Morbidity Outcomes of Very Low Birth Weight Neonates Receiving Parenteral Nutrition with Fish Oil Enriched Lipid Emulsion or Lipid Emulsion with Soybean Oil: An Observational Study

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Abstract

Intralipid (Fresenius Kabi) was the most commonly used lipid emulsion in parenteral nutrition (PN), with a 100% soybean oil composition, a low vitamin E content, and a ω-6: ω-3 ratio of 7:1. A recent alternative formulation is SMOFlipid (Fresenius Kabi), with a ω-6: ω-3 ratio of 5:2 and higher vitamin E content. A retrospective observational study was conducted to determine neonatal morbidity in very low birth weight (VLBW) premature infants during two periods: P1, when PN was based exclusively on Intralipid, and P2, when only SMOFlipid was supplied. In total, 170 VLBW neonates were analyzed, of whom 103 received PN for more than 6 days, 56 during P1, and 47 during P2. In both periods, the antenatal and neonatal characteristics of the cohort were comparable. In this analysis, the prevalence of associated comorbidities was determined. During P2, there were fewer cases of moderate to severe bronchopulmonary dysplasia (BPD) and of cholestasis, but more cases of late sepsis, mainly *Staphylococcus epidermidis*. No changes in the prevalence of other neonatal comorbidities were observed. We believe that the SMOFlipid used in PN could discreetly improve the prevalence of cholestasis or BPD.

Keywords

- parenteral nutrition
- neonatal morbidity
- long-chain polyunsaturated fatty acids
- bronchopulmonar dysplasia
- late onset sepsis
- necrotizing enterocolitis
- intraventricular hemorrhage
- persistent ductus arteriosus

Adequate nutrition of the very low birth weight (VLBW) preterm infants is essential to adequate growth and development and reduces short- and long-term comorbidities.[1] Therefore, parenteral nutrition (PN) must sometimes be supplied to ensure the neonate receives an adequate caloric intake from the first hours of life, although neither enteral nor PN exactly reproduce intrauterine nutritional conditions.[2] Total 70% of energy consumption during fetal growth is employed in the development of the brain. Lipids comprise 50 to 60% of brain tissue (dry weight), hence their importance in neonatal nutrition.

Lipids are a fundamental source of energy in PN due to their high energy density. They are also a source of long-chain polyunsaturated fatty acids (LC-PUFAs), the structural constituents of most cell membranes.[3] There are two groups of LC-PUFAs considered essential for humans. The LC-PUFAs of the ω-6 series, whose 18-carbon representative is linoleic acid (LA) and the LC-PUFAs of the ω-3 series, whose 18-carbon representative is the α-linolenic acid (ALA). Both LA and ALA compete for the same desaturases so that the excess substrate of one and the other series affects the formation of their metabolites of 20 and 22 carbons, respectively:

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eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) for ALA and arachidonic acid (ARA) for LA.

SMOFlipid is a blend of soybean (30%), coconut (30%), olive (25%), and fish (15%) oils. This emulsion has a higher concentration of vitamin E (500 µmol/L) and of ω-3 fatty acids EPA and DHA than Intralipid. In view of well-known anti-inflammatory effects of ω-3 fatty acids, a priori we expect SMOFlipid to have a beneficial effect against various chronic inflammatory diseases.[4] ω-6 and ω-3 LC-PUFAs share the same desaturases in their metabolism so that an increase in the amount of ω-3 in lipid emulsions inhibits the cyclooxygenase pathway, favoring lipoxygenase, and decreasing pro-inflammatory prostaglandins.[5]

Previous studies have examined the early administration of lipids in PN of VLBW preterm infants, seeking to determine its relationship with weight gain, neurological development, and the prevalence of neonatal comorbidities such as bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), and retinopathy of prematurity (ROP).[6–8] A systematic review[6] suggested that the early administration of lipids in PN is safe and well tolerated, and does not provoke a higher incidence of adverse events. However, other studies[9] have related the prolonged use of intravenous lipid emulsions with a higher incidence of *Candida sepsis*, hyperbilirubinemia, cholestasis, or BPD.[10]

Until a few years ago, lipid emulsions based on soybean oil (Intralipid, Fresenius Kabi) were the most commonly used, with a ω-6:ω-3 ratio of 7:1 and low vitamin E content compared with SMOFlipid.[6] These lipid emulsions contain 60% LC-PUFAs mostly as linoleic acid (LA), which will be metabolized to ARA in a variable proportion and that could exceed daily LA requirements for VLBW preterm infants (estimated at 0.25 g/kg/day). For this reason, soybean oil emulsions may increase oxidative stress[11] and hence aggravate the consequences of BPD. Lipid emulsions based on a combination of soy and coconut oils provide higher proportions of medium chain triglycerides (MCT), enabling faster plasma clearance and greater resistance to lipid peroxidation.

