

910 Hypersensitivity Drug Reactions (HDR) In Latin America. Similarities and Differences Between Children and Adults

Dr. Ricardo Cardona-Villa, MD¹, Dr. Edgardo J. Jares, MD², Dr. Maximiliano Gómez³, Dr. Luis Felipe C. Ensina, MD⁴, Dr. Mario Sánchez-Borges, MD, FAAAAI⁵, **Dr. Alfredo Arias Cruz⁶**, Dr. Carlos Serrano⁷, Dr. Mabel Noemi Cuello, MD⁸, Ivan Cherrez⁹, Dr. Andrea Zanacchi¹⁰, Prof. Alicia De Falco¹¹, Dr. Silvana Monsell¹², Dr. Adolfo Salvatierra¹², Dr. Susana Barayazarra¹⁰, Dr. Susana Diez-Zuloaga¹, Dr. Blanca Maria Morfin-Maciél, MD¹³, Dr. Paola Toche Pinaud¹⁴, **Dr. Sandra González Díaz⁶**, Dr. Juan F. Schuhl, MD, FAAAAI¹⁵; ¹Universidad de Antioquia, Medellín, Colombia, ²C.M.P. SA, Buenos Aires, Argentina, ³Hospital San Bernardo, Salta, Argentina, ⁴Universidade Federal de São Paulo, São Paulo, Brazil, ⁵Clinica El Avila, 6a transversal Altamira, piso 8, consultorio 803, Caracas., Caracas, Venezuela, ⁶Hospital Universitario, Monterrey, Mexico, ⁷Fundación Valle del Lili, Cali, Colombia, ⁸Consultorios San Juan, San Juan, Argentina, ⁹Respiralab - Hospital Kennedy, Guayaquil, Ecuador, ¹⁰Nuevo Hospital San Roque, Córdoba, Argentina, ¹¹Universidad Nacional de La Plata, La Plata, Argentina, ¹²Fundair, San Luis, Argentina, ¹³Hospital Mocel, Mexico City, Mexico, ¹⁴Clínica Las Condes, Santiago, Chile, ¹⁵British Hospital, Montevideo, Uruguay.

RATIONALE: HDR are frequent motives for consultation in Allergology services. Possible etiologic factors and clinical presentation differences between Latin American children and adults have not been described yet. **METHODS:** An observational cross sectional study using a modified ENDA questionnaire was implemented in 19 allergology units in 11 Latin-American countries, reporting patients presenting HDR in the last year before consultation. Causal relationship was categorized according to WHO-UMC Causality Categories: certain, probable, possible, unlikely and conditional.

RESULTS: 727 patients, 144 (19.8%) of them under 18 years old, presented 732 reactions. Female gender was 71.7% in adults, and 50% in children. Atopic history was present in 44.9 and 63.8% and a history of previous drug reaction in 31.9 and 36.9% of adults and children, respectively. Fourteen percent of adult, and 10.7% of children had presented previous reactions with the same drug. The clinical picture of the reaction in adults and children was angioedema in 47.9 and 48.6%, urticaria in 44.5 and 41.8%, maculopapular and macular exanthema in 20.3 and 22.6 %, erythema multiforme and SJS in 3.6 and 2.7% respectively. Certain and probable causal relationships were attributed in adults and children to NSAIDs in 55.7 and 60.3 %, beta lactams in 11.2 and 19.8%, non beta lactam antibiotics in 8.4 and 2.5 %, anticonvulsants in 3.2 and 1.7%, chemotherapy 0.8 and 2.5% of patients, respectively.

CONCLUSIONS: Female sex was predominant in adults but not in children. NSAIDs and antibiotics were the drugs implicated in more than 75% of patients. Beta lactam antibiotics were more frequently involved in children.

911 Copy Number Variations In ALOX5 and PTGER1 Genes Are Associated With Susceptibility To AERD and Mnsaid-UA

Mrs. Maria Del Carmen Plaza Seron, Bsc¹, Dr. Pedro Ayuso Parejo, PhD¹, Dr. Natalia Blanca-López, MD, PhD¹, Dr. Inmaculada Doña, MD, PhD², Dr. Jose A. Cornejo-Garcia, PhD³, Dr. María José Torres, MD, PhD², Dr. Javier Fernández⁴, Dr. Jose Julio Laguna, MD, PhD⁵, Veronique Godineau³, Ms. Miriam Osorio⁶, Mrs. Luisa Galindo, RN², Dr. Gabriela Canto, MD, PhD¹, Dr. Miguel Blanca, MD, PhD²; ¹Allergy Service, Infanta Leonor Hospital, Madrid, Spain, ²Allergy Service, Carlos Haya Hospital, Málaga, Spain, ³Research Laboratory, Carlos Haya Hospital, Málaga, Spain, ⁴UMH Alicante G.University Hospital - Allergy Sect., Alicante, Spain, ⁵De La Cruz Roja Hospital, Madrid, Spain, ⁶Research Laboratory, Carlos Haya Hospital-FIMABIS, Málaga, Spain.

