

153 Cooperative Effects between CRTh2 and CCR3 on Eosinophils and Basophils in Chronic Spontaneous Urticaria

Eric T. Oliver, MD, Kristin L. Chichester, MS, and Sarbjit Singh Saini, MD, FAAAAI; Department of Medicine, Division of Allergy and Clinical Immunology, Johns Hopkins University School of Medicine, Baltimore, MD.

RATIONALE: Chronic spontaneous urticaria (CSU) lesions are characterized by infiltrates of eosinophils and basophils. Studies have suggested a role for the PGD₂/CRTh2 and eotaxin/CCR3 pathways in eosinophil recruitment to CSU lesions. Eosinophils produce PGD₂ in response to eotaxin, however the effects of PGD₂ on CCR3 expression have not been examined. Therefore, we explored CCR3 and CRTh2 as shared recruitment/activation pathways for eosinophils and basophils.

METHODS: We recruited adult CSU subjects (n=22) and non-allergic controls (n=8). Whole blood was analyzed for baseline CCR3 and CRTh2 expression on basophils and eosinophils by flow cytometry. CCR3 expression was examined in samples stimulated with PGD₂ in the presence or absence of a CRTh2 antagonist (AZD1981).

RESULTS: Basophils from CSU subjects exhibited lower CRTh2 and CCR3 at baseline compared to healthy controls (p=0.0277 and p=0.0001). Eosinophil CRTh2 expression was also significantly lower in CSU subjects compared to controls (p=0.0049). CRTh2 and CCR3 were positively correlated on basophils (p=0.0157) and eosinophils (p=0.0036). Increasing concentrations of PGD₂ reduced eosinophil CCR3 expression to a lesser extent in CSU subjects compared to controls (AUC 521.7 vs 624.6, p<0.0001). AZD1981 inhibited reductions in eosinophil CCR3 induced by PGD₂ (10^{-6.5} M) in CSU subjects (p=0.0001) and healthy subjects (p=0.0469).

CONCLUSIONS: Reductions in basophil and eosinophil CRTh2 and CCR3 surface expression were positively correlated in CSU subjects. PGD₂ exposure reduced eosinophil CCR3 expression in CSU and healthy subjects which was partially inhibited by CRTh2 antagonism. Further studies examining the coordination of these pathways may provide insights into the observed clinical benefits of CRTh2-targeting in eosinophilic subgroups.

Mexico, ¹²Universidad Autonoma de Nuevo Leon, Monterrey, Mexico, ¹³Universidad De Antioquia, Medellin, Colombia, ¹⁴Hospital Universitario Monterrey, NL UANL, Monterrey, Mexico, ¹⁵Hospital Universitario UANL, Monterrey, Mexico, ¹⁶Instituto Alas, Salta, Argentina, ¹⁷Centro Médico Bolívar, San Luis, Argentina, ¹⁸Hospital San Roque, Cordoba, Argentina, ¹⁹Fundación Valle de Lili, Cali, Colombia, ²⁰Avda Italia 2420, British Hospital, Montevideo, Montevideo, Uruguay, ²¹Hosp. J.J.Aguirre, Providencia, Chile, ²²Universidad de Antioquia, Medellin, Colombia, ²³Htal. Zonal de Lobos & Consultorio, Lobos Pcia., Argentina, ²⁴ASBAI, Rio de Janeiro, Brazil, ²⁵Salvador Allende General Hospital, C. de La Habana, Cuba.

RATIONALE: Urticaria/angioedema are the most frequent clinical manifestations of drug hypersensitivity. However, data from Latin America on this topic is limited.

METHODS: A retrospective, cross-sectional study assessed characteristics of drug induced urticaria (DIU) and angioedema using the European Network of Drug Allergy questionnaire in 22 allergy units from 11 Latin American countries. Clinical characteristics, demographics, causal relationship with specific drugs, confirmatory diagnostic evaluation, and treatment were assessed.

RESULTS: From 1,031 hypersensitivity drug reactions (HDR) evaluated, 697 (67.6%) met DIU diagnostic criteria. The mean age was 35.4-year-old (1-85); Female:Male for adults >17 y/o was 2.6:1 whereas for children/adolescent 0-17 y/o was 0.87:1 (P<0.0001).

Severe reactions were present in 21.6% of non-atopic and 15% of atopic patients (p<0.05). A history of a previous HDR to the causal drug was present in 13.3% of patients. The most frequently reported DIU inducers were nonsteroidal anti-inflammatory drugs (NSAIDs) (68%) followed by beta lactam (13%) and non-beta lactam (8%) antibiotics. Provocation tests (n=320) were performed in 244 cases (35%) with NSAIDs (68.1%), beta-lactams (12.8%) and non-beta lactam antibiotics (6.6%) being the most frequent drugs challenged. Skin prick (16.6%) and intracutaneous (10.4%) tests were the second and third most frequent diagnostic procedures performed. Antihistamines (79.5%) and corticosteroids (60.1%) were the most frequently prescribed therapies.

CONCLUSIONS: Female gender predominated in adults but not in children/adolescents. Personal history of atopy was associated with less severe reactions. NSAIDs and antibiotics were the most common drugs implicated. These results provide much needed data on the prevalence and nature of HDRs in Latin America.

154 Drug-induced urticaria (DIU) and angioedema in Latin American Countries

Edgardo J. Jares, MD¹, Mario Sanchez-Borges, MD, FAAAAI², R. Maximiliano Gomez, MD, PhD³, Carlos D. Serrano, MD⁴, Luis Felipe C. Ensina, MD⁵, Ivan Cherrez-Ojeda, MD⁶, Jonathan A. Bernstein, MD, FAAAAI^{7,8}, Alicia Mabel De Falco, MD⁹, Mabel Noemi Cuello, MD¹⁰, Blanca Maria Del Refugio Morfin Maciel, MD, FAAAAI¹¹, Alfredo Arias Cruz, MD, FAAAAI¹², Ricardo Cardona Villa¹³, Sandra Nora González-Díaz, MD, PhD, FAAAAI, FAAAAI, EAACI¹⁴, Alejandra Macias-Weinmann, MD¹⁵, Silvana Beatriz Monsell¹, Galie E. Mimessi, MD¹⁶, Raul Adolfo Salvatierra, MD¹⁷, Andrea Zancacchi¹⁸, Luis F. Ramirez Zuluaga¹⁹, Norma Susana de Barayzarra, MD¹⁸, Juan F. Schuhl, MD, FAAAAI²⁰, Paola A. Toche Pinaud²¹, Susana Diez²², Miguel Angel Vinuesa, MD²³, Mara Morelo Rocha Felix²⁴, and Ada Del Castillo Mendez, MD²⁵; ¹LIBRA FOUNDATION, Buenos Aires, Argentina, ²Centro Médico Docente La Trinidad, Caracas, Venezuela (Bolivarian Republic of), ³Instituto Médico Alas, Salta, Argentina, ⁴Fundacion Valle Del Lili, Cali, Colombia, ⁵FEDERAL UNIVERSITY OF SAO PAULO, SAO PAULO, Brazil, ⁶Kennedy Hospital, Guayaquil, Ecuador, ⁷Bernstein Allergy Group, Inc, Cincinnati, OH, ⁸University of Cincinnati, Cincinnati, OH, ⁹Hosp. Interzonal de Agud. Prof. Rossi, La Plata, Argentina, ¹⁰Hospital Infantil, San Juan, Argentina, ¹¹Hospital Angeles Mocol, Mexico,