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Influence of n-3 Fish Oil-Enriched Intravenous Lipid Emulsion on Length of Stay and Mortality in Infants Post Intestinal Surgery

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ABSTRACT

Background: Parenteral nutrition plays an important role in the infants post intestinal surgery. Currently, n-6 soybean oil-based intravenous lipid emulsion (IVLE) is used as a standard. n-6 have been shown increases biomarkers of inflammation while n-3 have shown positively influence clinical outcomes due to their immunomodulatory action. The aim of this study is to investigate the influence of n-3 fish oil-enriched IVLE on mortality and length of stay in infants post intestinal surgery. **Methods:** A medical record retrospective study was undertaken in infants post intestinal surgery at Dr. Soetomo Hospital in 2016-2017. Infants with intestinal atresia who had PN for at least three days were included. The n-6 soybean oil-based and n-3 fish oil-enriched IVLE were used. Incomplete data was excluded. **Results:** There were 19 infants (12/19 boys) included in this study. 10/19 infants received the n-6 soybean oil-based IVLE. The duration and dose of IVLE used were 16.52±11.34 days and 1.80±0.44 g/kg/day. Mortality rate was significantly lower in n-3 fish oil-enriched IVLE group (P=0.02) while there was no difference on length of stay (P=0.484).**Conclusion:** Infants who received the n-3 fish oil-enriched IVLE have a lower mortality rate but there is no difference on length of stay.

Keywords: Infants, Intestinal surgery, Intravenous lipid emulsion, Length of stay, Mortality

INTRODUCTION

Background

Parenteral nutrition (PN) has a very important role in the management of patients who are unable to take oral or enteral nutrition, especially for pediatric patients undergoing intestinal surgery[(1),(2)]. Intravenous Lipid Emulsions (IVLE) is an important source of essential fatty acids (EFA) in PN that is recommended in children post intestinal surgery as a source of energy and are necessary to prevent EFA deficiency[(3)]. The IVLE used conventionally as a standard until now is Soybean Oil (SO) based, which is rich in n-6 Polyunsaturated Fatty Acid (PUFA) linoleic acid, or 50:50 mixture of vegetable oils that are rich in medium chain saturated fatty acids and soybean oil (often called Medium Chain Trygliceride (MCT) / Long Chain Tryglyceride (LCT) to show a mixture of medium and long chain triglycerides[(4)].

Some experimental studies and clinical trials show that n-6 PUFA is associated with a decrease in cell mediated immunity and increases the potential risk of increasing the severity of the inflammatory response[(5)]. This can aggravate the clinical outcomes of patients after intestinal surgery, who have a high risk of death,

infection and organ failure[6]. Several trials and clinical trials have shown that n-3 PUFA enriched IVLE can improve infection and reduce inflammation post surgery[7],[8],[9]. Research shows that n-3 PUFA enriched IVLE is better at modulating fatty acids and is useful for increasing immunity in postoperative patients and reducing the duration of hospitalization compared to LCT[10].

Purpose

Until now, the use of fish oil-enriched fat regimens compared to n-6 soybean oil based IVLE regimens in post-gastrointestinal pediatric patients in Indonesia has not been studied. The aim of this study is to investigate the influence of n-3 PUFA enriched IVLE on length of stay and mortality in infants post intestinal surgery.

METHODS

This study was a retrospective study using medical records performed on children after gastrointestinal surgery at Dr. Hospital. Soetomo from January 1, 2016 to December 31, 2017. The inclusion criteria in this study were children with intestinal atresia who had undergone gastrointestinal surgery and received parenteral nutrition therapy for at least 3 days. The exclusion criteria were if the data from the medical record were not complete enough to support the research or medical records could not be found. The statistical analysis used was by Chi Square Test or by Fisher's Exact Test if it did not meet the requirements with a p-value <0.05. The software used was SPSS For Mac.

RESULTS

Based on this study, there were 38 infants with intestinal atresia who underwent gastrointestinal surgery but only 19 infants who met the inclusion and exclusion criteria. A total of 10/19 infants had jejunoileal obstructions. 12/19 infants of male sex. The average duration of IVLE use in PN was 16.52 ± 11.34 days with an average IVLE dose of 1.80 ± 0.44 g / kg / day. The basic characteristics of the research subjects are shown in table 1.