Although in some studies,[12] olive oil and fish emulsions can reduce mortality in critically ill patients, no significant evidence has been reported in different meta-analysis.[6] Clinical studies have observed a slight decrease in the prevalence of persistent ductus arteriosus (PDA) in VLBW preterm infants given SMOFlipid, absence of changes in the prevalence of NEC and ROP,[13] and an association with decreased BPD and more favorable lipoprotein profile.[9]

DHA is an LC-PUFA of 22 carbons, also defined as ω-3 VLC-PUFA, is an important component in the development of the central nervous system and the retina.[14,15] It also plays a significant role in resolving inflammatory processes and in the immune response. Although the VLBW preterm infant can synthesize small amounts of DHA from ALA, a deficiency of DHA is frequently observed when the neonate's diet consists of lipid emulsions based on soybean or olive oil, with a predominance of ω-6 LC-PUFAs, plant oil-based emulsions contain the DHA precursor ALA but only trace amounts preformed DHA.[14] These emulsion may contain a small amount of DHA from the egg phospholipids, and that this fraction can probably be batch dependent.

Zhang et al[15] analyzed nutritional supplementation with ω-3 LC-PUFAs for VLBW preterm infants, associating it with a reduced incidence of NEC and of BPD. Moreover, the inclusion of ω-3 LC-PUFAs in the diet can reduce the pathological neovascularization of the retina and thus decrease the need for laser treatment.[16]

The aim of the present study is to determine whether the prevalence of neonatal comorbidities during two different periods changes when lipid emulsions containing fish oil (SMOFlipid) are routinely included in PN formulation in a neonatal hospital unit.

Materials and Methods

A retrospective cohort study was designed and applied to compare rates of neonatal comorbidity during two periods, before and after the inclusion in PN of a lipid emulsion containing fish oil (SMOFlipid, Fresenius Kabi), for VLBW preterm infants at the neonatal intensive care unit at our hospital. In the first period, P1, from 1 July 2014 to 30 June 2016, PN was based on Intralipid (Fresenius Kabi). During the second period, P2, from 1 July 2016 to 30 June 2018, the Intralipid was replaced by SMOFlipid (►Fig. 1).

Ethical Considerations

The protocol was approved by the ethics committee of the hospital and all current regulations regarding data confidentiality were complied with.

Inclusion and Exclusion Criteria

All newborns admitted to our NICU with a gestational age less than or equal to 32 weeks or a birthweight below 1,500 g and who also received total or partial PN for more than 6 days were included in this study. Patients with intestinal atresia or pathological conditions that indicated prolonged PN beforehand were not included in any of the periods.

Nutritional Management

The nutritional strategy at our neonatal unit was applied in accordance with the recommendations of the Nutrition and Metabolism Group of the Spanish Neonatology Society[17] and the standard protocol of the neonatal unit. It can be summarized as follows. In most cases, early PN was started during the first 2 hours of life, with an initial provision of glucose at 5 mg/kg /minute, together with 2 g/kg of an amino acid solution. The infusion of Intralipid or SMOFlipid lipid solution was initiated during P1 and P2 from 24 hours of life at 0.5 g/kg/day, with daily increments of 0.5 g/kg/day to reach 3 g/kg/day by the end of the first week of life. In all cases, 1.2 µm filters were used for PN (Pall, Medical).

