Supportive and palliative care for people with end-stage renal disease

Advanced renal failure has a mortality rate worse than for most cancers with significant symptom burden. Despite this palliative care for this group has been poor. This article summarizes the role that palliative and nephrology teams can play in optimizing end-of-life care.

With an ageing population, the number of people dying with and from chronic kidney disease is growing; however, end-of-life care has previously been neglected in this patient group. Chronic kidney disease is classified into five stages, with advanced disease referring to stage 5 (*Table 1*). The UK annual incidence of stage 5 chronic kidney disease is 100 per million of population (Hamer, 2006) and growing. The rise has been in particular groups such as the elderly and those with multiple comorbidities (Ansell et al, 2008). With technical advances and increasing availability of dialysis and transplantation, renal replacement therapy has been regarded by some as the gold standard treatment for even the frailest patients. However, evidence is growing that these patients experience significant morbidity and mortality and such interventional treatment may not always be appropriate.

The median age for commencing renal replacement therapy in the UK is around 65 years. Patients who receive a renal transplant survive on average 10.4 years, those on haemodialysis 2.9 years and peritoneal dialysis 2.0 years. However, with an increasing incidence of elderly patients and those with significant comorbidities requiring renal replacement therapy many such patients are not eligible for transplantation, with only 22% of those over 65 years of age having a functioning transplant compared to 59% of those under 65 years. Overall approximately 67% of over 65-year-olds therefore opt for haemodialysis, with significant regional variation, and most of these will need to attend hospital three times a week to receive dialysis (Caskey et al, 2011).

Table 1. Chronic kidney disease classification

Stage	Glomerular filtration rate	Note
1	>90 ml/min	Normal glomerular filtration rate with other evidence of kidney disease
2	60–90 ml/min	Slight decrease in glomerular filtration rate, with other evidence of kidney disease
3	30–60 ml/min	Moderate decrease in glomerular filtration rate, with or without other evidence of kidney disease
4	15–30 ml/min	Severe decrease in glomerular filtration rate, with or without other evidence of kidney disease
5	<15 ml/min	Established renal failure

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Despite such medical advances in managing end-stage renal failure the overall mortality rates for these patients remain worse than for most cancers, with a median overall survival of under 6 years (Ansell et al, 2009). This deteriorates further with advancing age, with a less than 20% 5-year survival after starting renal replacement therapy in those aged over 75 years. Thus not all patients benefit from dialysis and some may experience a significant deterioration in quality of life because of the demanding and arduous nature of dialysis. In response to this, there has been increasing recognition of the need for specialist palliative care for patients with end-stage renal failure and the National Service Framework for Renal Services (Department of Health, 2005) advocates close collaboration between nephrology and palliative care services.

This article explores the role of palliative care in managing end-stage renal failure and how such services can be integrated with evolving nephrology management. In addition, it discusses the challenges of helping individuals make shared informed decisions regarding life-prolonging treatment such as dialysis and which factors studies have shown to be important when considering withholding and withdrawing treatment. Finally it describes how to manage some of the complex symptoms experienced by end-stage renal failure patients as well as management of the terminal stage.

The role of specialist palliative care

Many patients starting dialysis are old and frail, which both increases morbidity and mortality and limits the individual's ability to cope with dialysis. There is now a growing evidence base aiming to identify which patients do not benefit from dialysis in the hope of preventing patients unnecessarily undergoing dialysis and its complications. Patients over the age of 75 years, with multiple

comorbidities, poor performance status or frailty are considered to do less well, and such patients have been shown to gain no survival benefit from dialysis (Mallick and El Marasi, 1999; Munshi et al, 2001, 2003; Murtagh et al, 2007b).

In addition to determining clinical factors affecting outcome, Murtagh et al (2006) stated it is crucial that health-care professionals shift from a predominantly disease-focused approach towards a patient-focused approach. This is because often patients' wishes and preferences may not be related to their renal failure but to other pertinent factors that determine their individual quality of life, such as being the primary carer of a loved one, geographical location and a wish to have no life-prolonging treatment regardless of expected benefit.