Tabel 1. Characteristic of samples

Characteristic	n-6 soybean oil based-IVLE (n=10)	n-3 fish oil enriched IVLE (n=9)	p-value
Age (days, median, ±SD) 9.42±4.77	10.9±4.88	7.77±4.32	0.156
Sex			0.057
Boy	4	8	
Girl	6	1	
Body Weight (gram, mean±SD) 2295.26±645.26	2298±842.10	2292±372.60	0.985
Duration of PN (days,mean±SD) 16.52±11.34	12.80±7.20	20.66±13.93	0.290
Type of Surgery			0.070
Duodenal Atresia	7	2	
Jejunoileal Atresia	3	7	
IVLE dosage (g/kg/d, mean±SD) 1.80±0.44	1.79±0.45	1.82±0.46	0.868

The results of this study showed no significant differences in age, sex, weight, duration of administration of PN, type of surgery and IVLE dose used in the group of children who received n-6 soybean oil based IVLE and n-3 PUFA enriched IVLE.

Table 2. Relationship between type of IVLE and length of stay

		Type of IVLE		
		n-6 soybean oil based IVLE (n=10)	n-3 PUFA enriched IVLE (n=9)	p-value
Length of Stay	1-6 days	0	1	0.484
	7-13 days	5	2	
	14-20 days	1	5	
	21-27 days	0	0	
	>28 days	4	1	

There was no significant difference on length of stay between both IVLE groups (P-value = 0.484).

Table 3. Relationship between type of IVLE and mortality

	Died				p-value
	Yes	%	No	%	
n-6 soybean based IVLE	7	70	3	30	0.020
n-3 PUFA enriched IVLE	1	11.11	8	88.89	
Total	8	42.11	11	57.89	

The n-3 PUFA enriched IVLE group significantly had a lower mortality rate compared to n-6 soybean oil based IVLE group. (P-value = 0.020)

DISCUSSION

Intestinal atresia is the most common cause of gastrointestinal obstruction in children with rates ranging from 0.4 to 3.1 / 10,000 live births. Infants with intestinal atresia have a high risk of morbidity and mortality due to intestinal dysfunction and parenteral nutrition dependency[11]. In this study, the incidence of intestinal atresia was 38 cases in the last 2 years (2016-2017).

Parenteral nutrition (PN) is a postoperative management therapy that must begin within 24 to 48 hours after surgery[1]. This is similar to the ESPGHAN recommendation, which is immediate parenteral nutrition if nutrition cannot be fulfilled via oral or enteral[12]. Long-term parenteral nutrition is needed in short bowel syndrome caused by Necrotizing Enterocolitis (NEC), intestinal atresia, gastroschisis, or aganglionic long segments requires long-term parenteral nutrition[13].

A total of 19 children in this study received IVLE (10 children with n-6 SO based IVLE and 9 childrenwith n-3 PUFA enriched IVLE). Intravenous fat emulsion (IVLE) is one component in parenteral nutrition which plays an important role as an energy source and source of essential fatty acids in the prevention of essential fatty acid deficiencies[12]. The American Society for Parenteral and Enteral Nutrition / ASPEN (2012) classified the generation of IVLE into 4 categories based on fatty acid derivatives and the inflammatory response generated by the intravenous fat formula itself (Figure 1). The first generation containing 100% SO which is pro-inflammatory, second generation (50:50 mixture of SO and MCT) and third (80:20 olive oil/ OO) and SO) are neutral inflammation while the fourth generation accompanied by fish oil (fish oil / FO) is an anti-inflammatory[3],[14].

Long-chain triglycerides and n-6 essential fatty acids are available in the first generation IVLE. LCT plays a role in phagocytosis and chemotaxis in the immune system which can help increase infection. n-6 which

is precursors that form prostaglandin E2 (PGE2), prostaglandin I2 (PGI2) and thromboxane A2 (TXA2) via the cyclooxygenase (COX) pathway as well as leukotrin B4 (LTB4), leukotrin C4 (LBC4) and leukotrien E4 (LTE4) from arachidonic acid (AA) have a pro-inflammation role (Figure 2). Fish oil (FO) included in the generation IVLE containing n-3 which is a precursor that forms prostaglandin E3 (PGE3), prostaglandin I3 (PGI3) and thromboxane A3 (TXA3) via the cyclooxygenase (COX) pathway as well as leukotrien B5 (LTB5), leukotrien C5 (LBC5) and leukotrien E5 (LTE5) via lypooxygenase (LOX) from eicosapentanoid acid (EPA). n-3 inhibits the activity of n-6 by directly substitutes AA to EPA and inhibits AA production and directly does not alter inflammatory genes at the level of transcription factors and decreases proinflammatory cytokines. AA production is inhibited which causes EPA production so the mediator shifts towards anti-inflammatory conditions[12][16].

