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Research Article

Safety and Efficacy of Intravenous Lipid Emulsion Containing Soyabean Oil, Medium Chain Triglycerides, Olive Oil, and Fish Oil (SMOF Lipid) vs. Conventional Lipid Emulsion: A Single-Center, Double Blind Randomized Controlled Trial in Neonates Requiring Parenteral Nutrition

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Abstract

Background: Intravenous lipid emulsions are an integral part of the PN in neonates. Because of their high content of PUFAs and limited content of αtocopherol, they deplete antioxidant defences. The need for more appropriate lipid emulsions in neonatal care is well recognized.

Aims and Objectives: To evaluate the safety and effects of two different intravenous lipid emulsion in neonates requiring total parenteral nutrition.

Materials and Methods: This study was a single center, double blind randomized controlled trial conducted in NICU of a tertiary care hospital, from December 2017 to November 2018. Eighty premature newborns of < 34 weeks gestational age were randomized equally to two groups - SMOF lipid and Intralipid. Anthropometric measurements and biochemical variables including serum triglycerides, total and direct bilirubin, SGOT, SGPT, GGT and BUN were assessed in laboratory at 7 and 14 days.

Results: The two groups were comparable at baseline with regards to gestational age, weight, length, and head circumference. Comparison between SMOF group and IL group for anthropometric parameters, Duration of NICU stay and number of days taken to reach birth weight showed that both groups were comparable ($p > 0.05$). Triglycerides, SGOT, SGPT, GGT, BUN were significantly higher in IL group than SMOF group at 7 ($p < 0.05$) and 14 ($p < 0.05$) days.

Conclusion: SMOF is safe and well tolerated in preterm neonates requiring parenteral nutritionand using of SMOF lipid might be advantageous with regard to better biochemical parameters compared to conventional Intralipid.

Keywords: *Parenteral Nutrition; Preterm; SMOF Lipid; Intralipid*

Introduction

Parenteral nutrition (PN) has been used for many years as an efficient therapy in preterm neonates [1,2]. When enteral feeding is not tolerated or insufficient to meet the requirements, PN must be instituted after birth and lipid emulsions are an integral part of the PN regimen [3,4]. Well-balanced fatty acid supply during the neonatal period is crucial for growth, visual and cognitive development [3,5]. Soybean oil-based lipid emulsions (Conventional) contain high amounts of linoleic acid (LA; C18:2 ω6) relative to αlinolenic acid (αLNA; C18:3 ω3) but low amounts of arachidonic acid (AA; C20:4 ω6) and no ω3 long chain polyunsaturated fatty acids (LCPUFAs) such as eicosapentaenoic acid (EPA; C20:5 ω3) and Docosahexaenoic Acid (DHA C22:6 ω3) [6]. Because of their high content of PUFAs and their limited content of αtocopherol, increases the risk of lipid peroxidation. EPA functions as a precursor for the LC-fatty acid synthesized in the retina [7].

SMOF lipid 20% is a new ILE containing a physical mixture of 30% soybean oil, 30% medium-chain triglycerides (MCTs), 25% olive oil, and 15% fish oil. Soybean oil providing LA and α-LNA for EFA; olive oil rich in monounsaturated fatty acids, which are less susceptible to lipid peroxidation than PUFAs; MCTs showing a faster metabolic clearance; and fish oil for the supply of ω3 L1C-PUFA EPA and DHA [8,9]. SMOF lipid 20% has a ω6:ω3 FA ratio of approximately 2.5:1, which is in accordance with current recommendations [10,11].

Whether to use SMOF lipid as a standard of care in the preterm neonate remains a research question.

Aims and Objectives

Aim: To evaluate the safety and efficacy of two different intravenous lipid emulsion in neonates requiring total parenteral nutrition.

Primary objectives:

1. Clinical:
    - Weight, length, and head circumference at the end of 7 days, 14 days, and at discharge in the two groups.
    - Time taken to achieve birth weight in the two groups.
2. Biochemical:
    - Serum triglyceride, total and direct bilirubin, SGOT, SGPT, GGT, and BUN level at 7 days and 14 days of TPN in the two groups.

