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NURSING BEST PRACTICE GUIDE

Myeloma kidney disease

This document is one of the Myeloma Academy Nursing Best Practice Guides for the Management of Myeloma series. The purpose of this Guide is to enhance knowledge and inform nursing practice of myeloma kidney disease in the care of myeloma patients.

After reading this, you should be able to:

- Define myeloma kidney disease
- Understand the cause, symptoms and consequences of myeloma kidney disease
- Be aware of the clinical testing and assessment tools for myeloma kidney disease
- Understand the treatment for myeloma kidney disease
- Understand the nurse's role in the assessment, intervention and management of myeloma kidney disease and in the patient education of this complication

The information contained within this Guide should be used in conjunction with local policies, protocols and best practice guidelines in oncology.

Background

Myeloma kidney disease refers to a common and potentially serious complication of myeloma which can result in renal failure. It represents one of the major causes of morbidity and mortality in myeloma.

Myeloma kidney or cast nephropathy (MCN) occurs as a result of the co-precipitation of excessive myeloma free light chains and Tamm-Horsfall proteins within the distal renal tubules[1]. Their interaction forms waxy casts which block the renal tubules and causes interstitial inflammation and fibrosis[2-4].

In addition to myeloma kidney disease, in myeloma, the free light chains are also

KEY FACTS

- Myeloma creates a burden on the kidneys and many patients have, or are at risk of developing, renal complications
- The most common cause of renal impairment is cast nephropathy or myeloma kidney disease
- Early diagnosis and intervention is key to preventing irreversible renal damage and improving overall outlook and survival

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directly toxic to the proximal renal tubules adding further to the impairment of renal function[4, 5]. At diagnosis, up to 20% of patients present with acute renal failure (less than 15% renal function) as a result of myeloma kidney disease. Of these, 10% of patients will require dialysis[6].

Renal impairment can also evolve over time with an estimated further 40% of patients affected during the course of their myeloma[2, 7]. This is because many factors common in myeloma can contribute to renal impairment. These factors include dehydration, hypercalcaemia, urinary tract infection and sepsis, exposure to nephrotoxic drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics and contrast media[8]. Other comorbidities including diabetes, hypertension, prostatic obstruction and congestive heart failure also contribute to renal failure.

More rarely, plasma cell infiltration, amyloid or light chain deposition disease may cause renal impairment[9].

In general, the risk of myeloma kidney disease is directly proportional to the level of urinary free light chain excretion[10, 11] but is independent of the light chain class and presence or absence of intact paraproteins. Many patients, however, can excrete large amounts of free light chains without any effect on renal function[12]. Renal failure, however, reflects a high tumour burden, more aggressive disease and poorer prognosis[13].

The clinical consequences of myeloma kidney disease include:

- ★ Metabolic acidosis
- ★ Uraemia
- ★ Anaemia
- ★ Fluid and electrolyte imbalance
- ★ Cardiovascular, gastrointestinal and neurological complications
- ★ Renal failure

Provided patients are diagnosed early, rapid intervention to remove free light chain load can in most cases successfully reverse renal impairment and improve survival outcomes; outcomes remain inferior to those for patients with normal renal function at diagnosis[14].

However, diagnosis can be difficult as symptoms are not often apparent until renal impairment is quite advanced. Symptoms at this stage may include shortness of breath, fatigue, headache and swelling in the ankles or feet.

Identifying myeloma patients at risk of renal impairment and diagnosing those with existing renal impairment early is therefore a priority so that preventative and therapeutic interventions can be initiated to reduce the impact of renal complications.

The following describes the medical approach to the treatment of myeloma kidney disease and provides guidance on nursing interventions and nursing management of patients with myeloma kidney disease.

GENERAL RECOMMENDATIONS:

- ★ All myeloma patients should have their renal function assessed at diagnosis and monitored on a regular basis
- ★ Signs and symptoms of renal impairment should be recognised and be managed immediately
- ★ Drugs or conditions that contribute to myeloma kidney disease should be avoided or controlled to reduce the risk of further renal impairment
- ★ Light chain burden on the kidney should be monitored by measuring serum free light chain levels

NURSING RECOMMENDATIONS:

- ★ Patients undergoing rehydration therapy should be monitored closely for fluid balance and renal output and have daily weight checks
- ★ Bisphosphonate treatment for hypercalcaemia should be administered safely to avoid kidney toxicity
- ★ Blood samples should be taken at the appropriate times to monitor kidney function in response to treatment
- ★ Patients and their families should be made aware of the importance of keeping hydrated to maintain kidney health and the need to report new symptoms as soon as possible

Medical Approach

In most cases, renal function in patients with myeloma kidney disease improves by exercising certain measures. The following section describes the general medical approach to the treatment of myeloma kidney disease which usually involves a referral to the renal team.

Assessment

The most common laboratory findings which suggest renal impairment in myeloma patients are asymptomatic proteinuria and/or elevated serum creatinine levels.

