The Relationship Between Hla-Dpb1, Hla-Drb1 And Cbd/bes

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Background: Chronic beryllium disease (CBD) is the result of a cell-mediated immunologic response to beryllium and subsequent development of lung granuloma formation. Beryllium sensitization (BeS) is the presence of a cell-mediated immune response without granuloma formation. Many studies have identified a strong association between having a glutamic acid at position 69(E69) in the HLA-DPB1 gene and CBD or BeS; less studied has been the relationship between having a glutamic acid at position 71(E71) of the HLA-DRB1 gene in conjunction with E69 carriage and risk of CBD or BeS. **Objective**: The main objective of this study was to clarify the role of E71 in conjunction with E69 and risk for CBD and BeS in the largest pooled population to date. **Methods:** We enrolled 714 CBD/BeS (cases) and 557 beryllium-exposed controls using standard case definitions, from machining, nuclear or primary beryllium industries who gave informed consent for participation. Non-Hispanic Caucasian cases and controls were frequency matched by industry. HLA-DPB1 and HLA-DRB1 genotypes were determined using sequence specific primer PCR and/or sequence-based typing. Genotypes were grouped as E69 positive or E69 negative, and as E71 positive or E71 negative depending on allele carriage. Comparisons were modeled using multivariable logistic regression including an interaction term between E69 and E71 carriage. **Results:** The study population was over 80% male. The comparison group for all ORs was both E69 and E71 negative. The highest risk of being a case occurred among E71 negative subjects who were E69 positive [OR(95%CI) 12.0(8.6-16.7)]. The risk of being a case among E69 negative subjects was increased in those subjects who were also E71 positive [OR(95%CI) 4.1(2.6-6.4)]. A similar risk was noted in subjects positive for both E71 and E69 [OR(95%CI) 3.1(2.0-4.9)]. Results were similar for CBD vs. control and BeS vs. control comparisons. The only difference noted was among E71 negative/E69 positive subjects, comparing CBD to BeS subjects [OR(95%CI) 2.0(1.1-3.5)]. **Conclusion:** The presence of E71 appears to modify the risk of E69, as those with the E71 genotype have a decreased risk of BeS and CBD in the presence of E69. The risk of CBD and BeS is increased in the presence of E71 in those without E69. Examining amino acid sequences for each of these genes will give more specific information on possible antigen binding.

This abstract is funded by: Government Funding : 2 P01 ES11810-06A1

Am J Respir Crit Care Med 189;2014:A5207

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