Enteral nutrition with breast milk if possible, or otherwise with premature formula, was started early whenever possible at 10 mL/kg/day and with a progressive daily increase of 25 mL/kg/day. After reaching volumes of 80 mL/kg/day and after the first week of life, breast milk was fortified with a commercially available cow's milk-based fortifier (FM85,

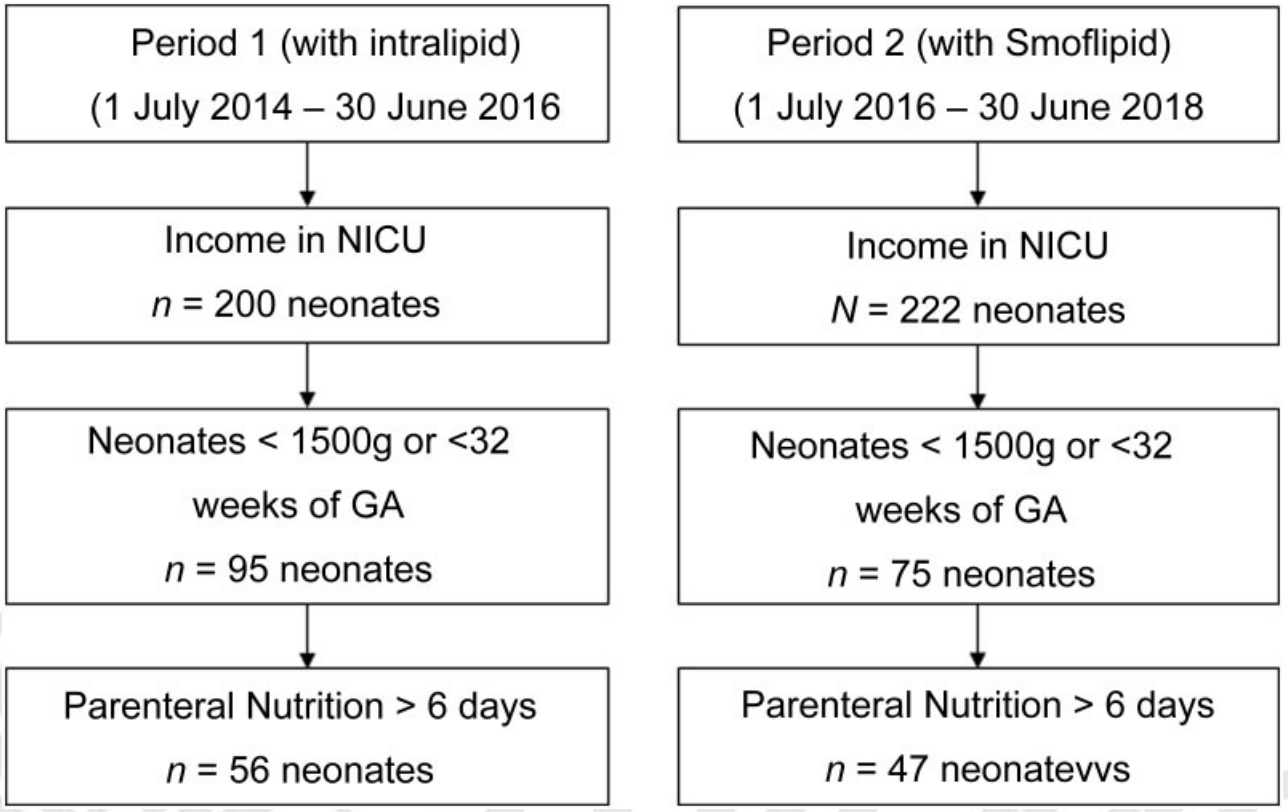

Fig. 1 Flow diagram.

Nestlé). The inputs of liquids, energy, proteins, carbohydrates, and lipids during the first week of life were recorded retrospectively (►**Table 1**).

Anthropometry

The weight, length, and cephalic perimeter are recorded when entering the neonatal unit. The change in weight is recorded daily, with weekly records of length and cephalic perimeter. ►**Table 1** includes the weights and z-score at birth and the week of life of the newborns in both periods. For the calculation of the z-score, the Fenton tables were used.[18]

Morbidity

The presence of any degree of BPD was recorded. According to the thresholds proposed by NIHCD[19] and by Jobe and Bancalari,[20] BPD is defined as a need for supplemental oxygen >21% at 28 days of life and/or a need for supplemental oxygen >21% or for positive airway pressure at 36 weeks of corrected gestational age. BPD is classified as mild, moderate, or severe.

