The ESPGHAN Cystic Fibrosis Working Group: Defining DIOS and Constipation in Cystic Fibrosis With a Multicenter Study on the Incidence, Characteristics, and Treatment of DIOS

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In 2005 a group of pediatric gastroenterologists convened at the annual meeting of the European Society for Pediatric Gastroenterology and Nutrition (ESPGHAN) to reevaluate some important gastrointestinal manifestations of cystic fibrosis (CF). It had become evident that the key gastrointestinal symptoms of the disease, such as distal intestinal obstruction syndrome (DIOS), meconium ileus equivalent (MIE), and constipation, were ill-defined. Such a limitation could not only represent a bias for clinical studies evaluating the incidence and prevalence of these gastrointestinal manifestations in CF but also negatively influence the diagnosis and treatment of these manifestations of CF. The results of the activity of the ESPGHAN CF Working Group appear in this issue of *JPGN*, specifically in the article by Houwen et al (1).

Cystic fibrosis is the most common fatal autosomal recessive disease among white populations, with a frequency of 1 in 2000 to 3000 live births. It is generally thought of as a lung disease because much of the associated morbidity rate and mortality rate is related to pulmonary complications (2).

However, gastrointestinal complications also have become an increasingly important cause of the morbidity rate in part because of the improved life expectancy of patients with CF. The underlying pathophysiology of CF is related to abnormal chloride transport caused by mutations in the CF transmembrane conductance regulator gene (*CFTR*) located on chromosome 7. The mutations cause the production of abnormally tenacious mucus and secretions in the lungs, gut, pancreas, and hepatobiliary system.

The gastrointestinal manifestations of CF can be broken down into 3 categories: intestinal, pancreatic, and hepatobiliary. One of the most common intestinal abnormalities is the DIOS, formerly known as ''meconium ileus equivalent,'' which is characterized by complete or partial obstruction of the bowel lumen by intestinal contents. Distal intestinal obstruction syndrome is caused by inspissated intestinal contents that completely or partially block the intestinal lumen, although a detailed understanding of this process remains unclear. In the last few years, different definitions of DIOS, MIE, and constipation in patients with CF have been used, but better definitions for the 3 conditions would now seem to be necessary for an improved assessment and management of these patients (3,4).

The new definition proposed by the ESPGHAN CF Working Group for incomplete or impending DIOS is ''a short history (days) of abdominal pain and/or distension and a faecal mass in ileocaecum, but without signs of complete obstruction.'' Constipation was defined as ''abdominal pain and/or distension or a decline in the frequency of bowel movements in the last few weeks to months and/or increased consistency of stools in the last few weeks or months, while the symptoms are relieved by the use of laxatives.'' Meconium ileus equivalent was identified with DIOS. The most important outcome of the consensus is that these specific definitions could avoid misdiagnosis between DIOS and constipation in patients with CF, as sometimes occurred in the past.

The practical result of this update was immediately seen in the study because the impact of this review was evaluated in a questionnaire-based multicenter survey in which the new definitions were applied to a large number of patients younger than 18 years with CF, enrolled between 2001 and 2005 in 8 medical centers. Using the new criteria, the incidence of both DIOS and meconium ileus at birth resulted to be far higher than that reported in previous studies. It seems clear that the higher incidence of DIOS is mainly due to the newly established definitions, although new therapeutic approaches could have partly influenced the results of other recent studies.

The authors have also reevaluated the correlation between DIOS and *CFTR* mutations, as organized into 5 classes (I–III severe mutations, IV–V mild mutations), comparing the *CFTR* genotype with the DIOS-positive or DIOS-negative phenotype. The great majority of the subjects with CF had a severe genotype, being homozygous for the most common mutation, ΔF508. The results of the present study seem to confirm the association between major *CFTR* dysfunction and DIOS, whereas the possible role of other genetic factors such as dysmotility and inflammatory status could be evaluated in the next clinical trials.

In conclusion, the new definitions established by the consensus conference of the ESPGHAN CF Working Group are important for 2 main reasons: the epidemiology of the gastrointestinal complications of CF could be profoundly modified, and the new definitions will help the clinician perform a more specific diagnosis of MIE, DIOS, and constipation, thus improving not only the diagnostic accuracy but also the effectiveness of treatment.

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