



Factors Associated with Self-Reported Multiple Drug Allergies in a Large Chronic Urticaria Cohort

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Abstract

Rationale: While drug allergy can trigger urticaria, the true incidence of drug allergies in chronic idiopathic urticaria (CIU) is unknown. Drug allergy in the general population is estimated at 5-25%. We aimed to characterize self-reported drug allergies in a cohort of CU patients.

Methods: 362 adult CIU patients seen at the University of Pittsburgh Allergy Clinic from 2007-2017 were identified. Multiple drug allergies (MDA) were defined as allergy to ≥ 2 chemically unrelated drugs. We compared demographic features of MDA, single drug allergy (SDA) and no drug allergy (NDA) using a Chi-square or Wilcoxon analysis.

Results: Overall, 202 CIU patients (56%) reported any drug allergy. Of those, 57% (n=115) reported MDA. Compared to SDA and NDA, MDA associated with Caucasian race and female gender (p=0.026, p=0.006, respectively). MDA and SDA associated with older age of CIU onset vs. NDA (median 39, 38.5 vs. 32years, p=0.0003, respectively). Higher BMI associated with MDA and SDA vs. NDA (median 28.6, 28.6 vs. 26.6, p=0.013, respectively). MDA reported a higher prevalence of self-reported asthma vs. SDA and NDA (39%, 15%, 23%, p=0.0002, respectively). Compared to SDA, MDA reported a higher rate of penicillin, cephalosporin, sulfa, non-steroidal anti-inflammatory drugs, opiate and radiocontrast allergy (all p \leq 0.025).

Conclusions: In CIU, the prevalence of self-reported drug allergies was higher than the general population. MDA associated with older age of CIU onset, female gender, Caucasian race, higher BMI, asthma, and antibiotic allergies. This population should be further studied to avoid the potential for comorbidity associated with less efficacious and more costly drugs.

Background

- Drug allergy: prevalence of drug allergy in CIU is unknown
- Estimated prevalence of drug allergy in the general population = 5-25%
 - It is difficult to perform skin and drug provocation testing in CIU as antihistamine cessation may not be tolerated
 - CIU patients recently reported to have higher rates of penicillin allergy than the general population⁴
 - Mean delay from urticaria onset to diagnosis in CIU patients = 24 months and can lead to unnecessary avoidance of suspected triggers including drugs⁵
- We examined the frequency of self-reported drug allergy in our CIU cohort

Hypothesis

- Patients with CIU would have a higher prevalence of reported drug allergies than the general population.

