Doncaster and Bassetlaw Hospitals NHS
NHS Foundation Trust

Analgesia in patients with impaired renal function – Formulary Guidance

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1. Aim

The aim of this document is to enable health care professionals to assess the impact of renal function on treatment of pain and provide safe and effective analgesia for patients with impaired renal function. This guidance applies to adult patients (over 18 years).

2. Introduction

Analgesia is problematic in patients with chronic kidney disease for several reasons. Some drugs may accumulate as they are renally excreted, whilst others may have increased toxic effects in patients with renal disease. Drugs with nephrotoxic effects need to be used with particular caution. There is evidence that pain in patients with chronic kidney disease is undertreated with significant consequences for the patients[1,2].

3. Assessment of renal function

To safely prescribe analgesia an assessment needs to be made of the level of renal function. In patients with stable renal function the most useful measure is the estimated GFR calculated by the CKD-EPI equation (now reported on all U&E samples). eGFR should be regarded with caution in extremes of size and patients with amputations. It is not validated in pregnancy and is not useful in children (under the age of 18). eGFR readings are meaningless in patients undergoing any form of dialysis or haemofiltration.

Table 1: Modified KDOQI staging of Chronic Kidney Disease

eGFR	CKD G stage	Notes for prescribing
> 60	Stage 1 or 2 if other evidence of kidney disease present (eg proteinuria)	No specific adjustment required
30-60	3	Caution advised, especially with high risk drugs (eg gentamicin) and nephrotoxic agents
15-30	4	All prescribing should take renal function into account and both dose and choice of agent should be checked. Specialist advice should be sought where appropriate.
< 15	5	
On dialysis	5D	

Acute kidney injury (AKI) refers to a sudden deterioration in renal function and is common in hospital inpatients. The presence and severity of acute kidney injury can be determined using the KDIGO staging system.

Table 2: KDIGO staging of Acute Kidney Injury

AKI stage	Definition	Notes for prescribing
1	Increase in serum creatinine 1.5-1.9 fold or increase by > 26.5 umol/L	Caution advised, especially with high risk drugs (eg gentamicin) and nephrotoxic agents
2	Increase in serum creatinine 2-2.9 fold	The patient should be treated as having severe renal failure and prescribing adjusted accordingly. Specialist advice should be sought where appropriate.
3	Increase in serum creatinine > 3 fold or rise to > 354umol/L	

Guidance on dosage adjustment according to degree of renal failure can be found in the BNF. More details (particularly prescribing for dialysis patients) can be found in the Renal Drug Handbook or Renal Drug Database. If you need access to information from these resources then contact your pharmacist.

4. Choice of Analgesics

Pain severity should be assessed and treated following the World Health Organisation (WHO) pain ladder. Pain severity should be assessed on a scale of 0-10 where 1-3 = mild pain, 4-7 = moderate pain, 8-10 = severe pain, and documented on the physiological observations chart. Non-pharmacological approaches should be considered.

Stage 1 – Mild-moderate pain

- Paracetamol: No dosage adjustment required. Can be given orally or IV (when the oral route is unavailable)
- Consider adjuvant analgesia (see below)

Stage 2 – Moderate-severe pain

- Paracetamol: No dosage adjustment required. Can be given orally or IV (when the oral route is unavailable)
- Weak opioid e.g. codeine phosphate or tramadol. Reduced doses are advisable in patients with eGFR<30, monitor closely for signs of toxicity.
- Consider adjuvant analgesia (see below)

Stage 3 – Severe pain

- Paracetamol: No dosage adjustment required. Can be given orally or IV (when the oral route is unavailable)
- Strong opioid
- Consider adjuvant analgesia (see below)

5. Use of strong opioids in patients with renal impairment

Short term/initial management:

Morphine is problematic in patients with reduced renal function due to the risk of accumulation of active metabolites and therefore is generally avoided. Pethidine should not be used due to the risk of seizures from accumulation of norpethidine. Oxycodone is a reasonable first line strong opioid, but it is partly renally excreted so there is some prolongation of the half life so doses should be reduced in patients with severe renal impairment. It is important to monitor patients regularly for evidence of opioid side effects. Oxycodone is significantly cleared by haemodialysis, therefore additional dosing is likely to be required after haemodialysis.
Alfentanil is not significantly renally excreted and is a good alternative for parenteral analgesia where staff have experience with using this drug.

Table 3: Suggested dose adjustment for oxycodone

CKD/AKI stage	**Starting dose of oral oxycodone**
CKD stage G3-4 or AKI stage 1	5mg
CKD stage G5 or AKI stages 2-3	2.5mg

Medium to long term use:

Prolonged release oxycodone can be used in patients with mild to moderate CKD but may be more problematic in patients with stages G4-5 CKD. Transdermal fentanyl or buprenorphine are not renally excreted and should be considered. The lowest possible dose should be used initially unless the patient is already established on other opioids, in which case dose conversion can be undertaken as usual. Monitor closely for signs of toxicity. Patients with stage G5 CKD who have severe ongoing pain are at high risk of adverse events from analgesia and should usually be managed jointly by a nephrologist and pain specialist.

6. Use of adjuvant analgesics

Non steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs are useful for nociceptive pain associated with tissue inflammation (e.g. arthritis). These drugs are usually contraindicated in patients with CKD 4-5 who are not on dialysis due to the significant risk of causing deterioration in renal function. In patients with stable CKD stage G3 where there is a strong indication (e.g. severe arthritis) then a trial of NSAIDs with close monitoring of renal function may be appropriate. In patients with CKD and preserved renal function (eGFR>60, CKD stage G1-2) short courses of NSAIDs are usually fine but care should be taken with long term use as there is a risk of progressive renal fibrosis. Ibuprofen 200 to 400mg TDS is a reasonable first

line drug, with co-prescription of a proton-pump inhibitor where appropriate for gastric protection. NSAIDs may also be used in dialysis patients who are anuric (i.e. have no significant residual kidney function) although there is also an increased risk of gastrointestinal side effects.
Topical NSAIDs can be effective for localised pain and are generally safe to use over a limited surface area in CKD patients.

Nefopam
Nefopam is an atypical analgesic which can be used as an adjuvant in mild-moderate pain. It is not renally excreted or nephrotoxic so can be used safely in patients with renal impairment. Side effects include gastrointestinal upset and confusion, and it should be avoided in patients with epilepsy. Efficacy is variable and some patients do not get substantial benefit, however it can be a useful adjuvant in some cases.

Gabapentin and Pregabalin
These anticonvulsants are effective in neuropathic pain (e.g. diabetic neuropathy). They are renally excreted and the dose should be adjusted accordingly. Information on dosage adjustment can be obtained from the renal drug handbook or renal pharmacist. Patients with severe renal failure taking gabapentin or pregabalin have a higher incidence of neurological side effects and should be monitored regularly.

Amitriptyline
Tricyclic antidepressants such as amitriptyline are used for relief of neuropathic pain (e.g. diabetic neuropathy). These drugs may be particularly beneficial at night where pain is disturbing the patient's sleep. Amitriptyline is not renally excreted and can be used at normal doses (10-25mg daily, titrated up to 75mg daily according to response) in patients with renal impairment.

6. References

1 Davison SN (2003) Pain in hemodialysis patients: prevalence, cause, severity and management Am J Kidney Dis 42:1239-1247
2 Roy PJ et al (2020) Pain management in patients with chronic kidney disease and end stage kidney disease Curr Opin Nephrol Hypertens 29(6) 671-680