

Kidney Patient Safety Committee: Safe prescribing of opiates in kidney disease

Contents

Contents.....	1
Background	2
Why is this area important?.....	2
Recommendations	3
Education	3
Medical students (through medical schools).....	3
Foundation trainees.....	3
Specialty trainees (through Royal Colleges)	3
Non-medical prescribers	3
Patient Assessment	4
Assess the patient’s kidney function	4
Assess the patient’s pain.....	4
Prescribing	4
Key considerations for prescribing opiates in the setting of reduced kidney function	4
Electronic Prescribing.....	5
Standard References.....	5
Patient Monitoring	5
Communication and dissemination of these guidelines.....	6
Authors.....	6
References	7

Background

Following the death of a patient with end stage kidney disease with multiple co-morbidities, the Coroner's report stated that this was a *“direct consequence of the over-prescription of Morphine on two occasions which resulted in a significant respiratory collapse.”*

Following this death, a Regulation 28 was issued on 7th January 2019 by the coroner with the following concerns:

“The junior doctors claimed to be insufficiently aware of important guidelines requiring a significant reduction in the prescription of morphine to those with end stage renal failure. Their unwillingness to seek advice even though they were basically aware of guidance strongly suggests that they had little idea of the significance of the issue”

This was felt to be partially due to a lack of training and induction particularly in non-specialist areas. It is believed this lack of knowledge/education is widespread.

There were also concerns by the prescriber about the availability of alternative opiates.

This case has highlighted the need to produce national recommendations for safe prescribing of opiates in kidney disease.

Why is this area important?

15% of the population has chronic kidney disease and acute kidney injury is seen in up to 20% patients who are admitted to hospital for emergency care. Pain affects more than 50% of patients with advanced chronic kidney disease, with more than half describing this as moderate to severe¹.

Despite its high prevalence, the recognition of pain and its management in patients with renal impairment is complicated and poorly understood. Prescribers' awareness of the choice of opioids and methods of assessment of renal impairment shows great variability² and often there is limited knowledge in care settings where specialist renal input is not available.

Factors which may contribute to difficulties in prescribing analgesia to patients with renal impairment or acute kidney injury include:

- Identification of patients with renal impairment
 - Renal impairment may be previously unrecognised and function deteriorating faster than is initially apparent on intermittent clinical and biochemical assessment.
 - Poor understanding of the limitations of various calculations used to assess renal function. Estimated GFR (eGFR) is not accurate in acute kidney injury, extremes of age or cachexia. This may lead to a failure to modify the dose of some medications appropriately in these clinical settings.
- Increased susceptibility to complications from analgesics due to
 - Accumulation of drugs excreted by the kidney and their metabolites in patients with renal impairment.
 - Increased sensitivity of patients with renal impairment to pharmacological agents. Opioid use is associated with increased risk of altered mental status, fall and fractures

even at lower dosing recommended in the haemodialysis population³. Higher doses have also been shown to correlate with increased risk of death and hospitalisation in dialysis patients⁴.

- Increased susceptibility to non-renal side effects amongst patients with renal impairment e.g. gastrointestinal ulceration may be exaggerated by use of NSAIDs due to the effects of the uraemic milieu on GI mucosal integrity.
- Polypharmacy contributing to significant drug interactions.
- Multiple co-morbidities.

There are no long-term studies or prospective evidence to support safe use of opioids in a clinical environment with gaps in the pharmacokinetic data on opioid use. So, in the absence of good supportive clinical data, recommendations are based on expert clinical experience and consistent pharmacological data of potential toxicity.

These recommendations have been produced by a multi-professional sub- group of the Kidney Patient Safety Committee.

Recommendations

Education

Dose adjustment for prescribing in respect of kidney function is a core part of training for any prescriber and should be embedded in their clinical practice. We recommend that safe prescribing in renal impairment (Chronic Kidney Disease (CKD) and Acute Kidney Injury (AKI)) is included in curricula for, and is taught to, the following groups:

Medical students (through medical schools)

- Prescribing in renal impairment should be mandatory on the Prescribing Safety Assessment (PSA)⁵ (currently it includes two mandatory questions on opioid prescribing, but although it generally includes questions on renal impairment these are not mandatory).
- Students should receive feedback on their performance in the PSA including areas for improvement and recommended resources to access this training.
- The General Medical Council (GMC) 'Outcomes for graduates' document⁶ should include prescribing in renal impairment in the safe prescribing competencies list.

Foundation trainees

- Feedback from the PSA should be reviewed with the trainee's Educational Supervisor in F1 and areas for improvement included in PDP for Foundation training.
- Completion of an online module on prescribing in renal impairment should be mandatory (for example through online training resources e.g. Script).

Specialty trainees (through Royal Colleges)

- Safe prescribing in renal impairment should be included in core competencies/curriculum. Competence could be demonstrated through portfolio/professional examinations.

Non-medical prescribers

- Safe prescribing in renal impairment should be included in core competencies/curriculum and as part of regular update sessions. Non-medical prescribers should only prescribe in areas they feel competent so should recognise if a patient with renal impairment needs be referred.

- Competence should be demonstrated by meeting the Royal Pharmaceutical Society competency framework by applying understanding of the mode of action and pharmacokinetics of medicines and how these may be altered in renal impairment⁷
- Trusts should ensure prescribers know the importance of prescribing in renal impairment by having access to, and knowing how to access, appropriate local and/or national guidelines for prescribing in renal impairment.
- Trusts should ensure their practice aligns with relevant local and national guidelines for prescribing in renal impairment. It may be appropriate for Trusts without a renal unit on site to collaborate with the local renal unit when these guidelines are updated.
- Trusts should provide prescribers with opportunities for training covering prescribing in renal impairment.