Secondary objective:

1. The duration of NICU stays in the two groups.

Materials and Methods

Material used in the study

Intravenous intralipid 20% and Intravenous SMOF lipid 20% (Both manufactured by FRSENIUS KABI).

Study area and duration

The study was conducted in the Neonatal intensive care unit, Jaipur Golden Hospital, 2-institutional area, Rohini sector3, Delhi110085 from December 2017 to November 2018.

Study design

A single-center, double blind randomized controlled trial.

Sample size

Our sample size calculation was based on biochemical parameters at the end of TPN in the two groups. With reference to the previous study [18], the total sample size was set as 78 calculated from an assumed effect size of 0.67 in any biochemical parameters between two groups with a power of 90% and at an α of 0.05.

Inclusion criteria:

1. Premature newborns (less than 34 weeks gestational age) admitted to the Neonatal ICU of Jaipur Golden Hospital.

Exclusion criteria:

1. Major congenital anomalies
2. Chromosomal abnormalities
3. Antenatal suspicion of liver or renal diseases
4. Enrollment into other studies.

Methodology

The babies were randomly allocated into two groups by a random number table. (Available at https://www.graphpad.com/quickcalcs/randomN1.cfm). As per the sequence generated, the serial numbers of babies were enrolled in one of the following groups:

1. Babies receiving SMOF lipid 20%.
2. Babies receiving conventional intralipid 20%.

In both group babies received lipid @ 2 gm/kg/day on Day 1, 3 gm/kg/day on day 2 and onwards and amino acid @ 1.7 gm/kg/day on day 1, 2.1 gm/kg/day on Day 2, and 2.7 gm/kg/day on day 3 and onwards (Recommendation by NEON trial [13]).

To ensure blinding, the study and control infusions were of the same size and identical appearance. Infusions used in study period were prepared in blinded ethylene-vinyl acetate bags in the hospital pharmacy and provided to the unit could be identified only by the patient number printed on the outside of the packaging.

Assessment of variables

Babies were weighed on an electronic weighing scale with an accuracy of 5g. Weighing was done immediately after birth and subsequently daily till achievement of birth weight and up to 14 days. The length was measured (in cm) by placing babies on Infantometer and Head Circumference was measured by putting non-stretchable measuring tape in cm. Weight, Length, and head circumference were mea-

sured by an investigator at birth, at the start of TPN, at 7 days, at 14 days, at the end of TPN, and at discharge. Serum triglycerides, serum bilirubin, BUN, SGOT, SGPT, GGT level were measured at 7 days and 14 days of TPN.

Statistical analysis

The data was entered in Microsoft EXCEL spreadsheet and analysis were done using Statistical Package for Social Sciences (SPSS) version 21.0.

Continuous variables are presented as mean ± SD. Categorical variables are expressed as frequencies and percentages. Quantitative variables between the two groups were compared using unpaired t test for data which was normally distributed, and Mann-Whitney test for data which was not normally distributed. Data within the group at 2 intervals were compared using paired t test for data which was normally distributed, and Wilcoxon signed rank test for data which was not normally distributed. Data within the group at more than 2 intervals were compared using repeated-measures ANOVA test for data which was normally distributed, and Friedman's test for data which was not normally distributed. Nominal categorical data between the groups were compared using the Chi-square test or Fisher's exact test as appropriate. For all statistical tests, a p-value of less than 0.05 was taken to indicate a significant difference.

Ethical and scientific committee approval was taken before the start of the study from the institutional ethics committee vide letter number JGH/DNB/SRC/2017/ dated 14 November 2017.

Informed consent was taken from the parents/guardian.

Results

Recruitment of patients

102 neonates were screened for the study. Of these, 9 were excluded as they fit into the exclusion criteria. At the end of recruitment, 80 neonates, with 40 in each group were enrolled. The study outline is described in the flow chart (Figure 1).

