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Theraputic Plasmapheresis in Neurological Disorders, Baghdad/Iraq

Basim Hanoon Jabar, Bahaa A. Hassan

Neurology Department, Neurosciences Teaching Hospital, Baghdad, Iraq

Email address:
theneurologistbahaa@gmail.com (B. A. Hassan)

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Abstract: *Background:* plasma exchange (PE) involves the separation and removal of plasma from corpuscular blood and the replacement of it with various fluids, while plasmapheresis only refers to the removal of plasma. *AIM OF STUDY:* To study our experience with PE in our 487 patients of different neurological disorders, determined most referring diseases. *Materials and Methods:* Retrospective study of PE procedures done during a period of 36 months, from January 2013to January 2016 in a neurosciences hospital in Baghdad/Iraq. Data analysis is used SPSS 20. *Results:* The main indication for PE was CIDP (339 patients; 69.20%). Age of patients ranged from 8-85 (mean = 46.22 years). Up to our knowledge is largeset number of patients used in that period, no mortality found. *Conclusion:* The analysis of 487 cases of PE done in our department shows that PF is usually well tolerated. Possible adverse reactions mainly relate to vascular access.

Keywords: Chronic Inflammatory Demylinating Polyneuropathy, Plasmapheresis, Therapeutic Plasma Exchange

1. Introduction

Apheresis is a general term that describes removal of abnormal blood constituents by extracorporeal blood purification methods. To date, therapeutic plasma exchange (PE) is the most common apheresis procedure [1, 2]. Plasma exchange, the unselective removal of all plasma constituents, has been applied, with varying degrees of success, to an increasing number of disorders. Because of the high cost of plasma exchange, largely the result of expensive homologous replacement solution, and other reasons, alternatives have been sought. Selective removal of plasma components permits the use of autologous plasma as replacement which is less costly, more physiologic, and in some cases, a more efficient alternative to plasma exchange. The selective removal of plasma components whose presence is associated with a disease process can be accomplished presently by physical or chemical means with either on-line or off-line systems. 2It was first employed in 1952 in patients with multiple myeloma to control the hyperviscosity. By the 1970s PE had evolved as a treatment modality inA variety of possible mechanisms for the actions of therapeutic PE have been proposed, including removal of antibody, alloantibody, immune complexes, monoclonal protein, toxin or cytokine(s) and the replenishment of a specific plasma factor [3, 4]

Most neurological disorders that are treated with PE are associated with presumed aberrant humoral immune responses, including myasthenia gravis, Guillain-Barré syndrome (GBS), and chronic inflammatory demyelinating polyneuropathy (CIDP) [5]. In contrast to immunoadsorption, PE is a nonspecific treatment modality with elimination of the entire plasma. The therapeutic effect is based on the removal of circulating, pathogenic immune factors including autoantibodies. Currently, PE is used for treatment of several immune-mediated neurological disorders. While first experiences relate to acute life-threatening conditions, such as treatment of Guillain–Barré syndrome or myasthenic crisis, therapeutic success was also shown in chronic diseases where immunosuppressive therapy is often required for long-term management [6].

Here we report the experience on PE in 487 patients with various neurological diseases treated in the Neurology department of a neurosciences hospital in Baghdad/Iraq.

2. Materials and Methods

Retrospective study reviewed all the PE procedures performed during a period of 36 months, from January 2013

to January 2016 in neurology department.

The subclavian vein was catheterized in 222 patients and femoral vein was accessed in 265 patients with a double lumen catheter, under local anesthesia, under aseptic precautions. Patients were preloaded with 1.5-2 L of normal saline to get an adequate hydration status before the procedure. Once target plasma filtrate was obtained, procedure was stopped. All PE procedures were administered by staff nurses trained in dialysis units under the supervision of a senior resident in Neurology assigned to the case.

The Dialysis machine marketed by HEAMONETIC MCS+ and SPECTRA OPTIA and was used for doing the PE.

3. Results

Altogether 1699 PE procedures were performed on 487 patients. There were 299 male patients and188 female patients. Age ranged from 8to 85 years (mean 46.22). Number of patients in different age-groups is given in the Table 1.

Table 1. *Age distributions.*

Age group	No of patients
20	45
20-40	280
40-60	95
60	67
total	487

Neurological diseases for which PE were done are given in Table 2. The patients with myasthenia gravis (MG) who underwent PE were in myasthenic crisis. PE was done on an average of 7 days after the onset of symptoms in GBS. In patients with acute disseminated encephalomyelitis (ADEM) and neuromyelitisoptica (NMO), it was done after inadequate response with steroids. Result show that CIDP is the most frequent disease in our unit which 337(69%) of our patients, form them 117(24.02%) are diabetic patients

Table 2. *Neurological diseases.*

Diseases	No. of patients (%)
Chronic inflammatory demyelinating polneuropathy	337(69%)
Guillain barre syndrome	65(13.35%)
Myasthenia gravis	30(6.16%)
Acute disseminated encephalomyelitis	9(1.85%)
Neromyelitisoptica	33(6.78%)
Multiple sclerosis	13(2.67%)
Total	487(100%)

PE protocol was five exchanges in all the patients, only 149 (30.60.3%) patients could not complete all the five sessions. Various reasons for incomplete PE sessions were filter related problems like poor filtration, filter block or clot formation (n =37, 7.60%), while 112(25.05), improvement after less number of exchanges, asgiven in the Table 3.

