Work productivity loss due to flares in patients with chronic gout refractory to conventional therapy

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Original article
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Abstract

Objective:
Joint pain and swelling during gout flares may lead to considerable morbidity and disability, having an impact on patient work productivity and social participation. The objective of this study was to assess how gout flares affect these activities in patients with chronic gout refractory to conventional therapy.

Methods:
A 1-year prospective observational study was conducted among patients with symptomatic disease in the United States in 2001. Inclusion criteria required patients (1) to be age 18 years or older, (2) to have documented, crystal-proven gout, (3) to have symptomatic gout, and (4) to be intolerant or unresponsive to conventional therapy, reflected by SUA ≥ 6.0 mg/dL. Patients were evaluated every 2 months. At each visit, patients completed a gout diary, which included number of flares experienced, duration and severity of each flare, and whether the flare caused: (1) work loss, (2) missed appointments or social events, or (3) impairment of self-care activities. The Short-Form Health Survey (SF-36) was also completed each visit.

Results:
Analyses were restricted to those who completed the first 6 months of the study ($n = 81$). Mean number of flares per patient per year was 8.8. Of the patients who were <65 years, 78% reported at least 1 work day lost due to a gout attack during the year. Mean annual work day loss for those <65 years was 25.1 days. A total of 545 of patients reported at least one flare per year that impaired social activities, with a mean of 17.1 social days lost and 52% reported at least one flare per year that compromised normal self-care activities, with a mean of 16.9 days impairment. Correlations between the diary reports and activity-related questions from the SF-36 were significantly positive.

Limitations:
The study is limited by small sample size, lack of reference group, and inability to explicitly collect employment information. Age under 65 years was used as a proxy for employment eligibility.

Conclusion:
Flares in patients with chronic gout refractory to conventional therapy significantly affect patient work productivity and social activities.

Introduction

Gout is a disorder in which urate crystal deposition in joints and soft tissues results in episodic acute arthritis and can ultimately lead to chronic arthropathy and tophus formation. Management of recurrent or progressive gout aims to reduce and maintain serum uric acid (SUA) levels below 6.0 mg/dL, a goal

usually requiring a urate-lowering agent such as a xanthine oxidase inhibitor (e.g., allopurinol or febuxostat), a urico-suric agent (e.g., probenecid) or both.

Progression of gout to a chronic disabling disorder is encountered most often among patients who are intolerant to currently available urate-lowering agents or who have medical comorbidities limiting their use; persons not pre-scribed or not adherent to sufficient urate-lowering ther-apy; and patients with organ transplants whose immunosuppressant therapy may diminish renal function and result in hyperuricemia.

Chronic gout that is refractory to conventional urate-lowering therapy with a high burden of symptoms, such as frequent flares and tophi, is estimated to occur in approx-imately 25,000–100,000[1] of the 3–6 million Americans who suffer from gout[2,3]. Prevalence of gout of all types is believed to be increasing[4–9].

The economic burden of treatment-refractory chronic gout contributes disproportionately to the overall health-care burden of the gout population. A study of the insur-ance claims (1999–2005) of 13 million beneficiaries in 40 private health plans in the US, estimated that older adults (≥65 years) with gout and SUA levels greater than 9 mg/dL incurred an additional \$3,100 per year in incremental costs as compared to those with SUA levels below 6 mg/dL[10]. In addition, the study found that presence of tophi contributed an additional \$5,500 in regression-adjusted all-cause health care costs[10].

The loss of work and social activity in a population of patients with chronic gout refractory to conventional urate-lowering therapy has not been previously reported, although two studies have examined productivity loss in the general gout population. As reported by Roubenoff (1990)[11], the National Health Interview Survey, self-iden-tified gout patients reported that gout restricted their activities an average of approximately 16.8 days per year. An analysis of absenteeism records of 300,000 employees of several large US employers found that 1,171 gout patients missed work an average of approximately 4.6 more days than the employees without gout[12]. Another analysis of the same data included a calculation of the productivity dollar difference between gout and non-gout as \$1,337, including sick leave, short-term disability, long-term disability, and worker's compensation[13]. Patients with chronic gout refractory to conventional therapy gen-erally have greater disease burden and are likely to expe-rience greater compromise in productivity.

To gain a better understanding of treatment-refractory chronic gout, a natural history study has been conducted in which individuals with chronic gout refractory to conven-tional urate-lowering therapy were followed for up to 1 year. Results on health-related quality of life and func-tional ability have been published[14]. The results indicated that treatment-refractory chronic gout is associated with functional disability and poor health-related quality of life.

This adverse impact is especially prominent for patients who experience more gout flares and have a greater number of involved joints.