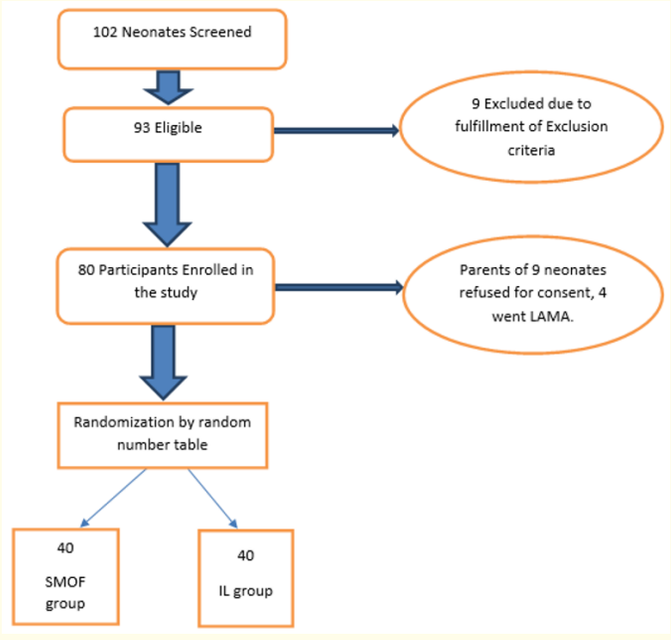

Figure 1: *Flowchart of patient recruitment.*

Baseline characteristics

The SMOF and IL groups in the study had comparable baseline characteristics with a mean gestational age of 30.1 ± 2 weeks and 30.1 ± 1.9 weeks, respectively.

Changes in anthropometric variables

When the comparison between SMOF group and IL group was done at different time intervals for weight length and head circumference, it showed that the weight at 7 days, 14 days, and at the time of discharge was comparable and did not show a significant difference ($p > 0.05$). The relative increase in weight was observed at 14 days in SMOF 3.5 ± 7.7% and IL 3.4 ± 5.9%, while weight was decreased at 7 days compared to baseline in both the groups.

Variables	SMOF	IL	P-value
Gestational age in weeks	30.1 ± 2	30.1 ± 1.9	0.863
Weight in grams	1345.9 ± 462.2	1305.6 ± 400.3	0.847
Length in cm	39.9 ± 3.3	39.9 ± 2.4	0.985
Head circumference in cm	28.4 ± 2.5	28.4 ± 2.3	0.945

Table 1: *Comparison of anthropometric variables.*

Changes in biochemical variables

In present study at 7 days, TG levels was 61.3 ± 16.9 mg/dl and 76.8 ± 24.6 mg/dl, SGOT levels was 32.4 ± 9.7 mg/dl and 39.1 ± 10.6 mg/dl, SGPT levels was 25.5 ± 8.4 mg/dl and 31 ± 8 mg/dl, GGT levels was 32.6 ± 10.3 mg/dl and 55.4 ± 17.9 mg/dl, BUN levels was 15.2 ± 3.3 mg/dl and 18.2 ± 3.2 mg/dl in SMOF group and IL group respectively. When the SMOF and IL groups were compared together, it revealed that triglycerides, SGOT, SGPT, GGT, and BUN levels at 7 days and 14 days were

Variables		SMOF	IL	P-Value
Triglycerides in mg/dl	7 days	61.3 ± 16.9	76.8 ± 24.6	0.002
	14 days	57.9 ± 16.9	72.2 ± 21.9	0.002
Total bilirubin in mg/dl	7 days	9.1 ± 1.8	10.2 ± 2.5	0.028
	14 days	6.4 ± 1.1	6.3 ± 1.2	0.737
Direct bilirubin in mg/dl	7 days	1.1 ± 0.3	1.5 ± 0.6	< 0.001
	14 days	0.8 ± 0.2	0.8 ± 0.2	0.734
SGOT in IU	7 days	32.4 ± 9.7	39.1 ± 10.6	0.004
	14 days	31.8 ± 6.1	34.9 ± 7.7	0.047
SGPT in IU	7 days	25.5 ± 8.4	31 ± 8	0.004
	14 days	24.9 ± 6	29.7 ± 6.6	0.001
GGT in U/L	7 days	32.6 ± 10.3	55.4 ± 17.9	< 0.001
	14 days	34.2 ± 9.3	48.5 ± 16.9	< 0.001
BUN in mg/dl	7 days	15.2 ± 3.3	18.2 ± 3.2	< 0.001
	14 days	13 ± 3.3	15.7 ± 3.2	< 0.001
Duration of NICU stay in days		29.2 ± 14.7	31.2 ± 14.8	0.378
Number of days taken to reach the birth weight		12.1 ± 4.8	13.8 ± 4.9	0.127

