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ORIGINAL ARTICLE

The duodenal microbiota composition in children with active coeliac disease is influenced by the degree of enteropathy☆

F. Girón Fernández-Crehuet[a], S. Tapia-Paniagua[b], M.A. Morinigo-Gutiérrez[b], V.M. Navas-López[a,c], M.J. Serrano[a], J. Blasco-Alonso[a,c], C. Sierra-Salinas[a,c,*]

[a] *Unidad de Gastroenterología y Nutrición Infantil, Hospital Materno Infantil, Málaga, Spain*
[b] *Departamento de Microbiología, Facultad de Ciencias, Málaga, Spain*
[c] *IBIMA, Spain*

Received 4 May 2015; accepted 4 June 2015
Available online 24 October 2015

KEYWORDS
Coeliac disease;
Microbiota;
MARSH;
Lactobacillus

Abstract
Objectives: To establish whether the duodenal mucosa microbiota of children with active coelic disease (CD) and healthy controls (HC) differ in composition and biodiversity.
Material and methods: Samples of duodenal biopsies in 11 CD patients were obtained at diagnosis, and in 6 HC who were investigated for functional intestinal disorders of non-CD origin. Total duodenal microbiota and that belonging to the genus *Lactobacillus* using PCR-denaturing gradient gel electrophoresis (DGGE) were analyzed. The banding patterns obtained in the resulting gels were analyzed to determine the differences between the microbiota of CD patients and HC (FPQuest 4.5) while environmental indexes (richness, diversity and habitability) were calculated with the past version 2.17 program.
Results: The intestinal microbiota of patients with Marsh 3c lesion showed similarity of 98% and differs from other CD patients with other type of histologic lesion as Marsh 3a, Marsh 3b and Marsh 2. The main differences were obtained in ecological indexes belonging to the genus *Lactobacillus*, with significant richness, diversity and habitability reduction in CD patients. In CD bands were categorized primarily with *Streptococcus*, *Bacteroides* and *Escherichia coli* species. In HC the predominant bands were *Bifidobacterium*, *Lactobacillus* and *Acinetobacter*, though the *Streptococcus* and *Bacteroides* were lower.

☆ Please cite this article as: Girón Fernández-Crehuet F, Tapia-Paniagua S, Morinigo-Gutiérrez MA, Navas-López VM, Serrano MJ, Blasco-Alonso J, et al. La composición de la microbiota duodenal en niños con enfermedad celíaca activa está influenciada por el grado de enteropatía. An Pediatr (Barc). 2016;84:224–230.

* Corresponding author.
E-mail address: carlos.sierra.sspa@juntadeandalucia.es (C. Sierra-Salinas).

Conclusions: The celiac patients with major histological affectation presented a similar microbiota duodenal. The ecological indexes applied to the genus *Lactobacillus* were significantly reduced in CD.

PALABRAS CLAVE
Enfermedad celíaca;
Microbiota;
MARSH;
Lactobacillus

La composición de la microbiota duodenal en niños con enfermedad celíaca activa está influenciada por el grado de enteropatía

Resumen
Objetivo: Comprobar diferencias en la microbiota duodenal al diagnóstico de la EC en relación con grupo control.
Material y Métodos: Se obtuvieron muestras de biopsias duodenales en 11 pacientes con EC al diagnostico y en 6 controles. Se analizó la microbiota duodenal total así como la perteneciente al género *Lactobacillus* mediante la técnica molecular PCR-Electroforesis en gel con gradiente desnaturalizante (DGGE). Los patrones de bandas obtenidos en los geles resultantes fueron analizados para determinar las diferencias presentes entre la microbiota de pacientes con EC y controles (FPQuest 4.5) mientras que los índices ecológicos (riqueza, diversidad y habitabilidad) fueron calculados con el programa Past versión 2.17.
Resultados: La microbiota intestinal de los individuos con histología Marsh 3c presentó similitud del 98% y fue diferente del resto de pacientes celiacos. Las principales diferencias se obtuvieron en los índices ecológicos pertenecientes al género *Lactobacillus*, con importante reducción de especies en los celiacos respecto al grupo control (riqueza, diversidad y habitabilidad). En los pacientes con EC las bandas principalmente fueron catalogadas con las especies *Streptococcus*, *Bacteroides* y *E. coli*. En los controles las bandas predominantes fueron *Bifidobacterium*, *Acinetobacter* y *Lactobacillus*, sin embargo los *Streptococcus* y Bacteroides fueron más bajos.
Conclusiones: Los índices ecológicos aplicados al género *Lactobacillus* fueron significativamente reducidos en los pacientes celíacos. Los casos con mayor afectación histológica presentaron una microbiota duodenal similar.

Introduction

Coeliac disease (CD) is a chronic inflammatory disorder of the small intestine characterized by a permanent intolerance to dietary gluten occurring in genetically predisposed individuals.[1] This disease can occur at any age and with a variety of clinical features, but typical cases often present in early childhood. Patients with CD may be asymptomatic, only with extraintestinal symptoms or silent forms. Currently, CD with a classical gastrointestinal symptoms is diagnosed by demonstrating mucosal villous atrophy, crypt hyperplasia and infiltration of intraepithelial lymphocytes.

CD is a multifactorial disorder that involves interactions between genetic and environmental factors. Environmental factors include early life gluten exposure, short duration of breastfeeding, intestinal infections and changes in microbiota.

Recently, scientific evidence showed changes in the intestinal microbiota composition in these patients.[2] So far, differences in the microbiota composition and related metabolites between CD patients and healthy controls (HC) have been reported mainly in feces.[3,4] Increased bacterial diversity and changes in several bacterial groups in the duodenal microbiota of pediatric CD patients have also been reported.[5–7] However, other studies have failed to show major microbiota differences between CD and HC.[8–10] Cheng et al.[10] describe a similar microbiota composition in the duodenal mucosa between the CD and healthy children but a sub-population profile comprising eight genus-like bacterial groups was found to differ significantly between the study groups, probably with a specific role in the epithelial disruption in CD.

Changes in the duodenal microbiota have been described in coeliac patients, adults and children, with active disease[5,9,11] and when they were also under gluten free diet.[12] Wacklin et al.[13] found differences in the diversity and composition of the intestinal microbiota in adults with classic intestinal CD symptoms and extraintestinal symptoms; this indicated that the composition of mucosa-associated microbiota in the duodenum of the patients differed depending on the manifestations of CD.

This study was designed to establish whether the duodenal mucosal microbiota of children with active CD and controls differ in composition and biodiversity in order to explain the differences in microbiota of pediatric CD patients and HC.