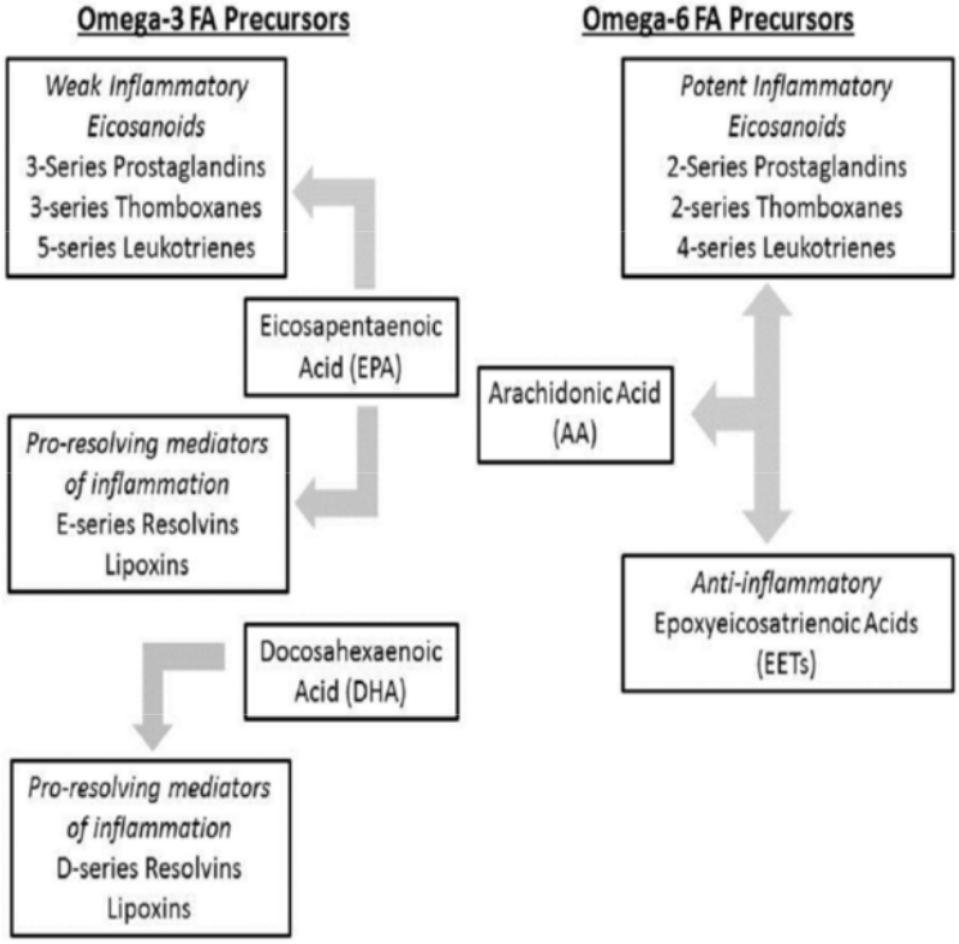

Figure 1. Metabolites of n-3 and n-6 *essential fatty acid* (EFA)[14]

Some studies showed that n-3 fish oil enriched IVLE significantly reduced the incidence of systemic inflammatory response syndrome (SIRS), morbidity and mortality in patients post surgery. The mechanisms underlying the clinical benefits are likely to be related to normalization of cellular immune function and modulation of the inflammatory response after surgery. It has been shown that ω-3 fatty acid emulsions can improve immune function after surgery, thus decrease the mortality rate[15][16][17].

CONCLUSION

The n-3 fish oil IVLE can reduce mortality in infants after gastrointestinal surgery compared to n-6 soybean oil IVLE.

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