Impact of Intravenous Omega-3-Enriched Lipid Emulsion on Liver Enzyme and Triglyceride Serum Levels of Children Undergoing Gastrointestinal Surgery

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Impact of Intravenous Omega-3-Enriched Lipid Emulsion on Liver Enzyme and Triglyceride Serum Levels of Children Undergoing Gastrointestinal Surgery

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ABSTRACT

Purpose: To investigate the impact of omega-3-enriched lipid emulsion (LE) on liver enzyme (aspartate transaminase [AST] and alanine aminotransferase [ALT]) and triglyceride (TG) levels of children undergoing gastrointestinal surgery.
Methods: This experimental randomized controlled group pretest-posttest design study included 14 children who underwent gastrointestinal surgery due to duodenal atresia, jejunal atresia, esophageal atresia, and need for parenteral nutrition for a minimum of 3 days at RSUD Dr. Soetomo Surabaya between August 2018 and January 2019. These children were divided into two groups, those who received standard intravenous LE (medium-chain triglyceride [MCT]/long-chain triglyceride [LCT]) and those who received intravenous omega-3-enriched LE. Differences in AST, ALT, and TG levels were measured before surgery and 3 days after the administration of parenteral nutrition.
Results: Liver enzyme and TG levels in each group did not differ significantly before versus 3 days after surgery. However, TG levels were significantly lower in the omega-3-enriched intravenous LE group (p=0.041) at 3 days after surgery, and statistically significant difference in changes in TG levels was noted at 3 days after surgery between MCT/LCT intravenous LE group and the omega-3-enriched intravenous LE group (p=0.008).
Conclusion: The intravenous omega-3-enriched LE had a better TG-lowering effect than the MCT/LCT intravenous LE in children undergoing gastrointestinal surgery.

Keywords: Omega-3; Fatty acids; Parenteral nutrition; Gastrointestinal surgery

INTRODUCTION

The role of parenteral nutrition is critical in patients who cannot receive oral or enteral nutrition, particularly pediatric patients undergoing gastrointestinal surgery [1]. Pediatric patients who undergo gastrointestinal surgery are more likely to suffer from malabsorption [2].

Conflicts of Interest and Sources of Funding

The authors have no financial conflicts of interest.

Meanwhile, patients who are unable to obtain oral nutrition within 3 days should be given parenteral nutrition within 24–48 hours [3]. Chawla and Teitelbaum [4] stated that parenteral nutrition is highly recommended in cases of impaired intestine absorption.

Some studies have shown an increased risk of liver injury in patients receiving parenteral nutrition [5,6]. Other studies reported a higher risk of hypertriglyceridemia in patients receiving soybean oil–based parenteral nutrition [7,8].

Soybean oil-based intravenous fat, one of the most common types of intravenous lipid emulsions (LEs), mainly contains linoleic acid (omega-6) or a 50:50 mixture with vegetable oil rich in medium-chain triglyceride/long-chain triglyceride (MCT/LCT). An intravenous LE enriched with fish oil containing docosahexaenoic acid and eicosapentaenoic acid (omega-3) was proven as a balanced source of fat that exhibits anti-inflammatory properties; it also exhibits hepatoprotective properties in infants weighing <1,500 g [9]. To date, no studies have aimed to compare the effects of an MCT/LCT intravenous LE to those of an omega-3-enriched LE on liver function and TG levels in children after gastrointestinal surgery in whom oral nutrition had not yet been resumed.

This study aimed to investigate the impact of omega-3-enriched LE on liver enzyme (aspartate transaminase [AST] and alanine transaminase [ALT]) and TG levels in children undergoing gastrointestinal surgery.

MATERIALS AND METHODS

This experimental randomized controlled group pretest-posttest design study aimed to explain the effect of omega-3-enriched LE in parenteral nutrition therapy on liver function and TG levels in pediatric patients post gastrointestinal surgery compared to standard LEs.

Participants of this study were pediatric patients undergoing gastrointestinal surgery at RSUD Dr. Soetomo Surabaya between August 2018 and January 2019, with the inclusion criteria of 0-18 years of age, having undergone gastrointestinal surgery due to duodenal atresia, jejunal atresia, or esophageal atresia; patients requiring parenteral nutrition for at least 3 days; and willingness to participate in the study (informed consent provided by their parents/guardians). The exclusion criteria of this study were one or more chronic diseases involving the heart, liver, or kidney; and history of fish/egg/soy/nut protein allergy. The drop-out criteria for the participants included withdrawal during the study, passing away before receiving parenteral nutrition for 3 days, loss to follow-up, and any allergic reaction to fish/egg/soy/nut protein.

SMOFlipid (Fresenius Kabi USA, Lake Zurich, IL, USA), a brand of omega-3-enriched intravenous LE, contains 30% soybean oil as a source of LCT, 30% coconut oil as a source of MCT, 25% olive oil, and 15% fish oil. SMOFlipid is given for 3 consecutive days at a dose of 1–4 g/kg/day [10]. The standard intravenous LE is Lipofundin 20% (B. Braun, Melsungen, Germany), which contains 50% soybean oil as a source of LCT and 50% coconut oil as a source of MCT. Lipofundin 20% is given for 3 consecutive days at a dose of 1–4 g/kg/day. Differences in liver function levels, namely AST and ALT, and TG levels were measured before surgery and 3 days after the administration of parenteral nutrition. Statistical analyses were performed using paired sample *t*-tests to investigate the effect of omega-3-enriched intravenous LEs on liver function and TG levels.

