

PLASMAPHERESIS: A REVIEW FROM THE UNIVERSITY HOSPITAL, KUALA LUMPUR.

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Summary

Plasmapheresis using a continuous flow cell separator was performed on six patients over the past three years. Three of the four myasthenic patients who underwent plasmapheresis responded dramatically. The response of the two patients who presented with hyperviscosity syndrome secondary to **IgM** paraproteinaemia and multiple myeloma were equally gratifying. Significant complication was seen in one patient who recovered uneventfully. Plasmapheresis is a costly procedure and is associated with definite risks. Therefore it should only be used in well defined clinical settings.

INTRODUCTION

The **Fenwall Centrifuge II** blood cell separator was acquired by the University Hospital in 1982. This continuous flow cell separator is able to carry out procurement of specific components for transfusion and therapeutic apheresis. The operating principle is the creating of an interface between different constituents of blood based on the differential effect of centrifugation.

Plasmapheresis is an expensive procedure. In terms of materials alone, a single procedure costs up to **M\$900**. This paper reviews six patients who underwent plasmapheresis for various diseases over a period of three years in the University Hospital, Kuala Lumpur.

MATERIALS AND METHODS

The case records of six consecutive patients who underwent plasmapheresis in the University Hospital during the 3 year period between 1982 and 1984 were studied with particular reference to their clinical features, therapeutic response and problems encountered.

About 1.5 times of the calculated plasma volume of the patient was exchanged in each procedure. The replacement fluid consisted of either plasma protein fraction or fresh frozen plasma. Whenever possible, plasma protein fraction was preferred in view of less side effects such as severe allergic pulmonary edema which has been reported with the use of fresh frozen plasma' .

RESULTS

Case 1

This 25 year old Indian man was diagnosed as a case of myasthenia gravis in October 1984 when he presented with ocular and bulbar muscle weakness at the Ipoh General Hospital. He showed poor response to conventional

treatment (high dose cholinesterase inhibitor and steroid) and was referred to the University Hospital in December 1984. Soon after admission, he developed respiratory muscle weakness requiring ventilation on and off. Thymectomy was performed on 29th March 1985 and histopathological examination confirmed a thymoma with no evidence of **capsular** invasion. He did not improve after thymectomy. In April 85, after being ventilated for three weeks for an episode of myasthenic crisis, **plasma**pheresis was performed. He responded rather dramatically. Within four days, he was weaned off completely from the ventilator and thereafter made steady recovery. He was discharged with prednisolone 60mg daily, pyridostigmine 60mg 4 hourly and probanthine 15mg qid. He was last seen on follow up in July 85 and was noted to be well.

Case 2

This 30 year old Chinese hawker was diagnosed to have myasthenia gravis in January 1984 at the Penang Medical Centre where he presented with ocular weakness and motor weakness of all four limbs. He was referred to the University Hospital 4 days later. His chest X-ray showed an anterior mediastinal mass. His condition deteriorated and he developed respiratory and bulbar muscle weakness **despite** treatment with steroid and **choline**-sterase inhibitor. Thymectomy was performed on 9th February 1984. Histological examination revealed thymic hyperplasia. He did not show much improvement after thymectomy and lapsed into myasthenic crisis requiring ventilation on 10th May 1984.

He was started on azathioprine **150mg** daily on the same day. He was ventilated for three weeks and could not be weaned off. Plasmapheresis was performed on 1st June

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1984. The response was swift and he was extubated the next day without any problems. He was discharged well two weeks later. At follow up on 24th May 1985, he was well and had started working as a hawker again. He is currently on aziathioprine 150mg daily, prednisolone 20mg EOD and pyridostigmine 60mg 4 hourly.

Case 3

This 37 year old Malay clerk was diagnosed as a case of myasthenia gravis in September 1983 when he presented with respiratory failure at the Assunta Hospital, Petaling Jaya. He was subsequently referred to the University Hospital where he was started on high dose cholinesterase inhibitor and steroids. His response to treatment was unsatisfactory and he required ventilation on several occasions. Thymectomy was performed in March 84 and histological examination showed a thymoma with no evidence of capsular invasion. He continued to have refractory illness. Plasmapheresis was performed on four occasions in April 84 with slight improvement but he still required ventilatory support most of the time. In May 84, he developed cavitating pneumonia which progressed to septicemia and he died on 1st June 85 despite vigorous treatment.

