Effect of a Probiotic Preparation (VSL#3) on Cardiovascular Risk Parameters in Critically-Ill Patients

Sarvin Sanaie1, Mehrangiz Ebrahimi-Mameghani2, Ata Mahmoodpoor3, Kamran Shadvar4, Samad EJ Golzari4,5

1Student Research Center, Faculty of Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran
2Nutrition Research Center, Faculty of Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran
3Anesthesiology and Intensive Care Department, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
4Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
5Students’ Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

ABSTRACT

Introduction: Cardiovascular disease (CVD) counts for a major portion of morbidity and mortality globally mostly accompanied by lipid abnormalities. Being at increased risk of cardiac injury, critically ill patients suffer from various lipid disorders. Lipid homeostasis has been efficiently restored by the introduction of probiotics. The aim of this trial was to determine the effect of probiotics on inflammation, antioxidant capacity and lipid peroxidation in critically ill patients.

Methods: Forty patients admitted to the intensive care unit were randomized to receive placebo or probiotic for 7 days. Serum levels of triglyceride (TG), total cholesterol, HDL-C, LDL-C and high-sensitivity C-reactive protein (hs-CRP) were measured before initiation of the study and on the 7th day.

Results: There was a significant difference between two groups regarding the levels of TG, HDL and hs-CRP at the end of the study (P = 0.043, <0.001 and 0.003, respectively); however, there was not a significant difference in total cholesterol and LDL-C levels.

Conclusion: Administration of probiotics in critically ill patients reduced the levels of TG and hs-CRP and increased HDL-C levels. However, no significant change was detected in levels of total cholesterol or LDL-C.
of high-sensitivity C-reactive protein (hs-CRP), a marker of systemic inflammation and a mediator of atherothrombotic disease, is in significant correlation with cardiovascular disease risk; inflammation is a major factor in atherothrombotic disease.\(^6\) Global risk assessment uses hs-CRP as an index in the primary prevention of cardiovascular disease.\(^{17}\)

Probiotics, live microorganisms providing a health benefit on their host when used in adequate amounts,\(^{18}\) are of beneficial effects in the prevention and treatment of different disease. Heterogeneous results have been given on the effects of probiotics consumption on the plasma lipid profile in different studies; yet, positive changes in lipid profile have been observed with the use of probiotics.\(^{19,20}\) In addition, probiotics not only are of useful effects on cellular immunity but also help to preserve the balance between pro- and anti-inflammatory cytokines.\(^21\) Despite the introduction of numerous pharmacologic lipid lowering therapies, there are known side effects.\(^22\) Hence, the use of probiotics considering their natural and safe properties and low ability of triggering adverse effects\(^23\) seems logical for serum lipid improvement.

The purpose of this randomized clinical trial was to determine the effect of probiotic containing lactobacillus, bifidobacterium and streptococcus thermophilus on lipid profile and hs-CRP levels in critically ill patients in the intensive care unit.

**Methods**

After approval of ethics committee of Tabriz University of Medical Sciences and obtaining written informed consent from the patients or their legal guardians, 40 patients who were admitted between December of 2011 and October of 2012 to the ICU of the Shohada Hospital (Tabriz, Iran) were enrolled in this trial. Inclusion criteria were critically ill patients who were expected to stay in ICU for at least 7 days aged 18 to 40 years old receiving enteral nutrition. Exclusion criteria were patients who could not tolerate enteral nutrition, those with unstable hemodynamic, immune disorders, history of diabetes mellitus and hyperlipidemia, intestinal obstruction or ischemia, cancer and patients who were expected to expire in the next 24 hours. Patients were randomized to two 20-person groups; the first group received standard treatment plus placebo and the second group received standard treatment plus VSL#3, 2 sachets daily for 7 days. Each sachet of probiotics (VSL#3; VSL Pharmaceuticals, Ft Lauderdale, FL) contained 450 billion viable lyophilized bacteria consisting of 4 strains of *Lactobacillus* (*L. casei, L. plantarum, L. acidophilus*, and *L. delbrueckii* subsp. *Bulgariicus*), 3 strains of *Bifidobacterium* (*B. longum, B. breve, and B. infantis*) and *Streptococcus salivarius* subsp. *Thermophilus*.

