

# 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 PGD<sub>2</sub>/CRTh2 and eotaxin/CCR3 pathways in eosinophil recruitment to CSU lesions. Eosinophils produce PGD<sub>2</sub> in response to eotaxin, however the effects of PGD<sub>2</sub> 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 PGD<sub>2</sub> 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 PGD<sub>2</sub> 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 PGD<sub>2</sub> (10<sup>-6.5</sup> 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. PGD<sub>2</sub> 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, <sup>12</sup>Universidad Autonoma de Nuevo Leon, Monterrey, Mexico, <sup>13</sup>Universidad De Antioquia, Medellin, Colombia, <sup>14</sup>Hospital Universitario Monterrey, NL UANL, Monterrey, Mexico, <sup>15</sup>Hospital Universitario UANL, Monterrey, Mexico, <sup>16</sup>Instituto Alas, Salta, Argentina, <sup>17</sup>Centro Médico Bolívar, San Luis, Argentina, <sup>18</sup>Hospital San Roque, Cordoba, Argentina, <sup>19</sup>Fundación Valle de Lili, Cali, Colombia, <sup>20</sup>Avda Italia 2420, British Hospital, Montevideo, Montevideo, Uruguay, <sup>21</sup>Hosp. J.J.Aguirre, Providencia, Chile, <sup>22</sup>Universidad de Antioquia, Medellin, Colombia, <sup>23</sup>Htal. Zonal de Lobos & Consultorio, Lobos Pcia., Argentina, <sup>24</sup>ASBAI, Rio de Janeiro, Brazil, <sup>25</sup>Salvador 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, MD<sup>1</sup>, Mario Sanchez-Borges, MD, FAAAAI<sup>2</sup>, R. Maximiliano Gomez, MD, PhD<sup>3</sup>, Carlos D. Serrano, MD<sup>4</sup>, Luis Felipe C. Ensina, MD<sup>5</sup>, Ivan Cherrez- Ojeda, MD<sup>6</sup>, Jonathan A. Bernstein, MD, FAAAAI<sup>7,8</sup>, Alicia Mabel De Falco, MD<sup>9</sup>, Mabel Noemi Cuello, MD<sup>10</sup>, Blanca Maria Del Refugio Morfin Maciel, MD, FAAAAI<sup>11</sup>, Alfredo Arias Cruz, MD, FAAAAI<sup>12</sup>, Ricardo Cardona Villa<sup>13</sup>, Sandra Nora González-Díaz, MD, PhD, FAAAAI, FAAAAI, EAACI<sup>14</sup>, Alejandra Macias-Weinmann, MD<sup>15</sup>, Silvana Beatriz Monsell<sup>1</sup>, Galie E. Mimessi, MD<sup>16</sup>, Raul Adolfo Salvatierra, MD<sup>17</sup>, Andrea Zancchi<sup>18</sup>, Luis F. Ramirez Zuluaga<sup>19</sup>, Norma Susana de Barayazarra, MD<sup>18</sup>, Juan F. Schuhl, MD, FAAAAI<sup>20</sup>, Paola A. Toche Pinaud<sup>21</sup>, Susana Díez<sup>22</sup>, Miguel Angel Vinuesa, MD<sup>23</sup>, Mara Morelo Rocha Felix<sup>24</sup>, and Ada Del Castillo Mendez, MD<sup>25</sup>; <sup>1</sup>LIBRA FOUNDATION, Buenos Aires, Argentina, <sup>2</sup>Centro Médico Docente La Trinidad, Caracas, Venezuela (Bolivarian Republic of), <sup>3</sup>Instituto Médico Alas, Salta, Argentina, <sup>4</sup>Fundacion Valle Del Lili, Cali, Colombia, <sup>5</sup>FEDERAL UNIVERSITY OF SAO PAULO, SAO PAULO, Brazil, <sup>6</sup>Kennedy Hospital, Guayaquil, Ecuador, <sup>7</sup>Bernstein Allergy Group, Inc, Cincinnati, OH, <sup>8</sup>University of Cincinnati, Cincinnati, OH, <sup>9</sup>Hosp. Interzonal de Agud. Prof. Rossi, La Plata, Argentina, <sup>10</sup>Hospital Infantil, San Juan, Argentina, <sup>11</sup>Hospital Angeles Mocol, Mexico,