Original Article

Clinical effects of multi-oil versus pure soybean oil-based lipid emulsions for preterm infants: An observational study

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Background and Objectives: Conventional soybean oil-based intravenous lipid emulsions (SO-ILEs) have high polyunsaturated fatty acid (PUFA) contents and phytosterols that may have adverse effects in preterm infants. Recently, the multi-oil-based intravenous lipid emulsion (MO-ILE), SMOFlipid, has been widely utilized in the neonatal intensive care unit (NICU), but significant benefits over SO-ILEs in low gestational age neonates have yet to be demonstrated. This study was performed to compare the effects of the SO-ILE, Intralipid, and the MO-ILE, SMOFlipid, on neonatal health outcomes in preterm infants. **Methods and Study Design:** We performed a retrospective review of preterm infants born at gestational week (GW) <32 receiving parenteral nutrition for longer durations (≥14 d) in the NICU between 2016 and 2021. The primary aim of this study was to investigate differences in morbidity between preterm infants receiving SMOFlipid and Intralipid. **Results:** A total of 262 preterm infants were included in the analysis, with 126 receiving SMOFlipid and 136 receiving Intralipid. The SMOFlipid group had lower rates of ROP (23.8% vs 37.5%, respectively; p=0.017), although the rate of ROP was not different in multivariate regression analysis. The length of hospital stay was significantly shorter in the SMOFlipid than SO-ILE group (median [IQR]=64.8 [37] vs 72.5 [49] days; p<0.001). **Conclusions:** The use of SMOFlipid as the lipid emulsion was associated with higher clinical efficacy than SO-ILE in preterm infants.

Key Words: lipid emulsion, preterm infants, SMOFlipid, intralipid

INTRODUCTION

Parenteral nutrition (PN) is a life-saving intervention for infants unable to feed by mouth, and consists of macronutrients (i.e., dextrose, lipids, and protein) and micronutrients.[1] In addition to providing calories, lipid emulsions are a rich source of essential fatty acids, such as linoleic acid (LA; ω-6) and alpha-linolenic acid (ALA; ω-3), which are precursors of the eicosanoids required for platelet function, immune response, inflammation, and early visual and neural development.[2]

Pure soybean oil (SO)-based intravenous lipid emulsions (SO-ILEs) have been widely used for several decades in adults, children, and infants.[3] A number of studies regarding the function of ω-6 fatty acids suggested that high-ω-6 fatty acid concentration have a negative impact on inflammation and oxidative stress, which may lead to adverse effects in preterm infants.[4-6] In addition, clinical studies have shown a strong correlation between the phytosterols present in SO-ILEs and PN-associated cholestasis (PNAC).[7-11] PNAC gradually onsets in infants receiving SO-ILEs. The incidence of PNAC from SO-ILEs varies markedly between centers, from 7% to 85%.[12]

Newer lipid emulsions comprised of fish oil (FO) and medium-chain triglycerides (MCT) show promise for reducing complications in infants. SMOFlipid (Fresenius Kabi, Bad Homburg, Germany) is the predominant multi-oil-based intravenous lipid emulsion (MO-ILE) used in Europe; it has also been approved for use in adults in the USA, with off-label approval for use in infants.[12] SMOFlipid contains 30% SO, 30% MCT, 25% olive oil (OO), and 15% FO.[13] Compared to pure SO-ILEs, SMOFlipid contains greater amounts of vitamin E and lower concentration of phytosterols.[14] However, the results of clinical trials on the efficacy of SMOFlipid over SO-ILEs for resolving PNAC have been mixed.[12]

Kapoor et al performed a systematic meta-analysis and thorough examination of the outcomes of SO-ILEs and SMOFlipid. There is currently insufficient evidence from randomized studies to determine with any certainty

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whether SMOFlipid offers advantages in terms of the prevention or resolution of PNAC, or any other clinical condition.[15,16] None of the currently available parenteral lipid emulsions prevent the postnatal deficits in docosahexaenoic acid (DHA) and arachidonic acid (ARA) in preterm infants. FO-containing lipid emulsions exacerbate the ARA deficit relative to 100% SO, increase eicosapentaenoic acid (EPA) concentration, and have an inverse ARA:DHA ratio compared to that observed at birth.[17]

Despite many previous intervention studies comparing SMOFlipid to alternate lipid emulsions, there are insufficient data regarding the clinical impact.[18] Our neonatal intensive care unit (NICU) implemented the use of SMOFlipid in routine practice in June 2019. The present study was performed to evaluate and compare the effects of two lipid emulsions, Intralipid and SMOFlipid, on neonatal health outcomes.