Table 2: *Comparison of biochemical variables.*

significantly higher in IL than SMOF group ($p < 0.05$). At 7 days, total bilirubin levels were 9.1 ± 1.8 mg/dl and 10.2 ± 2.5 mg/dl, direct bilirubin levels were 1.1 ± 0.3 mg/dl, and 1.5 ± 0.6 mg/dl in SMOF group and IL group respectively. When the SMOF and IL groups were compared together, total bilirubin and direct bilirubin at 7 days were significantly higher in IL than SMOF group ($p < 0.05$) but, at 14 days of SMOF and IL groups was comparable without statistical significance ($p > 0.05$).

Duration of NICU stay and days took to reach the birth weight

The duration of NICU stay in SMOF group and IL group was 29.2 ± 14.7 days and 31.2 ± 14.8 days which was statistically not significant ($p > 0.05$). The number of days taken to reach birth weight in SMOF group and IL group was 12.1 ± 4.8 days and 13.8 ± 4.9 days. But, the difference was not statistically significant ($p > 0.05$).

Discussion

Parenteral nutrition (PN) in preterm neonates is essential, and lipid is an integral part of PN. SMOF lipid is rich in MUFA and omega-3 LC-PUFAs and has a higher vitamin E concentration, which could be beneficial in high-risk preterm neonates.

The present study assessed the comparison between two types of intravenous lipid emulsions in preterm neonates requiring parenteral nutrition. The SMOF and IL groups in the study had comparable baseline characteristics with a mean gestational age of 30.1 ± 2 weeks and 30.1 ± 1.9 weeks, respectively. A study conducted by Maissa Rayyan., *et al*. [12] showed findings that are comparable with the present study. Also, in the NEON trial by Uthaya., *et al*. [13], there were 4 groups, those receiving low amino acid and IL had mean gestational age 27.8 ± 1.9 weeks, high amino acid and IL was 28.1 ± 2.1 weeks, low amino acids and SMOF was 27.5 ± 2.4 weeks and high amino acids and SMOF was 27.8 ± 2.1 weeks.

In present study, an increase in weight, length, and head circumference in both the groups was similar. There was no statistical difference in weight, length, and head circumference at 7 days, 14 days, and at the time of discharge. A similar observation was seen in studies conducted by Rayyan., *et al*. [12], Uthaya., *et al*. [13], Deshpande., *et al*. [14] and Repa., *et al*. [15] showed increase in weight was comparable and statistically not significant in between these groups. Compared to the current study, baseline anthropometric parameters in NEON trial [13], Repa., *et al*. [15] and Deshpande., *et al*. [14] were lower. E.g. the baseline head circumference of the neonates in the NEON trial was lower than our study. This might be due to the selection of extremely premature infants i.e. < 31 weeks in their study, whereas the same cut-off in the present study was 34 weeks.

Author	Group	Weight in gm or kg	Length in cm	Head circumference in cm
Present study	SMOF	1345.9 ± 462.2	39.9 ± 3.3	28.4 ± 2.5
	IL	1305.6 ± 400.3	39.9 ± 2.4	28.4 ± 2.3
Rayyan., *et al*. [12]	SMOF	1335.6 ± 408.8	38.9 ± 3.8	27.6 ± 2.7
	SO	1364.1 ± 339.7	39.1 ± 3.2	27.5 ± 2.0
Uthaya., *et al*. [13] [NEON Trial]	Low AA SMOF	1.05 ± 0.34@	34.6 ± 4.2	25 ± 3
	High AA SMOF	1.06 ± 0.29@	35.2 ± 5.2	25.6 ± 2.9
	Low AA IL	1.03 ± 0.29@	35.1 ± 3.5	25.3 ± 2
	High AA IL	1.04 ± 0.28@	35.1 ± 3.9	25.3 ± 1.9
Repa., *et al*. [15]	SMOF	788 [648 to 891]*	34 [31 to 35]*	24 [23 to 25] *
	SO	760 [610 to 884]*	33 [31 to 35]*	24 [23 to 25]*
Deshpande., *et al*. [14]	SMOF	935.58 ± 163.34	34.76 ± 2.37	24.35 ± 1.59
	OO	906.76 ± 313.42	34.14 ± 3.96	24.11 ± 2.28

