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Cost, utilization, and patterns of medication use associated with chronic idiopathic urticaria

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ABSTRACT

Background: The literature on chronic idiopathic urticaria (CIU) lacks large-scale population-based studies.
Objective: To characterize an insured population with CIU, including their demographic characteristics and comorbidities.
Methods: We conducted a cross-sectional analysis using insurance claims. We included patients with 1 outpatient claim with an *International Classification of Diseases, 9th Edition, Clinical Modification* (ICD-9-CM) code for idiopathic, other specified, or unspecified urticaria (ICD-9-CM 708.1, 708.8, or 708.9) and either (1) another of these claims 6 or more weeks later; (2) a claim for angioedema (ICD-9-CM 995.1) 6 or more weeks from the urticaria diagnosis; or (3) overlapping claims for 2 prescription medications commonly used for CIU.
Results: We identified 6,019 patients who had claims consistent with CIU. The mean age was 36 years. Fifty-six percent of patients had primary care physicians as their usual source of care, 14% had allergists, and 5% had dermatologists. Allergic rhinitis was diagnosed in 48%, asthma in 21%, other allergy in 19%, and atopic dermatitis in 8%. Sixty-seven percent of patients used prescription antihistamines, 54% used oral corticosteroids (OCSs), 24% used montelukast, and 9% used oral doxepin. Antihistamine users received a mean of 152 days of prescription antihistamines, OCS users 30 days of OCSs, montelukast users 190 days of montelukast, and oral doxepin users 94 days of doxepin.
Conclusions: Primary care physicians managed most patients with CIU. Antihistamines were the most common treatment for CIU, although OCSs were frequently prescribed. Thirty days of OCS supply among users may represent multiple steroid bursts each year. Given the known risks of OCSs, identifying other CIU treatments with more favorable safety profiles may be beneficial.

Introduction

Chronic urticaria is a frustrating condition for caregivers and affected patients. Urticaria is not a single disease but a reaction pattern that includes cutaneous mast cell degranulation and extravasation of plasma into the dermis. Urticaria is characterized by hives or wheals. In many patients, an extensive workup does not uncover a cause. Chronic idiopathic urticaria (CIU) is a diagnosis that requires wheals and pruritus to be present for 6 or more weeks with no obvious cause. The pathogenesis of this condition is not well understood, but many patients appear to have underlying autoimmune abnormalities. Patients presenting with a spectrum of symptoms, from localized urticaria to life-threatening angioedema, may be treated by a variety of specialists. No consensus guidelines exist in the United States (although a British guideline has been published),[1] and treatment may vary widely across geographic regions.

The literature on CIU contains a variety of investigations of underlying biologic mechanisms and small studies of treatments, but the epidemiology, treatment patterns, and burden of CIU have not been well described. The primary objective of this study was to characterize an insured population with CIU and, specifically, to describe these patients' demographic characteristics and common comorbidities and to identify the types of physician specialists who cared for them. The study also characterized the frequency of various treatments used for CIU and calculated the cost of care for this condition.

Methods

Data source and patients

This was a descriptive, cross-sectional statistical analysis using a Health Insurance Portability and Accountability Act–compliant

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commercial health care claims database. The data in the Ingenix Lab/Rx database are derived from claims for inpatient admissions, outpatient medical encounters, prescription drugs, and enrollment data on just over 10 million commercially insured individuals from every major region of the United States. Data on over-the-counter (OTC) medications are not available. The study was exempt from review by a human subjects protection committee because the database did not contain protected health information.

The *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code 708 refers to urticaria. There is no specific ICD-9-CM code for CIU; it may be coded as 708.1 (idiopathic), 708.8 (other specified), or 708.9 (unspecified). The study included patients who were continuously enrolled from July 1, 2007 through June 30, 2008 and had at least 1 outpatient ICD-9-CM code of 708.1, 708.8, or 708.9 combined with (1) a second such code 6 or more weeks later; (2) an ICD-9-CM code of 995.1 for angioedema at least 6 weeks from the urticaria diagnosis; or (3) a 90-day or longer period of an overlapping supply of a prescription antihistamine and a second prescription medication commonly used to treat CIU (a second antihistamine, montelukast, cyclosporine, methotrexate, or oral corticosteroids [OCSs]). We did not include the codes for allergic urticaria (708.0), urticaria attributable to heat or cold (708.2), dermatographic urticaria (708.3), vibratory urticaria (708.4), or cholinergic urticaria (708.5) in the algorithm under the assumption, supported by the 2 authors who treat CIU (M.W.C., D.J.H.), that these would not be used to code idiopathic urticaria.