METHODS

Procedure

This retrospective cohort study was conducted in the NICU of Zhejiang University School of Medicine, Sir Run Run Shaw Hospital. Approval to review data was obtained from the Hospital Human Research Ethics Committee (Protocol code 20200831-35 and date of approval 31/08/2020). Informed consent was not required as this was an observational study and all patient data were deidentified. In July 2019, we transitioned from using Intralipid to SMOFlipid as the primary lipid emulsion for PN in preterm infants. Hence, eligible participants were distinguished based on nutritional exposure: those who received pure SO-ILE (Intralipid 20%: SO, 200 g/L; egg phospholipids, 12 g/L; glycerol, 22.5 g/L) from June 2016 to July 2019, and those who received MO-ILE (SMOFlipid 20%: SO, 60 g/L; MCT, 60 g/L; OO, 50 g/L; FO, 30 g/L; egg phospholipids, 12 g/L; glycerol, 25 g/L; vitamin E, 200 mg α-tocopherol equivalent/L) from July 2019 to September 2021. Hospital electronic databases (medical records, pathology, and imaging) were then accessed to retrieve clinical data for the two cohorts. Both cohorts were cared for by the same multidisciplinary team, who provided medical, pharmacy, dietetic, nursing, and nutritional care.

Participants

Patients receiving SMOFlipid and Intralipid were divided into the SMOFlipid and SO-ILE groups, respectively. The inclusion criteria were as follows: preterm infants admitted to the NICU; low birth weight preterm infants born prior to gestational week (GW) 32; and receiving PN for ≥14 days. Preterm infants were excluded if they had severe congenital malformation or metabolic disorders prior to PN initiation, received more than one lipid formulation, or had insufficient/missing data in their medical records. Insufficient medical records of preterm infants are typically due to necrotizing enterocolitis necessitating transfer to another hospital for surgery. A flow chart of patient inclusion and exclusion is presented in Figure 1.

Parenteral nutrition protocol

PN was started for all preterm infants within 24 h of birth in the NICU. Amino acid solution was administered at a rate of 1.5–2.5 g/kg/day on the first day, and was increased by 1 g/kg every day up to 3.5 g/kg/day. Lipid emulsions were infused at 1.0 g/kg/day on the first day and increased by 1 g/kg every day up to a maximum of 3.0–4 g/kg/day. PN was administered by continuous 24h infusion. This was consistent between the two study periods. Infants also received trace elements, electrolytes, minerals, and vitamins as a standard part of the total parenteral nutrition (TPN) protocol. Enteral feeding commenced as soon as the medical team deemed the infant to be medically stable, and was performed according to a standardized feeding protocol, which was the same for both study periods.

Data collection

Data on the baseline characteristics of each group were collected, including sex, gestational age at birth, birth weight, length, head circumference, and the APGAR score of the preterm infants at 5 min. Data were also collected on maternal characteristics such as age, conception method, preeclampsia, premature rupture of membranes (PROM), antepartum hemorrhage (APH), cervical incompetence, antenatal steroid use (minimum of one dose), and delivery method. The primary outcomes were mortality prior to discharge, rates of neonatal cholestasis, patent ductus arteriosus, bronchopulmonary dysplasia, retinopathy of prematurity (ROP), necrotizing enterocolitis, and late-onset sepsis. Secondary outcomes included osteopenia of prematurity, number of days required to regain birth weight, illumination time, assisted ventilation time, rate of postpartum use of hormones, duration of PN administration, duration of invasive ventilation, duration of pressure support, days until toleration of enteral feeding, and length of hospital stay (LHS). Further analysis of preterm infants requiring prolonged LHS (>88.25 days) was performed to investigate risk factors. A cutoff of 88.25 days was chosen, as it represented the 75th percentile of LHS in our cohort.

