Factors Associated With Preventive Pharmacological Therapy Adherence Among Patients With Kidney Stones

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OBJECTIVE To determine adherence patterns for thiazide diuretics, alkali citrate therapy, and allopurinol, collectively referred to as preventive pharmacological therapy (PPT), among patients with kidney stones.

METHODS Using medical claims data, we identified adults diagnosed with kidney stones between 2002 and 2006. Through National Drug Codes, we determined those with one or more prescription fills for a PPT agent. We measured adherence to PPT (as determined by the proportion of days covered formula) within the first 6 months of starting therapy and performed multivariate analysis to evaluate patient factors associated with PPT adherence.

RESULTS Among 7980 adults with kidney stones who were prescribed PPT, less than one third (30.2%) were adherent to their regimen (indicated by proportion of days covered ≥ 80%). Among those on monotherapy, rates of adherence differed by the type of PPT agent prescribed: 42.5% for thiazides, 40.0% for allopurinol, and 13.4% for citrate therapy. Factors that were independently associated with lower odds of PPT adherence included combination therapy receipt, female gender, less generous health insurance, and residence in the South or Northeast. In contrast, older patients and those with salaried employment had a higher probability of PPT adherence.

CONCLUSION Adherence to PPT is low. These findings help providers identify patients where PPT adherence will be problematic. Moreover, they suggest possible targets for quality improvement efforts in the secondary prevention of kidney stones. UROLOGY 93: 45–49, 2016. © 2016 Elsevier Inc.

Kidney stones are a chronic medical condition, for which secondary prevention can play an important management role. In recognition of this, the American Urological Association and the American College of Physicians recently released clinical guidelines, outlining a rational approach to reduce kidney stone recurrence in adults.[1,2] Recommendations include a trial of a thiazide diuretic, citrate, or allopurinol—collectively referred to as preventive pharmacological therapy (PPT)—in the patient with active kidney stone disease who fails to respond to dietary modification alone.

However, although multiple randomized, controlled trials have shown PPT to be efficacious; getting patients to accept a prescribed regimen and adhere to it may be difficult because the benefits of treatment are not obviously apparent when patients are between symptomatic stone events.[3-7] Indeed, the literature on other chronic medical conditions like diabetes and hypertension suggests that medication adherence rates are about 50% at best.[8] Because nonadherence may mitigate treatment benefit or even cause harm, understanding baseline adherence rates among patients on preventive pharmacological therapy is important.[9,10]

In this context, we used medical claims data to identify adult patients with a diagnosis of kidney stones. Among those with a prescription fill for a PPT agent, we assessed their adherence using a validated metric. We then evaluated for changes in rates of adherence over time. Finally, we determined patient-level factors that were associated with higher adherence. Findings from our study serve to

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inform future interventions designed to increase the uptake of PPT among patients with kidney stone disease.

METHODS

Data Source and Study Population

For our study, we used Truven Health Analytics MarketScan Commercial Claims and Encounters Database (2002 to 2006). This longitudinal database contains medical and drug claims from a population of working-age adults with employer-sponsored insurance and their dependents.

Through an established International Classification of Diseases, Ninth Revision, Clinical Modification (ICD9) code-based algorithm,[11] we identified adults between the ages 18 and 64 years old with a diagnosis of urinary stone disease. To be eligible for inclusion, a beneficiary had to have continuous health insurance coverage for 180 days prior to the index stone claim and 180 days after his/her prescription fill for a PPT agent.

Because our analytic focus was on PPT, we then used appropriate National Drug Codes to abstract the subset of beneficiaries with a new prescription fill for a thiazide diuretic, alkali citrate therapy, and/or allopurinol during the 6 months after their index stone claim. Understanding that medications such as thiazide diuretics and allopurinol are not necessarily specific for metabolic stone management, we conducted a secondary analysis in which we excluded patients with a concomitant diagnosis of hypertension (ICD-9 codes 401.1, 401.9) or gout (ICD-9 274.0, 242.01, 242.02, 242.03, 274.89, 274.9). A complete list of the medications considered to be PPT is available upon request.

Measuring Medication Adherence

To estimate medication adherence, we used the proportion of days covered (PDC) formula. Although there are multiple ways of measuring and assessing medication adherence using secondary data, the PDC offers several important advantages. First, it provides a more conservative estimate of adherence (compared to other popular methods) when multiple medications are intended to be used concomitantly. Second, the PDC avoids double-counting of days of medication coverage because a day is only counted if all medications are available on that day.[12] Third, it is the only measure recommended by the Pharmacy Quality Alliance.[13]

With values ranging from 0 to 1, the PDC is calculated as the number of days available or "covered" by a certain medication divided by the total number of days in the follow-up period.[14] For our study, we used a 180-day follow-up period after a beneficiary's first prescription fill for a PPT agent. In the event that a beneficiary was prescribed multiple agents from different classes (eg, a thiazide diuretic and potassium citrate), we estimated adherence by calculating the average of class-specific PDC values. We then multiplied the PDC by 100 to express it as a percent. Consistent with prior studies, we defined a beneficiary as being adherent if this percent was at or above 80%.[15]

Statistical Analysis

For our initial analytic step, we assessed overall adherence to PPT by study year. To assess for changes over time in adherence, we used the Cochran-Armitage Trend test. Next, we examined for differences in adherence based on the class of agent prescribed.

We then made comparisons between adherent and nonadherent beneficiaries over a variety of sociodemographic factors. Specifically, we examined for differences related to their age at the time of the index stone claim, gender, employment classification (salaried vs hourly) and status (full-time vs part-time), generosity of health insurance, urban and/or rural status, geographic region of residence, and baseline health status. To determine the generosity of health insurance, we calculated the percentage covered by insurance for each prescription fill during the 180-day follow-up period and took the mean for each beneficiary. We then ranked beneficiaries by this mean, splitting into tertiles of low, medium, and high generosity. To assess baseline health status, we used a modification of the Charlson comorbidity index score. For all bivariate comparisons, we used *t* tests and chi-square tests where appropriate.

Finally, we used multivariate regression to understand the determinants of adherence. For our binary outcome, we fit log binomial regression models where our independent variable of interest was receipt of combination therapy. Our a priori hypothesis was that this would be associated with lower probability of adherence. We adjusted our models for the other patient-level factors described above.

We completed all analyses using the SAS statistical software package, Version 9.3 (SAS Institute Inc., Cary, NC). We performed two-sided significance with alpha set to 0.05. Our Institutional Review Board deemed that this study (based on de-identified data) was exempt from oversight.

RESULTS

Among the 7980 beneficiaries who met our study's inclusion criteria, majority were on thiazide (40.5%) or citrate (30.1%) monotherapy. Combination therapy was infrequently prescribed (Table 1). Among those on monotherapy, adherence rates were highest for thiazides (42.5%), followed by allopurinol (40.0%) and citrates (13.4%). Regardless of the agent prescribed, adherence to monotherapy was higher than combination therapy (31.4% vs 23.3%,

Table 1. PPT use by study population

Medication Class	Frequency	Percent
Thiazide monotherapy	3234	40.5
Citrate monotherapy	2484	31.1
Allopurinol monotherapy	1074	13.5
Thiazide and allopurinol	225	2.8
Thiazide and citrate	419	5.3
Citrate and allopurinol	461	5.8
Thiazide, citrate, and allopurinol	83	1.0

PPT, preventive pharmacological therapy.