Serum creatinine levels vary considerably depending on age, gender, ethnicity and body size, and are not usually raised until over 50% of total kidney function is lost. Therefore, creatinine measurement alone should not be used to assess renal function. Clinical laboratories typically publish their own reference ranges, and these should be used in assessing creatinine results.

For a more accurate assessment of kidney function, the estimated glomerular filtration rate (GFR) should be calculated using the Chronic Kidney Disease (CKD) Epidemiology Collaboration creatinine equation[15]. However, some laboratories may still use the Modification of Diet in Renal Disease (MDRD) equation[13].

CKD is now classified using the eGFR and the albumin/creatinine ratio (ACR)[15]. Severity is indicated by a score ranging from G1A1 which is normal kidney function, to G5A3, the most severe
(Appendix I).

In some instances, the estimated GFR is not sufficient. In these cases, clearance of radiolabelled EDTA provides a more accurate GFR value. This test requires patient preparation and repeated blood samples[16]. Nurses play an important part in preparation and support of the patient for this assay.

Creatinine clearance, measured from a 24hr urine collection, can also provide an accurate assessment of renal function. The normal value for creatinine clearance is >90ml/min but it is important to note that this value declines at a rate of 1ml/min/year in individuals over the age of 40.

During routine tests, assessment of other parameters will also provide an indication of renal function, including: full blood counts; albumin; urea; blood urea nitrogen; electrolytes; and parathyroid hormone.

For the most accurate assessment to define the degree and extent of renal damage as a result of myeloma kidney disease, a renal biopsy is required. However, renal biopsies do not form part of routine assessment for myeloma patients, unless renal amyloidosis or light chain deposition disease is suspected.

Treatment

The most effective way of treating myeloma kidney disease is to reduce the light chain load delivered to the kidney tubule by reducing light chain production from the myeloma cells. In addition, it is also essential to induce a high urine flow rate to minimise light chain precipitation.

Oral high-dose dexamethasone should be started without delay, but in most cases other supportive or mechanical approaches are initiated to rapidly reduce light chain load before other anti-myeloma treatments are administered. Bortezomib/dexamethasone-based regimens are the preferred regimens for most patients with myeloma who present with renal impairment, especially for newly diagnosed patients; however, other agents (thalidomide, lenalidomide) in combination with dexamethasone may also improve renal impairment in several patients[7].

Depending on the treatment, doses may need to be adjusted for patients based on the extent of renal impairment (see Appendix II).

Renal dialysis (haemodialysis or peritoneal dialysis) may be necessary for patients with severe renal impairment.

Supportive treatment

For the majority of myeloma patients with any degree of renal impairment at diagnosis, renal function will improve by exercising measures such as:

- Fluid rehydration with at least 3 litres of normal saline daily
- Correction of hypercalcaemia with modified doses of bisphosphonates
- Discontinuation of nephrotoxic drugs such as NSAIDs and aminoglycoside antibiotics
- Vigorous treatment of any infection

Volume replacement should be guided by monitoring central venous pressure if renal output is reduced. Renal function should start to improve within 48 hours of initial interventions but if not, further advice from the renal team should be sought.

Mechanical approaches

Light chain load can theoretically be reduced by their physical removal from the plasma.

Plasma exchange (plasmapheresis) has been used to decrease serum free light chain concentrations particularly in patients with acute renal failure, with varying degrees of success. If carried out, it should be done in conjunction with dexamethasone-based treatment to limit production of new light chains.

The recent development of extended haemodialysis with high cut-off dialysis is currently being investigated. Early indications suggest that it may be more efficient at removing free light chains than either plasmapheresis or conventional dialysis. At present, this new method of haemodialysis should only be considered within the context of a clinical study[6, 17, 18].

Other treatments

Treatment of other underlying causes of renal impairment such as hypertension and diabetes is also required.

Further supportive treatment in the form of erythropoietin (normally made by the kidney) or blood transfusions may also be necessary to prevent or treat chronic anaemia.

Nursing interventions and management

Myeloma kidney disease can be successfully managed through an integrated approach with the multidisciplinary team with key input from nurses.

The following provides best practice recommendations for nursing interventions related to the assessment, treatment and monitoring of patients with myeloma kidney disease, and for nursing management involving a more holistic approach to care for this patient group.

Interventions

- Be vigilant for signs of acute renal failure: headache, nausea, vomiting, fever, chills, pain, bleeding, weakness, fatigue, taste changes, oliguria. Inform the multidisciplinary team if the patient reports any new or worsening symptoms of renal impairment
- Be vigilant for signs of infection and alert the multidisciplinary team if action is required
- Ensure patients comply with prescribed treatments and supportive care for myeloma kidney disease

