Therapeutic Plasma Exchange; One Year Experience of Minia at Nephrology & Urology Hospital / Minia University

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Abstract

Background: Therapeutic plasma exchange (TPE) or interchangeably termed as plasmapheresis is a process involving extracorporeal removal of plasma from other components of blood and replacing it with physiological fluids. this procedure aimed at removes circulating antibodies, immune complexes and toxins from the blood. TPE has been effectively used in numerous disorders.

Aim of the study: to assess TPE in our nephrology unit at Nephrology &Urology Minia University Hospital after the 1st year experience, including indications, doses, complications and outcome.

Methods: This is a descriptive study, carried out through one year on patients who were treated using TPE; clinical data, investigations, number of sessions, type of used fluid for exchange, outcomes and complications were recorded and analyzed statistically.

Results: Thirty seven patients were included to this study; 8 patients had Systemic lupus erytheromatosus (SLE), 4 patients had Thrombotic Thrombocytopenic Purpura (TTP), 4 patients had multiple sclerosis (MS),3 patients had Myasthenia Gravis (MG), 3 patients had nephrotic syndrome(NS) , 3patients had pre transplant elevated autoantibobodies,2 patients had post-transplant Immune mediated rejection , 2 patients had autoimmune encephalitis, 2patient had Heamolytic Uremic Syndrome(HUS),1 patients had covid -19 infection,1 patient had Staff man syndrome,1 patient had RH-Alloimmunization with pregnancy,1 patient had Thrombotic Microangiopathy(TMA) , 1 patient had neuromyelitis optica and 1 patient had Guillane Baree syndrome(GBs) . the total number of sessions of TPE Throughout this year were 192 session , As regard complications; the most common complication was chest infection , twenty nine patients were improved and 3patients showed no improvement while 5 patients un fortunately died during the treatment course of disease.

Conclusion: TPE is a safe and effective adjuvant therapy for many diseases especially immune mediated disorders.

Key Words: Plasmapheresis, Outcome, SLE, HUS, GBS.

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The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Introduction:

TPE or plasmapheresis is a procedure which eliminates many pathological substances such as pathological circulating antibodies, immune complexes and cytokines from the blood as the blood is removed from patient and pass through an extracorporeal medical device, which separates the plasma from the blood [1]. The removed plasma is replaced with colloid solution (e.g., albumin and-or donated plasma).so, it is called apheresis as sometimes the replacement was done by other than plasma [2]. The removal and replacement of patients' plasma including the previous mentioned pathological substances was supposed to be the major mechanism of action of TPE. But this mechanism does not clarify the magnitude of response seen in some disorders. Additionally, a proof was found that TPE may have immunomodulatory effect further than the removal of immunoglobulins [3]. TPE has been successfully used in numerous immunologically and nonimmunological mediated disorders, Initially it has been restricted to blood bank centers but in the last two decades; it was carried out in intensive care units as TPE became more effective and simple after the wide utilization of hemodiafiltration machines [4]. Plasma exchange disappointingly had some disadvantages as significant declines had observed to occur in some coagulation factors such as factor V (FV), FVII, FVIII,FIX, FX, and VWF activity. However, coagulation factors are replenished at different rates as fibrinogen achieves 66% of pre-apheresis levels by 72 h. so, currently, there are no consensuses or national guidelines recommend that hemostasis management in patients undergoing TPE treatments, [5]. There were other complications of the procedure were reported as access or catheter-related complications including access thrombosis and infection [6] as well as hypotension and anemia respectively due to large extracorporeal blood volume and blood loss in the circuit. There are wide varieties of indications of apheresis according the Committee of the American Society for Apheresis (ASFA) that evaluates periodically the potential indications for apheresis and classifies them from I to IV on the basis of the available medical literature [7].