With increasing awareness of the poor outcomes on dialysis for certain patient groups and that some patients may actively opt for 'no dialysis', conservative kidney management is becoming a valid, positive option discussed during pre-dialysis education. Many such patients continue to live active lives with relatively few symptoms despite surprisingly low estimated glomerular filtration rate. These patients will not necessarily require palliative care input and will often be managed by the renal team or their GP. However, patients with significant symptoms, psychosocial and spiritual issues may require referral. Palliative care teams are often involved in managing such patients, either in the community and/or in palliative care clinics, which have been established by some centres within nephrology clinics.

The role of the palliative care team is wide-ranging including managing symptoms and skilled communication to facilitate decision making regarding treatment options. These decisions also need reviewing at significant intervals. An important role for all involved in the care of the patient, including the palliative care team, is to offer the opportunity for advance care planning. This enables a patient to specify his/her preferences for future care and communicate this to all those involved in their care (National End of Life Care Programme, 2011). It gives patients back some control when facing ongoing losses. The aim is to avoid unwanted hospital admissions, unwanted commencement of dialysis, and to establish the preferred place of care and death.

Palliative care physicians have also been involved in developing cause for concern registers for end-stage renal failure patients. Similarly to the Gold Standards Framework (2000), this ensures that the care needs of patients with deteriorating health are reviewed regularly and that all health-care professionals involved are aware of the priorities of care. These renal cause for concern registers should integrate with the local electronic palliative care registers currently being developed. A fundamental aspect of the palliative care team's role is to work in conjunction with the nephrologists, developing joint education programmes, joint clinics and managing the disease, symptoms and patient holistically.

Conservative kidney management

As their renal function deteriorates patients receive pre-dialysis education to enable them to decide whether they want to have dialysis and, if so, which modality of treatment. If a patient opts for no dialysis, i.e. conservative kidney management, he/she is given the choice to be managed in the community by the GP. In some regions the patient can also be followed up in conservative kidney management clinics, often by a palliative medicine consultant within a nephrology clinic (Russon and Mooney, 2010).

In conservative kidney management clinics patients continue to receive active management of their renal disease, including management of their bone disease and anaemia, but a palliative medicine consultant leads this rather than a nephrologist. A greater focus is placed on palliating symptoms of uraemia and comorbidities, providing psychosocial support, family support and advance care planning. Patients can also access community palliative care services, such as day hospice, community Macmillan nurses and chronic oedema clinics. Through accessing these services early in their disease trajectory patients are introduced to the concept of palliative care and become familiar with the hospice environment. Importantly, through continuing to attend the same nephrology clinic as before, patients also feel they have continuity of care, as they still see the same dieticians, social workers and clinical nurse specialists as before. Through this they gain an understanding that the palliative care team is working alongside and in close collaboration with the renal team to provide the best possible care.

Decision-making process

Helping patients make an informed choice regarding renal replacement therapy or conservative kidney management is the responsibility of both the nephrology and palliative care teams. Most centres have trained clinical nurse specialists who provide pre-dialysis education to patients, often in their home environment. In February 2000, the Renal Physicians Association and the American Society of Nephrology published a clinical practice guideline on shared decision-making in the appropriate initiation of and withdrawal from dialysis (Galla, 2000). A key recommendation was ensuring that patients and teams are involved in shared decision-making. This is characterized by patients making a choice about the health care available, informed by the best available professional knowledge (Murtagh et al, 2009). This requires health-care professionals to ensure that the patient and his/her family fully understand the consequences of opting not to have dialysis. First this involves an assessment of the patient's capacity to make such a decision. If the patient does not have capacity nor a valid advance directive to refuse treatment or Lasting Power of Attorney then, in accordance with the Mental Capacity Act 2005, a best interest decision is

taken. If the patient is assessed as having capacity the decision-making process typically requires several discussions over time, where the concept of conservative kidney management *vs* dialysis is introduced. The team explores and clarifies the patient's preferences and wishes, which through advance care planning can be documented and shared with all health-care professionals involved in the patient's care. Finally it is important that the patient and family are aware that they can change their mind at any point and that this is reviewed at appropriate stages, i.e. as symptoms progress.

