Patterns of Gout Treatment and Related Outcomes in US Community Rheumatology Practices: The Relation Between Gout Flares, Time in Treatment, Serum Uric Acid Level and Urate Lowering Therapy

Poster #1904

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ABSTRACT

BACKGROUND: Study patterns of gout treatment and related outcomes in US community rheumatology practices, specifically the relation between likelihood and severity of gout flares, time in treatment with current physician, serum uric acid (sUA) level and urate lowering therapy (ULT, which included, at any dosage level, allopurinol, febuxostat, pegloticase, probenecid).

METHODS: Fifty practices completed retrospective chart abstraction on their 25 most recently seen patients with gout. Data, abstracted from all visits in 2010-2011 using standardized case report forms, included demographics, gout history, co-morbidities, sUA, gout treatment, and visit type (flare-related or follow-up). This report includes all data from the subset of the total cohort which was available at time of abstract submission. Final dataset will comprise 1,250 patients.

Data were analyzed using logistic regression, with visit type (coded as severe flare, mild/moderate flare, non-flare related) as an ordinal response variable, and 3 predictor variables: time in treatment with current rheumatologist at start of chart abstraction (TxTime: new patient vs. > 2 months), ULT (absence vs. presence at time of visit) and sUA (≥ 6.0 vs. < 6.0).

RESULTS: The study population consisted of 479 gout patients from 21 sites, 79% male, 77% Caucasian, mean age 62 years, median disease duration 5.5 years.

Patients had a total of 2,460 visits during study period. Of these, 1,465 (59.6%) included all analysis variables and constitute the analysis sample. 273 (18.6%) of visits were flare-related. All 3 main effects were significant. Increased likelihood of a flare was associated with 1) shorter TxTime, 2) absence of ULT, and 3) higher sUA. Data are summarized in the table.

		n	Type of Visit (%) Flare-Related: Severe	Flare-Related: Mild/Moderate	Not Flare-Related	Any Flare vs. Non-Flare p-value OR (95% CI)
TxTime	New Patient	565	9.6	16.6	73.8	< .001
	> 2 months	900	5.2	8.7	86.1	1.62 (1.22-2.15)
ULT	Absent	277	18.1	29.2	52.7	< .001
	Present	1188	4.3	7.7	88.0	4.79 (3.52-6.52)
sUA	≥ 6.0	729	9.9	15.9	74.2	.004
	< 6.0	736	3.9	7.6	88.5	1.64 (1.21-2.22)

The only significant interaction effect was ULT by TxTime ($p < .01$). Patients who were already on ULT when referred to the current rheumatologist were no more likely to flare than the physician's current ULT patients. For patients not on ULT, however, new patients had triple the odds of flaring compared with current patients (OR=3.04, 95%CI=1.86-4.95).

CONCLUSION: Data depict aspects of current usage of gout therapy in US community practices and underscore importance of managing sUA levels. All patients regardless of sUA levels or treatment had some risk of flare, but risk was greatly mitigated by ULT therapy. These data suggest that failure to treat hyperuricemia in gout patients is associated with a greatly increased likelihood of a flare.

INTRODUCTION

Gout is an increasingly common condition in both primary care and specialist practices. It is the most common inflammatory joint disease in men (Lawrence, et al, 2008) and the most common inflammatory arthritis in older women (Doherty, 2009). Furthermore, there is evidence that both the incidence and prevalence of this disease are increasing worldwide (Weaver, 2008). Although not life threatening, gout is extremely painful and has a significant impact on quality of life (Sundy, 2006; Roddy, 2007).

The objectives of therapy for people with gout are first to relieve the symptoms of the acute flare and then reduce the serum uric acid level sufficiently that existing crystals are dissolved and new crystals no longer form. The current understanding in the medical community is that gout remains poorly managed by both primary care physicians and rheumatologists (Hamburger, 2011; Singh, 2008; Pascual, 2007).

OBJECTIVES

Study patterns of gout treatment and related outcomes in US community rheumatology practices, specifically the relation between likelihood and severity of gout flares and:

- Urate lowering therapy (ULT, which included, at any dosage level, allopurinol, febuxostat, pegloticase, probenecid).
- Time in treatment with current rheumatologist (Rheum)
- Serum uric acid (sUA) level
  - A secondary objective was to examine the extent to which Rheums are monitoring sUA in their patients

Hypothesis: A higher frequency of flares will be associated with:

- A shorter time in treatment with current Rheum
- Higher sUA levels, and
- Absence of ULT

METHODS

Design and Procedures

- Retrospective chart abstraction from all gout-related visits in 2010 and 2011 within the study population
- 45 geographically-dispersed U.S. community-based rheumatology practices
- 25 most-recently-seen patients at each site with primary diagnosis of gout
- Variables: Demographics, co-morbidities, time in treatment with current Rheum, sUA (baseline and at each visit, when available), gout treatments, visit type (flare-related or follow-up)

