MS* multiple sclerosis, *TM* transverse myelitis, *TPE* therapeutic plasma exchange, *IVIG* intravenous immunoglobulin, *FFP* fresh frozen plasma, *HES* hydroxyethyl starch, *CVA* central venous access, *PVA* peripheral venous access, *CR* complete response, *PR* partial response, *NR* no response

central venous access (CVA) in 97 % ($n = 61$) and through a PVA in 3 % of the patients ($n = 2$). Five percent solution of human albumin was used as replacement fluid in 49 % ($n = 31$), HES in 49 % ($n = 31$) and FFP in 2 % ($n = 1$) of the cases. Continuous flow cell separators Fresenius Com.Tec and Spectra Optia instruments were used in 81 and 19 % of procedures, respectively. Adverse reactions associated with TPE were recorded in 60 % of the patients. Total ratio of complications in 517 TPE procedures was 10.8 %. These were catheter related complications (30.3 %), allergic reactions (30.3 %), hypotension (21.4 %), hypocalcemia (3.6 %), tachycardia (3.6 %), abdominal pain (3.6 %), anxiety (3.6 %), hypertension (1.8 %) and bradycardia (1.8 %). All of the catheter-related complications were fibrin sheaths, which caused to catheter dysfunction and just 1.2 % of the procedures were terminated depending on these complications. Complication rate was 64.5 % for human albumin and 58.2 % for HES ($p = 0.602$) (Table 2). Complete and partial response rates after TPE were 35 and 46 %, respectively. There was no response in 19 % of the cases. Overall response rate was 81 % and there was no mortality related to TPE procedure (Table 1).

There were 22 patients with GBS who were all in clinical stage IV: 11 males, 11 females (median age, 48 years; range 1–81 years). TPE was used as frontline therapy in 21 patients and the procedure was performed within 7 days of their illness in these 21 patients. One patient on TPE as second line therapy had received corticosteroid and IVIG, but was not responsive to this therapy. A total of 101 TPE sessions were performed in patients with GBS and the median number of TPE was 5 per patient. HES, human albumin and FFP were used as replacement fluids in 12, 9 and 1 patients, respectively. The procedure was done through a CVA in 18 and through a PVA in 4 patients. Complications were seen in 11 patients during the procedure; these were device or catheter related hypotension, allergic reactions, abdominal pain and anxiety. Two CR, 9 PR in HES group and 2 CR, 5 PR in human albumin group were obtained. One patient in HES, 2 patients in human albumin and 1 patient in FFP group were unresponsive (4 CR, 14 PR, 4 NR). However, there was no difference between response rates when compared according to replacement fluids ($p = 0.380$). Furthermore, 4 CR, 14 PR (3 NR) were obtained in cases that the procedure done within 7 days ($n = 21$) and NR was seen in 1 case in which the procedure delayed (>7 days).

There were 21 patients with MG: 10 males, 11 females (median age, 51 years; range 3–75 years). Therapeutic plasma exchange was used as frontline therapy in 6 patients who were in myasthenic crisis. Fifteen patients on TPE as second/third line therapy had received corticosteroid, pyridostigmine, azathioprine and/or IVIG prior to TPE, but they were non-responsive to these drugs. A total of 247 TPE sessions were performed in patients with MG and the median number of TPE was 12 per patient. HES and human albumin were used as replacement fluids in 10 and 11 patients, respectively. The procedure was done through a CVA in all patients. Complications were seen in 13 patients during the procedure; these were device or catheter related hypotension, hypertension, allergic reactions, abdominal pain, bradycardia and tachycardia. Nine CR in

Table 2 Complications of therapeutic plasma exchange

Complication type	Albumin (No of procedures = 348)	HES (No of procedures = 161)	FFP (No of procedures = 8)	Total (No of procedures = 517)
Catheter related (n)	7 (2.0 %)	10 (6.2 %)	1 (12.5 %)	18 (3.5 %)
Fibrin sheaths				
Allergic reactions (n)	10 (2.9 %)	7 (4.3 %)	–	17 (3.3 %)
Hypotension (n)	8 (2.3 %)	5 (3.1 %)	–	13 (2.5 %)
Hypocalcemia (n)	2 (0.6 %)	–	–	2 (0.4 %)
Tachycardia (n)	2 (0.6 %)	–	–	2 (0.4 %)
Abdominal pain (n)	2 (0.6 %)	–	–	2 (0.4 %)
Anxiety (n)	2 (0.6 %)	–	–	2 (0.4 %)
Hypertension (n)	1 (0.3 %)	–	–	1 (0.2 %)
Bradycardia (n)	1 (0.3 %)	–	–	1 (0.2 %)
Total	35 (10.1 %)	22 (13.7 %)	1 (12.5 %)	58 (11.2 %)

