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Deaminated Gliadin Peptide Antibody in the Diagnosis of Celiac Disease

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Celiac Disease (CD) is an immune-mediated gluten-sensitive enteropathy, characterised by intolerance to dietary gluten. [1] Indigestion of gluten containing food, among individual susceptible to CD will lead to immune-mediated inflammatory cascade primarily in small bowel mucosa, leading to intestinal villous atrophy. The worldwide prevalence of CD is around 1%, with slightly higher prevalence in certain part of the world. [2,3] Genetic predisposition plays a vital role in CD, with both the *HLA-DQ2* and *HLA-DQ8* genes are strongly associated with it. About 95% of patients with CD express *HLA-DQ2*, and the rest of them are usually *HLA-DQ8* positive. [1,3,4,5] Environmental exposure of gluten in the genetic susceptible individual is the key event in the development of CD. Gluten Free Diet (GFD) is the only proven effective treatment for CD as there is no other proven alternative to prevent intestinal mucosal damage due to gluten exposure, among population with CD.

The gold standard for diagnosis of CD is the histopathological analysis of small intestinal biopsy (usually second part of duodenum). [1] A few serological blood tests like anti Gliadin antibody (AGA), Endomysial antibody (EMA), tissue Transglutaminase antibody (tTG), and more recently Deaminated Gliadin Peptide (DGP) antibody are used for screening, diagnosis and follow up for patients with CD. [6] Celiac serological test is very useful diagnostic tool in the diagnosing process of CD. Serological screening tests can be used to identify patients at risk of CD to proceed with diagnostic gastroscopy and small intestinal biopsy. Apart from that, celiac serological tests can be utilized in monitoring the response and compliance to GFD [7,8].

AGA was widely used previously but the current utilization of AGA is limited due to its low sensitivity and specificity.[9] While both IgA anti-tTG and EMA would be the tests of choice in current clinical practice, DGP antibody test has been shown to have very good sensitivity and specificity.[10] In fact, several studies have demonstrated that IgG DGP antibody has a higher specificity and sensitivity than IgG tTG antibody in both adults and paediatric population population [11,12].

The low sensitivity and specificity of AGA has been attributed to the fact that the Gliadin used in the test was not deaminated. [13] DGP, which has been introduced as part of serological work-up in CD, enhances the antibody response by deamidation of gliadin peptides. Deamidation of gliadin plays a vital stage in the pathogenesis of CD. As gliadin entering the small intestinal mucosa is deamidated (the blinding of gliadin to HLA-DQ2 or DQ8 is strongly enhanced by deamidation), the modified antigens stimulate B-lymphocytes to create antibodies against the deamidated peptides. [10,13,14] The antibodies in subjects with CD will identify the deamidated gliadin peptides better than gliadin peptides. [13] Rashtak et al has demonstrated DGP Antibody is a better test for CD comparing to the AGA, with non-inferior performance comparing to IgA tTG antibody [6].

A meta-analysis by Lewis et al concluded that IgA DGP antibody is less sensitive comparing to IgA tTG antibody (88% vs. 93%). [14] While the study shows that the specificity of both IgA DGP antibody and IgA tTG antibody are high (>94% and >96% respectively), the study found that IgG DGP antibody is less sensitive, but more specific comparing to IgA-DGP antibody. However, there was a number of methodological weaknesses in both the primary studies included and the meta-analysis itself. [14] The trade off between sensitivity and specificity is always the centre of concern in a diagnostic test. [15] The ideal medical diagnostic test of 100% sensitive and 100% specific is virtually non-existence. The combination of IgG DGP antibody and IgA tTG antibody offers the best sensitivity and specificity in diagnosing CD. [1,9,14,16] This combination will increase the sensitivity in detecting CD, without lowering its specificity.

Around 2% of patients with CD are IgA deficient, and population with IgA deficiency will have higher risk of CD. [17] IgA tTG antibody alone will miss the case of CD with IgA deficiency, with false negative result. In such a scenario, IgG DGP or IgG tTG antibody can be very useful as part of the diagnosis cascade for CD.

Currently, there is 1 commercially available point of care test (POCT) which is based on DGP antibody. The DGP based POCT (Simtomax) available will detect both IgA and IgG DGP antibodies. [18] With its high negative predictive value of more than 99.1%, it was originally developed for screening of CD. [18] DGP based POCT (Simtomax) had a greater sensitivity than the other POCTs (Biocard and Coeliac Quick Test based on tTG antibodies) that were tested in patients referred with a positive EMA. [19] Mooney et al has demonstrated that the DCP based

POCT has comparable diagnostic accuracy to standard serological markers when used in an endoscopic setting. They have validated a clinically feasible diagnostic algorithm, based on DGP-based POCT, for identifying patients with CD in endoscopy setting. [19] DGP- based POCT is also shown to have a great potential be an instrument used to monitor compliance to GFD among patients with known CD. [7,8] As the sensitivity and negative predictive value of DGP-based POCT in predicting compliance to GFD were high, in routine Celiac clinic settling, the immediate availability of result (in detecting gluten ingestion) will allow for an on-the-spot management decision [7].

In conclusion, DGP antibody has proven to be an importance celiac serological test, along with more conventional tTG antibody and EMA, as part of the investigation for CD. DGP antibody also has the potential to be used as the individual celiac serological test or it can be used as a combination to other celiac serological tests. The combination of IgG DGP antibody and IgA tTG antibody provide the best diagnostic accuracy for CD. The availability of DGP-based POCT is particularly useful due to its instantaneous result, and its ability to be utilised in primary care settling, celiac clinic or even the endoscopy settling.

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