Variables

Patient demographic characteristics included age, sex, and geographic region; race/ethnicity was not reported in the database. We categorized "usual-care" physician specialty and "urticaria-care" physician specialty to describe the physicians who treated the study subjects. These specialties were identified using a previously validated method in which all evaluation and management service claims are reviewed, and the specialty listed on the plurality of these claims is defined as the usual-care specialty.[2] A similar method, but only including visits at which urticaria was coded, was used to identify the "urticaria-care" specialty. This was the specialty providing most of the evaluation and management services related to urticaria. We used the Charlson index, a validated claims-based measure of comorbidities, to characterize the burden of comorbid conditions.[3] The Healthcare Cost and Utilization Project Chronic Condition Indicator was used to count chronic conditions.[4,5] We identified several specific conditions that may be seen in conjunction with CIU, including atopic dermatitis (ICD-9-CM: 691.8), vasculitis and allergic purpura (ICD-9-CM: 287.0), allergic rhinitis (ICD-9-CM: 477.xx), asthma (ICD-9-CM: 493.xx), and other allergy (ICD-9-CM: 995.3, V15.x).

Claims do not associate a diagnosis with prescriptions, and no medications are specifically approved to treat CIU. To characterize treatment patterns, we identified 12 groups of prescription medications often used to treat CIU. These groups included 2 categories of antihistamines: nonsedating (cetirizine HCl, desloratadine, fexofenadine HCl, levocetirizine dihydrochloride, and loratadine) and all other prescription antihistamines (as noted, the database did not contain information on OTC antihistamines). Additional medication categories were OCSs, oral doxepin, montelukast, cyclosporine, methotrexate, H2 blockers, dapsone, sulfasalazine, and omalizumab.

We reported use of these drugs individually and in combination. Total and CIU-related charges were also reported. Total health service use included inpatient hospitalizations, emergency department (ED) visits, and physician office visits for all diagnoses during the 1-year period. Charges related to CIU included inpatient claims with a primary diagnosis of urticaria and outpatient claims with a primary or secondary diagnosis of urticaria. Urticaria-related pharmacy costs included any of the 12 groups of prescription medications used to treat CIU.

Statistical analysis

Descriptive statistics were reported for all measures. All data transformations and statistical analyses were performed using SAS version 9.2 (Cary, North Carolina). Means and standard deviations were reported for continuous variables; counts and percentages for categorical variables.

Results

A total of 7,555,991 individuals in the database met the 1-year continuous enrollment criteria, and 79,672 had at least 1 claim consistent with urticaria. Of these, 6,019 met the inclusion criteria, a prevalence rate of 1 per 1,255 (0.08%) enrollees. Having a second urticaria claim 6 or more weeks later was the most common reason for inclusion (n = 4,950), followed by an angioedema diagnosis 6 or more weeks distant from the urticaria claim (n = 1,255) and overlapping fills for prescription medications used to treat CIU (n = 1,008); 1,194 met more than one criteria.

The mean age of the 6,019 patients in the final study cohort was 36.0 years, and 66.7% (4,013) were female. The study population had a median of 2 chronic conditions identified in their claims and a median Charlson comorbidity index of 0, indicating relatively few serious concomitant conditions. Forty-eight percent of the group had allergic rhinitis, 21.2% had asthma, and 18.5% had other allergies in their claims. Atopic dermatitis affected 7.8%, and 0.3% were affected by vasculitis or allergic purpura. Anxiety and depression also were common, with both being identified in 9.4% of the population (Table 1).