There was no difference between the complication rates of albumin and HES ($p = 0.602$) (*HES* hydroxyethyl starch, *FFP* fresh frozen plasma)

Percentages were calculated as a proportion of the number of procedures done with each type of replacement fluid

HES group and 8 CR, 2 PR in human albumin group were obtained. One patient in HES and 1 patient in human albumin group were unresponsive (14 CR, 5 PR, 2 NR). However, there was no difference between response rates when compared according to replacement fluids ($p = 0.724$). In addition, 3 CR, 2 PR were obtained in patients in myasthenic crisis ($n = 6$), while no response was seen in 1 case.

There were 7 patients with CIDP: 6 males, 1 female (median age, 51 years; range 21–76 years). TPE was used as frontline therapy in 3 patients. Four patients on TPE as second line therapy had received corticosteroid or IVIG prior to TPE, but they were non-responsive to these drugs. A total of 95 TPE sessions were performed in patients with CIDP and the median number of TPE was 13 per patient. HES and human albumin were used as replacement fluids in 2 and 5 patients, respectively. The procedure was done through a CVA in all patients. Complications were seen in all patients during the procedure; these were device or catheter related hypotension, allergic reactions, hypocalcemia and bradycardia. PR was obtained 2 patients in HES and 4 patients in human albumin group, while no response was seen in 1 patient who is in human albumin group.

In 3 patients with polymyositis (2 males, 1 female; median age, 56 years), TPE was used as first line therapy. A total of 30 sessions were performed and the median number of TPE was 10 per patient. Human albumin and HES were used as replacement fluids in 2 and 1 patients, respectively. The procedure was done through a CVA in all patients. Catheter related complication and allergic reactions were seen in 2 patients during the procedure. PR was seen in all patients.

In 2 patients MMN (2 males; median age, 40.5 years), TPE was used as second line therapy after unresponsiveness to corticosteroid treatment. While PR was seen in 1 patient, there was no response in the other. In 2 patients with ADEM (1 male; median age 45 years), TPE was used as second line therapy after unresponsiveness to corticosteroid treatment. However, NR was seen in these patients. TPE was used as second line therapy after unresponsiveness to corticosteroid treatment in 2 patients with NMO (2 males; median age, 50.5 years). While PR was seen in 1 patient, there was no response in the other. There were 2 patients with MS (1 male; median age, 35 years) and TPE was used as first line therapy in one patient, while used as second line therapy after unresponsiveness to corticosteroid treatment in the other one. PR was seen in both of them. In 1 patient with LE (1 male, 40 years old), TPE was used as second line therapy after unresponsiveness to corticosteroid treatment. However, there was NR after TPE. In 1 patient with TM (1 male, 19 years old), TPE was used as fist line therapy and CR was seen.

Discussion

TPE is used alone as frontline and/or as second line adjuvant therapy to treat a number of neurologic conditions. ASFA divides the neurologic indications for apheresis into IV categories [15]. Acute inflammatory polyneuropathy (i.e., GBS) and MG are the two most common neurologic indications for apheresis (category I) [16–20]. Acute CNS demyelinating disease secondary to TM (category II), paraneoplastic neurologic syndromes (i.e., LE) (category III), monoclonal antibody with progressive multifocal leukoencephalopathy (category III), amyotrophic lateral sclerosis (category IV), polymyositis (category IV) are the other neurologic conditions occasionally treated with apheresis [15–24].

GBS is an acute inflammatory demyelinating neuropathy [25]. TPE or IVIG are used in patients with severe GBS [26, 27]. TPE was the first therapeutic modality to impact the disease favorably and several randomized studies have been performed to determine its efficacy [28–31]. And it is more beneficial when applied within the first 7 days of disease [32]. An international randomized trial compared TPE, IVIG and TPE followed by IVIG in 383 adult patients with severe GBS and found all three modalities to be equivalent; there were no differences in three treatment groups in mean disability improvement at 4 weeks [31]. However, there are no adequate randomized trials to determine whether TPE improves the long term outcomes. The decision to use TPE or IVIG must be weighed depending on availability and side effect profiles [33]. According to ASFA, typical TPE strategy in GBS is to exchange 200–250 ml of patient plasma per kg body weight over 10–14 days (5–6 TPE procedures) with 5 % albumin replacement. Eighteen out of 22 patients with GBS improved with TPE (4 CR, 14 PR) in our study, and since we did not determine any difference in terms of response rates according to replacement fluids, HES can be used as a very cost effective fluid in selected patients instead of human albumin. We think that NR was observed in 4 patients because of the natural history of disease; 2 patients died shortly after the initiation of procedure because of neurogenic respiratory failure and progressive disease developed in the other 2 patients.