RESULTS

Fourteen pediatric inpatients at RSUD Dr. Soetomo Surabaya took part in this study; all already met the inclusion and exclusion criteria. The study participants were classified into two groups: that receiving the MCT/LCT intravenous LE, and that receiving the omega-3-enriched intravenous LE.

As shown in **Table 1**, based on age, sex, weight at arrival, and surgery type, there were no statistically significant differences between the MCT/LCT intravenous LE group and the omega-3-enriched intravenous LE group (p>0.05). The duration of parenteral nutrition administration or hospitalization showed no statistically significant intergroup differences (p>0.05).

In this study, levels of hemoglobin, leukocytes, C-reactive protein (CRP), AST, ALT, albumin, and TG did not differ significantly before versus 3 days after surgery in either group (**Table 2**). However, TG levels were significantly higher in the MCT/LCT intravenous LE group compared to the omega-3-enriched intravenous LEs group (p=0.041) at 3 days postoperative (**Table 3**).

There was no statistically significant intergroup difference in changes in laboratory parameters for hemoglobin, leukocytes, CRP, AST, ALT, or albumin at 3 days postoperative. This study showed statistically significant difference in changes in TG levels at 3 days postoperative between the MCT/LCT intravenous LE group and the omega-3-enriched intravenous LE group (p=0.008) (**Table 4**).

Table 1. Subjects' characteristics

Characteristic	MCT/LCT IVLE	Omega-3-enriched IVLE	p-value
Age (d)	14.0±12.1	14.1±17.1	0.749
Sex			1.000
Male	6 (85.7)	5 (71.4)	
Female	1 (14.3)	2 (28.6)	
Weight on admission (g)	2,271.4±603.2	2,608.5±911.7	0.430
Underlying condition			1.000
Esophageal atresia	1 (14.3)	1 (14.3)	
Duodenal atresia	3 (42.8)	3 (42.8)	
Jejunoileal atresia	1 (14.3)	1 (14.3)	
Ileal atresia	2 (28.6)	2 (28.6)	
Duration of PN (d)	30.0±20.3	29.0±34.8	0.201
Length of stay (d)	32.2±23.1	31.5±38.6	0.406

Values are presented as mean±standard deviation or number (%).
MCT: medium-chain triglyceride, LCT: long-chain triglyceride, IVLE: intravenous lipid emulsion, PN: parenteral nutrition.

Table 2. Preoperative laboratory parameters

Variable	MCT/LCT IVLE	Omega-3-enriched IVLE	p-value
Hb (g/dL)	16.5±2.9	15.1±2.4	0.480
Leukocyte (10^3/L)	14,764.2±9,488.9	11,912.8±6,610.4	0.526
CRP	4.9±5.6	6.3±3.6	0.277
AST (U/L)	49.4±19.3	44.2±30.9	0.371
ALT (U/L)	25.5±25.8	24.8±15.0	0.848
Albumin (g/L)	3.2±0.3	3.1±0.5	0.782
Triglyceride (mg/dL)	104.5±34.9	132.1±75.8	0.400

Values are presented as mean±standard deviation.
MCT: medium-chain triglyceride, LCT: long-chain triglyceride, IVLE: intravenous lipid emulsion, Hb: hemoglobin, CRP: C-reactive protein, AST: aspartate transaminase, ALT: alanine transaminase.

Table 3. Laboratory parameters at 3 days postoperative

Variable	MCT/LCT IVLE	Omega-3-enriched IVLE	*p*-value
Hb (g/dL)	14.3±1.9	13.6±2.6	0.555
Leukocyte (10^3/L)	14,388.5±5,641.0	11,935.7±5,242.0	0.416
CRP	7.3±6.1	9.2±4.4	0.522
AST (U/L)	46.0±11.8	38.8±21.3	0.141
ALT (U/L)	28.2±21.5	19.2±11.4	0.348
Albumin (g/L)	3.1±0.3	2.9±0.2	0.611
Triglyceride (mg/dL)	256.0±132.2	126.7±24.3	0.041

Values are presented as mean±standard deviation.
MCT: medium-chain triglyceride, LCT: long-chain triglyceride, IVLE: intravenous lipid emulsion, Hb: hemoglobin, CRP: C-reactive protein, AST: aspartate transaminase, ALT: alanine transaminase.

