3. Plasma Exchange Therapy in the Treatment of Rheumatoid Arthritis

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In these years, plasma exchange (PE) has been paid attention as a therapy for diseases revealing various immunological disorders.

Since 1978, we have performed PE against collagen disease and autoimmune disease mainly rheumatoid arthritis (RA) and reported its results so far.

This time, we carried out the following four methods against RA and studied about its usefulness.

1. Membrane filtration plasma exchange (MFPE)
2. Double filtration plasma exchange (DFPE)
3. Immunoabsorbent (IA)
4. Lymphocytapheresis (LCP)

We employed Azathioprine for a combination therapy in either method of the above.

We established a definite criterion for the judgement of efficacy and based on it.

We could obtain the same result by MFPE and DFPE with that of plasma exchange which reported previously.

The decrease of immune complex and some variations of immunological parameter were noted by IA and ICP, respectively.

We studied about clinical symptoms, autoantibody, progress of immune complex, etc., and clinical effectiveness concerning each method.

4. Analysis and Clinical Significance of Cryogel Obtained from Patients with Rheumatoid Arthritis

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In recent years, plasmapheresis has been practiced on patients with rheumatoid arthritis (RA) and its clinical effectiveness has been reported. There are three techniques for plasmapheresis using a membrane filter: single-filtration,¹⁾ double-filtration²⁾ and cryofiltration (CF).³⁾ In this report, we examined the clinical effectiveness of CF on fourteen patients with RA and analyzed the chief components of cryogel using high-performance liquid chromatography (HPLC) and ouchtterlony test.

MATERIAL AND METHODS

1. CF system: CF system was performed according to the already established method.⁴⁾ AP-05H (Asahi Med. Co.) and PS 4000 (Terumo Japan Co.) were used as the first filter. AP-06 and CF 01 were used as the second filter. When the pressure in the second filter rose to around 250 mmHg, CF was finished.

2. Patients: CF was performed a total of 196 on fourteen patients with RA. Four were men and ten were women between the ages of 37–70 years.

4. Cryogel Obtained from Patients with RA

Period of contraction was between 3–23 years. Four of them were anatomic stage II, three were III and seven were IV. All of them were functional class II except two were III.

3. Analysis of cryogel: Analysis of cryogel by HPLC was performed according to the already established method.⁴⁾ Asahipak GS-520 column was used. For ouchterlony test, anti-IgG, A, M, D and E antibody (Sigma Chemical Co.) were used.

RESULT AND DISCUSSIONS

Therapeutic response on CF was divided into two patterns. One pattern showed marked rebound phenomenon after each CF at first. The other pattern did not show the marked rebound phenomenon. Seven patients showed positive rebound phenomenon and seven showed negative rebound phenomenon. α 1-globulin, RAHA, IgA, IgM and C3 were significantly different between two groups. However, difference of α 1-globulin and C3 were small, and variance of RAHA was large, and then these parameters were not good indicators which distinguish clinical response against CF. Serum IgM was sufficiently low in rebound phenomenon negative group. Moreover, there were significant negative correlationship between plugging time of the second filter and serum IgM concentration. It means serum IgM concentration is good indicator to distinguish clinical response and to predict the plugging time of the second filter before CF⁴⁾. We measured Lansbery scores before and after each CF to evaluate the improvement of clinical manifestations objectively. Fig. 1 shows Lansbery scores before and after CF to examine a short-term therapeutic effectiveness. Lansbery scores decreased significantly after CF. Fig. 2 shows Lansbery scores at entering and leaving the hospital and reduction rate between two column to examine a long-term therapeutic effectiveness. As we evaluate clinical effectiveness of CF as follows; excellent: reduction rate is above 50%, good: 30–49%, moderate: 15–29%, poor: below 15%, five patients showed excellent, six showed good, two showed moderate, one showed poor.

A chromatographic pattern of cryogel showed six peaks marked A, B, C, D, E and F. Repro-

Fig. 1. Comparison of Lansbery score between before and after cryo-filtration.

Case	Lansbery Score at entering the hospital (%)	Lansbery Score at leaving the hospital (%)	Reductin Rate of Lansbery Score (%)
	136	79	41.9
	78	23	70.5
	62	33	46.8
	123	74	39.8
	113	46	59.3
	38	26	31.6
	101	59	41.6
	104	75	27.9
	101	59	41.6
	79	36	54.4
	54	24	55.6
	149	117	21.5
	90	40	55.6
	22	20	9.1

Fig. 2. Lansbery score and reduction rate at entering and leaving the hospital.

ducibility was extremely good. Chief component of cryogel was A peak and this was divided into three peaks marked A1, A2 and A3. The molecular weights of these three were 1,300,000, 1,000,000 and 640,000. Moreover, we analyzed cryogel obtained from first, fifth and tenth CF of the same patient and cryogel obtained from different four patients. A chromatographic pattern of each cryogel did not change. For this results, we concluded that components of cryogel do not change during CF therapy and between the patients, quantitative change of cryogel is important factor

Fig. 3. Ouchterlony test of A₁, A₂ and A₃ peaks analyzed by HPLC.

for RA therapy.

We measured IgG, IgA, IgM, C3, C4 and im-

mune complex in 10 mg cryogel dissolved by isotonic saline. Concentration of immune complex was not high. From this result, we concluded that immune complex is not chief component of cryogel.

To examine the relation between A₁, A₂ and A₃ of cryogel and immunoglobulins, ouchterlony test was performed. Fig. 3 shows that immunoglobulins, especially native IgM, were not component of cryogel.

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5. Plasma Exchange Therapy in Systemic Lupus Erythematosus: Its Indication and Evaluation

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The purpose of this study is to clarify whether the measurement of T cell subsets, the splenic function, determined by the radiolabelled heat-damaged red blood cells and the chronicity index of the renal biopsy specimen are useful or not to determine the indication of plasma exchange therapy for patients with SLE.

Plasma exchange (PEX) was performed by the centrifugation method or double filtration plasmapheresis. Series of PEX consisted of 3 to 6 procedures and 5% albumin solution was used for the substitution fluid.

In 16 patients with SLE, the measurement of T cell subsets was carried out before and after

series of PEX by the flow cytometry using OKT monoclonal antibody (Ortho Pharmaceutical Corp.).

The splenic function was studied in 7 patients by the radiolabelled heat-damaged red cells before PEX and repeated within 1 to 5 weeks after series of PEX in 4 of 7 patients.

In 8 patients, renal biopsy was performed. The specimen was examined under the light microscopy and the lesions were scored as the chronicity index which is modified by Morel-Maroger's sclerosing index.

There were no significant changes in OKT3, 4 and 8 positive cells before and after PEX and also