Methods

this descriptive study carried out at our Nephrology unit at Nephrology & Urology Minia University Hospital during period from November 2020 to October 2021; the study included 37 patients indicated for TPE. The study included all patients for whom TPE was indicated to improve the course of disease and their quality of life such as; SLE, TTP, MG, HUS, NS and GBS. We excluded all patients indicated for TPE but unfit for the procedure as patients who have allergies to fresh frozen plasma or albumin depending on the type of plasma exchange or who were actively septic or hemodynamically unstable. Actually, exchanged plasma volumes were taken according apheresis protocols; patient plasma volumes (PPV) were calculated according to Sprenger as following: Plasma volume = 0.065 × body weight [kg] × (1-hematocrit) [1, 8]. TPE is performed either by using centrifugation (cTPE) devices that separate the plasma from cellular components based on density or by using membrane apheresis, based on molecular size (mTPE). [9] The earlier removes target substances at a higher plasma extraction ratio with a lower blood flow rate, while the later compensates the lower plasma extraction ratio with a higher blood pump speed. Both technologies are to a large extent equivalent in safety and efficacy [10]. Nephrologists largely favor mTPE, an adaptation of technology on the dialysis machine, while others use cTPE when possible. We used the two methods in our unit. in centrifugation method, prescription Details were outlined in regional anticoagulation with citrate infused to blood volume with a ratio of 1:32 and target concentration of post-filter ionized calcium 0.25-0.35 mmol/l as described by **Calatzis** [11]. All patients included in this study were subjected to full history taking, thorough clinical examination, laboratory investigations in order to diagnose ,follow up or detect improvement in the form of CBC (complete blood count), kidney and liver function tests, PT (prothrombin time), PTT (partial thromboplastin time), routine urine analysis, urine culture, arterial blood gas analysis (ABG), blood glucose level, s.sodium, s. potassium, s.Albumin and corrected Calcium in addition to special investigation according to the case such as; (ANA, Anti DNA, C3, C4 for SLE cases), (Nerve conduction velocity, Electromyography study (EMG) for GBs),(viral markers, and 24 hours proteinuria in NS),(C3, LDH, Blood culture, Stool analysis, Stool culture for HUS)…etc.

Ethics approval:

This study protocol and the consents were approved by the Ethical Committee of nephrology

unit at Nephrology & Urology Hospital, Minia University. Informed written consent was obtained in every case from patients or their relatives.

Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software then were imported into Statistical Package for the Social Sciences (SPSS version 25). The qualitative data represented as number and percentage; quantitative data represented as mean ± SD.

Results

In this study ;thirty seven patients who underwent TPE in our department, 8 patients had SLE (21.6%), 4 patients had TTP(11%), 4 patients had MS (11%),3 patients had MG (8 %), 3patients had pre transplant elevated autoantibodies (8 %),3 patients had NS (8 %), 2 patients had post-transplant Immune mediated rejection(5.4%), 2 patients had autoimmune encephalitis (5.4%), 2patient had HUS (5.4%) ,1 patients had covid -19 infection(2.7%),1 patient had Staff man syndrome(2.7%),1 patient had RH Alloimmunization with pregnancy(2.7%),1 patient had TMA (2.7%) , 1 patient had neuromyelitis optica (2.7%) and 1 patient had Guillain-Barré syndrome (GBs) (2.7%) .Concerning gender of the studied cases (59.5%) was females with mean age of all studied cases were 27.6± 9.1. We used albumin and saline in 27 (73%) cases while we used fresh frozen plasma in 10 cases (27%); the type of replacement fluid was selected according to disease. Throughout this year we delivered 192 sessions of TPE, number of sessions is <5 in 27 % of cases, 5-10 sessions in of 67.6 % of cases and >10 sessions in 5.4% of cases **(Table1).** As regard complications; the most common complication was chest infection of 6 patients (16.2%) it occurred regardless original disease or age of the patients followed by hypotension as it happened in 3 of cases (8.1%). At the end of TPE sessions we had 29 improved cases (78.4%), 3 cases weren't improved (8.1%) and unfortunately, we lost 5 cases ended by death (13.5%). **Table 2** showed that there was high significant relation between the disease type &outcome (p value=0.001). But there was no significant relation between either age, number of sessions or complications and outcome (p value=0.5, 0.72 and 0.89 respectively) **(table 2).** We found that there was significant decrease in urea level, creatinine and platelets on admission and at end of relapse while there is no significant change in TLC, HB and corrected Calcium. **(Table 4)**

Table 1: Number of sessions of the studied cases.

