Evolving protocols: utilising free light chain filter treatment for multiple myeloma-associated acute kidney injury

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Abstract

Acute kidney injury associated with multiple myeloma does not resolve with traditional haemodialysis, often resulting in stage five chronic kidney disease and permanent dialysis, which is an additional burden for patients with an uncertain future. The porous membrane of the high cut-off (HCO) haemodialysis filter is showing promising results in reducing levels of free light chains in serum and hence reverting acute kidney injury. This article focusses on the HCO haemodialysis treatment from a nursing perspective, outlining treatment frequency, anticoagulant and dialysate changes and the instigation of cytotoxic precautions. Experience gained with HCO filters has resulted in a protocol maximising patient safety and ensuring consistency in practice.

Keywords

Free light chain, multiple myeloma haemodialysis.

Disease manifestations and prognosis

Multiple myeloma (MM) is a type of cancer of unknown cause involving malignant plasma cells in the bone marrow. Although this cause of acute and later chronic kidney disease accounts for less than 2% of the dialysis patients nationally (Grace, Hurst & McDonald, 2011) and up to 10% internationally (Gondouin & Hutchinson, 2011), renal involvement in MM affects a staggering 30–50% of diagnosed patients. International data collection is being undertaken to evaluate if early treatment with high cut-off (HCO) haemodialysis filters may reduce the incidence of acute kidney injury (AKI) in this population. The challenge for the collaborating medical teams is to provide a timely diagnosis and instigation of combined treatments for both myeloma and renal impairment (Cockwell & Cook, 2012). Within our unit the instigation of free light chain (FLC) treatment is discussed by the renal consultant team with consideration given to the degree of AKI, including symptoms such as fluid overload, the patient's current state of health, and the level of FLCs evident. The timing of these interventions, coupled with the current health of the patients makes the course of the treatment and outcomes highly variable.

Cases of MM exhibit an overabundance of one particular immunoglobulin, kappa (κ) or lambda (λ). These immunoglobulins, known as FLCs reach a precipitation point either as MM develops or, because of declining kidney function related to infection, hypovolaemia, hypercalcaemia or medication reactions, resulting in AKI (Hutchinson *et al.*, 2011; Stringer, 2011). The level of FLC which triggers AKI is highly individual and influenced by the extent of compounding factors as mentioned (Hutchinson *et al.*, 2009).

FLCs are excreted in excess in the urine and consequently overwhelm the tubules of the kidney, which is then unable to process the increased amount of FLCs being produced. These FLCs precipitate with proteins to form waxy casts, which, in turn, block the flow of urine and cause interstitial inflammation. FLCs normally have a half-life of two to three hours, but due to impaired kidney function, increased levels will persist for two to three days or until treated (Pratt *et al.*, 2006).

The difficulty in removing the FLC relates to the relatively small size of the protein molecule, weighing κ 22.5kD and λ 45kD, respectively, which are found in similar concentrations in the serum, but with the majority (80%) found extravascularly (Gondouin & Hutchison, 2011). Therefore, traditional haemodialysis-related absorption or removal therapies have been unable to remove FLCs in significant quantities to prevent AKI. Plasma exchange procedures have shown minimal benefit due to the inability to consistently remove the destructive kappa and lambda light chains from both the intracellular and extracellular compartments (Gondouin & Hutchison, 2011). Plasma exchange may only remove 25% of FLCs, whereas specific FLC

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filters are predicted to remove up to 85% (Cockwell & Cook, 2012). Since 2009 the HCO filters with a molecular weight cut-off of 65kD have been more widely available in Australia (Cockwell & Cook, 2012).

The resolution of renal function is reliant on the early and ongoing reduction of FLCs with a 60% reduction (by day 21 after diagnosis) associated with recovered renal function in 80% of cases (Hutchinson, 2011*b*). However, if levels are not reducing, consideration needs to be given if FLCs are clumping into molecules of a higher molecular weight, which may not be able to be removed (Cockwell & Cook, 2012). Those patients that remain dialysis-dependent generally have poorer outcomes with mean survival rates being <1 year compared with those patients with MM alone [overall survival of around 44 months] (Cockwell & Cook, 2012).

Development of treatment methods

Availability of the HCO filters has enabled the unit to implement procedures and processes around the instigation and review of treatment and the required nursing care. Historically, as treatments were being trialled, various strategies were utilised, such as adding the convective force of haemodiafiltration (HDF) in an attempt to increase clearances.