Analysis

Descriptive statistics were generated from the collected data. All statistical analyses were performed using SPSS 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as the mean (standard deviation [SD]) or median (interquartile range [IQR]). Normally distributed data were analyzed by Student's t test and skewed data by Wilcoxon's rank-sum test. Categorical variables were analyzed by the chi-squared test. Multivariate and univariate logistic regression analyses adjusted for baseline variables were performed to determine the significant risk factors for ROP, and LHS. All tests for significance were two-sided and $p<0.05$ was taken to indicate statistical significance; 95% confidence intervals (CIs) were also generated.

RESULTS

Patient characteristics

A total of 1,142 preterm infants were admitted to the NICU during the study period, among whom 262 (GW

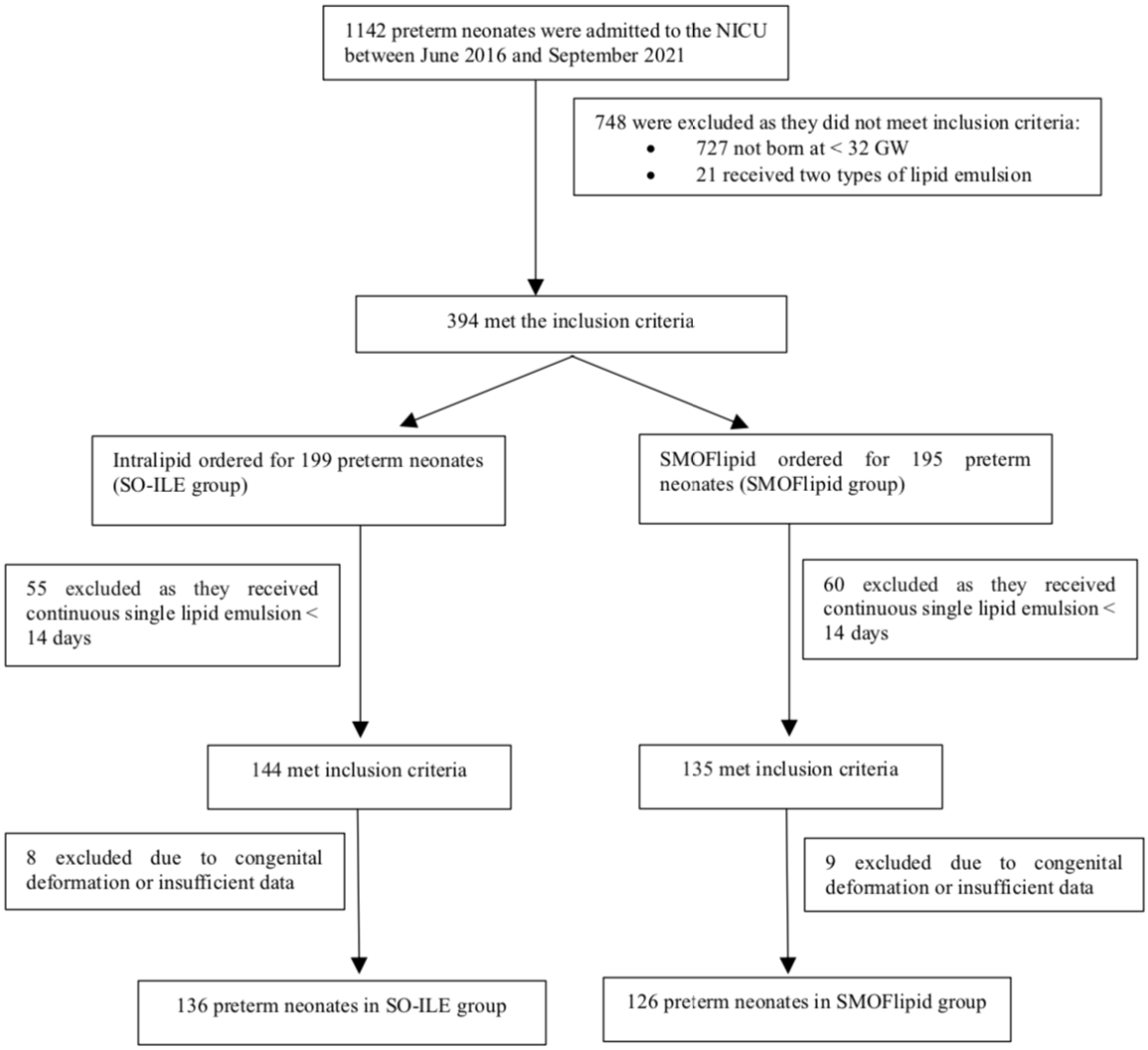

Figure 1. Participant flow chart.

<32) received either Intralipid or SMOFlipid for ≥14 days and were included in the study (Figure 1). Of these infants, 136 received Intralipid (SO-ILE group) and 126 received SMOFlipid (SMOFlipid group). Key demographic variables and baseline characteristics are shown in Table 1. The median gestational age at birth was not significantly different between the SO-ILE and SMOFlipid groups (28.6 vs 29.2 weeks; p=0.394). The groups were well balanced in terms of demographic and baseline characteristics, except for a higher proportion of PROM

Table 1. Baseline participant characteristics

	SMOFlipid (n=126)	SO-ILE (n=136)	*p*-value
Baseline maternal characteristics			
Maternal age, years†	31 (4)	31 (6)	0.705
Antepartum hemorrhage, n (%)	24 (19.0)	27 (19.9)	0.869
Premature rupture of membrane, n (%)	45 (35.7)	72 (52.9)	0.005
Cervical cerclage, n (%)	52 (41.3)	54 (39.7)	0.797
Preeclampsia, n (%)	19 (15.1)	8 (5.9)	0.014
