

Validation of The Binding Site latex IgG4 immunoassay antigen excess parameters

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Background:

Khosroshahi et al recently identified a prozone effect with IgG4 measurements in a significant proportion of IgG4-related disease (IgG4-RD) patients. Since the measurement of serum IgG4 is included in IgG4-RD diagnostic guidelines accurate IgG4 quantification is of importance. The antigen excess (AgXS) capacity of the Binding Site Group Limited (TBS) latex human IgG4 subclass liquid reagent kit was increased from 2400 mg/L to 49,000 mg/L. Here we validate the clinical utility of the new AgXS protocol for use on the Siemens BNII™ analyser.

Materials & Methods:

Serum samples were obtained from 10 pancreatic cancer patients (PC), 19 chronic pancreatitis patients (CP) and 28 autoimmune pancreatitis (AIP) patients (46:11 M:F, median age 67 years, range 37–86) diagnosed at Shinshu University Hospital, Japan. Serum IgG4 concentrations were measured using the antisera human IgG4 subclass liquid reagent kit (“antisera kit”) at diagnosis and for this study using the latex human IgG4 subclass liquid reagent kit (“latex kit”) (TBS, UK) on the Siemens BNII™ analyser. Serum IgG4 >1350 mg/L was considered elevated and used to validate the new protocol.

Results:

Measurement of IgG4 using the latex kit was highly concordant with the antisera kit (agreement PC: 90%, CP 95%, AIP 93% and all patients 93%, $P < 0.0001$). 24/28 AIP patients had elevated serum IgG4 and 22/24 were elevated on the latex kit. 2/24 were discrepant borderline samples (976.36 vs. 1358.10; 1219.79 vs. 1426.73). 19/24 AIP patients had serum IgG4 concentrations >2400 mg/L. 16/24 samples were >2400 mg/L on the latex kit (agreement 89%, $P < 0.0001$) and a concentration was reportable for all 16 samples (range 2731 – 17429 mg/L). 3/19 samples were below 2400 mg/L on the latex assay but all 3 samples had IgG4 >1350 mg/L. A concordant cut-off of 1220 mg/L was generated for identifying AIP patients with elevated IgG4 (AUC 0.95, sensitivity 82.1%, specificity 96.6%, likelihood ratio of 23.8).

Conclusions:

Our study validates the new antigen excess parameters for the TBS latex assay. These new parameters ensure that samples >2400mg/L do not go into antigen excess. This will increase the utility for using the measurement of IgG4 in IgG4-RD.