Journal of Nephrology & Therapeutics
ISSN: 2161-0959

Lipe, et al., J Nephrol Ther 2016, 6:3
DOI: 10.4172/2161-0959.1000249

Short Communication Open Access

Cost/Effectiveness Treatment of Acute Renal Failure Secondary to Multiple Myeloma with Filters High Cut off

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Received date: May 3, 2016; **Accepted date:** May 23, 2016; **Publication date:** May 31, 2016

Abstract

Introduction: Treatment of Multiple Myeloma with high cut off filters was started in 2007.

Working hypothesis: The High Cut Off hemodialysis is a cost-efficient treatment.

Objective: To demonstrate that a combination treatment of chemotherapy and High cut off dialysis improves patient survival and quality of life, while saving costs by chronic dialysis.

Methodology: Up to 13 treatments with HCO filters have been applied in the University Hospital Lozano Blesa of Zaragoza to patients with acute renal failure (ARF) secondary to Multiple myeloma.

Results: 13 treatments were performed on 12 patients with high cut off hemodialysis. Six patients were diagnosed with monoclonal gammopathy Kappa and 6 were diagnosed with monoclonal gammopathy Lambda, with high levels of light chains in serum over 500 mg/L (11,036 mg/L on average at the beginning). We have achieved an improvement of renal function and have allowed the patient to live without dialysis dependence in 77%. We demonstrated that the savings would be 11.782 Euros.

Discussion: This paper focused on the idea that although the high cost of high cut off filters is an inconvenience, this should not impede their use because the technique has been proven more effective and cost efficient

Conclusion: The treatment is cost-effective; cost savings can be estimated in more than 11,000 euros/patient.

Keywords: Multiple myeloma; Acute renal failure; Filters high cut off

Introduction

Multiple Myeloma (MM) represents 13% of hematologic cancers [1]. It is characterized by an uncontrolled proliferation of plasma cells, producing large amounts of free light chains (FLCs) which can cause obstruction of the renal tubule. Up to 40% of patients develop kidney failure and 10 to 15% require dialysis

The causes of renal dysfunction in patients with myeloma includes a proximal and distal tubular cell damage by alteration of the filtered light chains (FLCs), cast nephropaty, amyloidosis, deposition disease light chains or heavy [2], crioglobulinemia, interstitial infiltration by plasma cells, and rarely a proliferative glomerulonephritis or interstitial nephritis [3].

Life expectancy is less than 1 year with renal failure, although treatment can extend up to 5-7 years [4,5].

Treatment of acute renal failure rests on three pillars: eliminate factors that aggravate nephrotoxicity and forming cylinders, eliminate or reduce production by FLCs neoplastic cells, and eliminate or reduce FLC.

Three methods have been used to remove these free light chains in the blood: plasmapheresis, dialysis filters HCO, and recently supra HFR.

Treatments of Multiple Myeloma with high cut-off (HCO) filters were started in 2007, beginning with a 1.1 m^2 surface HCO filter, and then increasing to a 2.1 m^2 surface. In 2012 Hutchison [6] published 67 treatments of acute renal failure secondary to multiple myeloma and 2011 Grima [7] published in a study based on a cost-effective model, comparing treatment with HCO filters to conventional dialysis treatment. The cost savings explained by Grima are based on avoiding chronic hemodialysis; the model predicted a survival of 20 months in standard dialysis, as opposed to a survival of 34 months "using the HCO filters, and because treatment with HCO filters avoids the use of dialysis, the patients would also experience higher quality of life".

Working Hypothesis

The High Cut Off hemodialysis, is a cost-efficient treatment.

Objective

To demonstrate that a combination treatment of chemotherapy and High cut off dialysis improves patient survival and quality of life, while saving costs by chronic dialysis.

Methodology

This is a descriptive study. In the period between July 2011 and February 2015 (44 months). Up to 13 treatments with HCO filters had been applied in the University Hospital Lozano Blesa of Zaragoza to patients with acute renal failure (ARF) secondary to Multiple myeloma

Selection criteria

Patients with acute renal failure secondary to multiple myeloma requiring dialysis.