Table 4. Differences in laboratory parameters between preoperative and 3 days postoperative

Variable	MCT/LCT IVLE	Omega-3-enriched IVLE	*p*-value
Hb (g/dL)	−2.2±2.1	−1.5±3.86	0.443
Leukocyte (10^3/L)	1,260.0±13,247.9	−1,611.4±6,551.4	0.985
CRP	2.4±6.8	2.8±5.2	0.879
AST (U/L)	−3.4±21.1	−5.5±10.2	0.747
ALT (U/L)	2.7±28.9	−5.5±10.7	0.223
Albumin (g/L)	−0.2±0.5	−0.2±0.6	0.793
Triglyceride (mg/dL)	151.4±114.6	−5.4±60.7	0.008

Values are presented as mean±standard deviation.
MCT: medium-chain triglyceride, LCT: long-chain triglyceride, IVLE: intravenous lipid emulsion, Hb: hemoglobin, CRP: C-reactive protein, AST: aspartate transaminase, ALT: alanine transaminase.

DISCUSSION

This study showed no significant differences in laboratory parameters such as hemoglobin, leukocytes, CRP, albumin, AST, and ALT, before surgery or 3 days after surgery, between the MCT/LCT intravenous LE group and the omega-3-enriched intravenous LE group. These results are in accordance with those of several previous studies [11-13].

A study conducted by Jiang et al. [13] in children undergoing gastrointestinal surgery showed that AST and ALT levels did not differ significantly between the MCT/LCT intravenous LE group and the omega-3-enriched intravenous LE group at 2 weeks after surgery. However, when both emulsions were given for 4 weeks, statistically significant intergroup differences in ALT and AST levels were noted.

The administration of parenteral nutrition is a predisposing factor for gallstones formation and liver cholestasis due to a decreased synthesis of bile acids and lack of neurohumoral stimulation [14,15]. Postoperative sepsis and inflammation increase the production of cytokines, which inhibit bile secretion. Total parenteral nutrition can also worsen cholestasis. The purpose of MCT administration in intravenous LEs is to 'bypass' TG metabolism, so that the fatty acids produced by the metabolism can be utilized sooner as the energy source. LEs containing MCT also contain LCT because of the rapid metabolism of MCT and lack of essential fatty acids in pure MCT [15].

The composition of parenteral nutrition is also a determinant in lowering the incidence of hepatobiliary abnormalities. Several studies have shown the beneficial effects of fish oil on hepatobiliary function [16]. SMOFlipid LEs combine various components to leverage each component. Fatty oil-enriched emulsions are expected to reduce liver enzyme levels as they contain lower litogenic MCT levels than other intravenous LEs. Moreover, omega-3-enriched

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intravenous LEs also contain more LCT with higher phytosterol levels, which may reduce the risk of liver dysfunction. The content of olive oil in omega-3-enriched intravenous LEs is also less likely to induce hepatobiliary disorders [15].

In this study, we found no clinically significant differences in AST and ALT levels between the MCT/LCT intravenous LE group and the omega-3-enriched intravenous LE group. In contrast, several studies have shown significant differences in liver enzymes with the long-term use (more than 4 weeks) of intravenous LEs [17,18].

In accordance with several other studies [12,13], this study showed statistically significant intergroup differences in TG levels.

Carpentier et al. [16] stated that postoperative trauma might induce a catabolic response that causes hypercatabolism and impaired lipid tolerance. The synthesis of liver TGs is highly related to the availability of carbohydrate and fatty acid substrates. As a result, hyperlipidemia may occur in patients receiving parenteral nutrition after surgery [19]. In this study, postoperative TG levels in the omega-3-enriched intravenous LE group were significantly lower than those in the MCT/LCT intravenous LE group.

Wilk reported that the consumption of fish or fish oil can reduce cardiovascular risk by decreasing TG level. Our study findings are like those of a study of a healthy population that showed that intravenous LEs enriched in fish oil significantly improved lipid profile and counteracted dyslipidemia. More efficient TG elimination by omega-3-enriched intravenous LEs than LCT intravenous LEs has been reported by several studies in postoperative patients [20].

Shearer et al. [20] explained that TG levels are regulated by omega-3 as follows: fatty acids are transported throughout the body in two main forms, i.e. esterified fatty acid by very-low-density Lipoprotein (VLDL-TG) and non-esterified fatty acid by serum albumin (non-esterified fatty acid). These forms of fatty acids are then distributed to the different tissues according to energy requirements and hormonal status. In the tissues, fatty acids are utilized for adenosine triphosphate production via oxidation, re-esterification in TG for energy storage, incorporation into lipids that form cell membranes, and production of signaling molecules. Non-essential fatty acids can also be synthesized from other carbon sources. The liver acts as the main organ for fatty acid distribution and fatty acids processed from all sources. In hepatocytes, omega-3 reduces VLDL production and increases β-oxidation; in adipocytes, omega-3 increases fatty acid uptake from plasma TG lipoprotein lipolysis, decreases intracellular glycolysis in adipocytes, and increases β-oxidation. The omega-3 contained in fish oil also reduces the secretion of proinflammatory cytokines from adipose tissue macrophages and regulates plasma TG lipoprotein lipolysis and β-oxidation.

In conclusion, based on the results of this study, the administration of intravenous omega-3-enriched LE as parenteral nutrition therapy significantly lowers the TG levels of children undergoing gastrointestinal surgery compared to the standard intravenous LE and has no significant effect on liver enzyme levels.

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PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7