North of Tyne, Gateshead and North Cumbria recommendations for symptom management in renal patients (including symptom management at the end of life)

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Contents

Introduction

Patients with chronic kidney disease (CKD) are among the most symptomatic of any chronic disease group. Symptoms can be a direct consequence of renal disease, be dialysis-related or due to co-morbid conditions. Research has focused on symptoms experienced by dialysis patients, but evidence suggests that patients with stage 4 and 5 CKD (not on dialysis) report a similar number and severity of symptoms. This guideline is mainly intended to support clinicians managing patients with stage 4 and 5 CKD.

These guidelines are intended for use by clinicians in primary and secondary care in the North of England, and should be read alongside the following resources:

North of Tyne formulary:
http://northoftyneandgatesheadformulary.nhs.uk/

The Northern England Clinical Networks Palliative and End of Life Guidelines:
http://www.northerncanceralliance.nhs.uk/wp-content/uploads/2018/11/NECNXPALLIATIVEXCAREX2016-1.pdf

The North of Tyne and Gateshead guidelines for the detection, management and referral of adults with kidney disease:
http://www.northoftyneapc.nhs.uk/wp-content/uploads/sites/6/2017/03/NoT-and-Gateshead-Kidney-Guidelines-March-2017-Final-Release.pdf
If specialist renal advice is required, please seek advice via Advice and Guidance which can be found through the eReferral system.

Disclaimer

Many of the drug treatments described in this guideline are either unlicensed (i.e. the drug isn't licensed in the UK for the treatment of the condition specified) or off-label (i.e. the drug is licensed for the condition, but not for the patient group specified). Such treatments will be identified with a superscript "u".

It is assumed that clinicians will follow good-practice guidelines, such as those issued by the GMC (https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices) when prescribing medicines outside the terms of their licence.

It is also assumed that clinicians will exclude contraindications and interactions, referring to the BNF and local formularies as necessary, when prescribing treatments for individual patients. The guideline does not replace specialist renal or palliative care advice.

Anorexia/Loss of Appetite

Possible cause(s) and contributing factors	Uraemia. Taste disturbance. Dry mouth. Oral candidiasis. Poorly fitting dentures. Reduced intake due to dietary restrictions. Nausea & vomiting. Constipation. Pain. Oesophagitis/gastritis. Dyspepsia. Depression.
Management strategies	Identify and treat reversible causes. Avoid medicines which may exacerbate dry mouth. Advise small regular meals, particularly of favourite foods. Advise high-calorie foods (consider diabetes control where relevant). Refer to dietitian for further advice, including the use of nutritional supplements (this should be a specialist renal dietitian for patients requiring low phosphate or low potassium diets).
Treatment options	**Metoclopramide 10mg tds** improves gastric emptying. No dose adjustment needed but increased risk of extrapyramidal reactions in severe renal impairment. **I**f also needing treatment for depression see p5

Anxiety/Depression

Possible cause(s) and contributing factors	Burden of illness/self-care (including frequent clinic/hospital visits, dietary restrictions, medication burden). Functional impairment and physical symptoms. Awareness of increased morbidity and mortality. Personal issues (family, social, financial difficulties). Co-morbidities. Primary factors (e.g. genetic predisposition).
Management strategies	Identify and address modifiable contributing factors. Signpost to talking therapies. Refer to health psychology services if appropriate. Refer to psychiatric services if appropriate.
Treatment options	**Sertraline 25-100mg od.** Titrate slowly. **Citalopram 10-40mg od.** Caution if CrCl <10ml/min or prolonged QTc). **Mirtazapine 15-45mg at night.** Increases appetite. Severe renal impairment reduces clearance by 50%. In CrCl <20ml/min, start with low dose (15mg) and monitor for adverse effects. Avoid tricyclic antidepressants in dialysis patients – dry mouth may make fluid restriction more difficult. **Benzodiazepines** should only be prescribed for short-term use.

