

# Palliative care in end-stage renal failure

Little attention is given to palliative care for patients with non-cancer disease such as end-stage renal failure. Sometimes dialysis either cannot be started or needs to be stopped in elderly patients with multiple comorbidities. Palliative care for such people is advocated by guidelines, but many renal services do not have adequate palliative components. Management of symptoms is the main aim of treatment, and includes pain, nausea, constipation, depression, dyspnea, pruritis, and delirium.

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Care for people who are dying is an integral part of geriatric medicine, yet little attention is afforded to the palliative care of patients dying from non-cancer illnesses. This area must be addressed as our population ages and increasing numbers of people live with, and die from, chronic diseases. The Gold Standards Framework for Palliative Care<sup>1</sup> highlights the need to broaden the remit of palliative medicine to encompass all patients nearing the end of life. This article outlines symptoms commonly encountered in end-stage renal failure, and highlights the need for a planned approach to their management.

Medical advances have led to patients living longer with chronic diseases, and the number of patients with end-stage renal failure is therefore increasing. End-stage renal failure occurs when the kidneys' ability to excrete waste, concentrate urine, and conserve electrolytes deteriorates to the point at which haemodialysis or renal transplant is necessary for survival. An increasing proportion of these patients are elderly and have multiple comorbidities. This trend is forcing us to increasingly face the issues of either non-initiation or withdrawal of dialysis.<sup>2,3</sup> About 20% of patients presenting with end-stage renal failure choose conservative management.<sup>4</sup>

## Palliative care

The WHO's definition of palliative care is "active total care of patients whose disease is not responsive to curative treatment".<sup>5</sup> The goals of care are to "control pain, symptoms, and social, psychological, and spiritual problems" to achieve "the best quality of life for patients and their families".<sup>5</sup> Therefore, principles of palliative medicine should clearly be adopted when caring for patients who decline life-sustaining dialysis and those for whom it is no longer feasible.

Extending the role of palliative medicine to non-cancer patients presents major challenges; not least that of understanding the different paths of these diseases. A person with cancer typically experiences a period of treatment associated with relatively good function, which overlaps with increasing palliative care input. By contrast, a patient dying from single organ failure is more likely to decline gradually and unpredictably, and frail elderly people face a lengthy period of diminishing function.<sup>6</sup> Predicting a person's progress along the final two disease trajectories is more difficult, and it is therefore harder to know where and how care should be given.<sup>6</sup>

The American Society of

Nephrologists recommend that all patients who decline haemodialysis should be referred to palliative care.<sup>7</sup> Guidelines produced by the Renal Physicians' Association in conjunction with the American Society of Nephrologists suggest that care should be shared between nephrologists and palliative-care physicians with the aim of controlling symptoms, achieving good quality of life and facilitating a good death, as defined by the patient and their family.<sup>8</sup> Having a good death has been postulated as another measure of success in medicine.<sup>9</sup>

The National Service Framework for Renal Services 2005 also promotes good end-of-life care for renal patients through the development of combined palliative and renal services.<sup>10</sup> Provision of such services is still limited; a recent UK survey of palliative care in end-stage renal failure found wide variations across the country. Only 39% of renal units employed staff with palliative-care skills, and three-quarters of these staff spent less than 4 hours a week in this role.<sup>2</sup> Until the development of a joint service, physicians, and particularly geriatricians, should be confident in managing the care of patients with end-stage renal failure. This requires an understanding of the common symptoms and their treatment.

## Managing common symptoms

### Pain

Pain is defined as “an unpleasant sensory and emotional experience with actual or potential tissue damage”<sup>11</sup> with the total pain experienced being determined by emotional, psychological, behavioural, and cultural factors. Common types of pain in end-stage renal failure include bone pain due to osteodystrophy or osteomalacia, neuropathic pain, and leg cramps. The most common reason for

inadequate pain control is “the lack of proper pain assessment”.<sup>12,13</sup>

Pain in patients with end-stage renal failure should be assessed and managed routinely using WHO’s pain-control ladder. Non-steroidal anti-inflammatory drugs are best avoided because prostaglandin inhibition may cause further deterioration in renal function. Most opioids are renally-excreted or have renally-excreted metabolites, and will need a reduction in dose to avoid accumulation. Codeine, dihydrocodeine, pethidine, and slow-release preparations are most likely to accumulate and cause toxicity.<sup>14</sup>

Opioid-accumulation causes myoclonic jerks, sedation, or agitation. Tramadol, methadone, and hydromorphone are metabolised by the liver and tend to be safer in this population. The route of administration must also be considered. Transdermal analgesia may be appropriate for patients with stable pain already controlled by an opioid, whereas a subcutaneous syringe driver may be more appropriate for patients with acute or unstable pain or requiring multiple drugs. Table 1 outlines analgesics that can be used safely in renal failure.

