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Original Research Article

Therapeutic plasma exchange in neuro-immunological disorder

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ABSTRACT

Background: Therapeutic plasma exchange (TPE) is an extracorporeal blood purification technique used to remove high molecular weight substances from the plasma. Examples of these substances include immune complexes, pathogenic autoantibodies, endotoxin, cryoglobulins and cholesterol-containing lipoproteins and myeloma light chains. Therapeutic Plasma exchange is a well-established therapeutic procedure most commonly used in many neuro-immunological disorders. The benefit of plasma exchange occurs by elimination of pathognomonic inflammatory mediators, including complement components, autoantibodies and cytokines. Various studied have demonstrated that TPE plays an important role in neuro-immunological disorder (eg. Guillain-Barré syndrome, myasthenia gravis and other forms of immune neuropathies).
Methods: It is descriptive and prospective study on the effect of TPE in neuro-immunological disorders. TPE are studied prospectively for a period from September 2011 to August 2013. The amount of plasma to be exchanged during TPE was determined using the formula EPV = (0.065 x weight [kg]) x (1-hematocrit). TPE was performed using a Haemonetics MCS+ intermittent flow cell separator. An average of 1-1.5 plasma volume is removed on alternative days. Clinical outcome of TPE was assessed at the time of discharge.
Results: A total of 138 Therapeutic plasma exchange procedure were performed on 30 patients. In which the improvement begins within days of commencing the treatments and progressed steadily so that 25 out of 30 patients who responded favourably to TPE with a manageable adverse reaction. And only 5 patients failed to respond this therapy. So the clinical outcome for therapeutic plasma exchange for Neuro-immunological cases were 83.3% and remaining 16.7% doesn't show any improvement after five plasma exchanges.
Conclusions: Therapeutic plasma exchange is a first line of management for most of the neuro-immunological disorder. In our study there was an improvement in motor performance after 3-5 plasma exchanges which are mainly due to removal of unbound antibodies from the plasma. Although the statistical power of our study was not sufficient to allow definitive conclusion, the result strongly suggest that 3-5 procedures on alternative days with 1-1.5 volume of plasma exchange gives a better result in patient with neuro-immunlogical diseases. The success of therapeutic plasma exchange also depends on composition of the replacement fluid. The risk and complication associated with procedure are also minimal and easily manageable.

Keywords: Extracorporeal, Neuro-immunological, Myasthenia Gravis, Guillain-Barré Syndrome, Plasma exchange

INTRODUCTION

Neuro-immunological disorders consist of diseases in which the immune system seems to attack the nervous system. It is known that antibodies and immune complexes play a crucial role in many kinds of autoimmune disease. Removing these pathogenic substances from patient plasma may result in an efficient means of treatment. When therapeutic plasma exchange (TPE) became clinically available in the early 1970s, several spectacular treatment results in otherwise deleterious clinical situations were reported.[1] The clinical indications for TPE have been progressively growing although the clinical efficacy of TPE has been documented with randomized controlled studies only in limited numbers of diseases.[2,3]

Therapeutic plasma exchange (TPE) is a well-established therapeutic procedure most commonly used in many neuro-immunological disorders. TPE is an extracorporeal blood purification technique used to remove high molecular weight substances from the plasma. Examples of these substances include immune complexes pathogenic autoantibodies, endotoxin, cryoglobulins and cholesterol-containing lipoproteins and myeloma light chains. It is known that antibodies and immune complexes play a crucial role in many kinds of autoimmune diseases, removing these pathogenic substances from patient plasma will result in an efficient means of treatment.