Primary care (internal and family medicine) was the specialty of the usual-care physician for most (56.4%) of the patients, followed by allergy/immunology (13.9% of patients) and dermatology (5.4%). For 24.3%, the specialty of the usual-care physician was either unknown (3.8%) or was one of a variety of other specialties (20.5%), each constituting 2% or less of the total. In contrast, the specialty providing the most urticaria care was allergy/immunology in 42.7% of cases, primary care in 33.0%, dermatology in 13.3%, and other or unknown in 11.0% (Table 2).

Ten patterns described the use of prescription medications by 82% of the subjects; no data were available on OTC antihistamines. The most common pattern, seen in 16.8% of patients, was the combination of a prescription nonsedating antihistamine with at least 1 course of OCSs. Prescription nonsedating antihis-

Table 1
Characteristics of 6,019 patients with chronic idiopathic urticaria

Characteristic	N = 6,019
Age, mean ± SD, y	36.0 ± 19.6
Female, no. (%)	4,013 (66.7)
Charlson comorbidity index	
Mean ± SD	0.7 ± 1.2
Median	0
Number of chronic conditions	
Mean ± SD	2.7 ± 2.0
Median	2
Specific comorbid conditions, no. (%)	
Allergic rhinitis	2,882 (47.9)
Asthma	1,274 (21.2)
Allergy[a]	1,115 (18.5)
Anxiety	565 (9.4)
Depression	565 (9.4)
Atopic dermatitis	468 (7.8)
Vasculitis and allergic purpura	20 (0.3)

[a]Includes allergy to agents other than medications and allergy, unspecified.

Table 2
Specialty of usual-care and urticaria-care physician

Specialty	No. (%) of Patients $N = 6,019$	
	Specialty of Usual-Care Physician[a]	Specialty of Urticaria-Care Physician[b]
Dermatology	324 (5.4)	799 (13.3)
Allergy/immunology	836 (13.9)	2,571 (42.7)
Primary care[c]	3,397 (56.4)	1,986 (33.0)
Other/unknown[d]	1,462 (24.3)	663 (11.0)

[a]Specialty providing the plurality of evaluation and management services.
[b]Specialty providing the plurality of evaluation and management services at which a diagnosis of urticaria was recorded.
[c]Internal or family medicine.
[d]Patients for whom usual-care specialty accounted for ≤2% or less of the total or for whom a specialist could not be assigned because of missing information.

tamines (without OCSs) were used in 16.0%. The OCSs were the only prescription medication used in 11.6% of patients. Prescription nonsedating antihistamines plus montelukast, with (8.7%) and without (6.3%) OCSs, were the next most common patterns. Fifteen and a half percent of patients filled none of the 12 categories of prescription medications during the study year (Table 3).

Prescription antihistamines were used by 66.6% of the study group, with 64.0% using prescription nonsedating antihistamines and 7.9% using sedating prescription ones. Oral corticosteroids were the next most common medication (53.7% of patients), followed by montelukast (24.1%). Nine percent used oral doxepin, and 6.7% used H2 blockers. Less-common medications included cyclosporine (1.1% of patients) and methotrexate (0.7%). Of medications used by more than 1% of patients, montelukast had the greatest mean days supplied (190 days), followed by prescription antihistamines (152 days), oral doxepin (which is also a highly potent antihistamine; 94 days), H2 blockers (89 days), and OCS (30 days) (Table 4). Considering doxepin to be an antihistamine would raise the proportion treated with a prescription antihistamine to 68.1%, and considering H2 blockers as antihistamines would raise it to 69.5% (not shown).

Patients with CIU were frequent users of office-based care, with a median of 11 visits per year (mean ± SD, 14.5 ± 12.6). A median of 2 visits (mean ± SD, 3.1 ± 2.8) was urticaria related. Few CIU patients were hospitalized (mean ± SD, 0.4 ± 2.3) or went to the ED (mean ± SD, 0.5 ± 3.0 visits) during the year. During the year of observation, 9.5% of patients had a skin biopsy, and 16.8% had a test for antithyroid antibodies. The mean total annual charge for all health care per patient was $15,848 (median, $7,041), of which $1,762 (median, $1,298) was urticaria related. Medical claims (which do not include charges for prescription drugs) accounted for most of the charges, with a mean of $13,426 (median, $5,135) total and $1,252 (median, $700) for urticaria-related care. Prescription charges for urticaria-related medications were $510 (median, $243) (Table 5).