Gestational diabetes mellitus, n (%)	20 (15.9)	30 (22.1)	0.203
Cesarean section, n (%)	111 (88.1)	112 (82.4)	0.192
Baseline preterm neonate characteristics			
Sex, male, n (%)	60 (47.6)	75 (55.1)	0.223
Gestational age at birth, weeks†	29.2 (2.9)	28.6 (2.9)	0.394
Body weight at birth, kg†	1.29 (0.52)	1.25 (0.47)	0.752
Body length at birth, cm†	38 (6)	38 (5)	0.919
Head circumference at birth, cm†	27 (3)	27 (4)	0.396
Apgar score at 1 min†	8 (3)	8 (3)	0.773
Apgar score at 5 min†	9 (2)	9 (2)	0.615
Early onset sepsis, n (%)	67 (53.2)	61 (44.9)	0.178

†Data are presented as median (IQR) (Mann–Whitney U test).

in the SO-ILE than SMOFlipid group (52.9% vs 35.7%; p=0.005).

Clinical outcome variables

Comparison of morbidities and mortality between the groups indicated no significant differences in bronchopulmonary dysplasia, intraventricular hemorrhage, late-onset sepsis, necrotizing enterocolitis, cholestasis, gastrointestinal bleeding, pulmonary hemorrhage, patent ductus arteriosus, purulent meningitis, metabolic bone disease, mortality, or other serious adverse events. However, there were significantly fewer cases of ROP in the SMOFlipid than SO-ILE group (23.8% vs. 37.5%; difference, −13.7% [95% CI, 2.68%, 24.7%]; p=0.017). (Table 2).

Comparison of clinical characteristics between the two groups revealed no significant difference in TPN duration, noninvasive mechanical ventilation duration, days to regain birth weight, or weight on postnatal day 7 or 14. However, the LHS was significantly shorter in the SMOFlipid than SO-ILE group (median [IQR] 64.8 [37] vs 72.5 [49] days; difference, 13 [95% CI 7, 20]; p<0.001). The total incidence of prolonged LHS (>88.25 days) was significantly lower in the SMOFlipid than SO-ILE group (15.9% vs. 33.1%, respectively; difference, −17.2% [95% CI 27.4%, 37.2%]; p=0.001) (Table 3).