Case 4

This 24 year old Chinese ex-air hostess was diagnosed to have myasthenia gravis in December 1981. She had ocular, bulbar and respiratory muscle weakness on presentation. She was admitted to the University Hospital on several occasions between 1981 and 1983, and was treated with steroids and high dose cholinesterase inhibitor. Thymectomy was performed in January 1983. Her symptoms persisted and she had to be ventilated on several occasions. On 15th December 1983, she was admitted in a severe myasthenic crisis and was ventilated in the intensive care unit. She was still on the ventilator after two weeks.

Plasmapheresis was carried out on 11th January 1984. She responded well and was extubated the next day. Two weeks later, she was discharged on prednisolone 60mg daily and pyridostigmine 60mg 6 hourly. Since then she has been well.

Case 5

L.S., a 63 year old housewife, was first seen at the University Hospital in March 1983 when she complained of decreased effort tolerance. She was diagnosed to have 'mild' depression. Her symptoms however worsened and in April 83, she was referred by a private physician to the University Hospital for investigation of hyperviscosity syndrome.

On admission, she was drowsy and mildly tachypneic. Fundoscopic examination showed sausageing of blood vessels with haemorrhage and exudates. There were scattered crepitations all over the chest. No significant hepatosplenomegaly or lymphadenopathy were noted. The peripheral blood film showed marked rouleaux formation and lymphocytosis. Immunoelectrophoresis showed a marked increase in the level of IgM kappa chains. Bone marrow examination was not diagnostic of myeloma or Waldenstrom's macroglobinemia. She also had significant amounts of cryoglobulins. A diagnosis of IgM paraproteinemia with hyperviscosity syndrome was made.

An emergency plasmapheresis was performed on the second day of admission. After the procedure, she became more lucid and was no longer tachypneic. Her fundic vessels were less congested. Her paraprotein levels showed a significant decrease after the procedure (Table 1). Meanwhile she was started on chlorambucil. 5mg daily.

She has been well since discharge. She was taken off treatment after two months on chlorambucil. Her paraprotein level done on 19th April 1984 was 8 g/L. She was last seen on 12th July 1985 with no notable problems.

TABLE 1
CHANGE IN IG CONCENTRATIONS FOLLOWING PLASMAPHERESIS IN 2 PATIENTS

Case No.	Ig type	Before plasmapheresis	After plasmapheresis
5	IgM paraprotein (g/L)	40	10
6	IgG paraprotein (g/L)	82	38

Case 6

M.K. is a 62 year old retired engineer who was diagnosed in July 1981 as suffering from multiple myeloma on the basis of typical radiological and bone marrow findings and evidence on immunoelectrophoresis of IgG paraproteinaemia. During the subsequent 2 years, he was given 24 courses of cyclophosphamide and prednisolone. He was relatively well until the end of 84, when he developed anemia, pneumonia and bleeding from the gums requiring hospital admission on several occasions. On 27th June 1985, he was readmitted with bleeding from the gums and was noted to be drowsy, confused and rather tachypneic. His fundi could not be visualized due to the presence of dense cataracts. Hyperviscosity secondary to paraproteinaemia was suspected clinically and subsequently confirmed by laboratory findings. He underwent 3 plasmapheresis within one week, with gradual improvement. His paraprotein levels showed a significant drop after the first plasmapheresis (Table 1). Meanwhile, he was started on a multiple drug regime (donorubicin, vinblastine and bleomycin). He was discharged relatively well, lucid and with no evidence of bleeding. However, three weeks later, he was readmitted with similar problems of confusion and bleeding from the gums. In view of the advanced disease (myeloma which was no longer responding to chemotherapy), only symptomatic treatment was given. He was bed ridden and ill at the time of this report.