Constipation

Possible cause(s) and contributing factors	Fluid restriction. Reduced mobility. Medication (opioids, phosphate binders, iron supplements). Poor dietary intake. Dietary restriction of high-fibre foods such as fruit and vegetables due to potassium content. Depression. Reduced gut motility.
Management strategies	Review diet. Encourage fibre and fluid intake, within constraints of dietary and fluid restrictions (refer to specialist renal dietitian for advice if required). Encourage mobility and exercise where possible.
Treatment options	Enemas may be needed initially, followed by maintenance oral treatment to prevent recurrence. A combination of laxatives is sometimes required. Peritoneal dialysis can worsen constipation, and constipation itself can make peritoneal dialysis less effective, so ensuring frequent bowel movements is particularly important in this patient group. Avoid regular use of magnesium- and phosphate-containing laxatives (e.g. milk of magnesia, phosphate enemas) due to risk of hypermagnesaemia and hyperphosphataemia. Osmotic laxatives: **Lactulose 10-20ml od-bd** (adequate fluid intake required). **Macrogols (Movicol, Laxido) 1-2 sachets daily** (contains potassium and requires adequate fluid intake). Stimulant laxatives: **Senna 7.5-15mg at night.** **Bisacodyl 5-10mg at night.** Stool softener: **Docusate 100-200mg bd** (adequate fluid intake required). Enemas and suppositories: **Micralax micro enema 5ml prn.** **Glycerol suppository 4g prn.**

Cramps

Possible cause(s) and contributing factors	Dehydration (including excessive fluid removal during dialysis). Peripheral vascular disease. Poor glycaemic control in diabetics. Hypocalcaemia. Hypomagnesaemia. Iron deficiency. Hypothyroidism.
Management strategies	Encourage exercise and mobility where possible. Muscle stretching and massage (before bed if cramps are worse at night). Apply ice-pack or heat (e.g. warm bath, hot water bottle), but caution with use of heat/cold in diabetes and peripheral vascular disease. Encourage adequate fluid intake (unless fluid restricted). Limit alcohol and caffeine intake. Wear comfortable shoes.
Treatment options	**Quinine 200-300mg at night.** Note MHRA guidance to avoid routine use due to risk of thrombocytopenia and QT prolongation. Stop after 4 weeks if no benefit and avoid in patients with other risk factors for QT prolongation.

Dry Mouth

Possible cause(s) and contributing factors	Dehydration. Medication (anticholinergics, opioids). Oral thrush.
Management strategies	Optimise fluid balance and review contributing medication. Oral hygiene: - Brush teeth twice/day. - Floss nightly. - Use chlorhexidine mouthwash after brushing (only helpful as prophylaxis in a clean mouth). - Remove dentures at night and clean properly with a nailbrush and warm soapy water. Soak in chlorhexidine solution and rinse before re-inserting. - Avoid acids and alcohols. - If tongue coated, use a soft (baby's) toothbrush to gently clean mouth in between brushing if tongue is coated. Crushed ice/ice lollies. Treat oral thrush (ineffective treatment may indicate resistance – swab if no improvement).
Treatment options	Oral lubrication: **Biotene oral balance gel 1 application qds and prn.** Treat oral thrush: **Nystatin 100,000 units/ml 1ml qds** (continue for 48 hours after thrush has resolved). **Miconazole oral gel – normal adult dose** (be aware of interactions as per BNF) **Fluconazole** 50mg caps. - CrCl >10ml/min dose as per normal renal function. - CrCl <10ml/min or dialysis patient 50mg stat then 25mg (2.5mls of 50mg/5ml suspension daily) or 50mg post dialysis for 7-14 days. - Strong CYP450 inhibitor – may increase plasma concentration of other drugs including ciclosporin, tacrolimus, alfentanil, fentanyl, midazolam, haloperidol, warfarin, TCAs, antiepileptics.