Patient Assessment

Assess the patient's kidney function

- Consider kidney function as an integral part of the prescribing process.
- Refer to local guidelines for prescribing in CKD and AKI.
- For acutely unwell patients' current assessment of kidney function should be available to guide prescribing.
- When patients are assessed as clinically stable, assessment of their biochemistry before prescribing may not be necessary. However, any change in kidney function will alter the metabolism of most opiates.
- Systems should be put in place to identify patients with renal impairment to prescribers (for example alerts on electronic prescribing, inclusion in 'Allergies' box, alert cards for known renal patients).

Assess the patient's pain

Consider

- Intensity, chronicity, frequency and type of pain using a validated renal scoring system e.g. Edmonton Symptom Assessment System—revised: Renal ESAS-r:Renal1.⁸
- Developing a treatment plan including an explanation of the nature of the pain, condition and setting appropriate treatment goals.
- Analgesic agents available.

Prescribing

Key considerations for prescribing opiates in the setting of reduced kidney function

- Is the patient opiate naïve?
- Age, weight, co-morbidities, polypharmacy, dialysis and drug interactions.
- Individualise the dose and balance against the side-effects.
- Start with a low dose and longer dosing interval.
- Oral administration is preferred as usually safer.
- Assessing pain regularly and titrating analgesia slowly accordingly.
- Prescribe analgesia in a step wise fashion starting with non-opioids before proceeding onto low dose opioids.
- Opioids with hepatic metabolism e.g. fentanyl and alfentanil are preferred but extremely potent and often unavailable for acute pain outside the intensive care or palliative care

setting. Oxycodone is preferred to morphine, however can still accumulate in those with reduced kidney function.

- Fentanyl patches should never be used for acute pain and are contraindicated in opioid-naive patients remembering fentanyl is a potent opioid. A 12 microgram (μg) per hour fentanyl patch equates to daily doses of oral morphine of up to 45mg a day.¹¹
- Refer to local opiate prescribing guidelines (e.g. palliative care) for opiate dose equivalents.
- Check 'as required' prescription to ensure no duplication or inconsistency with dosing.
- Regular analgesia is only recommended for chronic pain.
- Slow-release formulations should be avoided in renal impairment. If essential, these should be used only for chronic pain and titrated very slowly every 3 or 4 days.
- Document a minimum time interval between doses on every opioid prescription. If supplementary analgesia is required within this time period, this should be discussed with a prescriber.
- Anticipate side-effects and manage pre-emptively
 - Prescribe laxatives to prevent constipation.
 - Prescribe naloxone alongside opiates in an inpatient patient setting.
- Local prescribing guidelines should consider the prescribing recommendations above.¹²

Electronic Prescribing

- If possible utilise electronic prescribing systems to support safer prescribing e.g. by forcing a review date and blocking duplicate PRN prescriptions.

Standard References

- We recommend commonly used references such as the Renal Drug Database and British National Formulary are updated to provide specific prescribing advice for opiates in opiate naïve patients.
- We recommend that all prescribers have access to:
 - The Renal Drug Database which has been updated to give more information relating to opiate dosing in renal impairment. (<https://renaldrugdatabase.com/>)
 - Palliative care analgesia guidelines e.g. Scottish guidelines.⁹
 - Local pain guidelines. These should be reviewed to ensure they include prescribing in renal impairment.
 - Suitable analgesia and availability should be reviewed considering local guidelines and supply.

Patient Monitoring

- Regularly assess the prescription:
 - Agree and document a regular prescription review interval
 - Repeat and review biochemical assessment
 - Regular review of inpatient prescriptions by a pharmacist
 - Clearly record any missed doses of opiates and reason why
- Regularly assess the pain:
 - Titrate analgesia accordingly
 - If dose is changed ensure original prescription is discontinued
 - Monitor patient after any dose change
 - Check and record observations at agreed intervals when commencing opiates and whenever a dose change occurs. Use NEWS 2 scoring¹³

- Review ongoing need for any opiate prescription
- Assess side effects and observe for signs of toxicity and record and escalate any changes in observations:
 - Marked confusion, delirium, or “acting drunk”
 - Frequent vomiting
 - Pinpoint pupils
 - Extreme sleepiness, or the inability to wake up
 - Intermittent loss of consciousness
 - Breathing problems, including slowed or irregular breathing
 - Respiratory arrest
- If patient has diabetes, be aware of symptoms of hypoglycaemia which can be similar to those of drug toxicity. Regularly monitor blood sugar and review insulin/oral hypoglycaemics.

Communication and dissemination of these guidelines

Even experienced clinicians may have difficulty in balancing risks and benefits of opioid analgesia in the setting of CKD and AKI. To mitigate against harm to patients, we advocate:

- High-quality pharmaceutical education at all levels of training and across all relevant professional disciplines, including (but not limited to) Medicine, Nursing and Pharmacy.
- Thorough evaluation of knowledge of opioid analgesia prescribing for trainees at all levels and across all professional disciplines.
- Access to appropriate reference resources for opioid prescribing in all clinical care settings.
- A culture of professional openness in all healthcare organisations to enable lessons to be learned effectively from any instances of avoidable harm that may occur.
- Universal access to renal, pharmacy and toxicology advice at all times.

We recommend a national educational campaign is provided to all areas that care for people with kidney impairment including primary care, paramedics, paediatrics, emergency departments, surgical, general medicine, care of older people and end of life care.

We will work with national bodies to ensure appropriate distribution of these recommendations and adoption into clinical practice.

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