ProCeDE – Prospective Celiac Disease Diagnostic Evaluation

Currently, the reference standard for the diagnosis of Celiac Disease (CD) combines the histological examination of duodenal biopsies and CD specific serology (antibodies against tissue Transglutaminase = tTG, endomysium autoantibodies = EMA, and deaminated gliadin peptides = DGP). During the last decade, the quality of serological markers highly improved, particularly in terms of specificity, while the unambiguousness of duodenal biopsy was questioned (Arguelles-Grande et al, J Clin Path 2012;65:242-247). A systematic review showed that endoscopy may be omitted in a subgroup of children with symptoms of malabsorption with high tTG-IgA (>10 times cut values) (Giersiepen et al, JPGN 2012;54:229-241). No such data are available for asymptomatic or oligosymptomatic children with high risk for CD (1st degree relative with CD or history of other CD associated disorders). Based on the available evidence new diagnostic criteria for CD in pediatric patients have been published by the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) (Husby et al, JPGN 2012; 54:136-160).

However, these estimates are based mostly on retrospective evaluations or data from single-center studies. Therefore, the working group of ESPGHAN on the diagnostic criteria of CD felt obliged to evaluate the new criteria on a large pediatric population in different countries and settings including a broad range of symptomatic and asymptomatic children which are referred for further work up because of a positive test result for antibodies against tissue transglutaminase. The ProCeDE (**Pro**spective **Ce**liac Disease **D**iagnostic **E**valuation) study aims to provide prospective data to assure that this diagnostic procedure is valid also in clinical practice with positive predictive value above 99%. Furthermore, inter-observer variability for histology and inter-test variability will be assessed and the impact of HLA-typing on diagnosis will be evaluated. Although the new criteria foresee the option to omit duodenal biopsies only in children with typical symptoms of celiac disease it was decided to include also children with no or minor symptoms which have been screened for celiac disease because of increased risk for the disease based on a celiac disease associated condition.

In total, 37 centres in 22 countries will collect data of paediatric patients aged 0.5 -18 years who undergo duodenal biopsies for suspected CD (fig. 1, 2). Patients are included if they have a positive tTG-IgA (IgG in case of IgA-deficiency) at any titre height, report symptoms and/or are at high risk for CD, eating a normal gluten-containing diet and parents have given written informed consent. Exclusion criteria are contraindication for endoscopy, primary or secondary immunodeficiency, existing malignancy or previous diagnosis of CD. At the day of endoscopy blood is drawn for local serology and central testing for EMA and tTG and DGP from at least 5 manufactures, and HLA-typing. All biopsies will be evaluated by local and a reference pathologist. Data on medical and family history, diet, physical examination and basic lab are collected. Confirmed CD cases will be followed-up at 3, 6, 12 and 18 months after starting gluten-free diet. A total sample size of 600 to 700 patients with high suspicion for Celiac Disease had been estimated. The project started in November 2011. Currently 400 patients have been recruited. The study is financially supported by manufacturers of serology test-kits and non-profit organizations as patient organisations and the ESPGHAN.