Management

- Inform all myeloma patients of risk of impaired renal function and how to recognise any signs or symptoms. In particular instruct them to be observant for any changes in urine output or the characteristics of their urination (change in frequency, cloudy, bloody)
- Encourage all myeloma patients to drink at least 3 litres of fluid daily to maintain renal health. This instruction should include showing what a litre of fluid is, using visual examples
- Educate patients on the need to avoid NSAIDs, aminoglycoside antibiotics and contrast dyes used in imaging scans
- Ensure patients understand the importance of reporting symptoms of renal impairment and they know how, when and to whom they should report
- Inform patients and their families of the different investigations for renal impairment and the different treatments involved. For example, provide instructions for 24 hour urine collection. Allow time to listen to their questions, concerns and anxieties
- Provide patients with written information to help them understand about myeloma kidney disease
- Discuss with and advise patients and their families of the benefits of lifestyle changes such as stopping smoking, exercise, diet and weight management, in reducing the risk of or in improving renal impairment
- Make regular assessments of symptoms, quality of life and psychological wellbeing and coordinate referrals to the palliative care team or counsellors if necessary
- Coordinate care with both renal and haematology teams to ensure successful management of each patient, advocating as required in difficult decisions about treatment
- Have a clear understanding of myeloma kidney disease and the technologies available for its treatment
- Ensure that drug doses are appropriate to renal function

Summary

Myeloma kidney disease is a potentially serious complication of myeloma which can cause a number of long-term serious consequences if it is not diagnosed early.

Prompt treatment and management can in most cases reverse the renal damage caused by myeloma kidney disease.

In this regard, nurses play a key role in assessing and monitoring the signs and symptoms of renal impairment and in providing timely management and support to optimise patient outcomes.

Abbreviations

- **ACR** Albumin to creatinine ratio
- **CKD** Chronic kidney disease
- **CrCl** Creatinine clearance
- **CTCAE** Common terminology criteria for adverse events
- **EDTA** Ethylenediaminetetraacetic acid
- **ESRD** End-stage renal disease
- **GFR** Glomerular filtration rate
- **MCN** Myeloma cast nephropathy
- **mg/mmol** Milligrams per millimolar
- **ml/min** Millilitres per minute
- **NSAID** Non-steroidal
- **od.** Once daily

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ABOUT THE NURSING BEST PRACTICE GUIDES

The Nursing Best Practice Guides have been developed by Myeloma UK and an expert nursing advisory group, with input from relevant specialist healthcare professionals. They have been developed to enhance nurse knowledge, inform nursing practice and support nurses in the delivery of high quality treatment and care to myeloma patients and families.

Nursing Best Practice Guide series:

- ★ Complementary therapies
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The Myeloma Academy provides healthcare professionals involved in the treatment and care of myeloma patients with access to comprehensive accredited learning resources and tools in an innovative online environment and through educational events.

It supports the education and continual professional development of myeloma healthcare professionals so they can provide optimum patient-centred treatment and care within the current UK health and policy environment.

For more information visit:
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ABOUT MYELOMA UK

Myeloma UK is the only organisation in the UK dealing exclusively with myeloma.

Our mission is to provide information and support to people affected by myeloma and to improve standards of treatment and care through research, education, campaigning and raising awareness.

For more information about Myeloma UK and what we do, please visit **www.myeloma.org.uk** or contact us at **myelomauk@myeloma.org.uk** or **+44 (0)131 557 3332.**

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Appendix I

Classification of Chronic Kidney Disease[15]

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol) description and range		
			< 3 Normal to mildly increased	3 - 30 Moderately increased	> 30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73m²) description and range	≥ 90 Normal and high	G1	No CKD in the absence of markers of kidney damage		
	60 - 89 Mild reduction related to normal range for a young adult	G2			
	45- 59 Mild-moderate reduction	G3a[1]			
	30 - 44 Moderate-severe reduction	G3b			
	15 - 29 Severe reduction	G4			
	< 15 Kidney failure	G5			

Increasing risk

Increasing risk

[1] Consider using eGFRcystatinC for people with CKD G3aA1

Appendix II

Recommended dose reductions in renal failure

Drug	Renal function	Dose change
Melphalan	GFR 30-50 ml/min GFR <30 ml/min	Reduce dose by 50% Stop use
Cyclophosphamide	GFR 10-50 ml/min <10 ml/min	Reduce dose by 25% (titration according to bone marrow toxicity for subsequent courses) Reduce dose by 50%
Velcade® (bortezomib)	Mild to moderate renal impairment (CrCl>20 ml/min/1.73m^2) Severe renal impairment (CrCl <20 ml/min/1.73m^2) requiring dialysis	No dose adjustment necessary Pharmacokinetics unknown. (Since dialysis may reduce Velcade concentrations, it should only be administered after dialysis)
Revlimid® (lenalidomide)	Mild renal impairment Moderate renal impairment (CrCl 30-50 ml/min) Severe renal impairment (CrCl <30 ml/min, not requiring dialysis) End-stage renal disease (ESRD) (CrCl <30 ml/min, requiring dialysis)	No dose adjustment required 10 mg od. (Increased to 15 mg od. after 2 cycles if patient is tolerating treatment but not responding) 15 mg every second day (increased to 10 mg od. if patient is tolerating treatment) 5 mg od. On dialysis days the dose should be administered after dialysis
Thalidomide		No dose reduction recommended. Renal impairment does not appear to lead to increased toxicity

Notes

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