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Paper Poster Session V

Improving fungal diagnostics

Comparative efficacy of five *Aspergillus*-specific IgG ELISAs for the diagnosis of chronic pulmonary aspergillosis (CPA)

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Objectives

Chronic pulmonary aspergillosis (CPA) is a fatal condition that is estimated to effect 2-3 million people worldwide. Measurement of *Aspergillus*-specific IgG is central to the diagnosis of CPA, alongside clinical and radiological features. In-house assays are in use in some referral centers, but cannot be easily reproduced in other laboratories. Various assays are commercially produced. Such assays might provide consistently reliable results that are reproducible across many areas.

Our major aim was to compare the efficacy of five commercial assays for the diagnosis of CPA in an untreated population. We also noted that the diagnostic cut-offs for these assays were largely determined in mixed groups of aspergillosis patients and may not be optimal for the diagnosis of CPA. Hence, we aimed reconsider the appropriateness of existing diagnostic cut-offs for these assays in our patient population.

Methods

We tested sera from 250 patients with untreated CPA at the UK National Aspergillosis Center. Diagnosis of CPA was taken from clinical notes and required appropriate symptoms, radiological changes and microbiological evidence of infection. 100 sera from adolescent Ugandan blood donors were tested as controls.

Intra-assay variability was measured for each assay by repeating a single test 20 times. *Aspergillus*-specific IgG was measured on all sera by five methods. ImmunoCAP was also performed during routine diagnostic work-up. We performed ROC curve analysis to compare the efficacy of each assay for CPA diagnosis. We suggest new diagnostic cut-offs for each assay and describe sensitivity and specificity with these cut-offs.

Results

Co-efficient of variation (CoV), Receiver-operator curve area under curve (ROC AUC) and sensitivity and specificity for each test are shown in table 1.

ROC curves are shown in figure 1.

Conclusions

The Siemens Immunolite assay has statistically superior efficacy to all other assays where ROC analysis was possible, for the diagnosis of CPA. It also has superior sensitivity to the ImmunoCAP assay, which is widely used in Europe. Its high sensitivity and specificity mean that it can be used with confidence for the diagnosis of CPA, when clinical and radiological features are also present.

TEST	CoV	Median *Aspergillus*-specific IgG in healthy controls (n=100)	Median *Aspergillus*-specific IgG in CPA cases (n=250)	Maximum *Aspergillus*-specific IgG in CPA cases (N=250)	ROC AUC (95% confidence interval)	New proposed diagnostic cut-off	Sensitivity with new cut-off	Specificity with new cut off
Siemens	3.4%	4 mg/L	390 mg/L	7660 mg/L	0.99 (0.981 - 0.999)	10 mg/L	95.6%	98%
					0.972 (0.957			

Serion	23.2% 6 U/ml	133 U/ml	3436 U/ml	0.972 (0.957 - 0.986)	35 U/ml	90.4%	98%
Genesis	11.1% 7 U/ml	60 U/ml	930 U/ml	0.902 (0.872 - 0.933)	16 U/ml	78.4%	97%
Dynamiker	12.1% 34 U/ml	126 U/ml	6118 U/ml	0.918 (0.890 - 0.946)	70 U/ml	75.2%	98%
ImmunoCAP					*40 mg/L*	87.6%	
Precipitins						59%	100%

Figure 1 - ROC analysis for diagnosis of CPA by *Aspergillus*-specific IgG ELISAs