Dyspnoea

Possible cause(s) and contributing factors	Pulmonary oedema. Acidosis. Anaemia. Respiratory tract infection. Pleural effusion. Co-morbid chronic respiratory disease. Fatigue/cachexia. Anxiety. End of life: un-cleared secretions.
Management strategies	Correct reversible underlying causes. Review fluid balance/diuretics/dialysis regimen. Consider oxygen if hypoxic. Recommend patient acquires a fan for symptomatic benefit. Physiotherapy if appropriate for fatigue management/rehabilitation. Occupational therapy – optimise functional adaptation. Psychological interventions if anxiety significant contributing factor. Pharmacological interventions: Target underlying cause.
Cautions/general prescribing information	Start low and go slow. When in doubt, seek specialist advice. Opioids are the first line pharmacological treatment for palliation of breathlessness with no reversible factors. Benzodiazepines may be used to manage associated anxiety/panic. A familiar, established and well tolerated opioid may be safer than switching to an unfamiliar but 'renally safer' agent. All Benzodiazepines are at risk of causing an enhanced central depression effect in renal failure. Avoid Diazepam. Undesirable effects may take days or weeks to become apparent, especially for opioids with long half-lives. Concurrent use with other drugs with CNS depressant activity increases the risk of toxicity. Unless specifically stated, all listed drugs can be used at the same doses for patients on PD or HD. For anticipatory prescribing at the **end of life**, refer to the regional End of Life Care guideline.

PTO for treatment options

Treatment options	Thick secretions/difficulty expectorating: **0.9% Sodium Chloride nebulisers 5ml qds**. Bronchoconstriction: **Salbutamol nebulisers 2.5mg prn max qds.** Consider inhaled/systemic **corticosteroids** (use normal doses). Opioids: **Oxycodone IR oral solution 1-2mg every 6 hours prn.** Once dyspnoea is controlled, consider **Buprenorphine transdermal patch** according to 24-hour prn requirement (**Fentanyl transdermal patch** is an alternative option if the opioid requirement is high). See this page for opioid conversion **Benzodiazepines** (break breathlessness-panic cycle): **Lorazepam 0.5mg sublingually[u] prn max bd** (but consider cautious titration).

Fatigue

Possible cause(s) and contributing factors	Anaemia. Uraemia. Insomnia. Depression. Loss of muscle mass.
Management strategies	Treat anaemia. Encourage good sleep hygiene. Treat depression. Consider rehabilitative interventions.
Treatment options	Anaemia: Consider specialist referral for IV iron and/or erythropoiesis stimulating agents in CKD stage 4 or 5. (Oral iron is only likely to be appropriate in CKD stage 3 and better. Avoid if constipation is already a problem.)

Insomnia/Sleep disturbance

Likely cause(s) and contributing factors	Pain. Restless legs. Sleep apnoea. Anxiety and Depression Excessive day time sleepiness Metabolic and biochemical changes Medication (steroid therapy)
Management strategies	Identify and address contributing factors. Encourage good sleep hygiene Consider sleep clinic referral. Consider short term use of 'Z drugs'.
Treatment options	**Consider non-pharmacological methods first** **Zopiclone** can be useful as a short term treatment using the lowest effective dose. **For CrCl < 10ml/min or dialysis start at 3.75mg at night** Longer term use is associated with a risk of dependence and tapering may be required if withdrawing therapy after continuous use of 4 weeks or more. **Mirtazapine**[u] can be useful for insomnia if the patient is also suffering from depression. **Start at 15mg at night and titrate slowly, this can be increased to 30mg if required after 2-3 weeks.**