Data Analysis

1. Relationship between Time in Treatment with Current Rheum (≤ 2 months vs. > 2 months) and frequency and level of sUA was assessed with chi-square
2. Relationship between Visit Type (severe flare vs. mild/moderate flare vs. non-flare related) and 3 predictors:
   - TxTime: time in treatment with current rheum at start of chart abstraction, coded as described in the previous analysis
   - ULT: absence vs. presence at time of visit
   - sUA: value obtained at the corresponding visit, dichotomized as ≥ 6.0 vs. < 6.0

   was assessed with multinomial logistic regression
3. Impact of sUA on Visit Type was further explored, treating sUA as a continuous variable, using logistic regression and graphical methods

RESULTS

1,045 patients met study inclusion criteria (at least 18 years of age, at least 1 gout-related visit in 2010 and 2011, not taking any investigational drugs for gout during the study period). Seventy-six (76) patients were dropped from the second and third analyses due incomplete sUA or ULT data.

TABLE 1: PATIENTS

Mean age (years): 62.1 (range: 21-99)	
Gender: Male 78.3%	
Ethnicity: White 72.4%	
Mean Duration of Disease (years, diagnosis to start of study period): 5.8 (range: 0-45)	
In Treatment with Current Rheum ≤ 2 months: 34.0%	
Comorbidities:	
Hypertension:	66.4%
Hyperlipidemia:	37.7%
Obesity (reported):	24.2%
Diabetes:	23.7%
CKD:	22.9%
CAD:	20.2%
Other:	22.1%
None:	13.5%
ULT Therapy at any time during Study Period:[1]	
Allopurinol only:	61.4%
Febuxostat only:	19.0%
Probenecid only:	1.8%
Allopurinol & Febuxostat:	7.8%
Febuxostat & Probenecid:	1.1%
Allopurinol & Probenecid:	0.9%
Febuxostat & Pegloticase:	0.5%
Allopurinol, Febuxostat & Probenecid:	0.2%
None:	7.2%
At least 1 visible tophus at any time during Study Period: 23.9%	

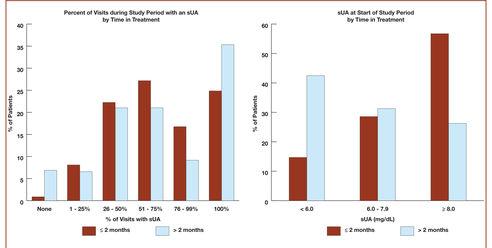
Note 1: Patients may have been on probenecid concomitantly with other ULTs. All other ULTs were used as monotherapy. Pegloticase was not used in conjunction with any other ULT.

TABLE 2: VISITS

Total Number of Visits: 3,189	
Median # of visits per patient during the 2-year study period: 5.0 (range: 2-20)	
Flare status (self-reported)[2]:	
Non-flare related:	83.9%
Mild/moderate flare:	11.1%
Severe flare:	5.0%
Visits while on ULT: 84.3%	
Visits with sUA <6: 51.5%	
Visits for patients in Treatment with Current Rheum > 2 months: 64.1%	

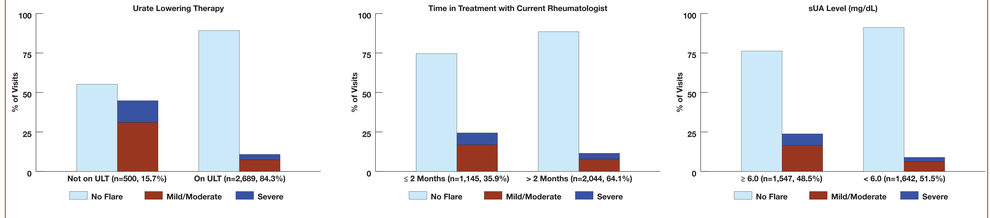
Note 2: This study only analyzed visits that resulted from a flare or follow-up visits. Data on patient-reported flares which occured between visits were also collected, but are not reported here. Patients reported at least 1 intra-visit flare at 27% of their visits (21.3% mild/moderate, 5.8% severe). Thus, it should be noted that the rate of flares reported here under-estimates the total number of flares which actually occurred during the study period.