Table 3. *Numbers of exchanges.*

No. of exchanges	No. of patients (%)
5	338(69.40%)
4	79(16.22%)
3	50(10.27%)
2	15(3.08%)
1	5(1.03%)
Total	487(100%)

Fever due to possible catheter related phlebitis occurred in 15 (3.08%) patients. Among the systemic complications, perioral and/or limb paresthesias and muscle cramps were occurring in 10 (2.05%) patients. These were mild and transient and never resulted in termination of the procedure.

Mild transient hypotension (systolic BP < 100 mmHg with only minimal or no symptoms) occurred in 70 (14.37%) patients during at least one of their PE cycles. This was readily corrected by reducing the pump speed or administering intravenous 0.9% saline. PE was continued in all of them without any significant symptoms or complications during or after the procedure.

Fifteen (3.08%) patients developed severe prolonged hypotension (systolic BP <80 mmHg) during procedure and required temporary stoppage of the exchange and administration of FFP or 0.9% saline. Eleven of these patients were having GBS and eight among them were hemodynamically unstable even before the procedure, most probably due to autonomic dysfunction, asgiven in the Table 4.

There was no procedure related mortality in any of the 487 patients.

Table 4. *Complications.*

Complications	No. of patients (%)
Hypotension	85(17.45%)
Fever(thrombophlebitis)	15(3.08%)
Paresthesia&numbness	10(2.05%)
No complications	377(77.41%)
total	487(100%)

Patient with chronic inflammatory demylinating polyneurolpthy 124(25.4%) are diabetic, while 213(43.7%) are non diabetic patients as shown in table 5.

Table 5. *Chronic inflammatory polyneuropathy.*

Chronic inflammatory polyneuropathy	No of patients
With diabetes mellitus	124(25.4%)
Without diabetes mellitus	213(43.7%)

4. Discussion

We report a series of 487 cases that underwent 1699 cycles of PE over 36 months for various neurological diseases. The major indication for the procedure was chronic inflammatory polyneuropathy (337 patients, (69.20). [7, 8, 9]

Majority of patients were adults and middle aged persons (Mean age: 46.22; range: 8-85) [17]. We employ PE in patients in the pediatric age group and the youngest patient in

our cohort was 8-year-old. In children, therapeutic PE procedures are associated with multiple and unique challenges relevant psychological issues, modification of protocols and technical hardware are often necessary for safe and effective treatment in children, but its still safe by expert hands [10].

Chronic inflammatory demyelinating polyneuropathy is believed to be due to immune cells, which normally protect the body from foreign infection, incorrectly attacking the nerves in the body instead. Recent studies have reported that patients with diabetes mellitus (DM) have a predisposition to develop chronic inflammatory demyelinating polyneuropathy (CIDP). Demyelinating neuropathy meeting the electrophysiological criteria for CIDP occurred in both types of DM, and its occurrence was significantly higher in diabetic than in nondiabetic patients.

Most patients visit our unit are CIDP patients (69%) and (24.02%) are diabetics which show that the cleared association between diabetes mellitus and CIDP, plasmapheresis better than steroid in diabetic patients [11].

In our series, there was a much higher incidence of hypotension (17.45%) compared to the 2.6-8.1% incidence in previous reports. Due to autonomic dysfunction, involavment because vast majority of our patients were havingCIDP& GBS.

These events (hypotension, arrythemia, nosia, vomitting) are usually mild and resolves without 1treatment. Because of problems related to vascular access, 4-5% of PE may have to be terminated. [11] Hypotension was treated by lowering the pump speed or temporarily stopping the procedure and infusion of normal saline or fresh frozen plasma (FFP). Blood pressure (BP) and pulse were monitored every 15-30 minute intervals during the sessions and patients were closely observed for changes in appearance, development of symptoms (e.g., lightheadedness, nausea, parasthesias, etc.). This is attributed the large fluid shifts between the intra and extra vascular compartments with associated electrolyte imbalances and the citrate content of the anticoagulant in the FFP which chelates the calcium. That's the same reported incidence of these symptoms ranges from 1.5%-9%. [12] Similarly, However, the previous lower rates of the reported adverse effects could be explained. we used FFP as the replacement fluid which has been associated with higher incidence of hypotension and other adverse events. The French Cooperative Group on plasma exchange in GBS has recommended albumin in place of FFP, as replacement fluid, [13] but we preferred FFP over albumin owing to the higher cost of the latter. Nevertheless, the high incidence of adverse events in our study is in agreement with some previous studies, including one large study from India. [14] The overall mortality rate in PE, neurological and non-neurological indications combined together, is estimated to be 1-3 per 10,000 procedures. [15, 16] Globally, neurological disorders constitute the leading indication for PE, followed by hematological, renal and rheumatologic disorders. Hyperviscosity syndrome, cryoglobulinemia, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome and idiopathic thrombocytopenia are some of the leading haematological indications [17, 18].

5. Conclusion

Our results show that PE is a safe and effective treatment, for various immune mediated neurological disorders.

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