Univariate and multivariate logistic regression analyses were performed to identify clinical risk factors. Univariate regression identified the type of lipid emulsion, gestational age at birth, body weight at birth, noninvasive mechanical ventilation duration, bronchopulmonary dysplasia, intraventricular hemorrhage, early onset sepsis, and late-onset sepsis as significant risk factors for the development of ROP. However, multivariate regression identified gestational age at birth (odds ratio [OR] 0.67; [95% CI 0.46, 0.97]; p=0.035) and noninvasive mechanical ventilation duration (OR 1.04; [95% CI 1.02, 1.05]; p<0.001) as significant risk factors for the development of ROP; the type of lipid did not influence the rate of ROP (OR 0.55; [95% CI 0.27, 1.12]; p=0.100) (Table 4).

Univariate regression analysis of LHS >88.25 days (Table 5) revealed 12 significant variables, which were thus included in the multivariate model (Table 5). Lipid emulsion type, gestational age at birth, cholestasis, bronchopulmonary dysplasia, and metabolic bone disease were risk factors for prolonged LHS, whereas lipid emulsion type (OR 0.099; [95% CI 0.033, 0.298]; p<0.001) and gestational age at birth (OR 0.506; [95% CI 00.317, 0.809]; p=0.004) were independent protective factors.

DISCUSSION

The results of this study on clinically relevant outcomes of lower GW preterm infants receiving neonatal PN (the SO-ILE Intralipid or MO-ILE SMOFlipid) in the NICU suggested that SMOFlipid was superior to SO-ILE in terms of LHS. The graphical abstract is presented in Figure 2. Preterm infants received continuous lipid emulsion for a minimum of 14 days as a component of PN, to ensure adequate exposure to the lipid formulations. As previous trials showed an influence of lipid emulsion treat-

Table 2. Comparison of morbidity and primary mortality from birth to discharge

	SMOFlipid (n=126)	SO-ILE (n=136)	Difference, % (95% CI)	p-value
Cholestasis, n (%)	37 (29.4)	43 (31.6)	−2.2 (13.3, −8.89)	0.692
Late-onset sepsis, n (%)	17 (13.5)	27 (19.9)	−6.4 (15.4, −2.58)	0.169
Patent ductus arteriosus, n (%)	38 (30.2)	44 (32.4)	−2.2 (8.83, −13.6)	0.702
Bronchopulmonary dysplasia, n (%)	47 (37.3)	55 (40.4)	−3.1 (14.0, −8.70)	0.603
Necrotizing enterocolitis, n (%)	11 (8.7)	15 (11)	−2.3 (9.49, −4.89)	0.534
Retinopathy of prematurity, n (%)	30 (23.8)	51 (37.5)	−13.7 (24.7, 2.68)	0.017
Intraventricular hemorrhage, n (%)	7 (5.6)	10 (7.4)	−1.8 (7.76, −4.16)	0.555
Gastrointestinal bleeding, n (%)	21 (16.7)	24 (17.6)	−0.9 (10.1, −8.25)	0.833
Pulmonary hemorrhage, n (%)	22 (17.5)	14 (10.3)	7.2 (3.21, −17.6)	0.092
Purulent meningitis, n (%)	16 (12.7)	13 (9.6)	3.1 (4.54, −10.7)	0.418
Metabolic bone disease, n (%)	22 (17.5)	20 (14.7)	2.8 (6.12, −11.7)	0.544
Extrauterine growth restriction, n, %	13(10.3)	22(16.2)	−5.9 (2.26, −14.1)	0.164
Mortality, n (%)	5 (4)	4 (2.9)	1.1 (3.31, −5.51)	0.907
Other serious adverse events, n (%)	15 (11.9)	11 (8.1)	3.8 (3.47, −11.1)	0.302