FIGURE 1: RESULTS OF ANALYSIS 1



- Over two-thirds of patients had an sUA on at least half of their visits
- 6.9% of existing patients (in treatment more than 2 months) had no sUAs at all during the study period
- Existing patients showed a high frequency (35%) of sUA at every visit – likely the result of being stable patients seen annually
- Existing patients had significantly lower sUA at the start of the study period ($p < .001$)
- Nevertheless, over half of the existing patients (57.6%) had an sUA ≥ 6 and 26.3% had an sUA ≥ 8

FIGURE 2: RELATIONSHIP BETWEEN VISIT TYPE (FLARE) AND 3 PREDICTOR VARIABLES



- The odds of a flare in the absence of ULT were nearly 50/50 (45.6% vs. 54.3%)
- Even when on a ULT, 11.2% of visits were flare-related
- The probability of a flare was reduced by over half after 2 months in the care of a rheumatologist
- The likelihood of a flare fell below 10% for visits where sUA was less than 6.0 mg/dL
- However, just over half (51.5%) of all visits met that criteria

ANALYSIS 2

All 3 main effects were significant. No interaction effects were significant. Increased likelihood of a flare was associated with 1) shorter TxTime, 2) absence of ULT, and 3) higher sUA. The table below summarizes the results of the regression analysis, showing odds ratios (OR), 95% confidence limits and p-values for each predictor.

Predictor	Flare Severity (vs. no flare)	OR	95% CI
ULT	Mild/Moderate	4.69	3.60-6.10
	Severe	4.55	3.16-6.55
TxTime	Mild/Moderate	1.95	1.54-2.47
	Severe	1.93	1.38-2.69
sUA	Mild/Moderate	1.95	1.50-2.54
	Severe	2.09	1.42-3.06

All $p < .001$

- Based on relative magnitude of odds ratios, largest effect is due to the presence of ULT
- The absence of ULT therapy is associated with over a 4 times greater risk of a flare, both for mild/moderate and severe flares
- TxTime and sUA are roughly equal in increased odds of a flare, with the greater risk group (shorter time in treatment and higher sUA) approximately doubling the risk of a flare

Figure 2 displays the percent of visits which fell into each flare category, broken down by the levels of each predictor variable. The hypothesized higher risk groups consistently showed a higher frequency of flares, and this relationship held for both mild/moderate and severe flares.

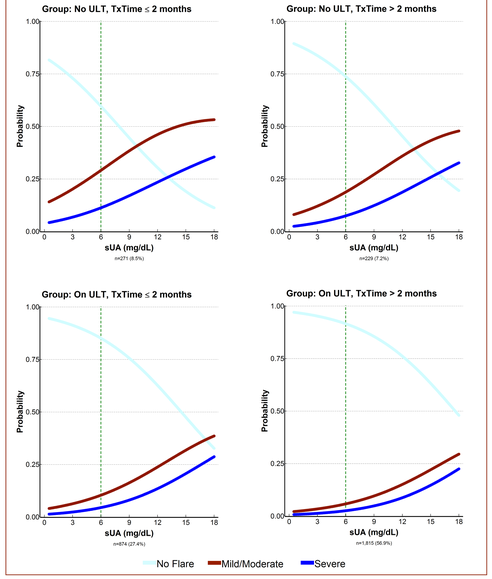
ANALYSIS 3

SUA is a continuous variable which, in the data presented here, varied from less than 1 to over 14. This analysis examines whether the relationship between likelihood of flare and sUA is best thought of as a step function (as implied in Analysis 2) or as a continuous function where flare risk increases proportionately to increased sUA.

A logistic regression analysis analogous to Analysis 2 was performed, treating sUA as a continuous rather than dichotomous variable, and results were comparable. Figure 3 displays the relationship between sUA and probability of mild/moderate, severe or no flare for, respectively, No ULT/TxTime > 2months, No ULT/TxTime ≤ 2 months, On ULT/TxTime > 2 months, and On ULT/TxTime ≤ 2 months.

- For all groups, the relationship between sUA and probability of a flare is curvilinear, i.e., as sUA increases linearly, risk for flare increases exponentially
- For the highest risk group (no ULT and in treatment ≤ 2 months), the probability of no flare decreases to below 50/50 at approximately 8 mg/dL, a moderate level which occurs frequently in our data (see Figure 1)

FIGURE 3: RELATIONSHIP BETWEEN VISIT TYPE (FLARE) AND SUA



CONCLUSIONS

- Data depict aspects of current usage of gout therapy in US community practices and underscore importance of managing sUA levels
- Although treatment by a rheumatologist significantly reduces the likelihood of a flare, over half the patients who had been in treatment for more than 2 months had a baseline sUA ≥ 6 and over one quarter had an sUA ≥ 8
- All patients regardless of sUA levels or treatment had some risk of flare, but risk was greatly mitigated by urate-lowering therapy
- The probability of a flare increases exponentially with a linear increase in sUA

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Acknowledgment: This study was supported by Savient Pharmaceuticals, Inc.

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