The objective of the present analysis of this longitudi-nal natural history study was to determine the effect of gout-related disability on work productivity and other daily activities in patients with treatment-refractory chronic gout. Newer therapeutic agents in development promise to provide the opportunity for much needed improvement in signs and symptoms and patient outcomes in the difficult to manage gout population[15]. The effects of the disease on productivity would help evaluate the eco-nomic value of these new drugs.

Patients and methods

Patient population

A 1-year prospective observational study was conducted among patients with symptomatic disease at 24 sites in the United States in 2001. Inclusion criteria required patients (1) age 18 years or older, (2) to have documented, crystal-proven gout, (3) to have symptomatic gout, and (4) to be intolerant or unresponsive to conventional therapy, reflected by SUA ≥ 6.0 mg/dL. Symptomatic gout was defined as having at least one of the following: recurring gout flares (≥3 per year); chronic synovitis/arthropathy; presence of tophi confirmed by radiographic or physical examination; or uric acid nephrolithiasis/nephropathy. No restrictions were placed on concurrent medications or procedures[14].

Evaluation

Following a baseline visit, subjects were evaluated at 2-month intervals for 12 consecutive months. During each follow-up visit, subjects completed a symptom diary, in which they were instructed to record information on the overall severity of pain within the preceding 2-month period and on any flare experienced within that time, including the duration of attack, severity (using visual analog scale), joint(s) affected, and treatment. A gout flare was defined as any worsening of signs or symp-toms that required the attention of a physician or required the subject to take new medication or an increased dosage or frequency of his/her current gout medication. For each flare, the subject was asked 'As a result of this flare, were you (check all that apply): unable to perform your usual work, unable to make an appointment or social event, or unable to take care of yourself as you normally do?' The responses were assumed to apply for the entire duration of the flare. Self-reported quality of life was measured at each visit using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36; Version 1)[16] (SF-36 is a

Table 2. Flares and activity loss.

	N	Mean	95% confidence interval	Median
Flares				
8 mg given as an intravenous infusion every 2 weeks. (2.1)	65	8.8	7.0, 10.7	6
Duration (days)	63	5.3	4.2, 6.3	4
Severity*	64	5.7	5.1, 6.4	6
Work productivity for age <65 years				
Patients with any loss	42	78%	65%, 88%	–
Days lost per year†	40	25.1	11.7, 38.6	12
Social activity				
Patients with any loss	65	54%	43%, 65%	–
Days lost per year†	63	17.1	7.7, 26.7	4
Personal care				
Patients with any loss%	65	52%	41%, 63%	–
Days lost per year†	63	16.9	7.7, 26.1	3

N number of patients with evaluable diary data.
*Scale is 0–10 with 10 being most severe.
†Average overall, including patients with no days lost.
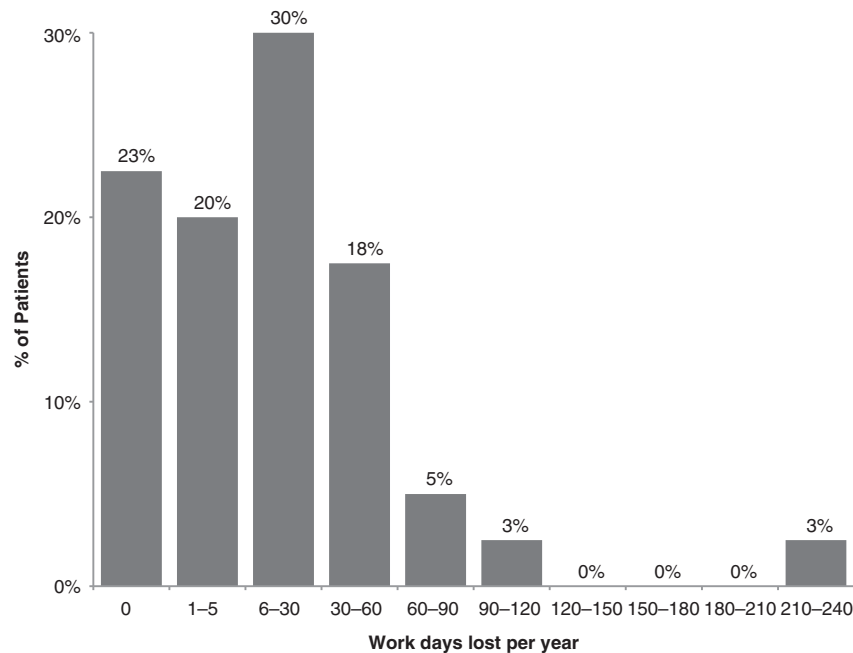
Figure 1. Patients by work days lost to flares, age <65 years, $n = 40$.

