Background: When serum uric acid rapidly increases or decreases due to such as alcohol consumption or fasting, free urate crystals are formed, which induce an acute joint inflammation referred to as an acute gout attack. In 86.4% of patients with gout, dual energy computed tomography demonstrated the deposition of urate crystals in vasculature, and urate crystals have been observed in coronary arteries and various tissues in 10.9% of patients with a heart transplant. However, whether hyperuricemia and urate crystal directly cause cardiovascular disease is not well known. We previously realanalyzed the CARES trial to calculate the mortality rates based on the median duration of exposure to study drugs and the median follow-up duration. A sharp increase in mortality was observed after allopurinol and febuxostat were discontinued. Even in view of the Sick-Stopper Effect, for about 40-fold increase in mortality following drug discontinuation, we postulated that the sharp increase in mortality may be associated with rapid changes in uric acid level and subsequent free urate crystal formation in the cardiovascular system (cardiovascular gout attack).

Objectives: Based on this hypothesis that some cardiovascular events may be cardiovascular gout attacks, we investigated the association between the cardiovascular event and initiation of hypouricemic agent, when is accompanied by acute gout attack and/or fluctuation of uric acid level, in gout patients.

Methods: Using the Korean National Health Insurance Service (KNHIS) database, which covers the entire Korean population, we conducted a population-based cohort study among gout patients who initiated allopurinol or febuxostat between 2012 and 2018. The initiators were defined as those who had no prior dispensing of any urate-lowering therapy for at least 60 days prior to the initiation date and continuous treatment for at least 30 days after the initiation date (i.e. index date) of either allopurinol or febuxostat. We excluded patients with a diagnosis of cancer and patients treated with benzbromarone. We investigated a composite cardiovascular event of hospitalized myocardial infarction, ischemic stroke, and cerebral hemorrhage.

Results: We identified hospitalizations for cardiovascular event (acute myocardial infarction (n = 3538), cerebral infarction (n = 5127), and cerebral hemorrhage (n = 1593)) that occurred within 2 year before and 2 year after initiation of allopurinol or febuxostat. Of these, 4333 cardiovascular event (0.014 per person-time, 95% confidence interval [CI], 0.014 to 0.015) occurred in 2 years before initiation of allopurinol or febuxostat, 1032 cardiovascular event (0.081 per person-time, 95% confidence interval [CI], 0.076 to 0.086) occurred in 30 days before initiation of allopurinol or febuxostat. And, 83 cardiovascular event (0.030 per person-time, 95% CI, 0.024 to 0.037) occurred in 7 days after initiation of allopurinol or febuxostat.

Conclusion: Initiation of febuxostat and allopurinol was significantly associated with acute myocardial infarction, cerebral infarction, and cerebral hemorrhage. Considering that allopurinol and febuxostat usually are initiated a few weeks after a acute gout attack. Acute gout attack and/or fluctuation of uric acid level might be significantly associated with cardiovascular event. Some of cardiovascular events might be cardiovascular gout attack.

References:

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1909

Figure. The cardiovascular event in gout patients who initiated and discontinued allopurinol and febuxostat.