Nausea and Vomiting

Possible cause(s) and contributing factors	Uraemia. Constipation (especially in peritoneal dialysis). Gastric stasis (diabetes mellitus/electrolyte disturbance/medicines). Poor oral hygiene/oral thrush. Medicines (e.g. antibiotics/opioids/antimuscarinics/SSRIs/cytotoxics). Uncontrolled pain. Cough/secretions – see 'Breathlessness' Infection. Hypercalcaemia.
Management strategies	Correct reversible underlying causes. Maintain good oral hygiene (see 'Dry Mouth') Encourage small frequent meals/snacks. Acupressure e.g. Sea Bands® or similar product/acupuncture. Pharmacological interventions: Target underlying cause.
Cautions/general prescribing information	Start low and go slow – some medicines may be associated with increased risk of enhanced central depression effect (cyclizine, haloperidol and levomepromazine). Accumulation may take weeks and signs/symptoms of toxicity may therefore be delayed. Caution with concurrent CYP450 inhibitors (increased risk of toxicity). Caution with concurrent drugs that prolong the QT interval. All listed drugs can be used at the same doses for patients on PD or HD. For anticipatory prescribing at the **end of life**, refer to the regional End of Life Care guideline.

PTO for treatment options

Treatment options	**Chemically-induced nausea and vomiting e.g. uraemia, medicines, electrolyte disturbance:** **Haloperidol 0.5mg up to every 2 hours prn**, max 2.5mg/24 hours (avoid in Parkinson's disease/movement disorders). **Levomepromazine[u] 3mg at night and up to every 8 hours prn**. Short term use only advised due to potential adverse effects, review after 7 days **Gastrointestinal stasis:** **Domperidone 10mg up to tds**. **Metoclopramide 10mg up to tds** (avoid in movement disorders and caution in children/young adults). **Intracranial disorders inc. vestibular disorders and raised intracranial pressure:** **Cyclizine 25-50mg up to tds**, max 150mg/24 hours (avoid in severe cardiac failure). **Unknown cause/intractable nausea and vomiting:** **Levomepromazine[u] 3mg at night and q8h PRN**. Seek specialist advice.

Pain

Possible cause(s) and contributing factors	Acute and chronic co-morbid conditions, including diabetic neuropathy, peripheral vascular disease, musculoskeletal and cancer-related pain. Disease physiology (e.g. kidney stones, polycystic kidneys) Complications of kidney disease (e.g. renal bone disease, calciphylaxis)
Management strategies	Correct reversible underlying causes. Physiotherapy if appropriate. Occupational therapy – optimise functional adaptation. Psychological interventions. Pharmacological interventions: Target underlying cause.
Cautions/general prescribing information	Start low and go slow for pharmacological treatments. A familiar, established and well tolerated opioid may be safer than switching to an unfamiliar but 'renally safer' agent, unless there has been a sudden significant deterioration in renal function. When in doubt, seek specialist advice. Undesirable effects may take days or weeks to become apparent, especially for opioids with long half-lives. Concurrent use with other drugs with CNS depressant activity increases the risk of toxicity. Unless specifically stated, all listed drugs can be used at the same doses for patients on PD or HD. For anticipatory prescribing at the **end of life**, refer to the regional End of Life Care guideline.

PTO for treatment options

Treatment options	**Musculoskeletal pain:** Topical agent: **ibuprofen 5% gel tds** (caution with quantity) Oral agent: **paracetamol 500mg – 1g every 6 hrs prn** max 4g/24 hours. Avoid **NSAIDS** unless anuric and on dialysis: use in normal doses (caution if comorbid cardiovascular disease). **Neuropathic pain:** Topical agent: **aqueous cream with menthol** Oral agent – stepwise approach: 1. Amitriptyline OR gabapentin. 2. Amitriptyline AND gabapentin. - If gabapentin not tolerated or effective, consider pregabalin as an alternative. 3. Seek specialist advice. **Doses:** **Amitriptyline[u] 10mg at night** (titrate with caution). **Gabapentin 100mg at night initially or pregabalin 25mg daily initially**, titrate with caution to response and tolerability, monitor for CNS side effects, avoid abrupt withdrawal. **Nociceptive pain (visceral/somatic):** **Paracetamol 500mg – 1g every 6 hrs prn** max 4g/24 hours. **Tramadol 50mg every 6hrs prn**, max 200mg/24 hours. **Oxycodone IR oral solution 1-2mg every 6 hrs prn**. Once pain controlled and stable, consider switching to a long acting opioid, for example **Oxycodone MR tablets** **Fentanyl transdermal patch** according to 24-hour PRN requirement. See here for appropriate opioid conversion. Buprenorphine patches can be used if dose too low for Fentanyl. **Refractory pain: Seek specialist advice.**