Table 3: *Comparison of anthropometric measurements of neonates at baseline.*

**Median [IQR], @in kg.*

Changes in biochemical variables

Premature neonates have only limited muscle and fat mass and thus decreased the hydrolytic capacity of the enzyme lipoprotein lipase. As a consequence, they are at higher risk for PN-associated hypertriglyceridemia, cholestasis, and PN-associated liver disease (PNALD) than term infants [15,16].

Author	Group	Triglycerides[#]	Total Bilirubin[#]	Direct Bilirubin[#]	SGOT[$]	SGPT[$]	GGT[$]	BUN[#]
Present study At 7 days	SMOF	61.3 ± 16.9	9.1 ± 1.8	1.1 ± 0.3	32.4 ± 9.7	25.5 ± 8.4	32.6 ± 10.3	15.2 ± 3.3
	IL	76.8 ± 24.6	10.2 ± 2.5	1.5 ± 0.6	39.1 ± 10.6	31 ± 8	55.4 ± 17.9	18.2 ± 3.2
	P value	0.002	0.028	< 0.001	0.004	0.004	< 0.001	< 0.001
Rayyan., *et al*. [12] At 8 days	SMOF	61.06 ± 35.4	5.54 ± 3.99	0.6 ± 0.34	-	9.8 ± 4.83	73.1 ± 33.99	-
	SO	59.29 ± 30.1	5.74 ± 4.37	0.75 ± 0.42	-	9.2 ± 4.11	63 ± 44.3	-
	P value	0.781	0.049	0.036	-	0.888	0.135	-
Repa., *et al*. [15] At discharge	SMOF	-	-	0 [0-0.22]*	41 [32-67]*	-	148 [95-243]*	-
	SO	-	-	0 [0-0.38]*	48 [34-80]*	-	157 [101-217]*	-
	P-value	-	-	0.67	0.13	0.4	0.94	-
Tomsits E., *et al*. [18] At day 14	SMOF	0.87 ± 0.41[@]	-	80.89 ± 62.14	-	11.96 ± 8.83	107.8 ± 81.7	-
	IL	0.82 ± 0.41[@]	-	80.31 ± 61.73	-	11.10 ± 7.56	188.8 ± 176.7	-
	P-value	NS	-	NS	-	NS	0.04	-
Deshpande., *et al*. [14] At 8 days	SMOF	-	-	118.76 ± 23.11	5.53 ± 3.04	-	-	-
	OO	-	-	109.35 ± 36.07	6.85 ± 5.12	-	-	-
	P value	-	-	NS	NS	-	-	-
Vlaardingerbroek., *et al*. [24] At 7 days	SMOF	1.93 ± 0.97[@]	81 ± 28	2.4 ± 3.0	34.59 ± 24.46	8.03 ± 5.39	-	-
	SO	2.13 ± 1.61[@]	89 ± 28	2.9 ± 3.4	23.97 ± 9.90	7.20 ± 6.38	-	-
	P-value	0.511	0.148	0.564	0.027	0.572	-	-

Table 4: *Comparison of biochemical variables at a subsequent time interval after initiating parenteral nutrition.*

**Median [IQR], [#]in mg/dl, [$]in IU/L, [@]in mmol/l, NS not significant.*

In present study, although in both the groups (SMOF and IL) biochemical parameters (TG, Total and direct bilirubin, SGPT, SGOT, GGT, BUN) were within the normal range, values were significantly higher in IL group. Studies conducted by Kapoor V., *et al*. [17], Tomsits., *et al*. [18], Finn KL., *et al*. [19], and Maissa Rayyan., *et al*. [12] did not show a significant difference in TG with SMOF/FO and control group when compared together. A similar finding of elevated SGOT and SGPT in the control group was reported by Stanislaw Klek., *et al*. [20]. Tomsits E., *et al*. [18] conducted a study that showed that at end of the study, γ- glutamyl transferase (GGT) was lower in the SMOF versus the control group (107.8 ± 81.7 vs. 188.8 ± 176.7 IU/L, $P < 0.05$). This finding was comparable with the present study findings. Whereas, a study conducted by Repa A., *et al*. [15], Uthaya., *et al*. [13] and Maissa Rayyan., *et al*. [12] reported no significant difference in GGT levels in the study and control group.