We conducted 2 sensitivity analyses. In the first we examined the extent to which our results reflected the single year in which we conducted the analysis. We compared the demographic characteristics of our study population with the characteristics of a population drawn from a study time frame exactly 1 year earlier. Mean age differed by less than 1 year, and the proportion of females was identical. The proportion cared for by each of the listed physician specialties differed by less than 1 percentage point.

To determine the extent to which our algorithms for identifying patients with CIU impacted our findings, we looked separately at all outcomes for patients meeting different inclusion criteria. For patients meeting the 3 different sets of inclusion criteria, the median number of office visits was 11 for those with 2 diagnoses of ICD-9-CM 708.1, 708.8, or 708.9 at least 6 weeks apart and for those with 1 diagnosis and angioedema, whereas patients who qualified by having 1 diagnosis and 2 prescription medications had a median of 13 visits. Urticaria-related visits varied from a median of 1 in the group with 2 prescription medications to 3 in both other groups. Total charges varied from a mean of $14,810 in the group identified on the basis of 2

Table 3
Most frequent patterns of prescription urticaria medication use

Medication	No. (%) $N = 6,019$
Nonsedating antihistamine + oral corticosteroid	1,009 (16.8)
Nonsedating antihistamine	963 (16.0)
No use of selected medications	935 (15.5)
Oral corticosteroid	699 (11.6)
Nonsedating antihistamine + oral corticosteroid + montelukast	522 (8.7)
Nonsedating antihistamine + montelukast	381 (6.3)
Nonsedating antihistamine + doxepin + oral corticosteroid	153 (2.5)
Oral corticosteroid + montelukast	100 (1.7)
Nonsedating antihistamine + other antihistamine + oral corticosteroid	100 (1.7)
Nonsedating antihistamine + doxepin + oral corticosteroid + montelukast	81 (1.3)

Table 4
Prescription medications and days supplied for urticaria patients

Any Use of Listed Medication	$N = 6,019$
No. (%) using prescription antihistamines[a]	4,009 (66.6)
Nonsedating	3,851 (64.0)
Other	477 (7.9)
Mean ± SD days of supply among users	152.2 ± 128.1
No. (%) using oral corticosteroids	3,235 (53.7)
Mean ± SD days of supply among users	29.7 ± 52.2
No. (%) using montelukast	1,451 (24.1)
Mean ± SD days of supply among users	190.1 ± 128.3
No. (%) with any use of doxepin	541 (9.0)
Mean ± SD days of supply among users	93.5 ± 102.7
No. (%) with any use of H2 blockers	406 (6.7)
Mean ± SD days of supply among users	89.1 ± 97.9
No. (%) with any use of cyclosporine	69 (1.1)
Mean ± SD days of supply among users	137.4 ± 111.1
No. (%) with any use of methotrexate	44 (0.7)
Mean ± SD days of supply among users	173.7 ± 113.5

[a]Data on OTC medications were not available in the database.

Table 5
Annual health service use and cost of care for 6,019 patients with urticaria

Variable	Total $N = 6,019$	Urticaria related
Office visits		
Mean ± SD	14.5 ± 12.6	3.09 ± 2.81
Median	11	2
ED visits or inpatient admissions		
Mean ± SD	0.9 ± 3.9	0.03 ± 0.47
ED visits		
Mean ± SD	0.5 ± 3.0	0.02 ± 0.42
Inpatient admissions		
Mean ± SD	0.4 ± 2.3	0.01 ± 0.20
Total health care charges ($)		
Mean ± SD	15,848 ± 30,607	1,762 ± 2,353
Median	7,041	1,298
Total medical charges ($)		
Mean ± SD	13,426 ± 29,290	1,252 ± 2,257
Median	5,135	700
Total prescription medication charges[a] ($)		
Mean ± SD	2,422 ± 3,844	510 ± 681
Median	1,264	243

[a]Data on OTC medications were not available in the database.

urticaria diagnoses to $20,611 in those with 2 prescription medications. The range of values for the other outcomes was similar to those reported here.

