PLASMA EXCHANGE IN SEVERE GLOMERULONEPHRITIS – WHO BENEFITS?

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Summary

Plasma exchange (PE) and immunosuppression was used in the treatment of 17 patients with severe glomerulonephritis and 17 acute rejections in transplant recipients. No response occurred in crescentic nephritis with anuria; a temporary improvement occurred in other nephritis patients but half of these relapsed on immunosuppression alone. Seven rejection episodes responded. Responses always occurred promptly and prolonged PE did not improve the results. Histology, serum complement or immune complex results did not predict a successful outcome.

Introduction

Plasma exchange (PE) and immunosuppression have been widely advocated and used for the treatment of Goodpasture’s disease [1], rapidly progressive glomerulonephritis [2] and acute rejection of renal transplants [3]. We report the results of this treatment from a regional nephrology unit serving a population base of 1.2 million.

Methods

Between 1975 and 1981, 17 patients were admitted with rapidly progressive renal failure secondary to a severe crescentic glomerulonephritis (excluding patients with SLE). Renal biopsy, serum complement (CH\(_{50}\), C\(_3\) and C\(_4\)), immunoglobulins, C1q binding activity for immune complexes, autoantibodies including anti-GBM antibodies and standard renal function tests were performed before, during and after treatment. Oral prednisone (1mg/kg/bodyweight), cyclophosphamide (2mg/kg) and azathioprine (3mg/kg) were administered daily, usually after PE.

Seventeen transplant recipients with biopsy-confirmed acute rejection were
treated after they had failed to respond to methylprednisolone 1 g i.v. daily for two to three days. Standard low dose oral corticosteroid and azathioprine were continued.

PE was performed on an Amicon (1975–1979) or Hemonetics (1979–1981) cell separator using an arteriovenous shunt. The exchange volume was 50 ml plasma/kg/body weight, using Plasma Protein Solution (Plasma Fractionation Centre, Edinburgh) or fresh frozen plasma and up to 1 L 0.9 per cent saline. Plasma exchange was performed daily for five to 12 days and followed three/week for two to three weeks. Calcium supplements were added to the PPS.

Results

Glomerulonephritis

Goodpasture’s syndrome

Seven oligo-anuric patients failed to show any improvement in renal function (Figure 1) despite control of anti-GBM antibodies in five. One patient (Figure 2).

![Rapidly Progressive Glomerulonephritis Non-Responders](image)

Figure 1. Renal function before and after PE in non-responders
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS RESPONDERS

![Graph showing plasma creatinine levels before and after plasma exchange with disease progression and response to treatment]

- Goodpasture's
- IgA
- PAN
- Proliferative
- MCGN I
- MCGN II
- Drug-induced Goodpasture's

Figure 2. Renal function before and after PE in responders showed a temporary improvement for 11 weeks, during which he became nephrotic (urine protein 5-14g/day) but then deteriorated.

**Idiopathic, crescentic glomerulonephritis**

Two oligo-anuric patients failed to improve (Figure 1).

**Other crescentic glomerulonephritis (Figure 2)**

a) Two patients with polyarteritis nodosa and one with Henoch-Schönlein vasculitis made a good initial response but then relapsed despite continuing immunosuppression.
b) One patient with mesangiocapillary glomerulonephritis (MCGN) type 1 made a temporary response only while two with MCGN type 2 made a good long-term recovery.

c) Other — three patients (penicillamine-induced Goodpasture’s syndrome, IgA nephropathy and post-infectious proliferative glomerulonephritis) made a good long-term improvement having failed to improve for several weeks prior to plasma exchange.

There were no differences in the percentage of glomeruli containing crescents (more than 70 per cent in all cases) or in the pre-PE plasma creatinine between long-term responders and non-responders in this group. The creatinine clearance post-treatment correlated best with the fall in plasma creatinine during the first ten days of PE (Figure 3).

Immune complexes were only detected in one patient with idiopathic crescentic nephritis and one with polyarteritis. Low \( CH_{50} \) and \( C_4 \) were seen in only three cases.

![Graph showing the relationship between percentage fall in serum creatinine and post-therapy creatinine clearance. The correlation coefficient is \( r = 0.76 \) with a p-value of \( p < 0.005 \).](image)

**Figure 3.** Percentage fall in serum creatinine after 10 days of PE in relation to one month post therapy creatinine clearance

**Transplant rejection**

None had hyperacute rejection and all had had a prior blood transfusion.
Live donor

One patient had a good long-term response and one did not respond at all.

Cadaver

Six cadaver grafts were successfully treated and nine did not respond. There was no difference between first, second or third grafts. Response was more common in swollen, tender grafts; pre-treatment urine volume, sodium concentration or albumen excretion were not helpful.

Discussion

PE is not generally indicated in anuric patients with Goodpasture’s disease or idiopathic crescentic nephritis. It may have a role in other varieties of severe glomerulonephritis complicated by crescent formation, but selection of cases remains empirical and more data on long term results are needed. There is no clear indication for the use of PE in transplant rejection but a subgroup of patients appear to respond. Short courses of PE appear to be effective and if an improvement in renal function does not occur within the first two weeks it is unlikely to do so thereafter. Critical evaluation of PE is still required and its use in nephrology restricted to research departments.

References


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Open Discussion

BONE (Liverpool) We had an impression in our patients that the follow-up immunosuppression was of some importance. This was shown by a patient who stopped taking his tablets and relapsed. He was re-biopsied again, he again had crescentic glomerulonephritis and he again responded to steroids. Do you have any comments on your patients who responded initially and then deteriorated with respect to their on-going immunosuppression?

SWAINSON Patients with systemic disease like polyarteritis were continued on steroids. Since immunosuppression has not been shown to be of benefit in the other categories of disease mentioned we did not continue with immunosuppression and tailed it off a week after the end of plasma exchange. I think the mechanisms of progression of renal disease and subsequent renal failure in these patients may be very different from the original pathogenetic mechanisms as Professor Cameron illustrated so well this morning. All plasma exchange can do is to deal with the acute pathogenetic events e.g. immune complexes, and it probably does
very little for other as yet unknown events which cause progression to chronic forms of nephritis.

DAVISON (Chairman) One of the points you emphasised in your talk was the follow-up of the patient prior to initiation of plasmapheresis, and you were showing a very clear deterioration. Are you sure that during that phase there was no iatrogenic disease such as diuretic induced interstitial nephritis because I think that is perhaps more common than most of us would believe.

SWAINSON Most of these patients were not on diuretics; two were on heavy doses of Frusemide. In some cases we did biopsies early in the course of the disease; every one of them had a biopsy immediately prior to plasma exchange and in none of these could the pathologist be certain they were seeing a drug-induced lesion. In every case the glomerular lesion was much worse where we had two biopsies to compare.

DAVISON Yes, but in many instances in rapidly progressive glomerulonephritis, crescentic nephritis, one sees interstitial changes that you would not be able to differentiate.

SWAINSON Yes, I think that is a fair point, but it would be very difficult to sort out.