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Communication

Parenteral nutrition in short bowel syndrome patients, regardless of its duration, increases serum proinflammatory cytokines☆

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ABSTRACT

Short bowel syndrome is a severe malabsorption disorder, and prolonged parenteral nutrition is essential for survival in some cases. Among the undesirable effects of long-term parenteral nutrition is an increase in proinflammatory cytokines. The aim of the present study was to measure the serum levels of interleukin-6, interleukin-10, tumor necrosis factor alpha, and transforming growth factor beta, in patients with short bowel syndrome on cyclic parenteral nutrition and patients who had previously received but no longer require parenteral nutrition. The study was cross-sectional and observational. Three groups were studied as follows: Parenteral nutrition group, 9 patients with short bowel syndrome that receive cyclic parenteral nutrition; Oral nutrition group, 10 patients with the same syndrome who had been weaned off parenteral nutrition for at least 1 year prior to the study; Control group, 13 healthy adults, matched for age and sex to parenteral and oral groups. The following data were collected: age, tobacco use, drug therapies, dietary intake, body weight, height, blood collection. All interleukins were significantly higher in the parenteral group compared with the control group as follows: interleukin-6: 22 ± 19 vs 1.5 ± 1.4 pg/mL, $P = .0002$; transforming growth factor β: 854 ± 204 vs 607 ± 280 pg/mL, $P = .04$; interleukin-10: 8 ± 37 vs 0.6 ± 4, $P = .03$; tumor necrosis factor α: 20 ± 8 vs 8 ± 4 pg/mL, $P < .0001$. We concluded that parenteral nutrition in short bowel syndrome patients, regardless of its duration, increases serum proinflammatory cytokines.

Abbreviations: PG, Parenteral nutrition group; OG, Oral nutrition group; CG, Control group; SBS, Short bowel syndrome; PN, Parenteral nutrition; TNF-α, Tumor necrosis factor α; IL-6, Interleukin-6; IL-10, interleukin-10; TGF-β, Transforming growth factor β.

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1. Introduction

In the United States, short bowel syndrome (SBS) affects 3 to 4 individuals per million. Fifteen percent of the adults with SBS have undergone intestinal resection; 75% and 25% of the resected patients have been submitted to massive intestinal resection and multiple resections, respectively [1].

SBS generally originates from intestinal ischemia, neoplasms, post-surgical events, inflammatory bowel diseases [1–3]. An extensive intestinal resection, including the ileocecal valve, in some cases, reduces the absorption area and impairs the secretion of gastrointestinal hormones. Consequently, individuals with SBS experience marked weight loss and malabsorption of nutrients, electrolytes, and fluids and require parenteral nutritional therapy (PN) [4], which is essential for survival and constitutes an adjuvant therapy along with the oral diet [5].

Since home PN is not a therapeutic option provided by the Brazilian public health system, our hospital provides intermittent parenteral nutrition to patients with SBS and severe malabsorption [6]. These patients are hospitalized every 10 to 30 days to receive PN for 3 to 8 days, depending on the severity of symptoms such as diarrhea, dehydration, and poor nutritional status [6].

Nevertheless, PN is not exempt from complications such as metabolic, mechanic, gastrointestinal, and infectious [7]. Other hazardous effects of PN are currently under investigation, especially those associated with the presence of inflammation [8–11]. Tumor necrosis factor α (TNF-α) and interleukin-6 (IL-6) are innate immune cytokines that exhibit systemic pro-inflammatory action. Higher levels of TNF-α receptors p55 and p75 have been described during the use of PN [8]. TNF-α, in turn, leads to increase in basal metabolic rate and stimulates the synthesis of IL-6. The higher basal metabolic rate might demand larger infusion of calories and proteins to maintain the nutritional status [11]. On the other hand, interleukin-10 (IL-10) is the only innate immunity cytokine that displays anti-inflammatory activity. It suppresses inflammatory responses that involve macrophages, the main sources of IL-6 and TNF-α. In fact, some T cells that produce IL-10 also generate transforming growth factor beta (TGF-β). Like IL-10, TGF-β inhibits inflammatory responses that rely on macrophages (the main sources of IL-6 and TNF-α).

Therefore the objective of the present study was to compare the inflammatory status of SBS patients that receive cyclic PN (PG) with SBS patients in ambulatory care (OG) and with a control group (CG) through the serum measurement of the following cytokines: IL-6, IL-10, TNF-α, and TGF-β. We hypothesized that the PN-dependent SBS PN group patients had higher pro-inflammatory cytokine levels when compared to the CG group.

2. Methods and materials

2.1. Selection and brief characterization of participants

This was a cross-sectional observational study approved by the Research Ethics Committee of the University Hospital of Ribeirão Preto Medical School, University of São Paulo (HCFMRP-USP) under process number 8667/2009. All the participants signed a written informed consent before entering the study. All the SBS patients were recruited from the Metabolic Unit and the Ambulatory Nutrology Unit of the University Hospital at the Ribeirão Preto Medical School, São Paulo University.

The participants were grouped as follows: Parenteral group (PG) patients with SBS that regularly receive parenteral nutrition therapy; Oral group (OG) patients with SBS in ambulatory care; Control group (CG). Exclusion criteria for PG, OG and CG were as follows: surgical procedure less than one year prior to data collection; signs or symptoms of infection [12], previous surgical resection due to neoplasm; impaired cognitive function. The CG was matched to PG and OG for sex and age.

2.1.1. *Patients that received parenteral nutrition therapy (PG)*

This group consisted of all the SBS patients that, at the time of data collection, met the inclusion criteria and received PN at the Metabolic Unit of the University Hospital at the Ribeirão Preto Medical School, São Paulo University.

2.1.2. *Patients in ambulatory care (OG)*

This group comprised SBS patients attended in the Ambulatory Nutrology Unit of the University Hospital at the Ribeirão Preto Medical School, São Paulo University.

The characteristics of PG and OG regarding remaining small intestinal length, proportion of remaining colon, duration of PN, amount of parenteral calories, type of PN lipid emulsion and time elapsed after weaning off PN are shown in Table 1.

2.1.3. *Control group*

This group included members of the staff of HCFMRP-USP, paired for age and sex to PG and OG who met the pre-determined inclusion criteria.

2.2. Experimental design

Initially we analyzed the medical records of all the patients with SBS attended in Metabolic Unit and in the Ambulatory Nutrology Unit of the University Hospital at the Ribeirão Preto Medical School, São Paulo University. The eligible SBS patients were informed about the study during hospital admission for parenteral nutrition therapy (PG), by phone call or in the ambulatory clinic (OG). Recruitment of the control group was completed via advertisement using the hospital intranet and included hospital staff members. After acceptance, the volunteers were invited to come to the hospital for the protocol implementation. They came in the morning, after an overnight fast and were submitted to data collection that included clinical examination, measurement of body temperature, heart and respiratory rates, blood pressure, anthropometry, habitual dietary intake, age, tobacco use, and drug therapies. We also draw blood for measurement of C-reactive protein, TNF-α, IL-6, IL-10, and TGF-β.

2.3. Habitual dietary intake

A Food Frequency Questionnaire was applied to assess routine food consumption [13]. The computation of nutrient intake was performed with the software Dietsys (U.S. Dept of Health and Human Services, Rockville, MD, USA).