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419 Understanding the Mechanism of the Disproportionately Reduced C1-Esterase Inhibitor (C1-INH) Levels in Hereditary Angioedema (HAE)



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RATIONALE: HAE is an autosomal dominant disorder caused by defects in the SERPING1 gene. HAE patients maintain one functional wild-type SERPING1 allele, therefore at least 50% of the normal C1-INH value is expected. However, serum antigen levels of C1-INH in HAE patients are usually 5-30% of normal. We hypothesize that the type of SERPING1 mutations and their impact on C1-INH protein structure and function lead to the variable degrees of C1-INH level in HAE patients.

METHODS: The Division of Allergy/Immunology at Washington University School of Medicine recruited 20 HAE patients, including Type I (17) and Type II (3). Genomic DNA and mRNA were isolated from peripheral blood cells. WES and mRNA sequencing (mRNA-seq) were carried out. Serum C1-INH levels were measured.

RESULTS: We identified 11 heterozygous mutations and 3 large deletions in the SERPING1 gene from our HAE cohort. The mRNA-seq analysis revealed that the overall expression levels of SERPING1 gene vary substantially among HAE patients and were disproportionate to their serum C1-INH levels. The mRNA expression levels of two alleles from a single nucleotide variant (SNV) were approximately equal across ~70% of HAE patients. A monoallelic expression pattern was observed for the patients harboring frameshift and large deletions.

CONCLUSIONS: Primary blood levels of serum C1-INH are disproportional with mRNA expression levels in our HAE cohort. The substantial variability in the C1-INH levels is less likely due to the selective allelic expression and is more related to the defective C1-INH protein. We shall continue to collect further data to confirm our observations.

420 Can COVID-19 vaccinations cause chronic urticaria?



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RATIONALE: Adverse reactions to COVID-19 vaccinations have garnered significant attention from both the public and medical community. Delayed onset urticaria has been described as an adverse reaction to COVID-19 vaccination, but this phenotype has not been fully characterized thus specific evaluation and treatment strategies have not been developed.

METHODS: We conducted a retrospective chart review of patients presenting for evaluation of urticaria (acute or chronic) to the University of Washington Allergy Clinics between 12/14/2020 and 12/14/2021. Records were reviewed for development of delayed onset, persistent urticaria occurring following receipt of a COVID-19 vaccination or a history of chronic spontaneous urticaria that worsened after COVID-19 vaccination. Demographic and clinical data including age, sex, co-morbid conditions, treatments attempted, and treatment response was obtained.

RESULTS: 22 total patients were determined to have urticaria thought to be attributed to Pfizer and Moderna COVID-19 vaccinations. Six of the 22 (27%) had pre-existing chronic spontaneous urticaria (CSU) which worsened notably after vaccination, and 16 (73%) had novel development of delayed urticaria following vaccination. Patients received a range of treatments including H1-antihistamines, H2-antihistamines, leukotriene inhibitors, oral steroids, omalizumab, cyclosporine, and acupuncture. The majority of patients had improvement or resolution while a minority had worsening urticaria despite treatments at the time of evaluation.

CONCLUSIONS: COVID-19 vaccinations may result in the development of chronic urticaria in select patients and may worsen control of urticaria in some patients with previously diagnosed chronic urticaria. Additional studies are needed to characterize these patients and determine optimal management strategies.

421 Comparison of Hereditary Angioedema Among Patients of Different Races and Ethnicities in the United States: Data From a Real-World Study



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RATIONALE: There are limited data describing how HAE is experienced by patients of different racial and ethnic backgrounds.

METHODS: Real-world data from the Adelphi HAE Disease Specific Programme™ were utilized. Physicians reported data on their consulting patients with HAE including demographics, insurance, severity, prescribed treatment, and hospitalizations.

RESULTS: These patients with HAE were categorized as White (n=309), African American (AA) (n=31), Hispanic (n=25), Asian (n=12), Middle Eastern or Mixed Race (MEMR) (n=7). Age range was similar across groups. AA and Asian groups had higher proportions of females (71.0% and 58.3%) than White, Hispanic, and MEMR (46.3%, 40.0% and 42.9%). White patients were more likely to live in a suburban area, and use commercial insurance than AA, Hispanic, Asian, and MEMR (74.4% vs 62.7% and 76.7% vs 61.4%, respectively). At diagnosis, HAE was categorized as severe more often among AA, Hispanic, and Asian (34.6%, 37.5%, and 45.5%) than White patients (20.4%). White and MEMR patients were prescribed both prophylactic and on-demand treatments more often (71.2% and 71.4%) compared to Hispanic and Asian (64.0% and 58.3%). More Hispanic, MEMR, and White patients currently had mild disease severity (68.0%, 70.6%, and 71.4%) compared to AA and Asian groups (58.1% and 50.0%). More AA, Hispanic, and MEMR patients were hospitalized in the last year due to their HAE (33.0%, 21.7%, and 28.6%) compared to White or Asian patients (12.9% and 0%).

CONCLUSIONS: HAE may be experienced differently across racial and ethnic groups. Research on disparities is important to ensure all races and ethnicities receive equity in healthcare services.