Table 3. Comparison of clinical characteristics and length of hospitalization

	SMOFlipid (n=126)	SO-ILE (n=136)	Difference (95% CI)	p-value
TPN duration, days†	33.50 (31)	41.0 (28)	3 (−1, 8)	0.118
Noninvasive MV duration, days†	37.0 (39)	47.5 (44)	7 (0, 14))	0.068
LHS, days†	64.8 (37)	72.5 (49)	13 (7, 20)	<0.001
LHS >88.25 d, n (%)	20 (15.9)	45 (33.1)	−17.2 (27.4, 7.2)	0.001
Days to regain birth weight†	8 (4)	8 (3)	0 (−1, 0)	0.418
Weight (kg)†				
7 days	1.31 (0.50)	1.23 (0.48)	−0.01 (−0.10, 0.07)	0.812
14 days	1.50 (0.60)	1.44 (0.61)	0 (−0.10, 0.10)	0.990

LHS: length of hospitalization; MV: mechanical ventilation; TPN: total parenteral nutrition.
†Data are presented as the median (IQR) (Mann–Whitney U test).

Table 4. Risk factors for retinopathy of prematurity in logistic regression models

Risk factor	Univariate		Multivariate	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Lipid emulsion type (SMOFlipid vs SO-ILE)	0.52 (0.30, 0.89)	0.017	0.55 (0.27, 1.12)	0.100
Gestational age at birth	0.45 (0.36, 0.55)	<0.001	0.67 (0.46, 0.97)	0.035
Body weight at birth	1.00 (0.95, 1.00)	<0.001	1.00 (1.00, 1.00)	0.388
Noninvasive MV duration	1.06 (1.04, 1.07)	<0.001	1.04 (1.02, 1.05)	<0.001
Bronchopulmonary dysplasia	5.10 (2.90, 8.96)	<0.001	1.00 (0.44, 2.24)	0.992
Intraventricular hemorrhage	2.70 (1.00, 7.28)	0.049	2.38 (0.72, 7.87)	0.155
Early onset sepsis	2.30 (1.34, 3.95)	0.002	0.91 (0.42, 1.87)	0.794
Late-onset sepsis	3.81 (1.95, 7.43)	<0.001	2.10 (0.91, 4.88)	0.084

MV: mechanical ventilation.
All covariates of multivariate logistic regression analyses are listed in the table.

Table 5. Factors predicting length of hospital stay in logistic regression models

Predictor	Univariate		Multivariate	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Lipid emulsion type (SMOFlipid vs SO-ILE)	0.38 (0.21, 0.69)	0.002	0.10 (0.03, 0.30)	<0.001
Gestational age at birth	0.39 (0.30, 0.50)	<0.001	0.51 (0.32,0.81)	0.004
Body weight at birth	0.99 (0.99, 1.00)	<0.001	1.00 (0.99, 1.00)	0.099
Cholestasis	5.19 (2.85, 9.46)	<0.001	3.51 (1.30, 9.46)	0.013
Early onset sepsis	2.82 (1.56, 5.09)	0.001	0.81 (0.31, 2.10)	0.665
Late-onset sepsis	3.61 (1.83, 7.11)	<0.001	0.95 (0.30, 2.95)	0.926
Bronchopulmonary dysplasia	15.2 (7.38, 31.48)	<0.001	10.7 (3.96, 29.1)	<0.001
Necrotizing enterocolitis	4.23 (1.84, 9.72)	0.001	3.07 (0.82, 11.5)	0.095
Patent ductus arteriosus, req. treatment	1.98 (1.03, 3.79)	0.039	1.01 (0.38, 2.70)	0.983
Pulmonary hemorrhage	2.51 (1.21, 5.23)	0.014	1.68 (0.52, 5.50)	0.389
Purulent meningitis	2.40 (1.08, 5.34)	0.032	1.99 (0.62, 6.44)	0.251
Metabolic bone disease	5.13 (2.56, 10.27)	<0.001	4.64 (1.56, 13.8)	0.006

All covariates of multivariate logistic regression analyses are listed in the table.

ment for at least 7–14 days on infant biochemical parameters,[19-21] we considered this an adequate period to meaningfully impact clinical outcomes.