In order to consider TPE as a therapeutic option, two conditions need to be present, a disease state related to the presence of a pathological substance in the plasma and the possibility of removing the substance in a sufficient amount to permit resolution of the disease. TPE is often employed as the last resort treatment of various diseases unresponsive to conventional therapy. TPE has been used for the past three decades to treat a variety of neurological and hematological disorders, and its use is becoming more extensive when compared with Intra Venous immunoglobins. Although generally regarded as a safe procedure, complications do occur. Neurological disorders are among the most common indications for TPE in many countries. TPE is used to treat immunologically mediated peripheral neuropathies including chronic inflammatory demyelinating polyneuropathy, Guillain-Barre syndrome and other disorders such as myasthenia gravis.[5] Only these three neurological disorders (myasthenia gravis, Guillain-Barre´ syndrome, and chronic inflammatory demyelinating polyneuropathy) are among the five most frequent indications for this therapy.[1,4] Most neurological disorders that are treated with plasma exchange are associated with presumed aberrant humoral immune responses, including myasthenia gravis (MG), Guillain-Barre´ syndrome (GBS), and chronic inflammatory demyelinating polyneuropathy.[5] In some of these disorders, the efficacy of plasma exchange has already been demonstrated in randomized controlled study, where as its role in the treatment of other diseases remains less clear.

METHODS

The study was done in the Department of Transfusion Medicine, Vinayaka Mission's KirupanadaVariyar Medical College and Hospital, Salem. It is descriptive and prospective study on the effect of therapeutic plasma exchange in neuro-immunological disorders. Patients with confirmed diagnosis of neuro-immunological diseases requiring Therapeutic plasma exchange are studied prospectively for a period from September 2011 to August 2013. Patient age between 14-80 years and body weight above 30kgs with stable vitals are included in this study and patients on treatment with Intra Venous immunoglobulin's and steroids were excluded.

After establishing the diagnosis of GBS by nerve conduction study and MG by electromyography (EMG) the patient was referred to the Department of Transfusion Medicine for TPE by neurologist. The patients were classified according to Hughes classification for GBS and Osserman classification for MG.

Patient was informed about the procedure in their own understandable language and informed consent was obtained. Detailed history of the patients were taken and assessed clinically. Therapeutic plasma exchange was performed in Medical intensive care unit under the supervision of Emergency physician. Venous access was secured by the emergency physician most preferably double lumen dialysis catheter in femoral vein. After ensuring adequate flow through the catheter TPE was started.

The amount of plasma to be exchanged (Estimated Plasma Volume) during TPE was determined using the formula

$$EPV = (0.065 \times \text{weight [kg]}) \times (1\text{-hematocrit})$$

TPE was performed using a Haemonetics MCS+ intermittent flow cell separator (single needle procedure). Patient vital parameters and adverse reactions during the procedure were monitored.

In a typical TPE procedure, an average of 1-1.5 plasma volume is removed on alternative days. The removed plasma volume was replaced with normal saline (20%), 6% Hydroxyethyl starch (30%) and fresh frozen plasma (50%) in all the patients. ACD solution was used as an anticoagulant in all cases in the ratio 1:16. Clinical outcome of TPE was assessed at the time of discharge.

RESULTS

This study was done among 30 patients, 17 patients (56.7%) were from GBS and 13 patients (43.3%) from

MG. Out of these 14 patients were male which makes 46.7% and 16 patients were female which makes 53.3%.

Table 1: Clinical outcome in GBS.

Clinical outcome	No of patients	Percent
Improved	14	82.35
Not Improved	3	17.65
Total	**17**	

The mean age was 50.73 years, with minimum of 16 years and maximum of 78 years. The haemoglobin mean value was 11.063 g/dl with minimum of 8.0 g/dl and maximum of 14.0 g/dl. Minimum duration of hospital stay was 3 days and maximum was 117 days with mean value 21.45 days. Out of 30 patients 14 patients (46.71%) were under ventilator support.

Table 2: Clinical outcome in MG.

Clinical outcome	No of patients	Percent
Improved	11	84.62
Not Improved	2	15.38
Total	**13**	

Table 3: Overall clinical outcome.