RATIONALE: Aspirin-exacerbated respiratory disease (AERD) and Multiple NSAID-triggered urticaria and/or angioedema and anaphylaxis in patients without pre-existing chronic urticaria (MNSAID-UA) are the main manifestations of hypersensitivity reactions. Both are mediated by a non-specific immunological mechanism based on NSAIDs capacity to inhibit COX-1 and evoke an unbalance of metabolic pathway of

arachidonic acid. Copy number variations (CNVs) are DNA segments present at variable copy number that may affect the expression of genes and be associated with susceptibility to diseases. The aim of this study was to analyze association of CNV in genes implicated in arachidonic acid pathway with MNSAID-UA and AERD.

METHODS: We studied a total of 150 patients with AERD, 310 MNSAID-UA and 315 tolerant controls. We used TaqMan® copy number assays to analyze CNVs in *PTGS1*, *PTGS2*, *LTC4S*, *ALOX5* and *PTGER1-4* genes. The results were analyzed using the Copy Caller Software and SPSS 11.5 program.

RESULTS: We found differences in *ALOX5* and *PTGER1* genes. All controls showed 2 copies of each gene analyzed. Concerning to *ALOX5*, we identified 7 AERD patients (5.0%; AERD vs. Controls $P < 0.001$) and 13 MNSAID-UA patients (4.17%; MNSAID-UA vs. Controls $P < 0.001$) with a single copy of this gene. Regarding to *PTGER1*, we identified 19 MNSAID-UA patients (6.11%; MNSAID-UA vs. Controls $P < 0.0001$) with a single copy of the gene, no AERD patients showed a single copy.

CONCLUSIONS: We found statistically significant differences in CNVs of genes *ALOX5* and *PTGER1* between healthy controls and MNSAID-UA and AERD. Whether these variations imply a dysfunctional gene expression require further studies.

912 Association Study Of Genes Involved In Mast Cell Activation and Mnsaid-UA

Dr. Pedro Ayuso Parejo, PhD¹, Mrs. Maria del Carmen Plaza-Serón, Bsc¹, Dr. Inmaculada Doña, MD, PhD², Dr. Natalia Blanca-López, MD, PhD¹, Dr. Jose A. Cornejo-Garcia, PhD³, Dr. Maria J. Torres, MD, PhD², Dr. Javier Fernández⁴, Dr. Jose Julio Laguna, MD, PhD⁵, Ms. Miriam Osorio⁶, Veronique Godineau³, Mrs. Luisa Galindo, RN², Dr. Cristobalina Mayorga, PhD³, Dr. Gabriela Canto, MD, PhD¹, Dr. Miguel Blanca, MD, PhD²; ¹Allergy Service, Infanta Leonor Hospital, Madrid, Spain, ²Allergy Service, Carlos Haya Hospital, Málaga, Spain, ³Research Laboratory, Carlos Haya Hospital, Málaga, Spain, ⁴UMH Alicante G.University Hospital - Allergy Sect., Alicante, Spain, ⁵De La Cruz Roja Hospital, Madrid, Spain, ⁶Research Laboratory, Carlos Haya Hospital-FIMABIS, Málaga, Spain.

RATIONALE: Non-steroid anti-inflammatory drugs (NSAIDs) are the compounds more frequently involved in hypersensitivity drugs reactions. Multiple NSAID-triggered urticaria and/or angioedema and anaphylaxis in patients without pre-existing chronic urticaria (MNSAID-UA) are considered the most frequent entities. The underlying mechanism proposed is based on the pharmacological properties of the NSAIDs. These reactions occur as a result of mast cell activation and subsequent degranulation and generation of lipid-derived mediators. These cells can be activated by IgE-dependent and IgE-independent mechanisms that share common signaling pathways. In this work, we aimed to analyze the association between single nucleotide polymorphisms (SNPs) in key genes involved in mast cell activation and MNSAID-UA.

METHODS: A total of 450 patients with MNSAID-UA and 500 individuals who tolerated NSAIDs were included. Nine SNPs in 5 genes (rs290986 in *SYK*, rs7140 in *LAT1*, rs2228246 and rs753381 in *PLCG1*, rs2307198, rs12749354 and rs12746200 in *PLA2G4A*; and rs35211496 and rs1805034 in *TNFRSF11A* genes) were genotyped using TaqMan® probes.

RESULTS: MNSAID-UA patients were subdivided according to the type of response and significant differences were found between MNSAID-UA patients who only developed urticaria and the following SNPs: rs2228246, OR=0.30 (95% CI =0.11-0.82; $P=0.031$) rs35211496, OR=2.67 (95% CI=1.37-5.19; $P=0.0024$) and rs12746200, OR=0.14 (95% CI=0.03-0.59; $P=0.019$). Nevertheless, statistically significant differences were not found in genotype frequencies of these SNPs between MNSAID-UA and tolerant.

CONCLUSIONS: We found an association between non synonymous polymorphisms rs2228246 *PLCG1* and rs35211496 *TNFRSF11A* and the non encoding SNP rs12746200, which could be involved in *PLA2G4A* regulation and urticaria induced by multiple NSAIDs.