

Analysis of Aspergillus fumigatus IgG Serologic Cut-Off Values to Increase Diagnostic Specificity of Allergic Bronchopulmonary Aspergillosis

Authors : Sushmita Roy Chowdhury, Steve Holding, Sujoy Khan

Abstract : The immunogenic responses of the lung towards the fungus *Aspergillus fumigatus* may range from invasive aspergillosis in the immunocompromised, fungal ball or infection within a cavity in the lung in those with structural lung lesions, or allergic bronchopulmonary aspergillosis (ABPA). Patients with asthma or cystic fibrosis are particularly predisposed to ABPA. There are consensus guidelines that have established criteria for diagnosis of ABPA, but uncertainty remains on the serologic cut-off values that would increase the diagnostic specificity of ABPA. We retrospectively analyzed 80 patients with severe asthma and evidence of peripheral blood eosinophilia (> 500) over the last 3 years who underwent all serologic tests to exclude ABPA. Total IgE, specific IgE and specific IgG levels against *Aspergillus fumigatus* were measured using ImmunoCAP Phadia-100 (Thermo Fisher Scientific, Sweden). The Modified ISHAM working group 2013 criteria (obligate criteria: asthma or cystic fibrosis, total IgE > 1000 IU/ml or > 417 kU/L and positive specific IgE *Aspergillus fumigatus* or skin test positivity; with ≥ 2 of peripheral eosinophilia, positive specific IgG *Aspergillus fumigatus* and consistent radiographic opacities) was used in the clinical workup for the final diagnosis of ABPA. Patients were divided into 3 groups - definite, possible, and no evidence of ABPA. Specific IgG *Aspergillus fumigatus* levels were not used to assign the patients into any of the groups. Of 80 patients (males 48, females 32; mean age 53.9 years \pm SD 15.8) selected for the analysis, there were 30 patients who had positive specific IgE against *Aspergillus fumigatus* (37.5%). 13 patients fulfilled the Modified ISHAM working group 2013 criteria of ABPA ('definite'), while 15 patients were 'possible' ABPA and 52 did not fulfill the criteria (not ABPA). As IgE levels were not normally distributed, median levels were used in the analysis. Median total IgE levels of patients with definite and possible ABPA were 2144 kU/L and 2597 kU/L respectively (non-significant), while median specific IgE *Aspergillus fumigatus* at 4.35 kUA/L and 1.47 kUA/L respectively were significantly different (comparison of standard deviations F-statistic 3.2267, significance level $p=0.040$). Mean levels of IgG anti-*Aspergillus fumigatus* in the three groups (definite, possible and no evidence of ABPA) were compared using ANOVA (Statgraphics Centurion Professional XV, Statpoint Inc). Mean levels of IgG anti-*Aspergillus fumigatus* (Gm3) in definite ABPA was 125.17 mgA/L (\pm SD 54.84, with 95%CI 92.03-158.32), while mean Gm3 levels in possible and no ABPA were 18.61 mgA/L and 30.05 mgA/L respectively. ANOVA showed a significant difference between the definite group and the other groups ($p < 0.001$). This was confirmed using multiple range tests (Fisher's least significant difference procedure). There was no significant difference between the possible ABPA and not ABPA groups ($p > 0.05$). The study showed that a sizeable proportion of patients with asthma are sensitized to *Aspergillus fumigatus* in this part of India. A higher cut-off value of Gm3 ≥ 80 mgA/L provides a higher serologic specificity towards definite ABPA. Long-term studies would provide us more information if those patients with 'possible' APBA and positive Gm3 later develop clear ABPA, and are different from the Gm3 negative group in this respect. Serologic testing with clear defined cut-offs are a valuable adjunct in the diagnosis of ABPA.

Keywords : allergic bronchopulmonary aspergillosis, *Aspergillus fumigatus*, asthma, IgE level

Conference Title : ICACI 2018 : International Conference on Allergy and Clinical Immunology

Conference Location : Singapore, Singapore

Conference Dates : March 22-23, 2018