S-5-6

RATIONALE FOR USE OF PLASMA EXCHANGE IN MOF

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Potency of current therapy - With ICU support, 10-30% of patients with MOF can expect to survive. New therapies target specific mediators of sepsis and are unlikely to be effective.
Experimental - Plasma from patients or animals with MOF is capable of inducing immunosuppression or MOF when used in cell systems or animals. From this we conclude that the plasma is harmful, however some patients recover suggesting that the means to recover is contained in plasma. Altering the balance of harmful:beneficial plasma is the logical progression from these observations.
Practicalities - Many patients with MOF already undergo extra-corporeal support so the addition of plasma filtration requires no extra equipment.
Economy - The daily cost of ICU patients is only a fraction higher with plasma exchange. True savings will only be made if survivors recover earlier. Risk - Benefit ratio - The risks of plasma exchange procedures are negligible on experienced units. Transfusion carries small risks of reaction and infection. The risk of not having the treatment may be death. On our own unit plasma exchange was used in 20 patients with MOF who were not expected to survive. 50% initially improved after such treatment and 40% survived MOF. Comparative survival rates for other patients with MOF were 25 - 30%.
Prospective evaluation of such treatment is urgently needed!

S-6-1

INEFFECTIVENESS OF PLASMAPHERESIS IN SLE NEPHRITIS

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We studied the effectiveness of plasmapheresis in patients who had severe glomerular inflammation associated with SLE. Entry into the study was determined on the basis of the presence of severe lupus glomerulonephritis, as defined by a panel of expert histopathologists.

Plasmapheresis, administered 3 times weekly for 4 weeks with concurrent standard prednisone and oral cyclophosphamide therapy, was compared to prednisone/cyclophosphamide alone in 86 patients. The mean follow-up was 136 weeks. During this time, 13% of patients in the standard therapy group died compared to 20% of patients in the plasmapheresis group. Seventeen percent of patients in the standard therapy group developed renal failure, compared to 25% in the plasmapheresis group. The overall clinical course and the course of renal function was signifcantly better in patients receiving standard therapy. These results occurred despite a significantly more rapid reduction in plasma concentrations of anti-double stranded DNA and cryoprecipitable immune complexes. Patient outcome was strongly determined by the initial serum creatinine irrespective of the treatment given.

We conclude, that, in patients with severe lupus glomerulonephritis, the outcome which can be expected from prednisone and short-term oral cyclophosphamide therapy is not improved by the addition of plasmapheresis therapy.

S-6-2

PLASMAPHERESIS AND SUBSEQUENT PULSE CYCLOPHOSPHAMIDE IN SLE: A CHANCE FOR TREATMENT-FREE REMISSION IN AN INCURABLE DISEASE?

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Seven controlled trials have demonstrated that plasmapheresis has no or only marginal long-term benefit when applied as an adjunct to conventional peroral immunosuppression. Alternatively, a protocol has been developed which attempts to utilize the antibody rebound mechanism by exploiting the enhanced susceptibility of activated pathogenic lymphocyte clones following antibody depletion for increased clonal deletion through high-dose pulse cyclophosphamide (Ctx). This approach induced treatment-free remission in 8 of 14 SLE patients (Arthritis Rheum 1994;37: 1784). Meanwhile a total of 19 patients with severe SLE (SLAM score: 13-37) were treated (recently with anti-Ig-adsorption instead of plasmapheresis). As of Nov-95, 13/19 patients are off all medication. The mean follow-up is 58 months, the longest observation amounting now to 9 years without signs of SLE activity. Patients in long-term remission retain very low titers of antinuclear antibodies. B cell activity and T4/T8 ratios have returned to normal. Thus, synchronization of plasmapheresis (or: anti-Ig-adsorption) with subsequent pulse Ctx appears to offer a chance for long-term remission without continuation of treatment in severe SLE.

S-6-3

DIFFERENTIAL EFFECTS OF DIFFERENT IMMUNOADSORPTION DEVICES IN COLLAGEN VASCULAR DISORDERS

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Connective tissue diseases and systemic vasculitides respond in general to immunosuppressive treatment; new therapies are mostly based on pathophysiological concepts. Removal of circulating immune complexes and other proinflammatory substances from blood was the basis for introducing apheresis in the management of SLE 20 years ago. Experiences showed that autoantibodies-titers and circulating immune complexes are reduced and RES function improved after plasmapheresis, but early studies already indicated that an additional immunosuppressive therapy is needed to prolong clinical benefit.
The efficacy in treating organ manifestations also depends on the kind of inflammation, the type of pathogenic antibody and the duration of organ involvement. In SLE and other systemic connetive tissue disorders, these pathophysiological factors are heterogenous, which may in part explain the differences in response. Therefore more selective extracorporeal therapies may offer advantages and reduce the risks of plasmapheresis resulting from its non-selective removal of all plasma proteins.
During the past decade, an increasing number of different adsorbers with heterogenous specificities have been used in variable connective tissue diseases with more or less defined, multiple indications. Although controlled trials are still in the pipeline, published data and our own results with diverse adsorbers in vitro and in vivo support the idea of a more disease- and indication-specific intervention by immunoadsorption. The opportunity for continuous regeneration and for reuse in the same patient offers a further improvement in response by a more significant antibody reduction.
In vitro selection of an adsorber by its binding specifities is in our experience not always anadequate indicator of a clinical response to the immunoadsorptive therapy. Our results document the need for early intervention to increase the response rate in organic manifestations.