Short-term probiotic therapy alleviates small intestinal bacterial overgrowth, but does not improve intestinal permeability in chronic liver disease

Dong Shin Kwak[a], Dae Won Jun[a], Jae Gu Seo[b], Won Seok Chung[b], Soon-Eung Park[b], Kang Nyeong Lee[a], Waqar Khalid-Saeed[a], Hang Lak Lee[a], Oh Young Lee[a], Byung Chul Yoon[a] and Ho Soon Choi[a]

Aim: **Although numerous animal studies suggest that probiotic therapy has beneficial effects in various liver diseases, the evidence for beneficial effects in human liver disease is controversial. This study was carried out to investigate the efficacy of probiotic therapy in alleviating small intestinal bacterial overgrowth (SIBO) and permeability in chronic liver disease.**

Methods: **Fifty-three patients with chronic liver disease were randomized to either probiotic therapy or placebo. Six bacterial species were used: *Bifidobacterium bifidum*, *Bifidobacterium lactis*, *Bifidobacterium longum*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, and *Streptococcus thermophilus*. After 4 weeks, changes in the composition of fecal bacteria, SIBO, intestinal permeability, and clinical symptoms were examined.**

Results: **Three of the six probiotic species, *B. lactis*, *L. rhamnosus*, and *L. acidophilus*, increased in the feces of the probiotic therapy group ($P < 0.001$), whereas there was no change in fecal microbiota in the placebo group. SIBO disappeared in many individuals of the probiotic therapy group, but none in the placebo (24 vs. 0%, $P < 0.05$). General gastrointestinal symptoms also improved more in the probiotic group and improvement in intestinal permeability was slightly but not significantly more frequent in the probiotic arm than the placebo arm (50 vs. 31.3%, $P = 0.248$). Numbers of lactobacilli in stool were correlated negatively with intestinal permeability (P for trend < 0.05). Liver chemistry did not improve significantly in either group.**

Conclusions: **We conclude that short-term probiotic administration in chronic liver disease is effective in alleviating SIBO and clinical symptoms, but ineffective in improving intestinal permeability and liver function.** ***Eur J Gastroenterol Hepatol*** **26:1353–1359 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

European Journal of Gastroenterology & Hepatology 2014, **26**:1353–1359

Keywords: chronic liver disease, intestinal permeability, probiotic, small intestinal bacterial overgrowth

[a]Department of Internal Medicine, Hanyang University School of Medicine, Seoul and [b]Cell Biotech Co., Ltd, Gimpo, Republic of Korea

Correspondence to Dae Won Jun, MD, Department of Internal Medicine, Hanyang University School of Medicine, Haengdang-dong, Sungdong-gu, Seoul 133-792, Republic of Korea
Tel: +82 2 2290 8338; fax: +82 2 972 0068; e-mail: noshin@hanyang.ac.kr

Received 27 June 2014 **Accepted** 26 August 2014

Introduction

Small intestinal bacterial overgrowth (SIBO) is defined as 10^5 CFU/ml or more bacterial cells present in the proximal small bowel [1]. SIBO increases intestinal permeability, which acts as a template for bacterial peritonitis and chronic inflammation in cirrhotic patients, and can lead to bacterial translocation [1–9]. The increased intestinal permeability associated with SIBO is considered to increase the influx of lipopolysaccharide (LPS) endotoxin to the liver, aggravate chronic liver diseases, exacerbate digestive symptoms, and ultimately lead to complications [1–5]. Increased intestinal motility and altered stomach acidity or bile acid composition are considered to be related to SIBO [10–13]. Various treatments such as probiotics, prokinetics, and antibiotics are used to treat SIBO [5,14,15]. The effects of probiotics on portal pressure and cirrhotic complications have been studied recently.

Even though many animal studies indicate that probiotic therapy has beneficial effects on various liver diseases, the evidence for beneficial effects in the clinical field is very limited. There are reports that administration of probiotics decreased systemic inflammation and portal pressure in cirrhosis [2,3,5,16]. However, Pereg *et al.* [4] found that probiotic administration to patients with decompensated cirrhosis for 6 months did not result in significant improvement in liver function. Loguercio *et al.* [3] reported that the administration of a composite probiotic in patients with various chronic liver diseases decreased malondialdehyde and 4-hydroxynonenal, but failed to alter the levels of tumor necrosis factor-α, interleukin-6, and interleukin-10. Lata and colleagues found that administration of *Escherichia coli* strain Nissle led to the restoration of colonic flora and improvement in Child–Pugh scores [2]. Despite the promising results in experimental models and limited clinical evidence in chronic liver disease, well-designed placebo-controlled studies are clearly needed.

Most previous clinical trials have focused on the improvement of clinical parameters, for example, liver

0954-691X © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/MEG.0000000000000214