A key challenge is that some individuals will try to delay the decision, especially while they remain asymptomatic. In such cases it is important to establish what the patient wishes to know, and how much he/she wants to be involved in the decision-making process. It is also crucial that the patient is aware that his/her renal function could suddenly deteriorate, and any decision would then need to be made in a crisis situation, where outcomes are known to be poorer (Chan et al, 2007). Nonetheless, advance care planning is a voluntary process and patients may require support over an extended period of time before making a choice.

Withdrawal from dialysis

Approximately 14% of dialysis deaths are caused by withdrawal (Caskey et al, 2011). This is most likely a reflection of the changing population, with more elderly patients with multiple comorbidities starting dialysis but not tolerating it well or experiencing significant burden on their quality of life. Withdrawal can be instigated by either the patient or the medical team. From a medical perspective withdrawal is usually considered if the patient's comorbidities progress significantly thus limiting his/her ability to tolerate dialysis, such as developing cardiac failure. Other important factors to consider are the patient's performance status and level of dependence, as well as a new diagnosis of a life-limiting malignancy or severe dementia. From the patient's perspective an important factor when considering withdrawal is if the burdens of treatment outweigh the benefits. Often patients will ask what their prognosis will be with and without the treatment, what to expect once the dialysis is stopped and how they will be managed.

If a patient requests or the team suggests withdrawal from dialysis, it is important to initially establish the reasons why this has been requested and ensure that there are no reversible factors which may optimize the patient's symptom control and quality of life before making such a decision. This would include the diagnosis and management of depression. An assessment of capacity is required to ensure the patient is able to engage in the decision-making process. For an informed decision to be made, the patient and family need to have an in-depth understanding of the implications of withdrawal as well as those of continuing dialysis. A period of reflection and opportunity for further discussions is therefore encouraged, to ensure the patient makes a choice in keeping with his/her wishes. This is why discussing withdrawal before the patient becomes progressively unwell is recommended, in order to give him/her the opportunity to weigh up the decision and communicate it to health-care professionals and loved ones.

Patients and families are informed that following withdrawal of dialysis the mean survival is 8 days (Birmele et al, 2004). Their preferred place of death will be established before withdrawal and symptoms of uraemia can be managed at home, in hospital or in the hospice. If the patient wants to be transferred to the hospice a bed should be made available before withdrawal of dialysis.

Symptom management

Following withdrawal or if the patient opts for conservative kidney management, symptom management is crucial and can improve quality of life significantly. There is variation in symptom prevalence, with those with more advanced disease or significant comorbidities often experiencing a greater symptom burden. It is well documented that treatment of pain and other symptoms is not managed well in patients with renal failure as a result of uncertainty about prescribing in this group (Bailie et al, 2004).

Pain

Studies show that approximately 53% of conservative kidney management patients and 47–67% of dialysis patients experience pain (Murtagh et al, 2007a). The cause of pain can be related to a multitude of factors including:

- Comorbidities
- Primary renal disease
- Complications of end-stage renal failure including bone disease
- Dialysis-related
- Spiritual and psychological factors.

Following an holistic assessment of the pain, analgesia should be titrated carefully. The World Health Organization analgesic ladder is slightly modified for patients with renal failure (*Figure 1*). For the first step paracetamol is recommended as it is metabolized by the liver. Non-steroidal anti-inflammatory drugs should be avoided if the patient has residual renal function but can be considered in patients undergoing dialysis and if the patient is thought to be in the last few days of life. There is no significant evidence to suggest any particular non-steroidal anti-inflammatory drug is safer than others in patients with renal failure.