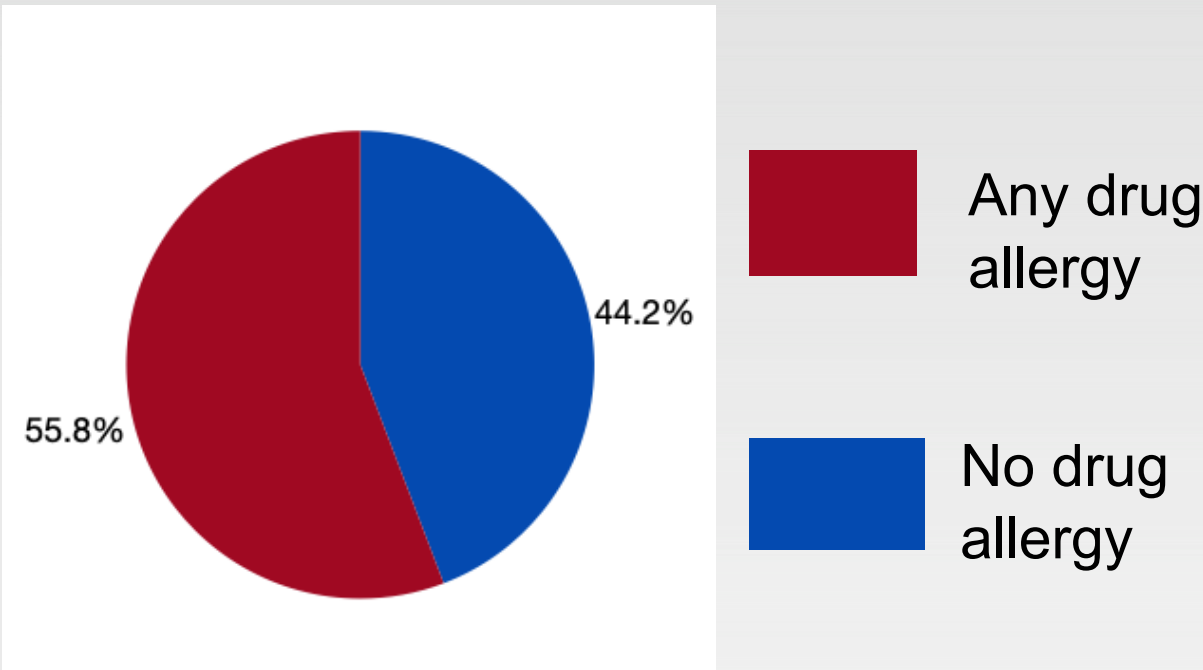
Methods

- Retrospective chart review of adult patients ≥ 18 years seen in the University of Pittsburgh Allergy and Immunology Clinic from 2007 to 2017
 - Diagnosis of chronic urticaria with or without angioedema (n=362)
 - Characteristics evaluated: drug allergies and associated demographic and comorbid features
 - Sub-analysis of CIU patients with single (SDA), multiple (MDA), and no drug allergy (NDA)
 - Data was analyzed with JMP Pro (Version 14.1.0, SAS Institute Inc., Cary, NC, 1989-2019)

