

Use of Opioids in Chronic Kidney Disease (CKD)

CKD can cause an increase in drug side effects by:

- Decreasing plasma protein binding capacity due to the loss of protein and to altered binding ability caused by uraemia.
- Allowing build up of active drug metabolites.
- Changes in hydration affecting the distribution of drugs in the body.
- Reduction in oral absorption of drugs because of vomiting, diarrhoea and gastrointestinal oedema.
- Increasing permeability of the blood brain barrier (in uraemia) which may exaggerate unwanted CNS side effects

Analgesic ladder for Chronic Kidney Disease [1,2]:

DRUG	CKD 3 eGFR 30-9mL/min	CKD 4 eGFR 15-29mL/min	CKD 5 eGFR <15mL/min	
			Not on dialysis	On haemodialysis (HD)
STEP ONE (NON-OPIOIDS)				
Paracetamol	ND	ND	Max 1g q8h	As for "not on dialysis"
STEP TWO (WEAK OPIOIDS)				
Tramadol	ND	50-100mg bd	Max 50mg bd	Max 50mg q8-6h
STEP THREE (STRONG OPIOIDS)				
Methadone	ND	ND	50% of ND (specialist prescription advised)	As for "not on dialysis"
Fentanyl	ND	75% of ND	50% of ND (e.g. sc 12.5mcg, starting 50-100mcg/24hr sc infusion)	As for "not on dialysis"
Alfentanil	ND	ND	ND (use when fentanyl > 600mcg/24h)	As for "not on dialysis"
Hydromorphone	ND	1.3mg 6h	1.3mg 8-12h	1.3mg 6h
ADJUVANTS				
Gabapentin	ND	ND	300mg alternate day	Loading: 300mg Maintenance: 200-300mg post HD
Amitriptyline	ND	ND	10mg nocte	As for "not on dialysis"

Common analgesics to be avoided in CKD:

NSAIDs

- NSAIDs decrease GFR compromising residual renal function
- Causing hyperkalaemia, raised BP, fluid retention, gastric mucosa effect, platelet inhibition, etc

Pethidine/Meperidine

- Neurotoxic metabolite normeperidine, which accumulates in renal insufficiency
- May cause seizures, death
- Should not be used in chronic dosing, regardless of renal function

Morphine

- metabolised to morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) in liver, both accumulate in CKD.
- Accumulation of M3G may cause clinical excitation or agitation.
- Accumulation of M6G, the useful analgesic metabolite, may account for symptoms of drowsiness, nausea & vomiting, respiratory depression and even coma.
- the use of long-acting preparations should be avoided in CKD.
- opioids which do not have active metabolites (such as fentanyl) may be more suitable for patients in renal failure than morphine or diamorphine.

Reference:

1. Brown E, Chambers EJ, Eggeling C. End-of-life Care in Nephrology. Oxford Specialist Handbooks. 2007
2. Ashley C, Currie A. eds. *The Renal Drug Handbook*. 3rd ed. Oxford: Radcliffe Publishing Ltd, 2009
3. Broadbent A, Khor K, Heaney A. Palliation and chronic renal failure: Opioid and other palliative medications - Dosage guidelines. *Prog Palliat Care* 2003;11(4):183-190