Various strategies have been investigated including use of:

i. *Single filter with surface area (SA) of 1.1m^2 (utilising the dialysis principles of diffusion and absorption)*

ii. *Double filters increasing SA to 2.2 m^2 (utilising diffusion and absorption)*

iii. *Single filter (1.1.m^2 SA) and pre-dilution HDF (utilising diffusion, convection and absorption)*

iv. *Double filter (2.2.m^2 SA) and pre-dilution HDF (utilising diffusion, convection and absorption)*

v. *With increased product availability now a single filter with surface area 2.1m^2 (utilising diffusion and absorption), has resulted in the previous treatments becoming obsolete. This treatment is now solely utilised as the current treatment regime in our unit.*

An international FLC data registry (ReFLeCt) is in place to collate patient data, treatment variabilities and patient outcomes. This will add to the knowledge base established by the EuLITE study, a mulit-centred randomised controlled trial undertaken in the United Kingdom and Germany, the results of which are eagerly anticipated (Hutchinson, Cook, Heyne *et al.*, 2008).

Nursing management

Once the diagnosis has been ascertained as a new or reoccurring presentation, the nephrologist will schedule treatments. Reoccurring disease is less likely to respond to treatment with HCO filters but may be considered dependent on the patient's clinical state. Once temporary central venous catheter (CVC) access is organised, liaison with the oncology unit is necessary in relation to the timing of chemotherapy treatments, and the resultant scheduling of HCO dialysis. Concurrent management plans including chemotherapy and HCO dialysis are considered essential to maximise efficiency of the treatment.

In preparing the filter and equipment, nurses need to ensure that the filter is thoroughly primed to minimise elevations in transmembrane pressure (TMP) during the treatment (which is indicative of clotting). Manufacturers advise to keep TMP greater than 100 mmHg to facilitate FLC flow across the dialyser membrane. Priming fluid is also forced across the membrane to ensure dialyser pores are fully open. Appropriate blood tests are taken (Table 1), the patient is connected to the machine, and treatment is commenced. The appropriate anticoagulant dose is administered with unfractionated heparin being the preferential medication due to ease of use, measurable effect and reversibility.

Table 1: Pathology monitoring regime

Time	Pathology
Pre-HDx	Free light chain (FLC) levels Electrolyte & liver function tests (ELFT) including phosphate, albumin & magnesium *(urgent)* Full blood count (FBC) Activated partial thromboplastin time (APTT)
4hr	ELFT inc. PO4, Alb., Mg *(urgent)* APTT
Post-HDx	FLC ELFT inc. PO4, Alb., Mg *(urgent)* FBC
Ongoing	Activated clotting times (recommended in units with available equipment)

The treatment lasts for eight hours, as extended time increases the rate of FLC removal from the serum, extravascular space and tissues. Blood flow rates ran at 250–300 ml/min dependent on the type of haemodialysis vascular access and patient tolerability, related to intercurrent illness. Blood flow rates remain at the established level for ongoing treatments in order to maximise blood/dialyser contact volume. Clinical observations including blood pressure, pulse, temperature, respirations and oxygen saturations are undertaken every 30 minutes during the first treatment. For ongoing treatments, the patients are individually assessed regarding their response to treatment in order to determine frequency of clinical observations.

Throughout the treatment pathology is reviewed and changes to dialysate occur (Table 2). Various complications, especially disequilibrium symptoms may become evident during the extended treatment time and nurses must independently assess for risk and manage these in consultation with the medical team (Table 3).

Optimum communication and documentation is required to monitor patient progress, evaluate treatment and ensure associated oncology and dialysis appointments are accurately planned. Scheduling of treatment is reviewed at three weeks and planned around guidelines included in Table 4.

Table 2: Dialysate concentration

Electrolyte	**Dialysate additions for extended treatment with HCO filter**
Potassium (K^+)	Additional of 4 mEq/L — diluted at a concentration of 1:35 parts with dialysis water
Phosphate (PO_4)	20–60 ml/5L utilising Fleet additive
Bicarbonate (HCO_3)	Machine settings are often reduced due to potential for alkalosis. Changing bicarbonate settings from the standard 35 i.e. +3 may be lowered to 33 (+1) and possibly as low as 30 (–2)
Calcium (Ca^{++})	Nil changes as results likely to be high due to MM

Once chemotherapy has commenced, patients are considered to be cytotoxic and appropriate precautions for staff safety need to be in place. This includes personal protection equipment for cytotoxic management, and education in the handling and disposal of wastes. Patients will remain cytotoxic for one week after the final dose of chemotherapy; therefore, this is ongoing through the HCO treatment regime.