	Characteristics	Advice
Codeine	Reduced clearance Accumulation of metabolites (codeine-6-glucuronide and morphine)	Reduce dose by 50%
Fentanyl	Reduced clearance Less constipation and sedation	Reduce dose by 50% Opioid of choice in severe renal failure
Morphine	Metabolites are renally excreted (morphine-3-glucuronide and morphine-6-glucuronide) and are neurotoxic when they accumulate	Reduce dose by 50% Increase dose interval by 6–8 hours
Methadone	Metabolites inactive 20% excreted unchanged in urine	Titrate to effect No significant dose alteration required
Oxycodone	Metabolites accumulate More likely to cause hallucinations	Reduce dose by 50%
Hydromorphone	Metabolised by liver Fewer active metabolites	Safe in moderate renal failure
Pregabalin	Negligible metabolism 90% excreted unchanged in urine	Reduce dose by 50% if creatinine clearance is 30–60 ml/min, and by a further 50% for each additional halving of creatinine clearance
Gabapentin	Reduced excretion Neurotoxic Useful in neuropathic pain and restless legs syndrome	Start at low dose (100 mg nocte) and increase
Carbamazepine	Half-life not changed in renal failure Useful in neuropathic pain	Give normal dose with caution

**Table 1:** Characteristics of analgesics used in renal failure<sup>13,15–18</sup>

### Nausea

Nausea is defined as “an unpleasant feeling of the need to vomit, often accompanied by autonomic symptoms”.<sup>11</sup> Common causes of nausea in end-stage renal failure include gastric stasis, gastritis, and metabolic disturbance. Identification, of the cause is important for initiation of appropriate treatment. Table 2 outlines treatment options for nausea in end-stage renal failure.

### Constipation

Constipation in end-stage renal failure can arise as a consequence of fluid restriction or hypercalcaemia. Constipation is the only opioid side-effect to which patients do not develop tolerance.<sup>14</sup> Laxatives containing phosphate or magnesium should be avoided because they can cause severe electrolyte disturbances, which may precipitate arrhythmias.<sup>15</sup>

### Depression

Depression is acknowledged to be under-recognised in patients with chronic diseases. The reported prevalence in end-stage renal failure varies from 10% to 25%.<sup>14</sup> Detection may be through observation, enquiring about symptoms, or using a screening tool such as the Geriatric Depression Scale.<sup>19</sup> Non-

pharmacological interventions such as psychotherapy or cognitive behavioural therapy may be beneficial, and pharmacological treatment using the newer selective serotonin reuptake inhibitors such as fluoxetine or citalopram can significantly improve a patient's quality of life.<sup>14</sup>

### Dyspnoea

Dyspnoea combines an “uncomfortable awareness of breathing”<sup>12</sup> with a psychological reaction to the sensation. It is an exhausting and distressing symptom that can severely affect quality of life and functional ability. Assessment should be both objective and subjective. Consider whether treating the cause of the breathlessness (eg, pneumonia or pulmonary embolus) will actually improve quality of life or whether interventions should focus on treating only the symptom.

Causes of breathlessness specific to renal failure include pulmonary oedema, anaemia, and the overwhelming fatigue which accompanies end-stage renal failure. Non-pharmacological measures include reassurance, breathing exercises, relaxation therapy, positioning, fans, and hypnosis.<sup>12,14</sup> Table 3 outlines drugs used to control breathlessness in end-stage renal failure.

### Pruritis

Itching is very distressing and is frequently seen in renal failure. Causes include uraemia, dry skin, iron-deficiency anaemia, hyperparathyroidism, opiates, hyperphosphataemia, and calcium phosphate deposits in the skin.

Cooled topical agents, UVB phototherapy, and sedating antihistamines are used to relieve this symptom. Naloxone (1.5–5 mg intravenously) may be used in opioid-naïve patients. Ondansetron (2–8 mg twice daily) and mirtazepine (15 mg nocte) are currently used off-licence for pruritis.<sup>17</sup>

### Delirium

Delirium is seen in up to 80% of patients dying from renal failure.<sup>14</sup> A combination of the underlying disease process, organ failure, toxin accumulation, and drugs are usually to blame. Delirium is generally irreversible, rapidly progressive and distressing for patient, their family, and carers. Once any obvious reversible causes have been excluded, sedation is often the only way to control a patient's distress. This is usually achieved with subcutaneous midazolam or levomepromazine (a dopamine antagonist with antihistamine and antimuscarinic properties).<sup>14</sup>

	Treatment of choice	Comment
Gastric stasis	Prokinetic (eg, metoclopramide 10 mg three times daily)	Allow for increased half-life and beware of extrapyramidal side-effects
Gastritis	Proton pump inhibitor	No dose alteration required
Metabolic upset	Metoclopramide (10 mg three times daily)	
	Haloperidol (1.5 mg nocte)	
	Levomepromazine (6.25–12.5 mg)	2nd-line agent

**Table 2:** Treatments for causes of nausea<sup>13,15,17</sup>

## Conclusion

Ongoing work is needed to understand how the palliative model of care can be adapted to meet the needs of elderly patients with renal failure at the end of life. In the meantime, it is ever more important that geriatricians are confident in managing symptoms commonly encountered during these final stages of life.

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	Mechanism of action	Advice
Opioids	Blunt perception of dyspnoea and reduce respiratory drive Rapid release is more effective	If already on opioids increase dose by 50% If not on opioids start morphine 2.5 mg every 8 hours and titrate as necessary
Anxiolytics (benzodiazepines)	Reduce anxiety (and therefore oxygen consumption)	Half-life is increased in renal failure, so reduce dose and titrate according to response
Corticosteroids	Thought to reduce inflammation and secretions Some bronchodilator effects	Monitor for fluid retention
Bronchodilators	Reduce the work of breathing via $\beta$ -agonist bronchodilatation	
Oxygen	Use if hypoxic or anaemic Can increase oxygen-carrying capacity of blood	
Anti-secretory agents	Reduce production of respiratory secretions	

**Table 3:** Treating breathlessness in end-stage renal failure<sup>14,15</sup>