In the present study, total and direct bilirubin at 7 days was significantly higher in IL group ($p < 0.05$) but, at 14 days SMOF and IL groups were comparable without statistical significance ($p > 0.05$). A similar finding of a significant increase of total bilirubin in study

groups seen in studies conducted by Goulet O., *et al*. [21], Finn KL., *et al*. [19], Maissa Rayyan., *et al*. [12], and Stanislaw Klek., *et al*. [20]. While a study conducted by Gawecka A., *et al*. [22], Uthaya., *et al*. [13] and Zhao Y., *et al*. [23] reported no significant difference in the rise of total bilirubin in between groups. In present study, there was no difference in time taken to regain birth weight in both the groups. There was shorter hospital stay observed in SMOF group though it was not statistically significant.

These findings, thus, show that both SMOF and IL are efficacious in terms of the treatment outcome. Though there were significant group differences in certain biochemical variables, the values in both groups were within normal clinical limits, with better tolerance and safety in the SMOF lipid group. Adverse events, anthropometric parameters, local tolerance, and clinical laboratory parameters did not show noticeable group differences, confirming the safety of study treatment revealed by the Tomsits E., *et al*. [18] study.

Our study findings are limited by the fact that we have not done a follow-up and hence cannot comment on the long term impact of our intervention. Yet, the short term impacts are significant and need to be shared. We hope that this will lead to replicative and/or larger studies to support our findings.

Conclusion:

1. The new lipid emulsion (SMOF lipid), based on a physical mixture of soybean oil, MCT, olive oil and fish oil was well tolerated and safe in preterm neonates requiring parenteral nutrition.
2. Infusion of the SMOF lipid emulsion was equally efficient as Conventional soybean emulsion in promoting the neonates' growth
3. Using of SMOF lipid might be advantageous with regard to better biochemical parameters compared to conventional intralipid.
4. We recommend the use of SMOF lipid in premature neonates requiring PN, however, to generalize the study finding in all neonates, multi-centric trials with larger sample size are required.
5. The effect of this novel lipid emulsion on neonates' mental and visual development has to be studied in future trials.

Contributor Credit:

JS - Manuscript first draft and study writing, Design of project, Data collection.

SB - Guide-idea incubation, design, supervision of data collection, analysis, intellectual inputs.

AG - Approval of study and manuscript, manuscript review, guided the entire process, and gave critical inputs to the manuscript.

VJ - Randomization and blinding assistance, data analysis, and intellectual inputs.

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Conflict of Interest

None of the authors has to declare any conflict of interest.

Bibliography

1. Shulman RJ and Phillips S. "Parenteral nutrition in infants and children". *Journal of Pediatric Gastroenterology and Nutrition* 36.5 (2003): 587-607.

2. Goulet O and Ruemmele F. "Causes and management of intestinal failure in children". *Gastroenterology* 130.2 (2006): S16-S28.

3. Koletzko B., *et al*. "Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), supported by the European Society of Paediatric Research (ESPR)". *Journal of Pediatric Gastroenterology and Nutrition* 41.2 (2005): S1-S87.

4. Krohn K and Koletzko B. "Parenteral lipid emulsions in paediatrics". *Current Opinion in Clinical Nutrition and Metabolic Care* 9.3 (2006): 319-323.

5. Innis SM. "Fatty acids and early human development". *Early Human Development* 83.12 (2007): 761-766.

6. Lee EJ., *et al*. "Essential fatty acid deficiency in parenterally fed preterm infants". *Journal of Paediatrics and Child Health* 29.1 (1993): 51-55.

7. Cetin I and Koletzko B. "Long-chain omega-3 fatty acid supply in pregnancy and lactation". *Current Opinion in Clinical Nutrition and Metabolic Care* 11.3 (2008): 297-302.

8. Sala-Vila A., *et al*. "Olive oil in parenteral nutrition". *Current Opinion in Clinical Nutrition and Metabolic Care* 10 (2007): 165-174.

