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].

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.

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 to 3 and documented on the physiological observations chart.

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)

Short term/initial management:

Morphine sulphate is appropriate as a first choice in acute pain. Dose should be reduced (see table for suggested doses) and the patient should be closely monitored. In severe pain a larger initial dose may be given but the patient should be watched closely to monitor response. Short acting preparations (e.g. IV or SC morphine, oramorph) should be used. Delayed release formulations (e.g. MST) should be avoided. In haemodialysis patients morphine is significantly cleared with haemodialysis sessions and therefore breakthrough analgesia is often needed towards the end of a dialysis treatment.
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 morphine

CKD/AKI stage	**Starting dose of oral morphine**
CKD stage 3 or AKI stage 1	10mg hourly
CKD stage 4	5mg hourly
CKD stage 5 or AKI stages 2-3	2.5mg hourly

Reduce doses by 50% for parenteral use

Medium to long term use:

Where a patient is likely to need longer term treatment (>3 days) risk of accumulation is higher with morphine.
Transdermal fentanyl or buprenorphine 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 5 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.

5. 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 who are not on dialysis due to the significant risk of causing deterioration in renal function. In patients with stable CKD stage 3 where there is a strong indication (e.g. severe arthritis) then a trial of NSAIDs with close monitoring of renal function may be appropriate. 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.

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