Levels of blood free light chain higher than 500 mg/L

Dialysis protocol: A Integra® monitor (Hospal®) was used, equipped with ultrafilters of 1.4 m^2, ultrapure water, bicarbonate cartridge (Bicart®) and centralized acid in a closed circuit, vascular access through a Shalldon® central catheter and heparinization with sodium heparin at 1%.

The dialyzer used in each case is a HCO filter with a surface of 2.1 m^2 made of polyarylethersulfone/polyvinylpyrrolidone (Theralite®) from Gambro®.

Dialysis treatments took place daily for six sessions, and later proceeded to happen every other day until levels of FLC in blood were reduced to less than 500 mg/L or the recovery of renal functions allowed them to dispense with dialysis.

The duration of dialysis was six hours INCLUDING a low blood flow between 250 and 300 ml/min, bath fluid flow 500 ml/min.

During dialysis sessions levels of renal function, FLCs, calcium, phosphorus, ions and albumin were monitored.

For the economic evaluation we took an approach similar to the one used by Grima used to calculate costs. Therefore, we have based our investigation essentially on the cost of the HCO filter, the albumin, dialysis lines, heparin circuit Prontoprime® priming liquid, dialysis bath fluid (bicarbonate cartridge Bicart® + centralized acid), Sodium heparin, 20 ml. syringe, physiological sodium solution and Shalldon® temporary catheter. Because these patients were considered as any other acute patients increased staff was not required and the two extra hours of nurse assistance included by Grima was not used.

In order to be able to compare the results we have chosen to accept the estimated survival time published by Grima. Survival of our patients should be evaluated in the long term, but so far we can claim that 3 patients have survived without dialysis for more than 3 years.

The two main limitations of the study were the lack of a control group and a small number of patients.

Results

We present our experience in the period between July of 2011 and February of 2015 (44 months). 13 treatments with high cut off hemodialysis were performed on 12 patients, 9 men and 3 women with a mean age of 60.8 years and range between 43 and 71 years. 6 patients were diagnosed with monoclonal gammopathy Kappa and 6 were diagnosed with monoclonal gammopathy Lambda, with high levels of serum free light chains over 500 mg/L (11.036 mg/L on average at the beginning).

A total of 151 dialysis sessions were performed, and patients stayed on a dialysis treatment with the HCO filter an average of 11.53 sessions with a range between 6 and 27 sessions. The patients, 9 male and 3 female, were on average 60.8 years old and their ages varied between 43 and 71 years old.

Regarding the bone marrow infiltration, we can say that we know the result in 10 patients and all of them had high levels of plasma cells (in a case there is evidence of plasmacytoma) that varied between 13% and 93%.

In 10 out of the 13 cases (77%) we improved the renal function of our patients enough to allow them to live without depending on a dialysis, proving the technique is effective in both the Kappa and Lambda chains, with a elimination percentage per dialysis of 58%, similar to the one obtained by other authors, who found loss between the 53 and 57% [7] and a final reduction in chains over 93%.

The cost of the HCO filter Theralite® from Gambro® in our hospital is 825 euros, the cost of each 50 ml vial of Human Albumin 20% solution is 17.68 euros, the rest of the material (lines, temporary catheter, dialysis bath, priming solution (Prontoprime®), Sodium heparin, physiological serum, and a 10 cc syringe) cost 82.06 euros. Thereby, the total cost of a dialysis with HCO filter is 924.76 (Table 1).

Material	Price
Dialyzer	825
Albumin	17,68
Linrd	4,73
Dialysis Bath	3,93
Prontoprime	3,87
Heparin	3,20
Physiological serum	0,66
Syringe	0,026
Temporary Catheter	65,67
TOTAL	924,76

Table 1: Cost of the hemodialysis with HCO filters. Material and medicine prices euros H.U Lozano Blesa Zaragoza Spain.

The total sessions that occurred during the 13 treatments was 151 sessions, each patient did an average of 11,53 sessions, for a total cost of 10.866 euros per treatment.

The cost per dialysis session in our hospital from the year 2011 to 2014 (the studied period) including the costs of pharmacy and supplies (dialysis equipment, lines, fluids, dialyzers, ultrafilters, catheters, etc.) was 87'11 euros per session on average, this information was obtained from the nephrology services reports.

A patient usually requires of 3 weekly sessions, 156 yearly sessions, for a total estimated cost of 13589 euros.

