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Initiation Dose of Allopurinol and the Risk of Severe Cutaneous Reactions in Older Adults With CKD: A Population-Based Cohort Study

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Rationale & Objective

Allopurinol should be started at lower doses in patients with chronic kidney disease (CKD) to avoid adverse effects. We examined the risk of severe cutaneous reactions in older adults with CKD who were newly prescribed allopurinol at varied doses.

Study Design

Population-based cohort study using linked health care databases.

Setting & Participants

Patients in Ontario, Canada (2008-2019) aged ≥ 66 years, with an estimated glomerular filtration rate (GFR) of < 60 mL/min/1.73 m², and who were new users of allopurinol.



Exposure

A new prescription for allopurinol >100 mg/d versus a dose ≤100 mg/d.

Outcome

The primary outcome was a hospital visit with a severe cutaneous reaction within 180 days of starting allopurinol. Secondary outcomes included all-cause hospitalization and all-cause mortality.

Analytical Approach

The exposure and referent groups were balanced on indicators of baseline health using inverse probability of treatment weighting on the propensity score. Weighted risk ratios (RR) were obtained using modified Poisson regression and weighted risk differences (RD) using binomial regression.

Results

Of 47,315 patients (median age, 76 years; median eGFR, 45 mL/min/1.73 m²), 55% started allopurinol at >100 mg/d. Starting allopurinol at >100 versus ≤100 mg/d was associated with an increased risk of a severe cutaneous reaction: number of events (weighted), 103 of 25,802 (0.40%) versus 46 of 25,816 (0.18%), respectively (weighted RR, 2.25 [95% CI, 1.50-3.37]; weighted RD, 0.22% [95% CI, 0.12%-0.32%]. Starting allopurinol at >100 versus ≤100 mg/d was associated with an increased risk of all-cause hospitalization but not with all-cause mortality.

Limitations

This study was underpowered to detect risk differences in the association of allopurinol dose with outcomes across eGFR categories (ie, 45-59, 30-44, and <30 mL/min/1.73 m²).

Conclusions

Older patients with CKD who started allopurinol at >100 mg/d versus ≤100 mg/d were twice as likely to visit a hospital with a severe cutaneous reaction in the next 180 days.

Index Words

[Allopurinol](#) • [chronic kidney disease \(CKD\)](#) • [drug dosing](#) • [drug safety](#) • [erythema multiforme](#) • [erythroderma](#) • [estimated glomerular filtration rate \(eGFR\)](#) • [exfoliative dermatitis](#) • [geriatric](#) • [hospitalization](#) • [hypersensitivity reaction](#) • [maculopapular eruption](#) • [older age](#) • [urticaria](#) • [serum urate](#) • [severe cutaneous reaction](#) • [skin eruption](#) • [Stevens-Johnson syndrome](#) • [toxic epidermal necrolysis](#) • [xanthine oxidase inhibitor](#)

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