Late sepsis is defined as the presence of a positive blood culture at 72 hours after admission to the neonatal unit and CRP >2 mg/dL (two positive blood cultures for *S. epidermidis*). A diagnosis of clinical sepsis was made when a NOSEP-1 score >8 was recorded. On this scale, the presence of CRP >1.4 mg/dL is assigned five points; that of neutrophils >50%, three points; thrombocytopenia $<150 \times 10^9$/L, five points; and fever >38.2°C, five points.

The diagnosis and staging of ROP were based on retinal examination before discharge from the neonatal unit, with severe ROP defined as stages 3 to 5.[21] In ROP, the presence of one or more of the following was classified as an unfavorable outcome: a retinal fold involving the macula; retinal detachment involving zone I of the posterior pole; retrolental tissue, or "mass"[22].

The diagnosis of IVH was based on Papile's classification.[23] All neonates received a transfontanellar ultrasound examination on the third day of life and every week thereafter.

For the diagnosis of NEC, patients were classified according to Bell's criteria.[24] Cholestasis was defined as an increase in direct bilirubin values >2 mg/dL (34.2 µmol/L). For this study only cases of secondary cholestasis detected after receiving PN are considered. No cases of primary cholestasis have been considered in this study.

Statistical Analysis

Study data were recorded in the e-Health record and in the Neosoft (Spanish Society of Neonatology) program. The descriptive data were summarized using medians and the interquartile range for continuous values and frequency distribution for categorical variables. Univariate comparisons of continuous variables were performed using the Mann–Whitney's test and by the Chi-square test for categorical variables. The risk assessment of BPD, ROP, NEC, and late sepsis was obtained by means of binary and multivariate logistic regression analysis (multinomial analysis) for the variables with one or more categories. In each analysis, the regressions were adjusted for possible confounding factors. The effects of the study periods were summarized as adjusted odds ratios (OR) with 95% confidence intervals (CI). The

Table 1 Gestational and neonatal characteristics (<1,500 g or <32 weeks of gestational age)

Characteristics	P1, $n = 95$	P2, $n = 75$	p-Value
	n (%)	n (%)	
Maternal			
PIH	3 (3.7)	8 (11.9)	0.05
Chorioamnionitis	8 (9.8)	6 (9.0)	0.86
Antibiotics	39 (47.6)	27 (40.3)	0.37
Glucocorticoids	69 (84.1)	61 (92.4)	0.12
PPROM	20 (24.4)	16 (23.9)	0.94
Gestation (weeks)[a]	30 (28–31)	30 (28–31)	0.80
Gestation ≤27 weeks	16 (19.5)	11 (16.4)	0.62
Twin birth	33 (40.2)	34 (50.7)	0.20
Caesarean section	63 (76.8)	55 (82.1)	0.43
Neonatal			
Birth weight (g)[a]	1,338 (1,046–1,583)	1,254 (975–1,437)	0.15
Birth weight (z-score)[a]	−0.46 (−1.03 to 0.03)	−0.44 (−1.05 to 0.27)	0.75
Weight 7 days (z-score)[a]	−1.13 (−1.53 to −0.66)	−1.18 (−1.61 to −0.57)	0.86
Male gender	49 (59.8)	38 (56.7)	0.70
Apgar ≤5 (5 min)	9 (11.1)	6 (9.1)	0.68
IUGR	11 (19.0)	13 (19.4)	0.95
Human milk feeding[b]	42 (54.5)	42 (68.9)	0.08
Length of NICU stay (d)[a]	25 (12–38)	27 (14–39)	0.52
Central venous catheter (d)[a]	6 (6–16)	9 (9–18)	0.64
Age at full feeds (d)[a]	10 (6–17)	10 (7–22)	0.26
Parenteral nutrition (d)[a]	10 (5–17.7)	10 (5–17.5)	0.37
Early parenteral nutrition	67 (70.5)	59 (79.7)	0.17
Probiotics	64 (67.4)	42 (56.0)	0.12
Respiratory support			
Oxygen	71 (87.7)	64 (97.0)	0.04
CPAP	61 (74.4)	56 (83,6)	0.17
Mechanical ventilation	41 (51.3)	35 (52.2)	0.90
Duration (h)[a]			
Oxygen	312 (96–1,398)	576 (216–1,056)	0.28
CPAP	72 (72–168)	72 (48–144)	0.30
Ventilation	24 (24–120)	24 (24–72)	0.94

