10th Euro-Global Conference on **Infectious Diseases**

5th International Conference on Histopathology & Cytopathology

September 27-29, 2018 Rome, Italy



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Relation of serum EpCAM levels with intestinal inflammation in children with Celiac Disease

Celiac disease is an autoimmune, chronic, inflammatory and systemic disease that is the result of gluten exposure in the diet. Epithelial cell adhesion molecule (EpCAM) is a non-classical adhesion molecule found in epithelial cells. It is found very much in small intestines and increases in chronic inflammatory events. The aim of the study is to determine the serum EpCAM levels and the effect of gluten-free diet (GFD) compliance on serum EpCAM levels in children with celiac disease. 46 celiac patients and 38 age-sex-matched healthy children were included in the study. Patients were divided into two groups as compliant with GFD or non-compliant with GFD. Serum EpCAM level was measured by ELISA method. Serum EpCAM levels in patients compliant with GFD were 62(34-83) ng/mL, while serum EpCAM levels in healthy children were 34(16-53) ng/ mL (P=0.023). Serum EpCAM levels in patients compliant with GFD were 34(16-53) ng/mL, respectively] (P=0.908). The serum EpCAM levels of children compliant with GFD were significantly lower than the serum EpCAM levels of patients non-compliant with GFD (P=0.029). Serum EpCAM level may be a sensitive marker for determining the intestinal inflammation and gluten free diet compliance.

Introduction: Celiac disease is an autoimmune, chronic, inflammatory and systemic disease resulting from the consumption of dietary gluten grains in individuals with genetic predisposition (1). Under normal conditions, harmful food or microorganism antigens entering the gastrointestinal tract are destroyed, while the harmless ones are tolerated. This condition of physiological unresponsiveness is called "oral tolerance". In celiac disease, oral tolerance to gluten is impaired, resulting in increased levels of interleukin-15 and inflammation in the intraepithelial area (2). Under the normal conditions, intestinal epithelium acts as a barrier against the molecules in the passage, and is not permeable to macromolecules such as gluten (3). However, since this permeability is impaired in celiac disease, the gluten may pass through the subepithelial area paracellularly or transcellularly, leading to prolonged intestinal inflammation (4). The epithelial cell adhesion molecule (EpCAM) is found in the intestinal epithelium. It is structurally unlike to classical cell adhesion molecules. Although other cell adhesion molecules are abundantly expressed in normal epithelium, expression of EpCAM is limited. EpCAM is up-regulated and is expressed highly in epithelial cells during and after inflammatory tissue regeneration (5). To assess the intestinal inflammation in children with celiac disease, we aimed to determine serum EpCAM levels, to compare them to healthy children and to determine the effect of gluten-free diet (GFD) on EpCAM levels.

Patients and Methods: The study included 46 celiac patients and 38 age-sex-matched healthy children. Patients were divided into two groups of gluten free diet compatible or not according to the results of anamnesis and celiac antibody. Those with a known chronic condition other than celiac disease were excluded from the study. Serum samples were stored at -80 °C for the measurement of EpCAM by ELISA. Binary groups were compared by student's t-test and Mann-Whitney U test, and more than two groups were compared by one-way ANOVA and Kruskal Wallis Variance analysis, as appropriate. Qualitative

Results:

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| Variables | Healthy controls, n=38 | Compliant with GFD, n=25 | Non-compliant with GFD, n=21 | Р |
|----------------------|---------------------------|-----------------------------|---------------------------------|-------|
| Age (years) | 12±3 | 12±4 | 13±3 | 0.280 |
| Gender Girls Boys | 22 (57.9%) 16 (42.1%) | 13 (52%) 12 (48%) | 12 (57.1%) 9 (42.9%) | 0.892 |
| EpCAM (ng/ mL) | 34 (16-53) | 30(20-49) | 62(34-83) | 0.013 |

GFD, gluten free diet.

Discussion: Celiac disease is the only autoimmune disease in which the trigger is apparent and which enters in remission when the agent is removed. Immunological response to gluten causes mucosal damage leading to intraepithelial lymphocyte increase in the small intestine, crypt hyperplasia, and finally villous atrophy (1). In chronic inflammation, the activation of leukocytes results in the production of millions of cytokines, increase of the production of adhesion molecules, which provide leukocyte migration to infiltrated tissue. Studies have shown that inflammatory cytokines and cell adhesion molecules increase both at tissue and serum as indicators of inflammation in celiac disease (6,7).

In our study, serum levels of EpCAM, a marker that is highly epithelium-specific in the small intestine, were investigated for the evaluation of intestinal inflammation in celiac disease patients. EpCAM levels were found to be the highest in patients non-compliant with GFD, while patients compliant with GFD were found to be similar results with the healthy children. Therefore, serum EPCAM levels may be a sensitive marker for determining the intestinal inflammation and gluten-free diet compliance.

Biography

Huseyin Kayadibi was born and raised in Istanbul, Turkey. He received a Degree in Medicine from the GATA School of Medicine (Turkey) in 2000. He is an Associate Professor in Medical Biochemistry at Hitit University School of Medicine, where he is the head of Medical Biochemistry. He worked at Pasarow Mass Spectrometry Laboratory, University of California Los Angeles in 2012 and 2017 as a visiting scholar. He has been a co-investigator on NIH and other international projects about metabolomic, proteomic and lipidomic analysis. He is the member of EFLM Working Group Test Evaluation and IFCC Working Group Cerebrospinal Fluid Proteins. He has published more than 70 papers in peer-reviewed journals. His research interests are non-invasive assessment of steatohepatitis, liver fibrosis, separation techniques and mass spectrometry.

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