

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

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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 ± 18,1seconds(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.

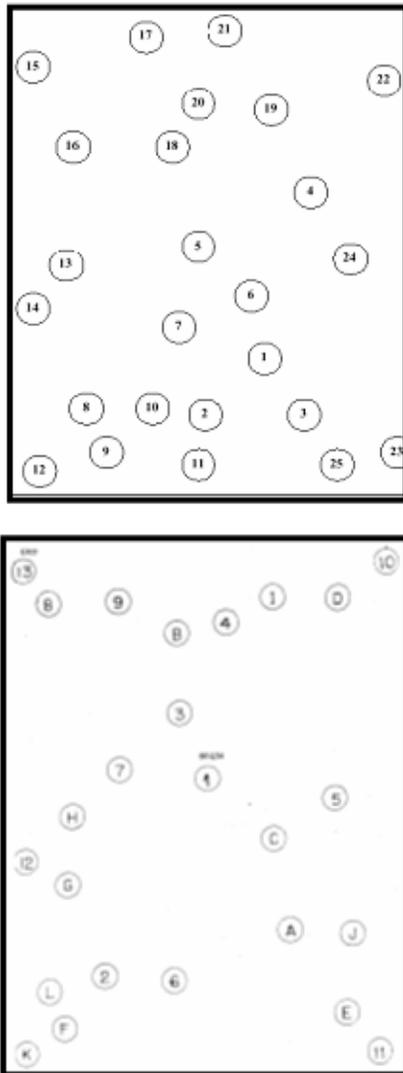


Figure 1. Psychometric tests NCT-A and NCT-B

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 750×10^6 and lactobacillus bifidus 250×10^6 living organisms, once a day at lunch time for 3 months.

The second group with 25 patients received usual medication plus Rifaximin $2 \times 550 \text{mg/day}$, 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= $315,08 \pm 22,78$ seconds to final mean time = $294,4 \pm 18,1$ seconds ($p < 0,01$).

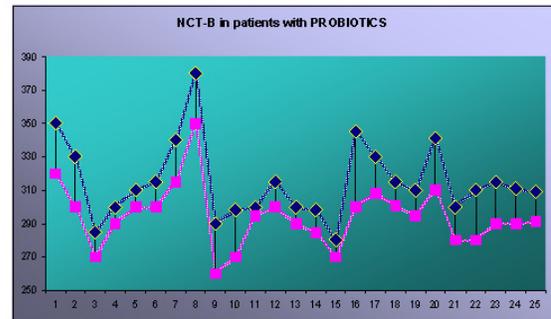


Figure 2. NCT-B before and after probiotics treatment

The second group who receive oral antibiotics also showed a significant reduction mean time necessary to complete NCT-B: from baseline $312,6 \pm 22,44$ seconds to $292 \pm 20,56$ seconds ($p < 0,01$). There was no significant statistically difference between the group with probiotic treatment versus the group with antibiotics : $294,4 \pm 18,1$ sec versus $292 \pm 20,56$ sec ($p = 0,6633$).

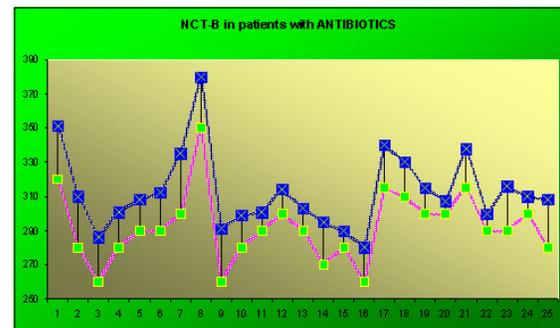


Figure 3. NCT-B in group with antibiotic treatment

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).

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

1. de Martin A. In live bacteria, food makers see a bonanza, *NY Times*. January 22, 2007, <http://www.nytimes.com/2007/01/22/business/22yogurt.html>
2. Friedrich MJ., Benefits of gut microflora under study, *JAMA.*, 2008, 299(2), 162, [doi: 10.1001/jama.2007.55-b](https://doi.org/10.1001/jama.2007.55-b)
3. Masco, Liesbeth; Marco Ventura, Ralf Zink, Geert Huys1, 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/ij.s.0.03011-0](https://doi.org/10.1099/ij.s.0.03011-0)
4. Bajaj J, Saeian K, Pajewski N, Pinkerton S., Is it cost-effective to treat minimal hepatic encephalopathy to prevent traffic accidents? A decision analysis., *Am J Gastroenterol.*, 2008, 103, 48, [doi:10.1111/j.1572-0241.2008.02139.5.x](https://doi.org/10.1111/j.1572-0241.2008.02139.5.x)
5. Merra G, Dal Lago A, Scarpellini E, et al., Small intestinal bacterial overgrowth of colonic-type carbohydrate fermentative bacteria in cirrhotic patients., *Am. J. Gastroenterol.*, 2008, 103, P852,