

# Renal Failure from Cast Nephropathy: Role of Plasmapheresis

## Short Communication

In multiple myeloma renal involvement is common, occurring in 50% of the patients and is an independent predictor of poor patient survival [1]. These circulating paraproteins can cause a variety of renal manifestations depending on the site of involvement, type and load of protein involved and mechanism of injury inflicted, resulting in glomerular diseases, proximal tubulopathy and obstructive nephropathy [2].

Light chain cast nephropathy is one of the common renal manifestations, resulting from circulating plasma free light chains. Improved renal recovery has been associated with early reduction of light chains. The evidence on the role of Plasmapheresis combined with chemotherapy alleviating renal failure by reducing the light chains load is conflicting. It does lower serum free light chains rapidly and might reduce renal toxicity, but its effects on patient survival and recovery of renal function by itself yet to be demonstrated [5].

In a systematic review of literature by Kumar et al. concluded that overall survival as well as the need for dialysis is not affected by plasmapheresis in multiple myeloma patients with acute renal failure [3]. Meta analysis by Alkhatib et al. suggested plasmapheresis might be beneficial in cast nephropathy patients proven by biopsy in combination with chemotherapy. This Meta analysis included 147 patients with more than 50% of them receiving plasmapheresis and treatment schedule varied from 4 to 7 sessions. Plasmapheresis group has lower risk of dialysis dependence compared to the control group but no overall difference in mortality risk at 6 months. There are ongoing clinical trials to assess high-cutoff dialysis as a promising alternative. Most of the clinical trials reported were before the introduction of proteasome inhibitors and immunomodulators which improved response, complete remission, progression free and overall survival compared to conventional chemotherapeutic agents [4]. Another systematic review in patients with acute renal failure from multiple myeloma reported no benefit of plasmapheresis in renal function improvement or overall survival. In this meta analysis, 8 articles met the inclusion criteria out of which 3 were Randomized Controlled Clinical Trials (RCTs). Two out of these 3 RCTs showed majority of patients attained dialysis independence, but showed no difference in survival. All studies demonstrated that the patients receiving plasmapheresis showed an improvement in renal function, however statistically significant improvement in renal function was proven only in 2 RCTs and one retrospective study [6].

Burnette et al. presented their experience of 14 patients over 6.5 yrs receiving proteasome inhibitor [bortezomib] and serial plasma exchange within a week of diagnosis of cast nephropathy. They reported 43% of the patients with complete and partial renal response respectively. Combined use of bortezomib and plasmapheresis is effective in improving the acute renal failure in patients with multiple



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myeloma presumed due to cast nephropathy [7].

In a study reported by Hutchison et al on multiple patients with severe renal failure and biopsy proven myeloma kidney, demonstrated that early reduction of serum free light chains correlated with improvement in renal function as well as improvement in median survival [8]. In another study reported by the same author involving 67 patients with multiple myeloma causing dialysis dependent renal failure [86% of them with cast nephropathy] was treated with high-cutoff dialysis in combination with chemotherapy with approximately two-thirds of the patients achieved independence from dialysis [9].

It is unclear whether reduction of the levels of free light chains represents the efficacy of proteasome inhibitors rather than the efficacy of plasmapheresis.

Two randomized clinical trials (MYRE and the EULITE) assigned patients with biopsy proven cast nephropathy causing acute renal failure with primary end point of discontinuation of renal replacement therapy to combination of proteasome inhibitor-based chemotherapy with either high Cut-Off Hemodialysis (HCO-HD) or High-Flux Hemodialysis (HF-HD). No difference in renal recovery was found in EULITE study. Patient who were in HCO-HD were independent of dialysis at 6 months as per MYRE study. Both studies were small, which makes any firm conclusions on the benefit of HCO-HD questionable. Based on the current knowledge, without more robust data, the routine use of HCO-HD cannot be recommended [10].

Generally, plasmapheresis is combined with chemotherapy to achieve a 50-60% reduction in serum free light chains. If dialysis is required on the same day, it is done after the plasmapheresis [8,11].

As per American Society for Apheresis 2016, indications for therapeutic apheresis and cytapheeresis procedures-plasmapheresis for renal failure from cast nephropathy in multiple myeloma falls under category 2 recommendation (Disorders for which plasmapheresis for renal failure from cast nephropathy in multiple myeloma is accepted as second-line therapy, either as a standalone treatment or in conjunction with other therapies) and evidence 2b

(Weak recommendation based on moderate quality evidence) [12].

Most of the clinical trials demonstrating the role of plasmapheresis were done before multiple combination therapies of proteasome inhibitors, immunomodulators, monoclonal antibodies which have significantly altered the management of myeloma with many patients achieving complete remission as well as significant improvement in progression free survival, and overall survival compared to conventional chemotherapy. Plasmapheresis might still be beneficial in a group of patients with cast nephropathy causing renal impairment in combination with chemotherapy. High-cutoff dialysis being another promising alternative to plasmapheresis.

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