Patterns of opioid dose escalation in patients with chronic kidney disease initiated on opioids for the treatment of non-cancer pain

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Abstract

Background Pain management in chronic kidney disease (CKD) is challenging due to altered drug metabolism, impaired excretion, and higher opioid toxicity risk. Despite this, opioids are commonly prescribed, yet real-world data on dose escalation in CKD remain limited. Objective To investigate patterns and timing of opioid dose escalation to ≥50 and ≥90 MME/day among new opioid users across kidney function levels. Methods This population-based cohort study used data from the Stockholm Creatinine Measurements (SCREAM) project linking diagnoses, prescriptions, and laboratory records. Adult new opioid users (no prior opioid in 12 months) from 2012–2021 were categorized by baseline eGFR (≥60, 30–59, < 30 mL/min/1.73m$^{2)\cdot}$ Opioids were identified using ATC codes, and daily doses (MME/day) were calculated based on strength, quantity, and equianalgesic ratios. Fine–Gray competing-risks regression assessed time to dose escalation (≥50 and ≥90 MME/day), accounting for death as a competing event. Results Of 81,987 adult new opioid users, 5,987 (7.3%) escalated to ≥50 MME/day comprising 7.4%, 6.8%, and 8.1% of patients with eGFR≥60, 30–59, and <30 mL/ min/1.73m^{2,} respectively. For ≥90 MME/day, 2,067 (2.5%) escalated, 2.5%, 2.3%, and 2.9% across the same eGFR categories. Competing risks regression showed significantly lower risks of escalation among patients with reduced eGFR levels. For ≥50 MME/day, the sub distribution hazard ratios (SHRs) were 0.67 (95% CI: 0.56–0.81, p<0.001) for eGFR 30–59 and 0.64 (95% CI: 0.42–0.99, p=0.043) for those with eGFR<30.For ≥90 MME/day, SHRs were 0.57 (95% CI: 0.43–0.75, p<0.001) and 0.31(95% CI: 0.15–0.65, p=0.002), respectively. Most escalation occurred within six months, with minimal increase thereafter. Conclusion Opioid dose escalation occurred across all eGFR levels, underscoring the need for cautious, individualized prescribing and close monitoring, especially in patients with reduced kidney function.

Indexed keywords

MeSH

Adult; Aged; Analgesics, Opioid; Cohort Studies; Dose-Response Relationship, Drug; Female; Glomerular Filtration Rate; Humans; Male; Middle Aged; Pain; Pain Management; Renal Insufficiency, Chronic

EMTREE drug terms

antidepressant agent; benzodiazepine; buprenorphine; fentanyl; ketobemidone; methadone; morphine; neuroleptic agent; nonsteroid antiinflammatory agent; opiate; oxycodone; tapentadol; tramadol; narcotic analgesic agent

EMTREE medical terms

adult; aged; Article; chronic kidney failure; chronic pain; clinical practice; clinical significance; cohort analysis; creatinine blood level; drug dose escalation; drug exposure; drug formulation; drug metabolism; estimated glomerular filtration rate; female; health service; human; kidney function; male; mental disease; middle aged; non cancer pain; non cancer pain; observational study; opioid use disorder; outcome assessment; pain; primary medical care; sensitivity analysis; analgesia; complication; dose response; drug therapy; glomerulus filtration rate; pain; pathophysiology; procedures

Device trade names

Commercial names given to devices, used for branding and differentiation in the market, commonly referenced in scientific and clinical research.

Stata version 19

Chemicals and CAS Registry Numbers

Unique identifiers assigned by the Chemical Abstracts Service (CAS) to ensure accurate identification and tracking of chemicals across scientific literature.

benzodiazepine	12794-10-4
buprenorphine	52485-79-7, 53152-21-9
fentanyl	437-38-7, 1443-54-5
ketobemidone	469-79-4

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