MG is a chronic autoimmune disorder affecting neuromuscular transmission [22]. Acute exacerbations of MG need effective and urgent treatment, since life-threatening hypoventilation may develop (myasthenic crisis). TPE is used principally to remove circulating autoantibodies, although both seropositive and seronegative patients respond to TPE [15]. IVIG and TPE have a similar clinical effect and a similar respond rate; however, there is no adequate randomized, controlled trial to determine whether

TPE improves the short-term outcome as well as long term outcome for MG [34–36]. TPE is especially used in myasthenic crisis, perioperatively for thymectomy, or as an adjunct to other therapies to maintain optimal clinical status. It works rapidly; clinical effect can be apparent within 24 h but may take a week [15]. The efficacy of TPE in the treatment of MG varies from 55 to 100 % [5]. ASFA recommends TPE in MG with processing a 225 ml/kg of plasma with albumin replacement over a period of up to 2 weeks; and the frequency of procedures depends upon the clinical scenario [15]. In our study, 19 out of 21 patients with MG improved with TPE (14 CR, 5 PR), and since we did not determine any difference in terms of response rates according to replacement fluids, HES can be used as a very cost effective fluid in selected patients instead of human albumin. There was NR in our 2 patients since they admitted too late after beginning of symptoms and they died shortly after the initiation of procedure because of respiratory failure.

CIDP is an acquired, autoimmune, peripheral neuropathic disorder [22]. Corticosteroids, IVIG or TPE are the treatment options with similar treatment outcomes; therefore a choice among them is based on cost, availability and side effects [15]. Maintenance therapy, including continuing steroids, periodic TPE or repeated infusion of IVIG, is usually required because discontinuation of therapy may be followed by relapse [15]. There have been 2 randomized, controlled, double-blinded studies that provide class I evidence that TPE is superior to placebo treatment in CIDP [37, 38]. However, TPE provides short-term benefit, but rapid deterioration may occur afterwards. This may necessitate maintenance treatment, with TPE and/or other immunomodulating therapies [15]. ASFA recommends TPE in CIDP with albumin replacement with a frequency of 2–3 times a week until improvement as initial therapy and with a frequency range from weekly to monthly as needed to control symptoms for maintenance therapy [15]. Although CIDP takes place in category I in ASFA guideline, some patients will not respond to TPE due to severe axonal loss. We observed NR in our 1 patient with severe axonal degeneration, but PR was obtained in 6 patients with TPE. HES was used as replacement fluid in 2 out of these 6 patients.

Dermatomyositis is a complement-mediated microangiopathy that affects skin and muscle. On the other hand, polymyositis is a T cell mediated inflammatory myopathy leading to muscle fiber necrosis [39]. Both of these inflammatory myopathies are generally responsive to corticosteroids, but could be refractory to them. TPE or IVIG with or without concomitant use of immunosuppressant drugs may provide improvement in dermatomyositis or polymyositis [18, 40–42]. Polymyositis/dermatomyositis takes place in category IV in ASFA guideline. However, in our 3 patients with polymyositis, TPE was performed as frontline therapy and PR was seen in all. But corticosteroid therapy was required in 2 patients after TPE. TPE can have a role in the therapies of refractory inflammatory myopathies, especially in acute forms and in combination with immunosuppressive therapies.

MMN is a very rare, progressively worsening condition where muscles in the extremities gradually weaken. IVIG is effective in almost 80 % of patients and some case reports show that MMN does not respond very well to plasmapheresis, even that plasmapheresis may be disadvantageous in MMN, since the immunoglobulins are washed out by plasmapheresis [43–45]. However, there is no randomized, controlled study showing the role of TPE in patients with MMN. In our study, 2 patients with MMN treated with TPE; PR was seen in one and there was NR in the other. Role of TPE needs to be further investigated with larger series of patients.

ADEM is usually a monophasic inflammatory demyelinating disease that affects the brain and spinal cord [26]. There is no standard therapy for ADEM. Corticosteroids are considered effective and there are also some reports in which TPE could be effective after corticosteroid failure [15, 46, 47]. Keegan reviewed 10 patients with ADEM who were treated with TPE for severe attacks of CNS demyelization; 4 patients had moderate to marked improvement after TPE [48]. In acute phase of ADEM, especially in patients who poorly respond to corticosteroids, TPE can be an effective treatment method, since it removes the cytokines and autoantibodies that play role in the pathogenesis of the disease [15]. ADEM takes place in category II in ASFA guideline, however in the present study, there was no response to TPE in our 2 patients who were also refractory to corticosteroids. If improvement is not observed early in treatment of ADEM, then it is unlikely a response will occur. But we cannot say that TPE is ineffective in ADEM, and the role of TPE should be investigated with larger series of patients.