All patients received enteral nutrition with Fresubin original fibre (*Fresenius Kabi, Homburg, Germany*) at the first 24-hour of admission via nasogastric tube. Energy requirements were calculated as 25–30 kcal/kg. Fasting blood samples were obtained from each patient to evaluate lipid profile and hs-CRP on days 1 and 7. Serum triglyceride, total cholesterol, and HDL-cholesterol concentrations were determined by routine clinical assays using commercial kits on an automated analyzer. Serum LDL-cholesterol concentrations were calculated based on the Friedewald calculation (LDL = TC - HDL - TG/5). Data were analyzed by SPSS 16. P values<0.05 were considered significant for all statistical tests.

**Results**

There were 20 patients in each group. No significant differences in patients’ demographic data between two groups were observed (Table 1). Levels of TG, total cholesterol, LDL-C, HDL-C and hs-CRP at the baseline and at the end of the study are shown in Table 2. There was a significant difference between two groups in levels of TG, HDL and hs-CRP at the end of the study (*P* = 0.043, <0.001 and 0.003, respectively); however, there was no significant difference in total cholesterol and LDL-C levels. In addition, levels of TG significantly decreased while levels of HDL-C significantly increased after the treatment period in probiotic group (*P* = 0.001 and 0.041, respectively). Levels of hs-CRP in both groups are shown in Figure 1.

**Table 1. Demographic data of patients**

<table>
<thead>
<tr>
<th>Control group</th>
<th>Probiotic group</th>
<th><em>P</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>35.60±5.03*</td>
<td>33.60±5.50</td>
</tr>
<tr>
<td>Male/Female</td>
<td>14/6</td>
<td>13/7</td>
</tr>
<tr>
<td>BMI</td>
<td>24.70±3</td>
<td>24.30±2.92</td>
</tr>
</tbody>
</table>

*Mean±SD, BMI: Body Mass Index*

**Figure 1. Mean (±SD) hs-CRP levels in two groups of patients.**

**Discussion**

The present study used a double-blind, placebo-controlled, randomized design to determine the effects of probiotics on lipid profile and inflammation in critically ill, enterally...
fed patients. A significant effect on the levels of TG and HDL-C was observed following adding probiotics to the enteral feeding of the patients; however, no significant effect was attained for total cholesterol and LDL-C in our study. In a study performed on 32 healthy subjects, it was reported that administration of probiotics was associated with a significant reduction in serum total cholesterol, LDL-C and TG and increase in HDL-C. In another study on type 2 diabetic patients, no noteworthy changes were reported in TG and HDL-C, while probiotic group had significantly decreased total cholesterol levels: HDL-C ratio and LDL-C: HDL-C ratio. In a meta-analysis, it was indicated that a probiotics rich diet decreases total cholesterol and LDL-C in participants with high, borderline high and normal cholesterol levels. The varied effects of probiotics on lipid profile observed in the studies might be as a result of the type of the patient population and also the used probiotic. In our study, probiotics could not have applied their LDL-C lowering effects, as we assessed their effects in critically ill population who generally present low LDL-C levels.

The patients who received probiotic showed a significant reduction in hs-CRP levels. hs-CRP as a marker of systemic inflammation is a strong independent predictor of risk of future myocardial infarction, stroke, peripheral arterial disease, and vascular death. In the present study, a significant reduction in hs-CRP concentrations following the treatment course with probiotics was observed. Similar findings were reported by Asemi et al. who studied the effect of daily consumption of probiotic yoghurt vs. conventional yoghurt on inflammatory factors in pregnant women. Their results showed that the probiotic yogurt decreased serum hs-CRP level, whereas there was no significant change in serum hs-CRP level in the conventional yoghurt group. In another study which compared a multifunctional (active) diet (AD) including a probiotic strain (Lactobacillus plantarum) with a control diet (CD) in healthy adults, CD did not alter the measured metabolic variables; however, AD changed hs-CRP levels significantly. Yet, the results of this study cannot be credited to the sole probiotic; as a mixed multifunctional diet was used and the obtained results might have been due to the use of antioxidant-rich foods, oily fish or wholegrain products.

In conclusion, the results of this randomized trial suggest that administration of probiotics in critically ill patients compared to placebo-treated patients significantly reduces the levels of TG and hs-CRP and increases HDL-C levels. However, it does not significantly affect the levels of total cholesterol and LDL-C. Hence, further studies with larger sample sizes are required to clarify their usefulness in this group of patients.

**Ethical issues:** The study was approved by the institutional review board, and written informed consent was obtained from all participants.

**Competing interests:** The authors had no competing interests to declare in relation to this article.

**References**

C-reactive protein and coronary heart disease in the MRFIT