Discussion

In this claims-based study, we identified a group of patients apt to have CIU, we described their common comorbidities, and we characterized their patterns of health service use. Just over 6,000 patients out of 7.5 million met our criteria, giving an estimated prevalence of 0.08%. Patients meeting our criteria had a mean age of 36 years, and two-thirds were female. Allergic rhinitis, asthma, and other allergies were common in our sample, as were anxiety and depression. Allergists were the most common provider of urticaria care, followed by primary care physicians and dermatologists. Most patients used both prescription nonsedating antihistamines and OCSs. Study patients were frequent users of outpatient care and prescription medications beyond those used for CIU, despite their relatively young age and lack of other chronic illnesses. Their total annual charges were $15,848, with $1,762 directly related to urticaria. Medications to treat urticaria cost $510/year on average.

Our findings are generally consistent with prior research. Because of the variability in diagnosis, the prevalence of CIU has been difficult to establish. Published lifetime prevalence figures of 0.1% to 0.5% and a typical disease duration of 4 to 5 years are consistent with our 1-year period prevalence estimate of 0.08%.[6,7] A US study of 50 nonimmunosuppressed patients with CIU reported a mean age of 43 years, with 74% female.[8] A study of 139 patients with chronic urticaria in Israel reported a mean age of 41 years, with 63% female,[9] whereas a Turkish study of 953 patients reported a mean age of 37 years with 68% female.[10] Our study identified patients with evidence of atopy in somewhat higher numbers than has been reported. 10 One element of the patient identification algorithm involved the use of antihistamines, which may have led to the inclusion of patients who took these agents for atopic conditions rather than for CIU. We found no prior research on the distribution of specialists caring for patients with CIU, but several other studies used populations of patients in specialty care rather than all insured patients.

DeLong and colleagues[8] studied the medical records of 50 patients attending allergy and dermatology clinics and reported on treatment patterns and cost. In that study, 72% used nonsedating antihistamines and 28% used OCSs, compared with our estimates of 64% and 54%, respectively. These investigators found that 8% used no medications in the preceding study (compared with 15.5% in our study) and that 46% used sedating antihistamines (compared with 8% in our study).

Several potential explanations exist for these differences. The dramatically higher rate of OCS use in our study may be explained by our inclusion of patients who received most of their care from primary care physicians in community practice rather than specialists in an academic setting. Furthermore, insurance claims do not link prescriptions with diagnoses, so some of the OCS prescriptions we identified may have been for conditions other than CIU.

Over-the-counter treatments were not available in our claims dataset because they are not reimbursed by insurance, leaving no record in claims to be analyzed. Combined with the wide availability of OTC antihistamines, this is a significant confounder and likely explains the lower rate of antihistamine use in this study compared with others. We were unable to address this problem within the confines of the dataset, and privacy rules made it impossible for us to contact the individuals we studied to ascertain their OTC antihistamine use. Although surveys and reviews of medical records are likely to be more reliable than studies of health insurance claims to estimate the proportion of patients using antihistamines overall, our estimate of prescription antihistamine use should be reliable.

Using 2005 prices, DeLong and colleagues calculated mean direct costs of care for CIU at $2,047 annually.[8] We reported a mean total annual urticaria-related charge of $1,762 using care between 2007 and 2008. De Long also reported medication costs using average wholesale prices and found a mean annual direct cost of $1,280[8] compared with our mean total annual medication cost of $510. The database we used reports actual charges, and our lower estimates of cost for medical care and for prescription drugs may be explained by the tendency of the average wholesale price to overestimate actual costs.[11] Adjusting for the 10% rise in the consumer price index from 2005 to 2008, the differences between the two studies would be slightly larger.