NMO and MS are demyelinating, inflammatory disorders of CNS [22]. Acute attacks are managed by high-dose steroids. However, TPE was found to be beneficial in patients who do not respond to initial corticosteroid treatment [49–51] and it takes place in category II in ASFA guideline. In a small retrospective study, 9 patients with NMO who received TPE after failing high-dose corticosteroids demonstrated immediate improvement after the second course of TPE [52]. In our 2 patients, TPE is used as second line treatment after corticosteroid failure and while PR was seen in 1 patient, NR was observed in the other who was 61 years old. The latter patient died shortly after the initiation of the procedure because of neurogenic respiratory failure. TPE is considered beneficial for patients with acute exacerbations of MS who do not respond to

high-dose corticosteroids (ASFA category II), rather than the patients with chronic progressive MS (ASFA category III) [53, 54]. PR was seen in our 2 cases with MS. One of our cases was unresponsive to steroids and the other was with acute exacerbation. However, in this study, there are not enough patients with NMO and MS to determine whether TPE is beneficial in the treatment of these disorders. Therefore, the roles of TPE need to be further investigated with larger series of patients.

Therapy of LE with or without a neoplasm is based on corticosteroids, IVIG, TPE and mycophenolate [55, 56]. LE takes place in category III in ASFA guideline and patients with antibodies directed against voltage-gated calcium channels may be more likely to respond to plasma exchange [15]. Our patient with LE did not have a neoplasm and we could not check the antibody level. He was treated with TPE after corticosteroid failure, however, there was NR.

Autoimmune TM is a focal disorder of the spinal cord [18]. Treatment consists of corticosteroids, TPE or cyclophosphamide [51, 57]. When high dose intravenous steroid treatment fails, TPE may provide improvement in TM cases. In our case, TPE was used as fist line therapy and CR occurred.

During the TPE procedures, some complications were reported such as hypotension, hypocalcemia, anemia, allergic reactions, anaphylaxis, hematoma, hypotension, acute pulmonary edema, myocardial infarction, death and complications related to catheter replacement [58, 59]. Henze at al reported complications of 291 TPE procedures in 39 patients with neurological diseases. They found that minor and major complications developed in 4.8 and 2.7 % of the patients, respectively, including one death [60]. In our study, the complications were recorded in 60 % of the patients; however, total ratio of complications in 517 procedures was 10.8 %. The most common complications were catheter related complications (30.3 %) and allergic reactions (30.3 %). There was no mortality related to TPE procedure in our series. In 2 different studies, TPE was performed via PVA in 70 % of patients [58, 59]. Contrary to this data, in our study, the procedure was performed trough a CVA in 97 % of patients. The relatively higher complication rate in our study compared to the others may be due to this higher rate of CVA in our patients. However, CVA has its own advantages in patients' improvement. Complications during and after TPE are based on the factors like extracorporeal volume and duration of the procedure, and vascular access plays role in volume removed and in duration of the procedure.

Human albumin is the recommended replacement fluid for TPE in neurological diseases [15]. In our study, albumin and HES were used as replacement fluid in 49 and 49 % of the cases, respectively. The ratio of CR for albumin and HES was 32.3 and 38.7 %, respectively ($p = 0.791$) and the ratio of PR for albumin and HES was 48.4 and 45.2 %, respectively ($p = 0.799$). There was also no difference between the rates of complications according to replacement fluids. Accordingly, complication rate was 64.5 % for human albumin and 58.2 % for HES ($p = 0.602$). Rock et al. also reported HES as a safe replacement fluid for PE in patients with GBS and MG [61]. These results show that HES can be used as a very cost-effective replacement fluid for TPE in neurologic disorders instead of human albumin, since HES is a cheap solution with similar efficiency and complication rates compared to albumin. However, further randomized, controlled studies are needed in this era.

In addition, there was no difference between the response rates according to the continuous flow cell separators Fresenius Com.Tec and Spectra Optia instruments ($p = 0.926$).

In conclusion, in our study, overall response rate of TPE in neurologic diseases was 81 % with mild to moderate and manageable side effects. TPE is an effective treatment in neurologic diseases where autoimmunity plays an important role in their pathogenesis, especially in GBS and MG. HES can be used instead of albumin during the procedure as replacement fluid, since it is much cheaper and have similar efficiency and complication rates.

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