Point of care testing for paediatric coeliac disease in the new ESPGHAN era

One of the challenges in coeliac disease is the significant under-diagnosis despite the increasing prevalence and international guidelines for serological screening in appropriate patient cohorts (1). Several point-of-care tests for coeliac disease have been developed over the past decade with the aim of improving case detection using rapid and convenient testing. Most point-of-care tests, such as Biocard, detect anti-tissue transglutaminase (tTG) IgA antibodies, whereas Simtomax uniquely detects anti-deamidated gliadin peptide (DGP) IgA/IgG antibodies. A recent head-to-head trial in adults comparing two tTG-based point-of-care tests (Biocard and Celiac Quick Test) and Simtomax found that Simtomax was superior to Biocard and Celiac Quick Test, with sensitivities of 92.7%, 72.2% and 77.8%, respectively (2). Laboratory DGP serology has been shown to be more sensitive than tTG serology in younger children, which sparks interest in the evaluation of the performance of a DGP-based point-of-care test in a paediatric cohort (3). Polanco et al. set out to address this question by testing the efficacy of Simtomax in children with suspected coeliac disease (4).

The authors prospectively recruited 100 children who had symptoms suggestive of coeliac disease or who had first-degree relatives with coeliac disease. All patients were tested with Simtomax and IgA-tTG serology. Those with IgA-tTG titres more than 10 times the upper limit of normal were diagnosed with biopsy-free approach, provided that the patient had positive endomysial antibodies and HLA DQ2/DQ8, according to the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines. This was based on a few studies showing good predictability of coeliac disease at such high tTG titres (3). Of the 47 patients with newly diagnosed coeliac disease in this study, 15 (31.9%) were diagnosed without biopsies, with the majority (11/15) being under two years of age. Those with elevated IgA-tTG titres of less than 10 times the upper limit of normal proceeded to duodenal biopsies as per the conventional approach. Those with negative IgA-tTG and normal IgA levels did not undergo further investigations unless coeliac disease was highly suspected or if the patient was less than two years of age. The prevalence of coeliac disease was 48%, with the sensitivity, specificity, positive and negative predictive values of Simtomax being 95.8%, 98.1%, 97.9% and 96.2%, respectively. Positive and negative likelihood ratios were 49.8 and 0.04, respectively. A subgroup analysis revealed that Simtomax was more sensitive for coeliac disease detection in children younger than 10 years of age (n = 70) as compared to those aged 11-18 (n = 30) (100% vs. 90%).

This is the first paediatric study evaluating the diagnostic performance of Simtomax versus the diagnostic reference standard set out by ESPGHAN since their guidelines were updated in 2012. This sets the study apart from other similar paediatric studies where the performance of Simtomax was not compared against ESPAGHN criteria or tTG serology alone. Nevertheless, the sensitivities of Simtomax reported by Polanco et al. are consistent with the literature. There are three other prospective studies evaluating the diagnostic accuracy of Simtomax in a paediatric population, showing high sensitivities of over 90% in detecting coeliac disease (5-7). As the authors mentioned, a limitation of this study was the high prevalence of coeliac disease (48%) in the study cohort. This referral bias might falsely elevate the positive predictive value (PPV) of Simtomax, limiting its generalisability. PPV may fall when Simtomax is used in real clinical practice, where coeliac disease prevalence has been shown to be approximately 3% when case finding in high-risk patient groups (8,9).

Importantly, the use of a simple, minimally invasive finger prick point-of-care test in the paediatric population may be immensely useful, as venepuncture can often be challenging and traumatic to children. Furthermore, with the advantage of providing antibody results within 10 minutes, point-of-care testing may have a significant potential role in case finding in the primary care setting. Rapid result availability not only offers convenience, but also allows discussion between patient, carer and clinician regarding results in real time. Referral to secondary care for further investigations and treatment may be accelerated, ultimately improving patient satisfaction and quality of care.

This study adds weight to the growing pool of promising evidence showing Simtomax to have a high diagnostic accuracy in detecting coeliac disease in a paediatric population at a tertiary centre, where the pre-test probability is high. Larger studies are required to evaluate the diagnostic performance of Simtomax in children in a lower-prevalence population, ideally with duodenal histology as the reference standard for all patients where possible. An interesting concept would be to establish if the intensity of the red line indicating Simtomax positivity correlates to the tTG titre, i.e., if a strong positive red line would correspond to tTG titres over 10 times the upper limit of normal and a diagnosis of celiac disease, as opposed to a faint red line. If so, one may hypothesize that a patient tested with a strong positive point-of-care test could potentially be diagnosed with coeliac disease at the outset, thus expediting commencement of a gluten-free diet. This could be food for thought for future research.
Further evidence from diagnostic performance studies on larger numbers and lower-prevalence cohorts would support a wider utility of this point-of-care test, which would be especially beneficial to children where coeliac screening is quick and minimally invasive.

Michelle S. Lau and David S. Sanders

Academic Department of Gastroenterology. Royal Hallamshire Hospital. Sheffield Teaching Hospitals. Sheffield, United Kingdom

DOI: 10.17235/reed.2017.5337/2017

REFERENCES