For step 2, both codeine and dihydrocodeine should be avoided in end-stage renal failure, as their toxic metabolites accumulate causing drowsiness and confusion. The kidneys excrete tramadol, so a dose reduction and immediate release preparations are recommended.

For step 3, morphine is to be avoided as again its metabolites are renally excreted and can accumulate quickly. Hydromorphone does not accumulate in end-stage renal failure nor is it removed by dialysis. For patients with estimated glomerular filtration rate 20–50 ml/min oxycodone is considered to be better tolerated than morphine, although there is limited evidence on its use in renal failure and it is primarily used as a short-term measure to titrate against pain, before switching to a transdermal preparation. Once the estimated glomerular filtration rate is <20 ml/min buprenorphine, alfentanil and fentanyl are preferred as their metabolites are excreted by the liver and are mostly inactive.

Transdermal preparations should not be used for titration – subcutaneous fentanyl or alfentanil can be used for greater flexibility. Methadone is a synthetic opioid metabolized by the liver to inactive substances and excreted mainly in faeces; this makes it a favourable option for complex neuropathic pain. In view of its prolonged pharmacological action, however, there is a risk of late accumulation and so methadone is usually managed only by specialists.

For neuropathic pain amitriptyline can be used in those without contraindications, and does not need dose adjustment. Gabapentin and pregabalin, however, do require adjustment, with a maximum dose of gabapentin 300 mg in those with estimated glomerular filtration rate <30 ml/min, although smaller doses such as gabapentin 50 mg once daily can be effective.

Pruritis

Itch can be localized or generalized, and is often worse at night and exacerbated by heat, dry skin and sweating. Causes of itch are often multifactorial in these patients and include renal osteodystrophy, uraemia, dry skin and low ferritin levels. Treating the underlying cause is key, such as with phosphate binders for osteodystrophy and moisturising the skin with emollients for dry skin. General measures including avoiding hot baths, not drinking alcohol, wearing light non-synthetic clothing and avoiding scratching can be helpful. Other pharmacological treatments for consideration are presented in *Table 2*.

Nausea

Nausea is thought to be primarily related to uraemia, but can also be caused by medication, fluid and electrolyte changes, gastric stasis and constipation. Management depends on establishing and treating the cause, while selecting the appropriate antiemetic. If the cause is thought to be primarily chemical related, i.e. uraemia and drugs, anti-emetics that act on the chemoreceptor trigger zone such as haloperidol and ondansetron are effective. Levomepromazine is often used second line because of its broad-spectrum activity. For gastric stasis reduced dose metoclopramide should be used first line.

Restless legs syndrome

Restless legs syndrome is distressing for both patients and partners. The pathogenesis is not fully understood, although dopamine is thought to play an important role (Satija and Ondo, 2008). Management includes adequate dialysis if appropriate, treatment of anaemia and avoiding precipitating factors such as caffeine, neuroleptics and tricyclic medication. Dopamine receptor agonists such as ropinirole can be tried first, but they require slow titration and can cause daytime somnolence. Benzodiazepines can be helpful, especially if restless legs syndrome is affecting sleep or the patient has entered the terminal phase, where clonazepam can be given subcutaneously. Gabapentin (adjusted dose) has also been tried.

Terminal phase

Recognizing the terminal phase is crucial as it allows the patient, family and health-care team to prepare and acknowledge that the emphasis of care has changed to symptom relief, avoidance of inappropriate prolongation of dying, and providing psychosocial and spiritual support. Although this is easier to predict in patients

Figure 1. Modified World Health Organization analgesic ladder for renal failure patients.