Number of sessions	No.	%
<5	10	27
5-10	25	67.6
>10	2	5.4

Table 2: The relation between type of diseases and outcome:

Disease Type	Improved (N = 29)	Not improved (N = 3)	Died (N = 5)	P Value
SLE	**6**	**0**	**2**	**0.001****
TTP	**3**	**1**	**0**	
MS	**3**	**0**	**1**	
MG	**3**	**0**	**0**	
NS	**2**	**0**	**1**	
HUS	**1**	**1**	**0**	
Immune mediated rejection	**2**	**0**	**0**	
Pre Tx elevated autoantibobo-dies	**3**	**0**	**0**	
autoimmune encephalitis	**2**	**0**	**0**	
covid -19 infection	**0**	**0**	**1**	
Staff man syndrome	**1**	**0**	**0**	
RH-Alloimmunizatio n with pregnancy	**0**	**1**	**0**	
TMA	**1**	**0**	**0**	
neuromyelitis optica	**1**	**0**	**0**	
GBs	**1**	**0**	**0**	

Table 3: The relation between age, number of sessions and complications and outcome or between and outcome:

	outcome	p-value
Age (mean ± SD)	27.6± 9.1	0.5
Number of sessions (mean ± SD)	5.32 ± 2.769	0.72
Complications: NO	81.1	0.89
Chest infection	16.2	
Hypotension	2.6	

Table 4: Comparison between laboratory data on admission and end of relapse:

	On admission	End of relapse	P value
TLC 10^3/dl Mean ± SD	11. 8±7.5	13.5±5.9	0.164
HB g/dl Mean ± SD	8.8±2.8	11.5±1.9	0.04*
Platelets 10^3/dl Mean ± SD	152.2±184.8	265.2±180.6	0.04*
Urea mg/dl Mean ± SD	100±106.4	13±21.7	< 0.001*
Creatinine mg/dl Mean ± SD	3.8±4.25	1.0±2.7	< o.o5*
Corrected Calcium mg/dl Mean ± SD	9±1.4	9.3±1.1	0.3

