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

By

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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 & sup2;). 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 & sup2;, 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.

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Data availability statement

The data used in this study originate from Swedish national healthcare registers and are protected under the General Data Protection Regulation (GDPR) and Swedish legislation. Therefore, the data cannot be shared publicly. Researchers interested in accessing Swedish register data may submit an application to the Swedish National Board of Health and Welfare (Socialstyrelsen) in accordance with Swedish law. Information on how to apply for data access is available from the Swedish National Board of Health and Welfare (Socialstyrelsen) website (https://www.socialstyrelsen.se/en/statistics-and-data/apply-for-data/) or via email (registerservice@socialstyrelsen.se).

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