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Robert Weinstein

Chief, Hematology and Transfusion Medicine, Caritas St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, Massachusetts, USA

Comunication with:
Robert Weinstein
Tel.:
E-mail:
bobbw@massmed.org

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Introduction

Monoclonal immunoglobulins or immunoglobulin fragments that accumulate in the plasma are referred to as M-proteins.[1] When the plasma concentration of an M-protein is low (generally < 3.0 gm/dL) and does not rise over time the M-protein is referred to as a monoclonal gammopathy of uncertain significance and the prognosis is generally benign.[2] However in certain M-protein disorders, notably multiple myeloma and Waldenström's macroglobulinemia, the plasma M-protein concentration usually increases and this may result in clinical disease.[1,2]

The complications of M-protein disorders that relate most directly to therapeutic apheresis are hyperviscosity syndrome and myeloma kidney.[3-6] Both of these are direct clinical complications of the M-protein in patients with Waldenström's macroglobulinemia or multiple myeloma, thus both are considered to be category II indications for plasma exchange by the American Society for Apheresis.[7] The designation category II means that therapeutic apheresis is accepted as a supportive or adjunctive treatment but is not ordinarily the only treatment that should be used.[7] Thus, chemotherapy would also be required to achieve long-term control of these disorders while plasma exchange is used for short-term control or relief of symptoms.[8,9]

Hyperviscosity

The first report of plasmapheresis for treatment of hyperviscosity in Waldenström's macroglobulinemia employed manual plasmapheresis in which 1000 mL of whole blood were removed by venesection, the plasma was removed by centrifugation, and the red blood cells reinfused.[8] The authors noted that removal of relatively modest volumes of plasma over several days would result in a similarly modest decrease in serum macroglobulin level but would also result in a marked decrease in serum viscosity. This was explained by the observation that the presence of a macroglobulin was associated with an expansion in plasma volume and red cell volume in approximately 2/3 of patients.[10] As the M-protein is removed, plasma volume progressively decreases, thereby improving the efficiency of M-protein removal with each procedure.

Hyperviscosity may be associated with microvascular thrombosis, anemia, coagulopathy, congestive heart failure, headache, peripheral neuropathy and other symptoms.[11] Removing the M-protein thereby alleviating hyperviscosity helps to resolve these symptoms, but Chopek and McCullough[12] determined over a quarter century ago that removal of M-proteins using plasma exchange was only half as efficient as would be predicted using standard calculations of plasma volume based on body weight and hematocrit. Because the goal of plasma removal, whether by plasmapheresis or plasma exchange, is to decrease viscosity thereby improving the patient's symptoms the amount of M-protein removed is less important than the extent to which viscosity is lowered. Removal of 5 to 6 liters of plasma will deplete more than 80 % of the M-protein from a patient with Waldenström's macroglobulinemia, but symptomatic relief and reduction of viscosity can be achieved by removal of only 1 to 3 liters in many patients.[6]

Palabras clave
✓ aferesis terapéutica
✓ recambio plasmático
✓ hiperviscosidad

Key words
✓ therapeutic apheresis
✓ plasma exchange
✓ myeloma treatment
✓ hyperviscosity

Myeloma kidney

Renal insufficiency is present at presentation in approximately 30 % of patients with multiple myeloma and occurs in approximately 50 % of cases overall.[13,14] Although several mechanisms of renal injury have been described in multiple myeloma, cast nephropathy, or myeloma kidney, is the most frequent.[15,16] Myeloma kidney results from immunoglobulin light chains that combine with Tamm-Horsfall protein in the renal distal tubule to form an obstructing intratubular cast.[17] Standard treatment includes volume expansion, alkalinization of the urine and diuretics to increase liquid handling by the kidney. Chemotherapy is used in order to diminish the production of the offending M-protein. Hemodialysis is used when necessary but will not influence the delivery of light chains to the distal tubule nor increase the potential for renal recovery.[18-20]

Plasma exchange was first reported as a means to improve renal function by reducing the delivery of light chains to the distal tubule in a 1976 case report.[21] A series of 3 patients was reported in 1979.9 Since that time three randomized trials have indicated that short term plasma exchange, in conjunction with fluid, alkalinization of the urine, diuretics and chemotherapy will improve the renal outcome (and in some cases the overall survival) of patients with multiple myeloma and myeloma kidney.[19,22,23]

Tandem plasma exchange and hemodialysis

A case report presented at the 2003 Annual Meeting of the American Society for Apheresis demonstrated the feasibility of continuing plasma exchange support, in tandem with hemodialysis, cyclophosphamide and supportive care, until renal function improves sufficiently to permit discontinuation of both hemodialysis and plasma exchange.[24] In order to permit outpatient treatment of this patient, and to minimize the number of visits he made to the hospital for treatment, plasma exchange and hemodialysis procedures were performed in tandem, at the same time, through the same venous access device. We have recently reported a series of three patients with M-protein disorders who received 23 to 80 tandem plasma exchange and hemodialysis procedures over 3 to 7 months largely in the outpatient setting.[25] Two of the patients were elderly men with multiple myeloma, and one was a middle aged man with amyloidosis and painful amyloid arthropathy.

The procedures were performed using centrifugal continuous-flow apheresis equipment that was connected to the dialysis tubing in parallel with the low pressure side of the hemodialysis circuit.[26] In order to determine whether the plasma exchange procedure would diminish the efficiency of hemodialysis we calculated the urea reduction ratio (URR):

$$URR = 100 \times [U_{reapre\text{-}dialysis} - Urea_{post\text{-}dialysis} / Urea_{pre\text{-}dialysis}]$$

for each patient, for three consecutive months, and compared the URR calculated during tandem treatments to URR calculated during hemodialysis alone. URR is an indicator of the adequacy of hemodialysis.[27]

All three patients were able to undergo tandem treatments as mentioned above. In all three cases there was no difference in URR during tandem treatments compared to URR during hemodialysis alone, demonstrating that plasma exchange did not compromise the efficiency of hemodialysis. After 3 months of tandem plasma exchange and hemodialysis one of the patients was able to discontinue both treatments because of the improvement in his creatinine clearance to 30 mL/min.

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