Pure SO-ILEs have been the standard lipid emulsions used in NICU worldwide for the last few decades.[22] However, there are concerns that lipid emulsions based purely on SO may increase lipid peroxidation, oxidative stress, and inflammation because of their high ω-6 polyunsaturated fatty acid (PUFA) and low ω-3 PUFA concentration. Newer lipid emulsions aim to decrease excessive ω-6 fatty acid content by using lipids from sources other than SO. More recently, lipid emulsions derived from multiple sources have become available for clinical use. SMOFlipid is a 30:30:25:15 mix of MCT, SO, OOS, and FO.15 Relative to Intralipid, SMOFlipid provides higher concentration of ARA (20:4 ω-6) and DHA (22:6 ω-3), as well as the ω-3 fatty acid EPA (C20:5 ω-3), with an ARA:DHA ratio of 1.0:3.5; thus, it may reduce oxidative stress and lipid peroxidation.[23] In addition, there is evidence suggesting that SMOFlipid may provide a more balanced nutritional supply, which may improve clinical and neurodevelopmental outcomes.[24] These factors may be related to the reduction of LHS in this retrospective cohort.

The use of SO-based emulsions in PN is a risk factor for cholestasis. A number of studies suggested that high ω-6 fatty acid concentration have a negative impact on inflammation and oxidative stress, making them possible causes of PNAC.[12] In addition, clinical studies have shown a strong correlation between the phytosterols present in SO-ILE and PNAC, which is supported by cell culture and animal model studies.[9-11] Lipid emulsion composition is a modifiable risk factor for PNAC that can reduce the likelihood of disease onset, and possibly also promote disease resolution. Recently, SMOFlipid has been utilized with the goal of avoiding cholestasis while maintaining energy intake. Use of SMOFlipid as the lipid emulsion component of PN may be beneficial for preventing PNAC in NICU patients receiving PN for ≥2 weeks.[1] However, the results of the present study showed no significant difference in the incidence of PNAC between preterm infants who received either Intralipid (31.6%) and SMOFlipid (29.4%) (difference, −2.2%; [95% CI 13.3%, −8.89%]; p=0.692). At present, understanding of how different components of parenteral fatty acids and their mixtures modify inflammatory and metabolic responses is limited.

Postnatal blood concentration of the essential fatty acids, DHA and ARA, are low in preterm infants, and are correlated with the progression of ROP.[25–27] Clinical trials supplementing preterm infants with DHA to improve the development of visual function and prevent ROP have yielded inconsistent results. Meta-analyses have shown benefits of the inclusion of FO as part of PN, as it significantly reduces the likelihood of severe ROP in preterm infants compared to other lipid emulsions without FO.[28] In the present study, the incidence of ROP was lower in the SMOFlipid than SO-ILE group, but this difference lost significance in the multivariate regression analysis; this may have been due to the small population size and

