Anti-dsDNA antibody testing in the clinic: Farr or ELISA?

Original article Neogi T *et al.* (2006) Anti-dsDNA antibody testing by Farr and ELISA techniques is not equivalent. *J Rheumatol* **33:** 1785–1788

SYNOPSIS

KEYWORDS dsDNA antibody testing, ELISA, Farr assay, systemic lupus erythematosus

BACKGROUND

Anti-double-stranded (ds) DNA antibodies are known to be highly specific for systemic lupus erythematosus (SLE) and are routinely used for the diagnosis of this disease. The specificity of dsDNA antibodies for the diagnosis of SLE however, is not necessarily correlated with their prognostic ability or the identification of organ-specific involvement.

OBJECTIVE

The objective of this study was to investigate the correlation between the efficacy of the Farr radioimmunoassay (RIA) and the enzyme-linked immunosorbent assay (ELISA) in detecting anti-dsDNA antibodies and their ability to measure disease activity.

DESIGN AND INTERVENTION

Patients who had anti-dsDNA antibody measured by both the Farr RIA and the ELISA techniques over a 2-year period were included in this study. Patients' details were obtained at every visit to the clinic at 3–4 month intervals and were stored in a database. Details included patient demographic characteristics, organ-specific disease-related symptoms, physical findings, current medications, and the latest laboratory measurements. The SLEDAI-2K (SLE Disease Activity Index 2000) was used to measure global disease activity for each patient, excluding the DNA component in order to assess the efficacy of the two anti-dsDNA antibody assays.

OUTCOME MEASURES

The primary outcome measure of this study was the correlation between the two anti-dsDNA antibody tests with measurements of global disease activity in patients with SLE. In this respect, Farr RIA values >7 U/ml and ELISA values >180 IU/ml were defined as abnormal.

RESULTS

A total of 550 patients, corresponding to 2,940 clinic visits, were included in this study. Analysis of first patient visits showed that the correlation between the Farr RIA and ELISA tests was 0.46 (95% CI 0.39–0.52, $P<0.0001$); this correlation was unchanged regardless of whether or not one test was abnormal. Abnormal Farr results were, however, associated with higher SLEDAI-2K scores compared with normal Farr results (6.2 vs 4.3 respectively, $P<0.0001$). This result was not observed with the ELISA test (5.9 vs 4.8 respectively, $P=0.04$). A total of 121 patients had active renal involvement, and had statistically significantly higher Farr RIA values; however, no differences in ELISA values were observed. The Farr RIA and the ELISA values were not found to correlate with central nervous system disease.

CONCLUSION

The authors conclude that there is poor correlation between the Farr RIA and ELISA in detecting anti-dsDNA antibodies in patients with SLE and that the Farr RIA should be used in clinical practice, as it correlates measures of global disease activity, renal involvement and vasculitis more effectively than the ELISA.

COMMENTARY

Michael Mahler and Marvin J Fritzler*

Anti-dsDNA antibodies are a serological hallmark for the diagnosis of SLE and are widely used as one of several disease classification criteria. Historically, anti-dsDNA antibodies have been mainly detected by a *Crithidia luciliae* indirect immunofluorescence test (CLIFT) and Farr radioimmunoassay. The Farr RIA is reputed to detect relatively high avidity anti-DNA antibodies because of the high ammonium sulfate concentration, which dissociates low avidity DNA–anti-DNA complexes. More recently, ELISA, line immunoassays, and multiplex assays have also been used for the detection of anti-dsDNA antibodies.[1]

This study by Neogi and colleagues shows that a commercial Farr assay (Trinity Biotech) is superior to a commercial anti-dsDNA ELISA (Zeuss Scientific) in terms of monitoring disease activity and predicting organ damage in this particular SLE cohort. These findings are in agreement with previous studies[1] and have obvious significance for clinicians who are challenged to follow the clinical course of patients with SLE and introduce timely interventions. It is difficult, however, to generalize this study to the anti-DNA immunoassays from other manufacturers that are widely used today. The basis for this reservation is that a validated anti-dsDNA assay depends on several factors, including the nature and the amount of the antigen, the isotype specificity of the detection antibody and the assay conditions.[1–3] Although an international reference serum is available, the standardization of anti-dsDNA immunoassays and the correlation between them is relatively poor. It is possible that an individual anti-dsDNA assay might demonstrate a good correlation with the Farr RIA and, therefore can be used as an equally reliable assay to follow disease activity and organ damage in patients with SLE. Novel approaches such as a fluorescence based immunoassay (EliA®, Phadia, AB, Uppsala, Sweden), the interpretation of the ratio between IgM and IgG to dsDNA, the use of oligonucleotide-based or chromatin based assays and the consideration of crossreactivity of anti-dsDNA antibodies to α-actinin have shown promising results.[1–5]

Despite some of its advantages, in a cost-conscious medical world the Farr RIA has several limitations. It is a laborious test to perform and because of the requisite use of radiolabeled DNA, pregnant technologists are not allowed to perform the test, leading to higher employee turnover. In countries with high personnel costs, the Farr RIA is significantly more expensive than the ELISA. The routine use of radioactive ligands such as DNA is attended by significant risk management and costs in laboratory and personnel certification, regular monitoring of the laboratory for contamination and exposure of employees, decontamination, arduous records of isotope inventory and disposal, and maintenance of and supplies for specialized detectors.

In conclusion, when clinical aspects (e.g. monitoring disease activity) alone are taken into account, the Farr RIA is generally believed to be superior to some anti-dsDNA ELISA tests. Overarching conclusions based on comparisons of only a few assays are unwarranted, however, until a full spectrum of kits that are used in clinical laboratories are evaluated in carefully designed study protocols.

References

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M Mahler is Director of Development and Production of the Dr Fooke Laboratorien GmbH, Neuss, Germany and MJ Fritzler is Professor of Medicine at the University of Calgary, AB, Canada.

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Competing interests
The authors have declared associations with the following companies/organizations: Dr Fooke Laboratorien GmbH, Immunoconcepts. See the article online for full details of the relationship.

Correspondence
*University of Calgary
Department of Medicine
Faculty of Medicine
3330 Hospital Dr NW
Calgary
AB T2N 4N1
Canada
fritzler@ucalgary.ca

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PRACTICE POINT
The Farr RIA is generally believed to be superior to some anti-dsDNA ELISA tests for disease activity monitoring purposes