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

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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.

Introduction

Cardiovascular disease (CVD) counts for a major portion of morbidity and mortality globally mostly accompanied by lipid abnormalities. Abnormal levels of high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C) and triglyceride (TG) could accompany a higher prevalence of CVD. Elevated LDL-C and reduced HDL-C levels are already-confirmed CVD risk factors with evidence suggesting that significant increase in HDL-C could be set as an important therapeutic goal. While critically ill patients frequently suffer from metabolic disturbances such as various lipid disorders, elevated triglyceride levels followed by increase in very low-density lipoprotein (VLDL), and low circulating HDL-C are their main characteristic in critically ill patients. LDL-C levels are also decreased. Commonly seen in critically ill patients, systemic inflammation and sepsis also accompany severe metabolic imbalances including decreases in HDL-C and LDL-C and high levels of TG. Association between systemic inflammation and lipid metabolism has been clearly established in many studies. In sepsis, enhanced production of hepatic VLDL and/or inhibited peripheral and hepatic VLDL clearance lead to increase in plasma TG within VLDL. In contrast, sepsis decreases plasma cholesterol within LDL-C and mainly HDL-C. Furthermore, lipid metabolism disorders are accompanied by worse prognosis in critically ill patients. Indices of lipid metabolism have been found to be related to the severity of illness, the occurrence of sepsis and survival in critically ill patients. In addition, ICU patients are at increased risk of cardiac disorders due to the underlying presence of coronary circulation atherosclerosis and other non-cardiac factors including increased tissue oxygen demands, anemia, sepsis, mechanical ventilation, and hemodynamic instability. Furthermore, assessment of myocardial injury as an independent determinant of hospital mortality would make it possible to recognize ICU patients at augmented risk of death. The incidence of myocardial injury is usually defined by elevated levels of cardiac troponin I.
of high-sensitivity C-reactive protein (hs-CRP), a marker of systemic inflammation and a mediator of atherothrombosis, is in significant correlation with cardiovascular disease risk; inflammation is a major factor in atherothrombosis. Global risk assessment uses hs-CRP as an index in the primary prevention of cardiovascular disease.

Probiotics, live microorganisms providing a health benefit on their host when used in adequate amounts, 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. 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. Despite the introduction of numerous pharmacologic lipid lowering therapies, there are known side effects. Hence, the use of probiotics considering their natural and safe properties and low ability of triggering adverse effects 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. Bulgaricus), 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.

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></th>
<th>Control group</th>
<th>Probiotic group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>35.60±5.03</td>
<td>33.60±5.50</td>
<td>0.238</td>
</tr>
<tr>
<td>Male/Female</td>
<td>14/6</td>
<td>13/7</td>
<td>0.500</td>
</tr>
<tr>
<td>BMI</td>
<td>24.70±3</td>
<td>24.30±2.92</td>
<td>0.677</td>
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</tbody>
</table>

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
Probiotics in critically-ill patients

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. 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.

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

70