Complications

One of the six patients developed significant complications while undergoing plasmapheresis. He developed hypotension associated with retrosternal discomfort and cold, sweaty peripheries towards the end of the procedure. The patient was on a ventilator. The FiO_2 was increased and one pint of hemocoel was given rapidly intravenously, whereupon his blood pressure was restored and his symptoms improved shortly. The procedure was completed without any further problems. The reactions observed could have been due to excessive vagal activity or hypocalcemia. The post plasmapheresis serum calcium level was 1.9 mmol.

Minor allergic skin rashes to the replacement fluids used were not uncommon but the reactions subsided rapidly with antihistamine administrations.

DISCUSSION

The popularity of therapeutic apheresis as a modality of treatment surged in 1976 following the reports of two British groups on their success in treating immunologically mediated diseases namely systemic lupus erythematosus² and Goodpasture's syndrome³. In the next seven years, apheresis was tried in a further 143 diseases with varying degrees of success ranging from the spectacular to the abysmal. Currently, the euphoria has subsided⁵. The use of this expensive modality of treatment should be confined to specific conditions where it is of proven value.

In our review, four myasthenic patients who underwent plasmapheresis had severe myasthenia gravis with respiratory muscle involvement. They were at the prime of their lives with their ages ranging from 24 to 37 years. Before plasmapheresis, all of them had undergone thymectomy and none had shown significant improvement. Three of them showed remarkable recovery after plasmapheresis (Table 2). They were on respiratory support for two to three weeks and after a single procedure of plasmapheresis they could be taken off the ventilator within one to four days.

Myasthenia gravis is thought to be an antibody mediated disease. More than 90% of the patients have demonstrable antibodies against acetylcholine receptors. There is generally good correlation between changes in the antibody titres and the disease activity⁶. Plasmapheresis probably acts by depleting the antireceptor antibody.

The indications for plasmapheresis in myasthenic patients⁷ include myasthenic crisis refractory to conventional treatment, pre and post thymectomy and stabilization of patients during start of steroid therapy. The indications for all our myasthenic patients was myasthenic crisis.

Hyperviscosity syndrome associated with macroglobulinaemia and multiple myeloma was the first disorder for which plasmapheresis was performed as a therapeutic manoeuvre⁸. The increase in plasma viscosity results from high levels of abnormal circulating paraproteins.

Our patient with IgM paraproteinaemia (Case 5) responded dramatically after plasmapheresis and there was an associated 75% decrease in the paraprotein level. As 75% of IgM is intravascular, plasmapheresis proved particularly effective. The patient with multiple myeloma (Case 6) also showed satisfactory response after plasmapheresis. There was a

TABLE 2
CLINICAL FEATURES AND RESPONSE OF MYASTHENIA GRAVIS PATIENTS

Case	Sex	Age (yr)	Duration of M.G. before plasmapheresis	Interval since thymectomy	Thymic lesion	Duration of steroid therapy before plasmapheresis	Immunosuppressive therapy	Response to plasmapheresis
1	F	24	2 yr	1 yr	?	1 yr	—	V. good
2	M	37	7 mth	1 mth	Thymoma	6 mth	Azathioprine (started after plasmapheresis)	Slight
3	M	30	5 mth	4 mth	Thymic hyperplasia	3 mth	Azathioprine (before plasmapheresis)	V. good
4	M	26	8 mth	1 mth	Thymoma	5 mth	—	V. good

M.G. = Myasthenia gravis

54% decrease in the **IgG** paraprotein level after a single procedure. The depletion of **IgG** is less effective than **IgM** as only about 52% of **IgG** is intravascular. However it is noteworthy that in both patients with the **hyperviscosity** syndrome, plasmapheresis served as a useful adjunctive treatment.

With regards to the technical aspect of the procedure, we found the use of arterial outlet line (size 20) to be very useful as the optimal outflow rate between 45–60 ml/min could then easily be attained and the procedure could be completed within two hours. In contrast, a venous outlet line was slow and the procedure could stretch up to **six** or seven hours to everyone's discomfort.

The cell separator is a new technology which provides a new modality in medicine. Plasmapheresis is adjunctive and not curative and is a short term treatment modality. **Definitive** therapy, if available, should be given **concomitantly**. Plasmapheresis is a costly procedure associated with definite risks. However, if used judiciously, it provides gratifying results as observed in the patients discussed in this paper.

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