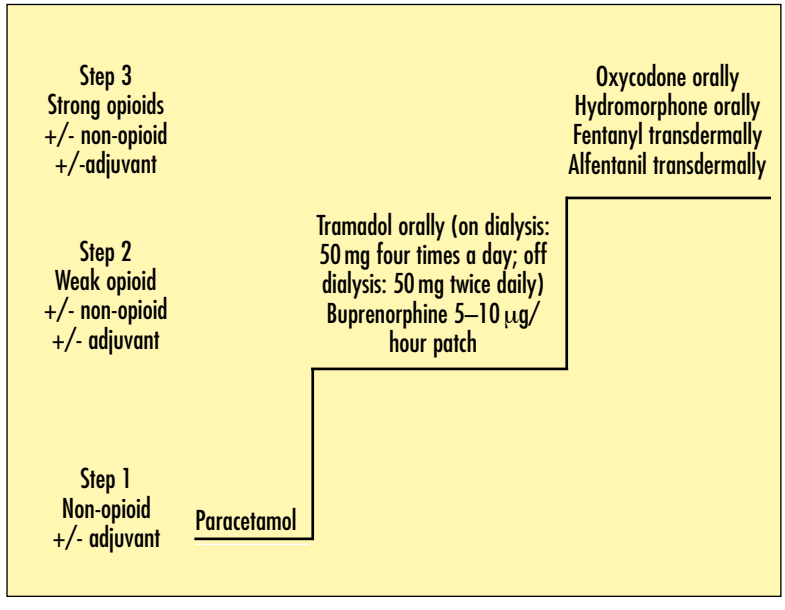

Table 2. Suggested pharmacological treatments for pruritis

Drug	Notes
Antihistamines	Limited evidence, easy to use and monitor
Phosphate binder (Calcichew)	If phosphate level >1.8 mmol/litre
Gabapentin	Some evidence, good choice if concomitant neuropathic pain
Mirtazapine	Limited evidence, good choice if depressed
Topical capsaicin	Some evidence, good for localized itching but some patients can not tolerate it because of the initial burning sensation
Ondansetron	Some evidence, good if experiencing nausea
Ultraviolet B phototherapy	Good evidence base, but burdensome treatment

withdrawing from dialysis, in others such as those choosing conservative kidney management this can be difficult. If a patient chooses to be managed conservatively in general the renal function deteriorates steadily over time and the patient dies soon after the estimated glomerular filtration rate goes below 5 ml/min; however, as many as 50% will die of another comorbidity before reaching this level, with sudden death being common.

Through providing support and symptom management at earlier stages of the disease trajectory, and providing opportunities for advance care planning, patients and families can feel supported even when the dying phase is sudden and unexpected. When patients are thought to be actively dying, bed bound, semi-comatose, and unable to take anything orally then the Liverpool Care Pathway should be instigated and used in accordance with the Department of Health (2008) guidelines for Liverpool Care Pathway prescribing in chronic kidney disease. Unnecessary medications, observations and investigations should be stopped, and regular mouth care and pressure area care should be prioritized alongside supporting the family.

Conclusions

Palliative care has an important role with nephrology services in providing good end-of-life care for patients with end-stage renal failure. There is a need for expansion of services throughout the UK, ensuring that palliative care and nephrology teams have the skills required to help patients make informed decisions regarding treatment, support advance care planning and manage symptoms. Further research is required to establish which patients do not benefit from dialysis as well as powered studies to establish the best treatment strategy for the large number of symptoms these patients face. Palliative care and nephrology teams have come a long way in improving palliative care for this vulnerable group of patients, but further collaboration and innovation is required to provide the optimal experience at the end of life. **BJHM**

KEY POINTS

- The overall mortality of patients with end-stage renal failure is worse than for most cancers.
- Patients over 75 years old, with multiple comorbidities, poor performance status or frailty, do less well on dialysis.
- Conservative kidney management (no dialysis) is a valid option for such patients and generally results in a steady decline in renal function.
- The role of the palliative care team includes complex symptom management, facilitating shared decision making, advance care planning and supporting families.
- Withdrawal from dialysis should be discussed as early as appropriate and results in a rapid deterioration in renal function.
- Patients with end-stage renal failure experience significant symptom burden – this area requires much-needed further research.
- Recognizing and actively managing the terminal phase is important and morphine should be avoided at this time.

Conflict of interest: none.

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