The extent to which gout affected work productivity, self-care, and social activity is associated with baseline severity. As shown in Table 3, subjects who reported a history of greater than six flares per year prior to study entry had more than twice the work days lost per year; social activities and personal care compared to those who experienced 1–2 flares per year.

Correlations between the gout diary reports and activity-related questions from the SF-36 were significantly positive, ranging from 0.39 to 0.56. Table 4 summarizes the correlations between SF-36 measures and diary reports.

Table 3. Mean activity days lost as a function of baseline number of flares per year.

Activity	Baseline number of flares per year*		
	1–2	3–6	>6
Work† ($n = 40$)	19.3	19.4	51.9
Social ($n = 63$)	8.4	11.2	36.2
Personal care ($n = 63$)	11.3	14.0	31.1

*Patient recall for the year prior to study entry.
†Only those who were <65 years old are included.

Table 4. Correlations* between SF-36 and diary-reported measures of activity loss, age <65 years, $n = 40$.

SF-36 measures†	Days lost calculated from diary report		
	Work	Social	Personal care
Percentage of work time decreased due to physical health	0.54	0.39	0.39
Percentage of work time decreased due to emotional health	0.28	0.24	0.18
Physical or emotional problems interfered with social activity	0.37	0.40	0.36
Pain interfered with normal work or housework	0.34	0.39	0.35
Physical or emotional problems affected time on social activities	0.40	0.34	0.38

*Pearson correlation coefficients.
†Patient's report on previous 4 weeks.

Full results on health-related quality of life in this longitudinal natural history study have been published elsewhere[14].

Seven of the 65 subjects who had flare diary data (10.8%) reported a total of 14 visits to the emergency room due to flares during the course of the study, corresponding to a mean of 0.22 visits per patient per year. Four patients (6.2%) had a total of nine flare-related hospital visits, corresponding to a mean of 0.14 visits per patient per year. The average length of stay per visit was 3.7 days.

Discussion

This longitudinal natural history study is the first prospective study to evaluate the loss of activity for work, self-care and social function, as well as health-related quality of life in patients with chronic gout refractory to conventional urate-lowering therapy. The results of the study demonstrate that treatment-refractory chronic gout significantly affected patients' work-related, self-care, and social activities. Based on the average 2006 US wage rate of $19.30 per hour, the mean of 25.1 work lost days would result in an approximately $3,900 per patient per year cost (median $1,850, 95% CI [$1,800, $6,000]). A mean of 17.1 social days and 16.9 self-care days were lost per patient per year.

The study findings suggest that, compared to gout population in general, patients who are refractory to conventional urate-lowering therapy are subject to significantly more work productivity and social activity loss. Previous studies described in the Introduction reported an average of 4.6–16.8 days per year of missed work days[11,12] and a total of $1,337 indirect costs associated with gout.

The present study has several limitations that limit the extent to which it can be generalized. The study examines a small sample size with limited follow-up and does not have a gout-free or moderate-gout control population. In terms of lost work productivity, the study did not explicitly collect employment information, so retirement age (65 years) was used as a proxy. There is at least a two-part limitation to using the subject's age as a proxy for employment eligibility. It fails to address those subjects younger than 65 years who may be unemployed due to gout or co-morbidity related disabilities as well as those older than 65 years who continue to be employed. Another limitation is that subjects were asked to report only about activities lost due to flares, not to tophi, arthropathy, or other gout-related complications.

More work days were lost than social days or personal care days as shown in Table 3. This may be due to the more demanding nature of work, or to patients' interpretation of the question about work fairly broadly (e.g., to include housework as well as how they define the totality of social events). The positive correlation of diary-reported activity loss with corresponding items on a well-established quality of life instrument (SF-36) supports the credibility of the diary reports.

The results are consistent with observed loss of productivity and activity in employed patients with rheumatoid arthritis (RA), another potentially debilitating chronic arthritic condition. A recent systematic review of several RA productivity studies found an average of 66% of individuals (range 36–84%) experiencing work loss due to their condition in the prior 12 months, for a median duration of 39 days (range 7–84 days)[17]. Others have reported that patients with a variety of musculoskeletal diseases reduce their work hours, take breaks, or may even be forced to change jobs to deal with the pain and disability of their conditions[12,18–20].

The costs of productivity loss, as well as lost days of self-care and social activities, in patients with chronic gout refractory to conventional urate-lowering therapy are significant. Considering only costs of medical management of treatment-refractory chronic gout, and not addressing the indirect costs associated with this condition, will likely underestimate the total cost burden. In order to accurately assess the true personal and societal costs of chronic gout refractory to conventional therapy, lost productivity and lost capability for personal care and social participation must be considered.

Transparency

Declaration of funding

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