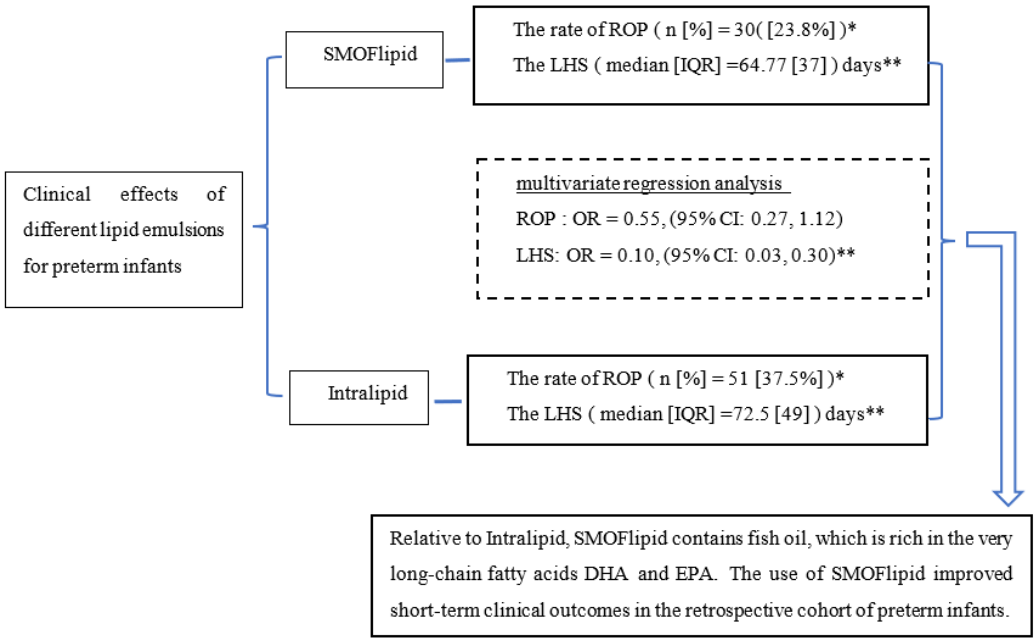

Figure 2. Graphical Abstract. SMOFlipid, a mixed lipid emulsion, contains 30% soybean oil, 30% medium-chain triglycerides, 25% olive oil, and 15% fish oil; Intralipid, soybean oil-based intravenous lipid emulsion, contains 100% soybean oil. ROP: Retinopathy of prematurity; LHS: length of hospital stay. $^{*}p<0.05$, $^{**}p<0.001$.

low incidence of ROP. Mixed results have been reported regarding the relationship between administration of lipid emulsions and the development of ROP. In 2019, Kapoor et al. published a meta-analysis of five studies (n=523) comparing SMOFlipid to SO-ILEs, and reported no statistically significant differences in clinical outcomes, including ROP, between groups.[15] However, recent studies showed that significantly fewer infants receiving MO-ILE developed ROP during their admission compared to those receiving SO-ILE.[2,29]

Despite multiple systematic reviews and meta-analyses, results remain inconclusive. The main limitation of intravenous supplementation is duration, as preterm infants only rely on PN for a limited time, usually in the range of a few days to weeks. None of the currently available parenteral lipid emulsions can prevent the postnatal deficits in DHA and ARA seen in preterm infants. FO-containing lipid emulsions exacerbate the ARA deficit relative to 100% SO, increase EPA concentration, and have an inverse ARA:DHA ratio compared to that observed at birth (and thus in utero).17 A recent cohort study showed that higher mean daily serum concentration of DHA during the first 28 postnatal days were associated with less severe ROP even after adjustment for known risk factors, but only in infants with sufficiently high ARA concentration.[30] These results suggest that maintenance of an adequate ARA concentration is required for DHA to exert protective effects against ROP.[25,31,32]

This is the first study to compare clinically relevant outcomes between preterm infants receiving the SO-ILE, Intralipid, and the MO-ILE, SMOFlipid, in China. The strengths of the present study included the comparison of long-term use of lipid emulsions between lower GW preterm infants and literature cases, and the fact that all of our patients were born in internal obstetric centers and transferred to the NICU. Therefore, antenatal follow-ups, delivery room resuscitation practices, and transport processes were standardized.

The limitations of this study include the retrospective design and analysis of historic cohort data. Advances in the management and care of premature infants inevitably occurred over the long study period, and changes in management practices over the study period could have influenced the detection or occurrence of the outcomes examined (e.g., a policy change requiring earlier initiation of prophylactic erythropoietin supplementation). The long study period would have led to inherent bias. Also, due to the retrospective nature of the study, no laboratory data were available regarding anti-inflammatory and antioxidant effects. Long-term follow-up may be useful to further assess the development of infantile complications, as the data analyzed in this study were limited to the date of discharge.

Conclusion

The present study demonstrated improved short-term clinical outcomes in a retrospective cohort of preterm infants provided with the MO-ILE, SMOFlipid, over the SO-ILE, Intralipid, for PN. The use of SMOFlipid in low GW preterm infants was associated with shorter LHS, and there was no evidence of adverse effects. Further sufficiently powered randomized controlled trials are necessary to determine the causal relationship between PN with SMOFlipid and decreased morbidity.

AUTHOR DISCLOSURES

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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