Discussion

Therapeutic plasma exchange has been successfully used in numerous immunological and nonimmunological mediated diseases in the last few decades. There has been profound improvement in the technique with advances in transfusion medicine; the outcomes of plasmapheresis as a therapeutic modality reported in nephrology literature are based largely on case reports in individual diseases [5]. So, the current study was conducted on 37 patients admitted to our unit in order to assess the outcome of therapeutic plasma exchange on the treatment of several diseases. The present study included 10 different disease identities; patients with SLE, TTP, MS, NS, MG, HUS, Staff man syndrome, GBS, autoimmune encephalitis and TMA with about 5 different indications of TPE as pre transplant elevated autoantibodies, post-transplant Immune mediated rejection, covid -19 infection, RH Alloimmunization with pregnancy, and neuromyelitis Optica. study revealed that about 21.6 % of cases indicated for TPE had SLE, 11% of cases had TTP ,11% of cases had MS , 8% of cases had MG ,8% of cases had pre transplant elevated autoantibodies ,8 % of cases had nephrotic syndrome ,5.4% of cases had Immune mediated rejection , 5.4% of cases had autoimmune encephalitis, 5.4% of cases had HUS, 2.7% of cases had covid -19 infection, 2.7% of cases had Staff man syndrome , 2.7% of cases had RH Alloimmunization with pregnancy,2.7% had TMA and 2.7% had neuromyelitis Optica and 2.7% had Guillain-Barré syndrome (GBs) . in our study About 78.4 % of cases showed improvement after therapy, 8.1% didn't improve and 13.5 % died. These results were close to **Ghonemy et al** study [12] as about (88.9%) experienced improvement while 2 patients showed no improvement and 6 patients died. At the present study the complications reported were chest infection as most common complication (16.2 %) followed by hypotension (2.6%). The present study reported that there was significant relation between the disease type and outcome (0.001). TPE is not currently among induction or maintenance therapy guidelines for treatment of Lupus Nephritis (LN) but is reported in current European guidelines as a treatment option in the setting of rapidly progressive glomerulonephritis [13]. In this study we found that 8 patients with SLE, 6 patients improved (75%) and other 2 patients died what matches David et al. study [14] who enrolled patients with SLE treated with TPE; the improvement in (78%) patients and the study concluded that TPE is safe and effective in patients with severe manifestations of autoimmune diseases. Also, **Hans et al.** [15] reported clinically significant improvement in the patients with SLE after plasma exchange suggesting that it can be an important component of treatment in patients of SLE with acute life-threatening complications concurrently with high dose steroid and cytotoxic drugs. Regarding to transplantation, Pre-transplantation desensitization protocols recommend use TPE for recipients with living donors who have an incompatible crossmatch from donor-specific human leukocyte antigen (HLA) antibodies. There is an obvious survival advantage with transplantation in these individuals when compared to remaining on dialysis. [16] The number of TPE sessions is determined by the degree of sensitization and HLA mismatch. The sessions are planned daily or on alternate days till crossmatch becomes negative leaving a week's window to transplantation before antibodies rebound. As regard to Post transplantation, Antibody-mediated rejection of kidney allografts occurs not only in up to 60% of high-risk recipients (HLA-sensitized or ABO-incompatible) but also in about 23% of unselected low-risk recipients [17].

We used daily or alternate days TPE using 5% HSA, and IVIG (a high dose 2 g/kg or a low dose of 100 mg/kg) to decrease donor-specific antibodies and suppress antibody production, respectively. Recent years has seen anti-CD20 antibody used alongside however the evidence toward safety and efficacy is still weak.[18] Regarding the patient who was presented by GBS (5.4%) in our study was improved as been evaluated pre and post TPE by electromyography (EMG), nerve conduction velocity, latency period, wave amplitude, f-wave and other laboratory investigation as the items of concern in evaluation of improvement. Regarding

the present study, patients with HUS 2 patients 1 improved and 1 patient did not improve. These results are consistent with a systematic meta-analysis which had reported that TPE is the most effective treatment in patients with HUS and should be considered as early as possible in the disease course. Patients with primary focal Segmental glomerulosclerosis developing NS are treated with steroids as first-line, then by calcineurin inhibitors can be used, and rituximab. TPE may be considered if previous treatments failed [19] in this study found that 3 patients had NS, 2 patients of them improved what was agreed with **Franke et al.** [20] who concluded that TPE is a useful option for treatment of steroid- and cyclosporine-resistant FSGS, especially if applied early in the course of the disease.in our study there were no significant relation between either age, number of sessions or complications and outcome in contrast to the results of **Sabry et al.** (21) who found that there was significant relation between number of sessions and outcome but agreed with our study as they concluded that there were no significant relation between age and outcome and high significant relation between the disease and outcome . Sessions in our current study in 80% applied every other day to give time for fibrinogen to be at a reasonable level. We use strict antiseptic measures in trial to diminish rate of vascular line infections as no cases of catheter related infection reported in our study.

Conclusions

we concluded that TPE is a useful therapeutic tool in management of numerous diseases especially in immune mediated disorders as SLE.

Recommendation

We recommend using TPE as an effective adjuvant therapy for many diseases and to share our experience to multiple centers to raise the skills and minimize complications.

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Conflict of interest

the authors declare no conflict of interest.

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