Clinical outcome	No of patients	Percent
Improved	25	83.3
Not Improved	5	16.7
Total	**30**	

Table 4: Incidence of adverse reaction.

Adverse reaction	No of patients	Percent
Nil	23	76.7
Allergic reaction	1	3.3
Catheter block	3	10.0
Citrate toxicity	1	3.3
Hypotension	2	6.7
Total	**30**	

A total of 138 Therapeutic plasma exchange procedure were performed on 30 patients. In which the improvement begins within days of commencing the treatments and progressed steadily so that 25 out of 30 patients who responded favourably to TPE with a manageable adverse reaction. And only 5 patients failed to respond this therapy.

So the clinical outcome for therapeutic plasma exchange for Neuro-immunological cases were 83.3% and remaining 16.7% doesn't show any improvement after five plasma exchanges. Most of the patients who underwent mechanical ventilation were cured after therapeutic plasma exchange and extubated (64.3%). Plasma exchange is highly effective in patient with respiratory distress. Not responding after five plasma exchange for more than 14 days is defined as a treatment failure that was seen in 16.7% of our patients that was similar with other studies.

DISCUSSION

Different studies showed that Therapeutic plasma exchange is effective in 55% - 100% of Neuro-immunological patients. This wide discrepancy between the reports can be due to difference in severity of disease, protocol of Therapeutic plasma exchange or different in study conduction.

Newsom-Davis 1979 compared the long-term effect of plasma exchange plus immunosuppressive drug in seven participants with myasthenia gravis to the effect of immunosuppressive drug alone in seven participants with myasthenia gravis. Plasma exchange was associated with improvement (100%) in all seven participants which has a higher outcome when compared to our study.[7]

Olarte MR studied effect of plasmapheresis in myasthenia gravis in 1978-1980 among 21 patients. 350 plasma exchanges were performed on 21 MG patients, in each exchange about two litres of plasma were exchanged for two weeks. No adverse effects were attributed to the procedure, except transient thrombocytopenia. Out of 21 patients, 17 patients (81%) improved and 4 patients failed to improve after TPE for 2 weeks which was very similar to our result.[8]

Behan PO et al studied Twenty-one patients with myasthenia gravis underwent a course of plasma exchange combined with immunosuppressive therapy. In fifteen (71%) there was dramatic clinical improvement which has been maintained for periods up to 19 months. In our study we had a better outcome that is 84.62% compared to the above study.[9]

Osterman 1984 studied 38 adult patients with GBS, out of which 18 patients received plasma exchange and 20 patents were given a supportive care. Clinical outcome for plasma exchange group was 77.7% whereas control group 30%. In the present study the clinical outcome was slightly higher than the above study 82.35%.[10] Hahn AF et al reported 80% improvement in GBS. 12 out of 15 patients completely respond to plasma exchange with substantial improvement in neurological function. Which is similar to our present study.[6]

In a study done by Valbonesi M et al the success rate of plasma exchange is 100%, which is much better than our result, but was evaluated only in six patients.[11] Kennard C et al, studied twelve patients with Guillain-Barre syndrome treated with plasma exchange. Examination two weeks after treatment was commenced showed that three had not improved and nine patients (75%) improved. But the present study showed an improvement of 82.35%.[12]

CONCLUSION

Therapeutic plasma exchange is a first line of management for most of the neuro-immunological disorder. In our study there was an improvement in motor performance after 3-5 plasma exchanges which are mainly due to removal of unbound antibodies from the plasma.

Although the statistical power of our study was not sufficient to allow definitive conclusion, the result strongly suggest that 3-5 procedures on alternative days with 1-1.5 volume of plasma exchange gives a better result in patient with neuro-immunological diseases. The success of therapeutic plasma exchange also depends on composition of the replacement fluid. The risk and complication associated with procedure are also minimal and easily manageable.

To conclude, therapeutic plasma exchange is an effective and safe procedure when performed with expertise in appropriate indication.

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