Probiotics versus antibiotics in the treatment of hepatic encephalopathy in cirrhotic patients

D. Georgescu1*, D. Radu1*, N. Basa1, I. Musta1, C. Gurban1, B. Rădoi2

1 "University of Medicine and Pharmacy “V. Babes”, Timisoara, Piata Eftimie Murgu 2, Romania
2 Banat’s University of Agricultural Sciences and Veterinary Medicine, Faculty of Food Processing Technology, Food Quality Department, 300645 Timișoara, C. Aradului 119, Romania

Received: 20 April 2011; Accepted: 14 May 2011

Abstract
The aim was assessment of efficiency of probiotic treatment versus oral antibiotics on hepatic encephalopathy in patients with nonalcoholic liver cirrhosis. Main results: The group with probiotics provided by natural yoghurt supplement had a significant reduction of time necessary to complete number connection test (NCT)-B from baseline mean time = 315,08 ± 22,78 seconds to final mean time = 294,4 ± 18,1 seconds (p<0,01). The second group who receive oral antibiotics also showed a significant reduction mean time necessary to complete NCT-B: from baseline 312,6 ± 22,44 seconds to 292 ± 20,56 seconds (p<0,01). There was no significant statistically difference between the group with probiotic treatment versus the group with antibiotics: 294,4 ± 18,1 sec versus 292 ± 20,56 sec (p=0,6633). NCT-A for the both groups was under the cut-off value (78 sec): 51,44 ± 7,32 versus 51,4 ± 6,92 (p=0,9842). In conclusions we noted a significant improvement of psychometric tests in patients receiving probiotics comparable to those with oral antibiotics with mitigation of neurocognitive dysfunction.

Keywords: probiotics, nonalcoholic liver cirrhosis, hepatic encephalopathy

1. Introduction
Probiotics are defined as living organisms that, when administered in sufficient numbers, are beneficial to the host [1]. The growing interest in probiotics comes as many scientists are now focused on the role of beneficial bacteria to aid digestion, boost natural defenses, and fight off bacteria that could cause health problems. Intestinal bacteria, being a part of a healthy human ecosystem, can benefit health by breaking down toxins, synthesizing vitamins, and defending against infection. They may also play a role in preventing such diseases as peptic ulcers, colorectal cancer, and inflammatory bowel disease [2]. *Bifidobacterium animalis* and *Bifidobacterium lactis* were previously described as two distinct species.

Presently, both are considered *B. animalis* with the subspecies *Bifidobacterium animalis* subsp animalis and *Bifidobacterium animalis* subsp lactis [3]. Recent studies reported that probiotic therapy could improve minimal hepatic encephalopathy (MHE) in patients with liver cirrhosis [4]. The aim of this study was the assessment of efficiency of probiotic treatment versus oral antibiotic in patients with nonalcoholic liver cirrhosis and MHE.

2. Materials and methods
Minimal hepatic encephalopathy (MHE) in a cohort of patients with liver cirrhosis and stage 0 for clinical hepatic encephalopathy according to West-Haven criteria, was diagnosed based on psychometric tests.
The psychological evaluation consisted on psychometric tests with separate assessment of NCT parts A and B, setting as cut-off values for part A: 78 seconds and for part B: 273 seconds with age related corrections. Results of NCT-A and B were reported as the number of seconds required to complete the task; therefore higher scores reveal greater impairment.

50 patients, sex ratio M/W=19/31, age between 35-54 years old, with nonalcoholic end stage liver diseases, Child-Pugh A (score 5 to 6 points) and MHE were enrolled in this open label study after taken patients informal consent and their families.

We randomly divided our patients in 2 groups. First group with 25 patients received usual treatment for liver disease plus probiotics as a mixture of lactobacillus acidophilus 750x10^6 and lactobacillus bifidus 250x10^6 living organisms, once a day at lunch time for 3 months.

The second group with 25 patients received usual medication plus Rifaximin 2x550mg/day, 10 days/month. After finishing 3 months of treatment we repeated gastroenterological, neurological and psychological evaluation.

3. Results and Discussions

The group with probiotics provided by natural yoghurt supplement had a significant reduction of time necessary to complete number connection test (NCT)-B from baseline mean time = 315.08±22.78 seconds to final mean time = 294.4±18.1 seconds (p<0.01).

The second group who receive oral antibiotics also showed a significant reduction mean time necessary to complete NCT-B: from baseline 312.6±22.44 seconds to 292±20.56 seconds (p<0.01). There was no significant statistically difference between the group with probiotic treatment versus the group with antibiotics: 294.4±18.1 sec versus 292±20.56 sec (p=0.6633).

Figure 1. Psychometric tests NCT–A and NCT–B

Figure 2. NCT-B before and after probiotics treatment

Figure 3. NCT-B in group with antibiotic treatment
NCT-A for both groups was under the cut-off value (78 sec): 51.44±7.32 versus 51.4±6.92 (p=0.9842).

Hepatic encephalopathy occurs due to the production of neurotoxins in the colon, largely by bacterial degradation of luminal contents. The small intestine is relatively free of bacteria in normal individuals. Merra and colleagues demonstrated that the small intestine in cirrhotic patients frequently has bacterial overgrowth [5]. Compared with noncirrhotic controls, 3.3% of whom demonstrated a positive lactulose breath test, 18 of 30 (60%) cirrhotic patients were positive. Bacterial overgrowth was more common in individuals with advanced cirrhosis (20%, 50%, and 80% in Child class A, B, and C cirrhosis, respectively). These findings suggest a role for bacterial overgrowth in the pathogenesis of hepatic encephalopathy.

In this view a possible mechanism involved in improvement of brain functions secondary to regular probiotics intake is modifying intestinal flora with diminishing ammonia producing flora and decreasing bacterial translocation. That might reduce the induction of inflammatory mediators that trigger some neurocognitive pathways via false neurotransmitters.

4. Conclusions

MHE is a neurocognitive complication of cirrhosis associated with an increased rate of progression to overt hepatic encephalopathy; detection being not possible by clinical examination only by psychometric tests. It occurs due to the production of neurotoxins in the colon secondary to bacterial overgrowth having as main treatment lactulose and oral antibiotics.

Our study noted a significant improvement of psychometric tests in cirrhotic patients receiving probiotics comparable to those with oral antibiotics, resulting in a significant mitigation of neurocognitive dysfunction.

References

3. Masco, Liesbeth; Marco Ventura, Ralf Zink, Geert Huys, Jean Swings, "Polyphasic taxonomic analysis of Bifidobacterium animalis and Bifidobacterium lactis reveals relatedness at the subspecies level: reclassification of Bifidobacterium animalis as Bifidobacterium animalis subsp. animalis subsp. nov. and Bifidobacterium lactis as Bifidobacterium animalis subsp. lactis subsp. nov., IJSEN, 54(4) doi:10.1099/ijs.0.03011-0