Managing CIU is a complex and difficult task. Although searching for and removing potential inciting factors may be the best first step, such a search is often fruitless. Symptomatic, nonpharmacologic measures also may be useful for some patients. Experts have recommended that initial pharmacologic therapy begin with oral antihistamines in the nonsedating category with the addition of a second antihistamine, either sedating or nonsedating, if an inadequate response results.[12] Our study suggests that this initial recommendation is commonly followed. Experts also suggest H2 blockers and "steroid-sparing" treatments, including leukotriene receptor antagonists, as further treatment. Our study suggests that patients are more commonly treated with OCSs than with corticosteroid-sparing drugs (eg, leukotriene receptor antagonists).

The most serious limitation of this study was our inability to confirm the diagnosis of CIU by review of medical records. In the absence of medical record confirmation, and lacking an ICD-9-CM code specifically for CIU, we were forced to use a variety of algorithms to identify likely CIU patients. Although these algorithms likely included some patients who did not have CIU and excluded others who did, our observed prevalence was consistent with published prevalence estimates. In a sensitivity analysis examining the impact of using different algorithms to identify patients, we did find variability, although the direction and magnitude of outcomes were similar across all groups.

A confirmatory analysis of the medical records of patients whose claims we analyzed would be the best way to test the sensitivity and specificity of our algorithm, but such an analysis was beyond the scope of the current project. Even if our algorithm were accurate, claims are generated for billing purposes, not for research, and consequently they lack important clinical details, including laboratory or allergen test results, use of OTC medications, and information on the study subjects' environment and behavior. Finally, claims are subject to errors such as under- or overcoding of conditions.

This large population-based study of commercially insured individual confirms prior estimates of the approximate proportion of the population diagnosed with CIU. The study suggests that many such patients are managed by primary care physicians and that although antihistamines are the most common pharmacologic treatment, use of OCSs is quite common. Although patients with CIU are relatively young and otherwise healthy, their health care charges are substantial, with approximately $1,700 per year related directly to care and treatment of urticaria.

References

[1] Powell RJ, Du Toit GL, Siddique N, et al. BSACI guidelines for the management of chronic urticaria and angio-oedema. *Clin Exp Allergy*. 2007;37:631–650.
[2] O'Malley AS, Pham HH, Schrag D, Wu B, Bach PB. Potentially avoidable hospitalizations for COPD and pneumonia: the role of physician and practice characteristics. *Med Care* 2007;45:562–570.
[3] Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992;45:613–619.

[4] Chronic Condition Indicator (CCI) for ICD-9-CM. Summary and Downloading Information. Oct 2009. Agency for Health Care Policy and Research, Rockville, MD. Available at: http://www.hcup-us.ahrq.gov/toolssoftware/chronic/chronic.jsp. Accessed November 8, 2011.
[5] Hwang W, Heller W, Ireys H, Anderson G. Out-of-pocket medical spending for care of chronic conditions. *Health Aff.* (Millwood) 2001;20:267–278.
[6] Greaves M. Chronic idiopathic urticaria. *Curr Opin Allergy Clin Immunol*. 2003;3:363–386.
[7] Greaves M. Chronic urticaria. *J Allergy Clin Immunol* 2000;105:664–672.
[8] DeLong L, Culler SD, Saini SS, Beck LA, Chen SC. Annual direct and indirect health care costs of chronic idiopathic urticaria: a cost analysis of 50 nonimmunosuppressed patients. *Arch Dermatol*. 2008;144:35–39.
[9] Toubi E, Kessel A, Avshovich N, et al. Clinical and laboratory parameters in predicting chronic urticaria duration: a prospective study of 139 patients. *Allergy*. 2004;59:869–873.
[10] Isik S, Karakaya G, Celikel S, Demir AU, Kalyoncu AF. Association between asthma, rhinitis and NSAID hypersensitivity in chronic urticaria patients and prevalence rates. *Int Arch Allergy Immunol*. 2009;150:299–306.
[11] Hay JW, Smeeding J, Carroll NV, et al. Good research practices for measuring drug costs in cost effectiveness analyses: issues and recommendations. *Value Health*. 2010;13:3–7.
[12] Grattan CE, Sabroe RA, Greaves MW. Chronic urticaria. *J Am Acad Dermatol*. 2002;46:645–657.