Results

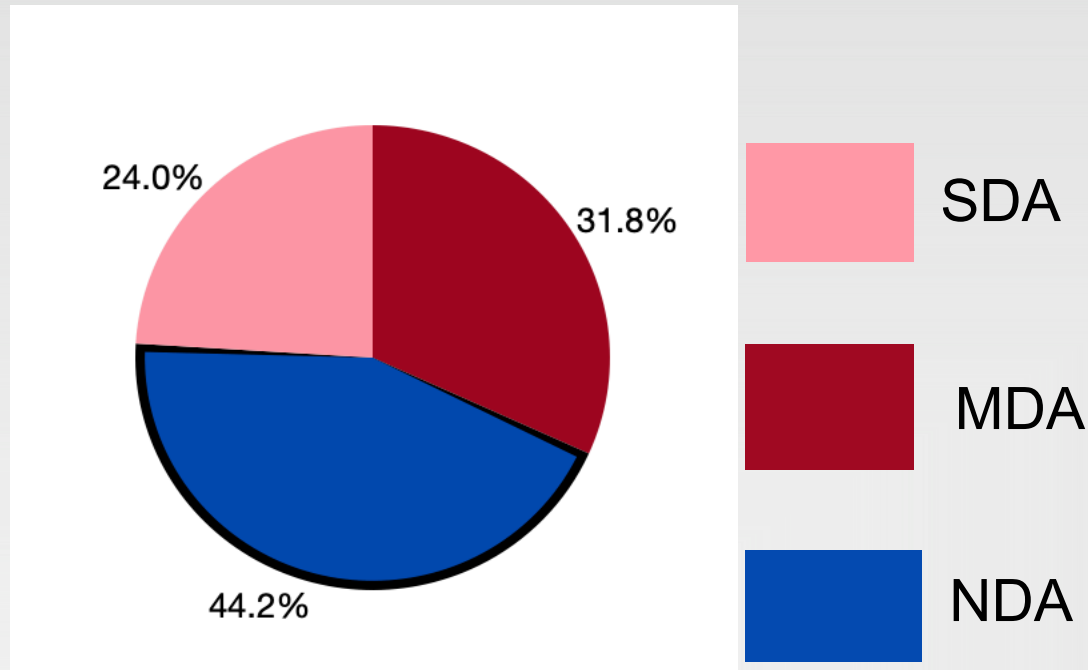
56% of CIU pts reported Drug Allergy

Figure 1: Patient reported drug allergies



MDA in 57% of drug allergic CIU pts

Figure 2: Patient reported SDA, MDA or NDA



Patient demographics

	Overall population (n=362)	Non-drug allergic (n=160)	Drug allergic (n=202)	P-value
Age of CIU Onset, yrs [†]	36 (26-50)	32 (24-46)	39 (28-54)	.002
Age at visit, yrs [†]	39 (29-54)	35 (25-49)	44 (31-57)	.0003
Sex (F:M)	255:107	109:51	146:56	.39
BMI, kg x m ^{-2†}	28 (24-34)	27 (23-32)	29 (25-34)	.004
Race (White/Black/Other)	272/60/24	111/27/16	161/33/8	.047
Presence of co-existing angioedema	223	98	125	.9
Presence of co-existing asthma diagnosis	94	36	58	.18

Demographic & Comorbid conditions in SDA vs. MDA

	SDA (n=87)	MDA (n=115)	P-value
Age of CIU Onset, yrs [†]	39 (25-52)	39 (30-55)	.19
Age at visit, yrs [†]	41 (29-53)	46 (33-59)	.03
Sex (F:M)	53:34	93:22	.002
BMI, kg x m ^{-2†}	29 (26-34)	29 (24-35)	.71
Race (White/Black/Other)	64/16/7	97/17/1	.02
Presence of co-existing angioedema	55	70	.73
Presence of co-existing asthma	13	45	.0002

[†] Median, IQR; * P value determined by Pearson χ^2 and Kruskal-Wallis test

§ There was no significant difference in the incidence of allergic rhinoconjunctivitis or atopic dermatitis

Results

PCN Allergy: 18% of CIU; 68% of PCN allergy had MDA

Figure 3: Reported PCN allergy

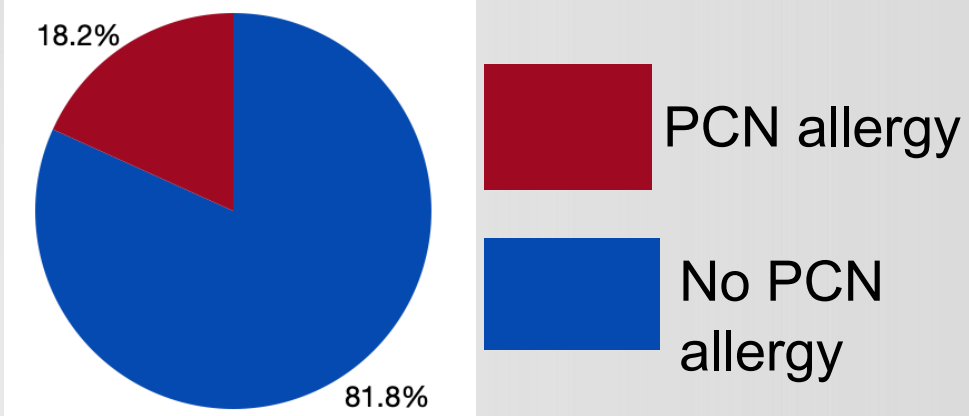
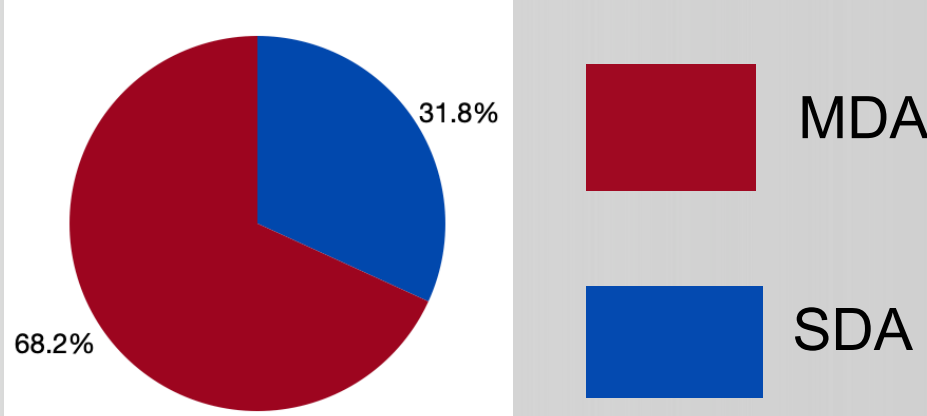


