Nutr Hosp. 2016; 33(1):182-184 ISSN 0212-1611 - CODEN NUHOEQ S.V.R. 318

Nutrición Hospitalaria

Nota Clínica

Synbiotic supplementation promotes improvement of chronic diarrhea of unknown etiology in patient with chronic kidney disease and provides better outcomes in dialysis

La suplementación con simbióticos promueve la mejora de la diarrea crónica de etiología desconocida en pacientes con enfermedad renal crónica y ofrece mejores resultados en diálisis

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Key words:

Chronic kidney disease. Microbiota. Synbiotics. Diarrhea. Hemodialysis.

Abstract

Background: Chronic kidney disease (CKD) patients often have gastrointestinal symptoms which may result in malnutrition and a negative impact on their quality of life. Modulation of the gut microbiota can be a strategy to promote host health and homeostasis.

Case report: The authors present a case of chronic diarrhea in a hemodialysis (HD) patient with an unknown etiology. After about one year and several failed interventions, synbiotic therapy was performed. The diarrhea episodes ceased after three months of daily supplementation and both biochemical and nutritional parameters improved. Synbyotic therapy promoted clinical benefits in this patient.

Discussion: Therefore, this simple therapy may be a promising alternative in CKD and it should be tested in larger studies.

Palabras clave:

Enfermedad renal crónica. Microbiota. Simbióticos. Diarrea. Hemodiálisis.

Resumen

Introducción: los pacientes con enfermedad renal crónica (ERC) a menudo tienen síntomas gastrointestinales que pueden provocar desnutrición y un impacto negativo en su calidad de vida. La modulación de la microbiota intestinal puede ser una estrategia para promover la salud del huésped y la homeostasis.

Caso clínico: los autores presentan un caso de diarrea crónica de etiología desconocida en un paciente en hemodiálisis (HD). Después de varias intervenciones fallidas durante un año, se realizó el tratamiento simbiótico. Los episodios de diarrea cesaron después de tres meses de la suplementación diaria y ambos parámetros bioquímicos y nutricionales mejoraron. La terapia con simbióticos promovió beneficios clínicos para este paciente.

Discusión: por lo tanto, esta sencilla terapia puede ser una alternativa prometedora en la ERC y debe ser probada en estudios más amplios.

Received: 08/10/15
Accepted: 08/11/15

Borges NA, Farage NE, Barros AF, Ferreira DC, Fouque D, Mafra D. Synbiotic supplementation promotes improvement of chronic diarrhea of unknown etiology in patient with chronic kidney disease and provides better outcomes in dialysis. Nutr Hosp 2016;33:182-184

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INTRODUCTION

The role of gut microbiota in human health and development of pathologies has recently emerged as an important issue. The gut microbiota has the ability not only to influence the physiology of the intestine but also affects several metabolic functions (1). Alterations to the commensal flora contribute to the pathogenesis of diverse illnesses such as inflammatory bowel disease, chronic inflammation, dyslipidemia, diabetes, atopic disorders, cardiovascular diseases, neoplasms and obesity (2). According to Barros et al. 2015, chronic kidney disease (CKD) patients may acquire an imbalance of gut microbiota (3). Modulation of gut microbiota has emerged as a promising therapeutic strategy to promote host health, including CKD patients (4,5).

The reestablishment of gut balance by using probiotics, prebiotics and synbiotics has been studied for various diseases (6). Probiotics are live microorganisms which when administered in adequate amounts confer a health benefit to the host (7). Prebiotics are selectively fermented ingredients that result in specific changes in the composition and/or activity of the gastrointestinal microbiota conferring health benefits to the host (8). Finally, synbiotics are a combination of probiotics and prebiotics administered together (6). Synbiotic therapy has been shown to be specifically effective for improving the intestinal environment in various medical conditions (9). Synbiotic therapy has been shown to reduce septic complications in major abdominal surgery, trauma and intensive care unit patients (10).

Studies concerning the effects of synbiotic therapy in CKD patients are uncommon. One study showed that synbiotic therapy resulted in a decrease of serum p-cresol levels (a uremic toxin from gut microbiota) and normalized bowel habits in hemodialysis (HD) patients (11) and another study in non-dialyzed CKD patients that received synbiotic therapy for four weeks also showed that total plasma p-cresol levels was reduced however the gastrointestinal symptoms were not ameliorated (12).

Bowel habit is a non-invasive indicator of bowel function and condition of the intestinal flora. Abnormal defecation is one of the symptoms that reduce the quality of life in CKD patients who are undergoing HD (11). Here, we describe the case of a CKD patient with chronic diarrhea of unknown etiology who received a synbiotic treatment.

CASE REPORT

A 66 year-old male HD patient has been suffering from reoccurring episodes of diarrhea for one year. He weighed 60 kg and had a body mass index (BMI) of 19.6 kg/m^2, and he had been diagnosed with diabetic nephropathy. He had been under renal replacement therapy (RRT) 3 times a week for four hours, for nine years. The patient's medical history showed high blood pressure, dilated cardiomyopathy and he underwent cholecystectomy several years ago. The patient was currently taking losartan, clonidine, folic acid and calcium carbonate. The fully informed consent was obtained in writing from patient.

The Subjective Global Assessment (SGA), a tool that assesses patients' medical history and clinical and physical examinations, revealed intensive diarrheal episodes (5-10 times a day), which interfered with the patient's sleep and caused the patient to miss his hemodialysis sessions frequently. Endoscopy was performed and showed gastritis. Colonoscopy and parasitological examination did not detect a specific disease.