If we consider Grima's work, average survival time of patients with Multiple Myeloma with dialysis' is 20 months, which represents a cost of 260 sessions x 87.11 euros, totaling 22.648 euros; therefore, we could save up to 11.782 euros (Table 2).

HD Type	Nº Sessions	Cost/Session	Total
HCO	11,53	842,45	10.866
Standard	250	87,11	22.648
Saving			11.782

Table 2: Cost savings. Comparison of the cost of a dialysis session with HCO filters or conventional average number of sessions patient, cost per session, total cost y total savings per treatment. High cut off (HCO) filters; Hemodialysis (HD): Number sessions (Nº sessions).

Discussion

The myeloma kidney treatment is oriented to reduce the exposure of the kidney to the FLCs. This is managed by acting on the Multiple Myeloma through chemotherapy treatment (dexamethasone, bortezomid, ciclophosphamide, etc) to reduce its production, at the same time they are used as adjuvant treatment techniques using extracorporeal depuration to eliminate FLCs [8-10].

The recovery of the renal function will depend not only on the reduction of the circulating FLCs, but also on the speed in which we can achieve this reduction, as Hutchison published [11].

Our results are similar to those published by Hutchinson in 2012 with sixty-seven patients with dialysis-dependent renal failure secondary to Multiple Myeloma, the median number of hemodialysis HCO sessions was 11 (range 3-45), the median number sessions in our Hospital was 11, 53 (range 4-27), 63% of population became independent of dialysis in the study of Hutchinson, versus 77% in our initial attempt to eliminate the plasma FLCs was performed with plasmapheresis, and although the initial studies seemed promising, later it was proved that the elimination of FLCs is limited, due to the distribution of FLCs in the body (80% extravascular) and to the extremely big size of the plasmafilter pores, which is why a high quantity of other essential proteins are lost [12].

Recently the hemodiafiltration with endogenous reinfusion (HFR) has emerged, a technique that combines convection, diffusion and adsorption. This treatment requires a capillary dialyzer with double chamber; initially a thin membrane with high permeability is used to allow the passing of FLCs, specially kappa, a ultrafiltration takes place and this ultrafiltration passes through a cartridge of adsorptive resin in which toxins attached to proteins are stopped, and theorically the FLCs are stopped as well, with the advantage of not adsorbing the albumin once regenerated the FLCs are infused between the two chambers of the dialyzer [13,14]. The second chamber of the dialyzer is a low permeability membrane and in it takes place a conventional HD.

In a recent report de Pascalli published in 2015 [15] supra-hemodiafiltration in combination with chemotherapy effectively reduced serum free light chains without need for albumin replacement, As in previous studies only 4 patients were treated, allowing us to draw few conclusions.

Considering the limitations of the HFR for the elimination of FLCs Lambda, and the reservations we must have because of the limited number of patients examined, we can only infer that the HFR achieves a reduction of the FLCs Kappa without having albumin loss, studies with more patients should be performed to confirm that is an effective technique for the treatment of acute renal failure secondary to multiple myeloma.

In our opinion and once we have examined the bibliography, the treatment modality in which we get the best results [16-19] is hemodialysis (HD) with dialysis membranes of very high permeability high-cut-off (HCO), these membranes have a pore size between 45 and 60 KDa, and are designed specifically for the kidney of the myeloma, but they present some disadvantages like the high loss of albumin and an elevated cost.

The treatment with HCO filters assures good results in the elimination of both Kappa and Lambda chains, overcoming the limitation shown by the HFR that only has good results in the elimination of Kappa chains.

In this study we have focused on proving that one of the main disadvantages discussed, high cost, shouldn't be an obstacle for its application, since it actually is the technique that has been proved to be most effective in our study and, that this technique is cost efficient we have made clear in this work, even without taking into account the indirect costs like sanitary transport, staff costs during the months the patient would stay on chronic hemodialysis, etc. Therefore, we believe that should treatment using high cut off filter be the chosen technique for a patient with acute renal failure secondary to kidney myeloma.

Conclusions

The combined treatment of chemotherapy and dialysis with HCO filters has been effective in treating acute renal failure secondary to multiple myeloma in 77% of the cases.

The treatment is cost-efficient, with savings estimated in more than 11,000 euros per patient.

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