Figure 4: PCN allergic patients with MDA



Conclusions

- CIU patients have a significantly higher prevalence of drug allergies vs. the general population (56% vs. 5-25%)
- Asthma was reported in 29% of our drug allergic CIU patients
 - MDA CIU patients had the highest asthma prevalence (39%)
 - This is higher than the reported asthma rates in our region and 2 other CIU cohorts in different regions (10-14%)^{6,7,8}
- Penicillin was the most common drug allergy (n=66, 18% total cohort, 33% of drug allergic CIU patients)
 - Similar to other studies,⁴ 68% of patients with penicillin allergy reported additional drug allergies

Discussion

- CIU pts are more likely to report a drug allergy and have a higher incidence of comorbid asthma
 - Actual prevalence of drug allergy difficult to determine as:
 - Self-reported drug allergy
 - Cessation of antihistamines for skin testing and challenge in the CIU population is difficult
- VCD has been associated with a misdiagnosis of asthma and a higher prevalence of drug allergy (vs. asthma and controls)⁹
 - VCD was not assessed in this cohort
- Misdiagnosis of asthma & drug allergy should be considered in CIU
- Physicians who care for CIU pts need to take detailed drug allergy and asthma histories

References

1. Wertenteil S, Strunk A, Garg A. Prevalence Estimates for Chronic Urticaria in the United States: a gender and age adjusted population analysis. J Am Acad Dermatol. 2019 Mar 11.
2. Bernstein JA, Lang DM, Khan DA, Craig T, Dreyfus D, Hsieh F, Sheikh J, Weldon D, Zuraw B, Bernstein DI, Blessing-Moore J, Cox L, Nicklas RA, Oppenheimer J, Portnoy JM, Randolph CR, Schuller DE, Spector SL, Tilles SA, Wallace D. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014 May;133(5):1270-7.
3. Sánchez J, Amaya E, Acevedo A, Celis A, Caraballo D, Cardona R. Prevalence of Inducible Urticaria in Patients with Chronic Spontaneous Urticaria: Associated Risk Factors. J Allergy Clin Immunol Pract. 2017 Mar - Apr;5(2):464-470.
4. Silverman S, Localio R, Apter AJ. Association between chronic urticaria and self-reported penicillin allergy. Ann Allergy Asthma Immunol. 2016 Apr;116(4):317-20.
5. Maurer et al. The burden of chronic spontaneous urticaria is substantial: Real-world evidence from ASSURE-CSU. Allergy. 2017;72:2005-2016.
6. Sánchez J, Sánchez A, Cardona R. Prevalence of Drugs as Triggers of Exacerbations in Chronic Urticaria. J Investig Allergol Clin Immunol. 2019;29:112-117.
7. 2010 Adult Asthma Data: Prevalence Tables and Maps. <https://www.cdc.gov/asthma/brfss/2010/current/tableC1.htm> Accessed January 13, 2020.
8. Isik SR, 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.
9. Traister RS, Fajt ML, Whitman-Purves E, Anderson WC, Petrov AA. A retrospective analysis comparing subjects with isolated and coexistent vocal cord dysfunction and asthma. Allergy Asthma Proc. 2013;34:349-355.

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