In the absence of an accurate diagnosis, the patient began taking anti-diarrheal medication and followed various dietary treatments including soluble fiber supplement, diet for Crohn's disease, lactose intolerance and gluten intolerance. There was no therapeutic success and the diarrhea persisted.

Approximately one year after the onset of the diarrhea episodes and after several failed interventions, the patient began taking synbiotics. Each dose (sachet) of the prescribed product was composed of *Lactobacillus paracasei* (10^8-10^9 Colony Forming Units [CFU]), *Lactobacillus rhamnosus* (10^8-10^9 CFU), *Lactobacillus aidophilus* (10^8-10^9 CFU), *Bifidobacterium lactis* (10^8-10^9 CFU) and fructooligosaccharides (FOS) (6 g).

Fifteen days later, without any other concomitant intervention for the treatment of diarrhea and using only the synbiotic supplement of one dose per day, the patient reported a reduction in the frequency of bowel movements. After one month of this daily supplementation, the patient reported alternate days without diarrhea and a normal sleep pattern was re-established, due to the absence of diarrhea at night time. After three months of daily supplementation the episodes of diarrhea had ceased totally and he did not miss his hemodialysis sessions anymore.

Improvement of various laboratory parameters was reported as a consequence of normalized attendance to the HD sessions regularly. The evolution of the biochemical parameters is shown in table I. After six months of synbiotic supplementation, there was no recurrence of diarrhea. The patient benefited from a weight gain of 5 kg (BMI = 21.2 kg/m^2) and reported that he felt more inclined to deal with his daily activities.

Table I. Biochemical parameters before and after the synbiotic therapy

Biochemical parameters	Before synbiotics	After synbiotics	
		(3 months)	*(6 months)*
Glucose (mg/dL)	130	120	127
Hemoglobin (g/dL)	8.8	12.5	11.0
Hematocrit (%)	27.0	36.4	32
Urea (pre-dialysis) (mg/dL)	210	150	154
Creatinine (mg/dL)	9.4	9.0	9.5
Albumin (g/dL)	3.9	4.1	4.3
Calcium (mg/dL)	10.0	9.1	9.8
Potassium (mg/dL)	5.7	5.3	4.5
Phosphorus (mg/dL)	6.5	5.5	5.7

DISCUSSION

This case report shows how synbiotic therapy may have clinical applicability in CKD patients. Fifteen days after starting to take the synbiotic supplement the patient improved and after three months the diarrheal episodes of unknown etiology had ceased completely.

Gastrointestinal (GI) symptoms tend to increase in CKD patients compared to the general population (13). Approximately 76% of HD patients exhibit such symptoms (14). Strid et al. in an observational study showed that pain, indigestion, constipation, diarrhea and eating dysfunction were significantly worse in CKD patients than the general population (15). GI symptoms may result in malnutrition and can cause impaired well-being in these patients.

In this case report, the diarrheal episodes may have influenced the levels of albumin, since after the synbiotic therapy and the cessation of the diarrhea episodes, there was an improvement in albumin levels. This study also observed improvements in other laboratory parameters such as hemoglobin, hematocrit, pre-dialysis urea, phosphorus and potassium, which can be attributed to the regular hemodialysis treatments that were reestablished after the episodes of diarrhea ceased. There are a number of benefits of synbiotic therapy for CKD patients, such as a reduction of uremic toxins and endotoxemia, improvement in GI symptoms and microbiota function providing an improvement in their quality of life (QOL) (13).

Evaluation of QOL of the patient was not applied. However, after synbiotic supplementation the patient was satisfied with his sleep, and he felt more disposed and more capable of carrying out his daily activities. In fact, studies suggest that an improvement in QOL following synbiotic therapy is a credible hypothesis (16-18).

In the present case the benefits achieved from the synbiotic therapy suggest that possibly dysbiosis led to the persistent diarrhea episodes. In CKD patients, increased urea plasma levels lead to urea secretion in the intestine and urease, expressed by some gut bacteria species, promotes hydrolysis of urea resulting in the formation of large amounts of ammonia, which could affect the growth of commensal bacteria. In addition, other factors such as disease complications, low-fiber diet, frequent use of antibiotics, metabolic acidosis, intestinal wall edema and oral iron intake, can negatively affect the balance of the intestinal flora (19).

Recently, the search for ways to restore symbiosis has been the focus of several studies and, synbiotic therapy is one of the alternatives. However, research related to CKD patients is scarce and there is no consensus on the adequate dosing or duration of synbiotic supplementation. Factors such as survival rates of the GI probiotic strains and the characteristics of prebiotic varieties differ widely and are crucial for the definition of therapeutic conduct (13,20).

The potential of pre, pro and synbiotics deserves further investigations in CKD patients through well-designed intervention studies in order to understand the effectiveness and benefits of this promising therapy in depth.

Synbiotic therapy proved to be a simple and effective measure in this case of chronic diarrhea of unknown etiology in a CKD patient. This therapy had beneficial effects that may go far beyond the intestine.

This case study shows how synbiotic therapy may have clinical applicability in CKD patients. Synbiotic supplementation can be a simple strategy to modulate the gut microbiota and promote significant clinical benefits.

ACKNOWLEDGMENTS

This work was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

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