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Letter

Frequency of Allopurinol Dose Reduction in Hospitalized Patients With Gout Flares

To the Editor:

The risk of subsequent flares after the initial diagnosis of gout remains high, according to the recent study, "Changes in the Presentation of Incident Gout and the Risk of Subsequent Flares: A Population-based Study Over 20 Years" by Elfishawi, *et al*[1]. This study found 60% of the patients have at least 1 subsequent flare episode within 5 years of their initial gout diagnosis. Despite an improved understanding of gout pathophysiology and treatment options, the prevalence of subsequent flares in the 2009–2010 cohort has not significantly improved compared to the 1989–1992 cohort. One of the identified risk factors was the persistently elevated serum uric acid (SUA). This finding highlights the importance of adequately treating gout to their target SUA. Limitations in their dataset may have precluded the authors from studying urate-lowering therapy (ULT) changes or discontinuation as a risk factor for subsequent flare. We report the results of our study below, in which we evaluated the frequency of inpatient adjustment of ULT in hospitalized patients with acute gout flares.

We used a clinical database to query patients with an International Classification of Diseases, 10th revision diagnosis of gout with active prescriptions for allopurinol who were admitted to the University of Washington Medical Center and Harborview Medical Center in Seattle, Washington from 2014 to 2019[2]. We included patients with acute gout flares during the hospitalization in the study. We reviewed the electronic medical records and extracted clinical characteristics including allopurinol doses on admission and discharge, and gout flares within 3 months of discharge. We used the Fisher exact test to assess for the difference between post-hospitalization gout flares between the allopurinol-reduced group (dosage reduced or discontinued) versus the comparator group (dosage unchanged or increased).

We identified 59 patients with a total of 73 admissions who met inclusion criteria (Table 1). Of all the admissions, 92% were males with a median age of 58 years. Allopurinol was either reduced or discontinued in 15 admissions (allopurinol-reduced group), which comprised 21% of total admissions. Allopurinol was increased or unchanged in the other 58 admissions (comparator group). The proportion with chronic kidney disease (CKD) was similar between the groups, while there was a greater proportion of patients with acute kidney injury in the allopurinol-reduced group versus the comparator group (60% vs 36%, respectively). There was a lower proportion of patients receiving flare prophylaxis in the allopurinol-reduced group than those in the comparator group at discharge. Rheumatology was consulted to assist with the management of gout flares in 39% of the total admissions. The allopurinol-reduced group had a significantly higher rate of gout flares within 3 months of discharge at 53% compared to the comparator group at 22% ($P = 0.03$).

Table 1. Baseline demographics, comorbidities, and posthospitalization gout flares between allopurinol-reduced and comparator groups.

	All Admissions, n = 73	Allopurinol Decreased or Discontinued, n = 15	Allopurinol Unchanged or Increased, n = 58
Age, yrs, median (IQR)	58 (16)	57 (15)	58.5 (16)
Male sex	67 (92)	14 (93)	53 (91)
Race, white	43 (59)	9 (60)	34 (59)
Acute kidney injury	30 (41)	9 (60)	21 (36)
Chronic kidney disease	53 (73)	10 (67)	43 (74)
Tophaceous disease	19 (26)	3 (20)	16 (28)
Flare prophylaxis	39 (53)	4 (27)	35 (60)
Rheumatology consult	29 (39)	2 (13)	26 (45)
Flare within 3 months of discharge	21 (29)	8 (53)	13 (22)*

Values are n (%) unless otherwise specified. *$P = 0.03$ for this comparison.

In hospitalized patients with gout who experienced acute flares at 2 academic medical centers, allopurinol was decreased or discontinued in nearly a quarter of admissions. There were significantly more gout flares after discharge in patients who had allopurinol reduced or discontinued, compared to those who did not. Inappropriate changes to allopurinol dosing during hospitalization can have a negative effect on gout-related outcomes. This is especially true in hospitalized patients, given that their risk of acute gout flares can be up to 10-fold greater, which is in turn associated with prolonged hospitalizations[3,4].

In our study, dose reduction was primarily driven by concerns that allopurinol, in the setting of gout flares and renal insufficiency, can worsen renal function and increase the risk of allopurinol hypersensitivity syndrome. However, studies have demonstrated no increase in adverse reactions in individuals with CKD who received maintenance allopurinol that was above the recommended maximum dose corresponding to their level of renal impairment[5,6]. A recent prospective cohort study found that allopurinol of at least 300 mg per day was associated with a 13% reduction in the risk of developing CKD stage 3 or higher[7]. Such renoprotective effect can be undermined by frequent flares and inappropriate discontinuation of allopurinol.

Certain limitations in our study must be acknowledged. First, this is a single-health system study with a small sample size, which limits the power to detect clinically relevant differences among subgroups of interest. As this was an observational study, there may be an imbalance of potential confounders between the allopurinol-reduced group and the comparator group. Finally, our study was performed in 2 US academic medical centers, which may limit its generalizability to other settings.

Our study demonstrates an association of increased gout flares following a decrease in allopurinol dosage in the inpatient setting, compared to no change in dosage. Current studies have supported the safety of allopurinol use for gout patients with concurrent renal insufficiency. Improved awareness of the current gout recommendations, as well as the risks and benefits of allopurinol in the setting of concomitant renal disease, is necessary to improve patient outcomes.

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