9. Koletzko B and Goulet O. "Fish oil containing intravenous lipid emulsions in parenteral nutrition-associated cholestatic liver disease". *Current Opinion in Clinical Nutrition and Metabolic Care* 13.3 (2010): 321-326.

10. Mayer K., *et al*. "Fish oil in the critically ill: from experimental to clinical data". *Current Opinion in Clinical Nutrition and Metabolic Care* 9.2 (2006): 140-148.

11. Mertes N., *et al*. "Safety and efficacy of a new parenteral lipid emulsion (SMOF lipid) in surgical patients: a randomized, double-blind, multicenter study". *Annals of Nutrition and Metabolism* 50.3 (2006): 253-259.

12. Rayyan M., *et al*. "Short-Term Use of Parenteral Nutrition with a Lipid Emulsion Containing a Mixture of Soybean Oil, Olive Oil, Medium-Chain Triglycerides, and Fish Oil: A Randomized Double-Blind Study in Preterm Infants". *Journal of Parenteral and Enteral Nutrition* 36.1 (2012): 81S-94S.

13. Uthaya S., *et al*. "Nutritional Evaluation and Optimisation in Neonates: a randomized, double-blind controlled trial of amino acid regimen and intravenous lipid composition in preterm parenteral nutrition". *American Journal of Clinical Nutrition* 103.6 (2016): 1443-1452.

14. Deshpande G., *et al*. "Fish Oil (SMOF lipid) and olive oil lipid (Clinoleic) in very preterm neonates". *Journal of Pediatric Gastroenterology and Nutrition* 58.2 (2014): 177-182.

15. Repa A., *et al*. "A Mixed Lipid Emulsion for Prevention of Parenteral Nutrition Associated Cholestasis in Extremely Low Birth Weight Infants: A Randomized Clinical Trial". *The Journal of Pediatrics* 194 (2018): 87-93.

16. Hanson C., *et al*. "Implementation, process, and outcomes of nutrition best practices for infants < 1500g". *Nutrition in Clinical Practice* 26.5 (2011): 614-624.

17. Kapoor V., *et al*. "Alternative lipid emulsions versus pure soy oil based lipid emulsions for parenterally fed preterm infants". *Cochrane Database of Systematic Reviews* 12 (2015): CD009172.

18. Tomsits E., *et al*. "Safety and efficacy of a lipid emulsion containing a mixture of soybean oil, medium chain triglycerides, olive oil and fish oil: a randomized, double blind clinical trial in premature infants requiring parenteral nutrition". *Journal of Pediatric Gastroenterology and Nutrition* 51.4 (2010): 514-521.

19. Finn KL., *et al*. "Impact of Providing a Combination Lipid Emulsion Compared with a Standard Soybean Oil Lipid Emulsion in Children Receiving Parenteral Nutrition: A Systematic Review and Meta-Analysis". *Journal of Parenteral and Enteral Nutrition* 39.6 (2015): 656-667.

20. Klek S., *et al*. "Four-week parenteral nutrition using a third generation lipid emulsion (SMOF lipid) - A double-blind, randomised, multicenter study in adults". *Clinical Nutrition Journal* 32.2 (2013): 224-231.

21. Goulet O., *et al*. "A new Intravenous fat emulsion containing soybean oil, medium chain triglycerides, olive oil and fish oil: a single center double blind randomized study on efficacy and safety in pediatric patients receiving home parenteral nutrition". *Journal of Parenteral and Enteral Nutrition* 34.5 (2010): 485-495.

22. Gawecka A., *et al*. "Tolerance of two lipid emulsions used in parenterally-fed premature infants - a comparative study". *Medycyna Wieku Rozwojowego* 12.3 (2008): 782-788.

23. Zhao Y., *et al*. "Safety and efficacy of parenteral fish oil-containing lipid emulsions in premature neonates". *Journal of Pediatric Gastroenterology and Nutrition* 60.6 (2015): 708-716.

24. Vlaardingerbroek H and van Goudoever JB. "Intravenous lipids in preterm infants: impact on laboratory and clinical outcomes and long-term consequences". *World Review of Nutrition and Dietetics* 112 (2015): 71-80.

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