Pruritus

Possible cause(s) and contributing factors	Uraemia. Dry skin. Reduced sweating. Abnormal metabolism of calcium and phosphorus/raised parathyroid hormone. Accumulation of toxins. Systemic inflammation. Neuropathy. Medicines, e.g. opioids. Co-morbid skin disease.
Management strategies	Correct underlying causes where possible. Aim to normalise electrolyte disturbance and optimise dialysis efficacy. Ensure good skin hygiene; prescribe a soap substitute e.g. Hydromol and a regular emollient. Consider Dermatology referral.
Treatment options	Topical agent: **aqueous cream with menthol.** Oral agent: **trial of antihistamines, e.g. chlorphenamine, cetirizine at usual doses**. Review efficacy after 7-14 days and discontinue treatment if no improvement observed.

Restless Legs

Possible cause(s) and contributing factors	Iron deficiency anaemia. Common sleep disorder in CKD of uncertain cause.
Management strategies	Correct iron deficiency (see 'Fatigue'). Recommend aerobic resistance exercise if appropriate. Encourage good sleep hygiene. Encourage reduction of alcohol, nicotine and caffeine. Muscle stretching and massage (before bed if cramps worse at night). Apply ice-pack or heat (e.g. warm bath, hot water bottle), but caution with use of heat/cold in diabetes and peripheral vascular disease. See treatment options below.
Treatment options	**See https://cks.nice.org.uk/restless-legs-syndrome** **Ropinirole not suitable at CrCl <30ml/min** **Pramipexole 88 microgram taken 2 – 3 hours before bedtime, titrate to effect.** Dose re-titration may be required if restarting after a few days. Maximum dose 540 microgram per day. Inform patient about MHRA warning re impulse control disorder. **Seek specialist advice.**

Sexual Dysfunction

Possible cause(s) and contributing factors	Impact of chronic illness on relationship roles. Depression. Fatigue. Low testosterone. Vascular disease. Antihypertensive treatment.
Management strategies	Check testosterone in men and consider Endocrinology referral. Treat underlying causes. Consider psychological management.
Treatment options	Erectile dysfunction: **Sildenafil 25mg** 1 hour prior to sexual intercourse. Avoid on dialysis days - increased risk of hypotension.

End of Life Care

Refer to the regional NECN Palliative and End of Life Care Guidelines (Fourth Edition 2016) http://www.northerncanceralliance.nhs.uk/wp-content/uploads/2018/11/NECNXPALLIATIVEXCAREX2016-1.pdf

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Renal Drug Database
https://renaldrugdatabase.com/

O'Connor et al, End-Stage Renal Disease: Symptom Management and Advance Care Planning. American Family Physician, 2012, vol 85, no 7, 705-710

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North of Tyne and Gateshead Area Prescribing Committee Formulary
http://northoftyneandgatesheadformulary.nhs.uk/default.asp

Resources for patients

The following websites contain useful information intended to be used by patients for learning more about their disease background, coping with symptoms, as well as the emotional and social impact of living with a chronic condition.

Tyneside Kidney Patient Association
http://www.tynesidekpa.org.uk/

The Renal Association
https://renal.org/information-for-patients/

National Kidney Foundation
https://www.kidney.org/

Edinburgh Renal Unit patient information
http://edren.org/ren/edren-info/

The Kidney Patient Guide
http://www.kidneypatientguide.org.uk/contents.php

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