Original Research

Association Between Colchicine and Risk of Diabetes Among the Veterans Affairs Population With Gout

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ABSTRACT

Purpose: This study aimed to determine the association between colchicine use and the incidence of diabetes in a cohort of patients with gout.

Methods: This is a retrospective study of 27,876 adults with gout identified via the Veterans Integrated Services Network 16 data warehouse. Patients had up to 11 years of follow-up (January 1999 through December 2010). The final study sample consisted of 1046 pairs of 1:1 propensity score–matched patients from the colchicine treated and control cohorts. Time to first diabetes development since the first gout diagnosis was modeled.

Results: After the propensity score matching, the 12-month baseline variables (eg, age, sex, race, index year, body mass index, serum uric acid, antigout drug use, and health care use) were comparable between the matched cohorts ($P > 0.05$ for all). Among the 1046 matched pairs, 234 patients who had taken colchicine and 224 patients who had never taken colchicine developed diabetes; the incidence rates were 38.95 and 39.02 per 1000 patient-years, respectively. In Poisson and Cox proportional hazards regression, the risk of incident diabetes was reduced with increased duration of colchicine use, but the difference was not statistically significant ($P > 0.05$). In a time-varying Cox proportional hazards model, the hazard ratio for incident diabetes among patients who had taken colchicine was 0.877 (95% CI, 0.662–1.163; $P = 0.362$) compared with those who had not taken colchicine.

Conclusion: This study suggests a possible duration- or dose-related association between colchicine use and reduced risk of diabetes in adults with gout even though the risk reduction was not significant. Further studies are needed to confirm findings from this study. (*Clin Ther*. 2015;37:1206–1215)

Key words: colchicine, diabetes, gout, veterans.

INTRODUCTION

Hyperuricemia is characterized by elevated levels of serum uric acid in blood (6 mg/dL for women and 7 mg/dL for men).[1] Hyperuricemia was present in 21.2% of men and 21.6% of women in data from the US National Health and Nutrition Examination Survey, which was conducted in 2007 and 2008.[2] This condition is often accompanied by comorbidities: metabolic syndrome, including diabetes, hypertension, and renal disease.[3,4]

The most well-known medical manifestation of hyperuricemia is gout, a chronic disease of the joints

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characterized by recurrent attacks of sudden severe pain[5] in one or more joints and inflammation due to deposition of monosodium urate or uric acid crystals in joints, tendons, and surrounding tissues. A range of comorbidities are often exhibited by patients with gout, including but not limited to hypertension, chronic kidney disease, obesity, and type 2 diabetes.[6,7] A 2007-2008 study based on the US National Health and Nutrition Examination Survey estimated the prevalence of gout as 3.9%.[2] Between 1996 and 2008, a total of 15.1% of the >177,000 US patients with gout were diagnosed as having diabetes. Men with gout were found to have a 34% to 66% higher risk of developing type 2 diabetes compared with those without gout after adjustment for various factors, such as age, body mass index (BMI), smoking, family history of type 2 diabetes, alcohol intake, dietary factors, and presence of individual components of the metabolic syndrome.[8] The standard pharmacologic management of acute attacks of gout involves use of oral colchicine, nonsteroidal anti-inflammatory drugs, or corticosteroids.[9,10]

Colchicine, an antigout and anti-inflammatory drug, is usually used to prevent gout attack and relieve the pain of gout attacks caused by hyperuricemia in adults.[11] Among the unique features of colchicine is its low therapeutic index. Effective steady-state plasma concentrations after short-term treatment range from 0.5 to 3 ng/mL, with toxic effects occurring at a level of approximately 3 ng/mL.[12]

Colchicine has hypoglycemic effects and may reduce the risk of diabetes mellitus.[13] This retrospective study is designed to examine the treatment pattern of colchicine and its association with the risk of incident diabetes in patients with gout. We hypothesized that colchicine use would be associated with a decreased likelihood of the development of type 2 diabetes.

MATERIALS AND METHODS

Data Source

The Veterans Affairs Veterans Integrated Services Network (VISN) 16 data warehouse was used for this research. The VISN 16 data warehouse contains all demographic (age, sex, race, and BMI), service use, and pharmacy data for patients treated in the South Central Veterans Affairs Health Care Network (Arkansas, Louisiana, Mississippi, Oklahoma and parts of Alabama, Florida, Missouri, and Texas), as well as certain clinical data, such as laboratory values and patient vital data. Data also include medical claims (inpatient and outpatient), pharmacy claims, laboratory test results, and vital data (height and weight). Data covering the period January 1999 through December 2010 were used for this study. Appropriate institutional review board approval was obtained before the study initiation.

Study Design

The study sample included adult patients (≥18 years) diagnosed as having gout in the VISN 16 data warehouse. The first diagnosis date of gout was defined as the index date. Patients diagnosed as having diabetes or any antidiabetes drug use before the index date were excluded. Patients were followed up from the index date to the onset of diabetes, the date of death, or the end of data availability, whichever came first. Everyone in this study had 1-year continuous enrollment eligibility before index date.

Variables

Patients with gout were identified using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code 274.xx. Patients with diabetes were identified using *ICD-9-CM* code 250.xx or any antidiabetic medication use. The comorbidities were identified using the following *ICD-9-CM* codes: cardiovascular diseases, 390 through 459 excluding 401-405; coronary artery disease, 410 through 414; angina, 410; myocardial infarction, 411 and 413; stroke, 430 through 438; peripheral artery disorder, 443; congestive heart failure, 398.91 and 428; hypertension, 401 through 405; diabetes, 250; kidney stone, 592, 594, and 274.11; and renal disease, 580 through 588, 250.4, 590, 593, and 791.0. The Charlson comorbidity index (CCI)[14] was also used based on diagnosis codes, such as heart disease, AIDS, or cancer (a total of 22 conditions). Each condition is assigned a score of 1, 2, 3, or 6, depending on the risk of dying associated with each one.[15]

Subjects

The VISN 16 data warehouse contained records for 46,409 unique veterans with at least one gout diagnosis. Patients had at least baseline information before the first diagnosis of gout and had to be ≥18 years old on the index date. Patients with any records of diabetes before first diagnosis of gout or first use of colchicine were excluded. Study participants were allowed to receive other standard of care medication for gout, including nonsteroidal anti-inflammatory drugs, corticosteroids,