Not only are patients nervous about pending treatments and their ongoing diagnosis, they are overwhelmed by the myriad of heath care professionals they encounter. It is the dialysis nurses' role to ensure information is clearly and accurately relayed and it is consistent with other team members. Education regarding cytotoxics is provided to the patient and family by oncology staff and reinforced by the nephrology nurses. Clear explanations are required regarding the HCO treatment, care of temporary CVC, and the increased risk of infections due to the patients' immunocompromised state.

Towards the completion of a treatment, intravenous albumin is routinely administered as serum levels decrease due to the high porosity of the HCO membrane (Table 3). On completion, final pathology tests are taken and the patient treatment is completed. The machine is cleaned with an additional, internal bleach disinfection to minimise any build-up of proteins in the dialysate lines. Once completed, dialysate lines are checked for residual bleach before the machine is used again.

Table 3: Nursing management

Treatment considerations for extended treatment time (8 hr) with HCO filter	**Nursing considerations**	**Rationale**
Potential for clotting	Monitoring clotting times and adjust anticoagulant as required	Extended treatment time increases clotting time and changes in coagulation result related to chemotherapy/anaemia
Potential for disequilibrium syndrome	Ensure urea levels reviewed prior to commencement of treatment and monitor patient for signs and symptoms	High urea level and consequent sudden decrease predisposes patients to disequilibrium syndrome
Variable fluid status	Fluid assessment at commencement of each treatment and regular medical consultation	Accurate assessment of ultrafiltration goal will minimise any risks of hypotension, cramps, nausea etc
Electrolyte imbalance	Daily monitoring and adjustments for first week then as individually assessed, dependent on extent of abnormalities	Electrolyte review identifies abnormalities and ensures appropriate dialysate prescription is administered and changed throughout treatment
Significant albumin loss	Monitor levels throughout treatment and electively supplement 1–2 bottles albumin 20% in last half hour of treatment (in line with the EuLITE study)	Due to the high porosity of the filter loss of albumin is evident and should be prevented (Hutchinson, Cool, Heyne *et al.*, 2008)

Patient data

MM is a devastating disease and, coupled with AKI, individuals are faced with multiple health challenges. Whilst FLC treatment aims to resolve the effects of AKI, the progression of MM is a dominant factor in the patient's state of health. Of the 10 patients that were managed in our unit from 2009 to 2012, three withdrew from treatment due to the consequences and negative health effects of MM. Whilst outcome data is beyond the scope of this article due to the small patient numbers, it is encouraging to note that 50% (5/10) of the patients were able to recover renal function and be independent of dialysis, 20% (2/10) remained dialysis-dependent and 30% (3/10) withdrew from treatment.

The age range of patients was 47–83 years, with an average of 64.7 years. Eighty per cent (8/10) were male. HCO dialysis treatment regimens ranged from five to 10 treatments, with most patients receiving the 10 treatments. The variation was related to individualisation of treatments based on patients' results, if a patient chose to cease treatment or was transferred to their home unit in a different city.

Treatment challenges

Disequilibrium syndrome occurred in one patient and was evident by headache, altered thought patterns and mild confusion and was related to due to the extended treatment time. This was negated in the remaining patients (5/10) by having consecutive, shortened haemodialysis sessions for several days prior to the commencement of HCO dialysis. Two patients had recurrence of MM with AKI so treatment was instigated at a lower level of renal decline; one patient did not required dialysis prior to treatment and one patient transferred from another unit and hence prescription of prior treatments were uncertain.

Due to the treatment initiatives to prevent complications (outlined in Table 4) patients did not experience any other side effects from the HCO treatment. However, one patient remained anaemic during this period and declined blood transfusions due to religious convictions. Nursing staff monitored the individual for signs of deteriorating health or increased symptoms but treatment and management of anaemia and changes in chemotherapy were managed by the oncology team.

Table 4: Treatment schedule

Frequency and duration of treatments
Daily for first six days then chemotherapy on the seventh day
Second daily for two weeks, chemotherapy as planned by oncology consultants around dialysis sessions
Three times a week for one week
Review and individualise prescription based on response to treatment Total treatments should be up to one month or a maximum of 18

Conclusion

Developing guidelines and nursing care parameters for the utilisation of HCO filters and eight-hour treatments has ensured ongoing safe practice in patient care. As new equipment and experience is evident, strategies need to be continually reviewed and potential risks identified. As we await further evidence, we will continue to be challenged in providing treatment to patients with MM and the variety of clinical symptoms that impact upon their kidney function.

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