Abbreviations: CPAP, continuous positive airway pressure; IQR, interquartile range; IUGR, intrauterine growth restriction; PIH, pregnancy induced hypertension; PPROM, preterm prelabor rupture of membranes.
[a]Median (IQR). p-valor C^2 for qualitative analysis, Mann–Whitney for quantitative analysis).
[b]Supplemented by less than 25% of the weekly volume with premature formula milk.

analysis was conducted on all neonates with <32 weeks of gestation. Characteristics that differed between study periods and other parameters considered to influence neonatal outcomes (e.g., maternal antenatal antibiotics) were also assessed during modeling. The analysis was performed using IBM SPSS 20.0 for Windows (IBM, Armonk, NY).

Reporting

The STROBE checklist for reporting observational studies was used.[25]

Results

Of the total of 170 neonates weighing <1,500 g or with a gestational age <32 weeks (hence, classed as VLBW), 103 received PN for >6 days. Of these, 56 received PN during P1 and 47 during P2.

As shown in ►Table 1, the antenatal and postnatal characteristics of the neonates included in P1 and P2 were broadly comparable, with no statistically significant differences although the birth weights of those included in P2 were slightly

lower. These circumstances were taken into account when making statistical adjustments in the regression analysis. Just over 70% of the neonates in P1 and 79.7% in P2 received early PN (►Table 1), and no statistically significant differences were observed between them. The percentages of neonates who were breastfed were also comparable in P1 and P2 (►Table 1). ►Table 1 shows z-score of weight for gestational age at birth and at 7 days, we did not observe growth differences between groups at 7 days of age, which is not surprising given that in both groups the caloric supply was equivalent. ►Table 2 shows the average daily nutrition received (liquids, calories, and macronutrients) during P1 and P2. There were no significant quantitative differences between the periods. ►Table 3 shows, for each period, the associations observed with the neonatal comorbidities analyzed. These results are discussed below. After considering the newborns who received PN for more than 6 days, we observed in P1 a weight of 1,216 g (786–1,625) and gestational age of 28.9 weeks (26.1–32.0); and in P2 a weight of 1,145 (775–1,464) and a gestational age of 28.9 weeks (25.9–31.1). No significant differences were observed for weight ($p = 0.31$) and gestational age ($p = 0.74$) between subgroups.

Outcomes for BPD

Although the differences were not statistically significant, the median duration of oxygen therapy was slightly greater in P2 than in P1, which is explicable by the slightly lower birth weight of these neonates (►Table 1). Without reaching statistical significance, the number of moderate to severe forms of BPD tended to decrease during P2, as the number of mild forms increased. In severe forms of BPD, the low number of cases during P2 (1 case) failed to perform statistical comparison (►Table 3). As shown in ►Table 1, the number of oxygen hours was globally greater in P2, which is justified by the case of severe BPD in P2 that deviated from the median number of hours received

Outcomes for Late Onset Sepsis

After the change of lipid emulsion between P1 and P2, there was a statistically significant increase in the incidence of late sepsis, with an OR of 3.15 (►Table 3) and a predominance of *S. epidermidis* infections (►Table 4). As shown in ►Table 1, we did not observe differences in the days of central catheter in both periods.

Outcomes for the Cholestasis

As shown in ►Table 3, we observed a decrease in cholestasis in the limit of statistical significance in P2.

Outcomes for other Morbidities

More cases of NEC with stage ≥2 were observed during P2 although this association was not statistically significant after adjustment with the related variables (►Table 3). We observed a low concordance between the cases of late sepsis and NEC ≥2 (Kappa = 0.20). No differences were observed between periods with respect to stage 3 NEC (►Table 3).

As previously reported,[26] the prevalence of ROP in our neonatal unit is low, which probably explains why there were no statistically significant changes in the prevalence of ROP in each period following the change of lipid emulsion in PN.

There were no differences in the number of cases of IVH and PDA recorded. However, the number of cases of cholestasis decreased during P2 although the difference was at the limit of statistical significance. After adjusting for days of PN and the presentation of late sepsis, we observe a tendency to decrease the risk of cholestasis associated with the change of lipid emulsion in PN.

Discussion

In our neonatal unit, the introduction of SMOFlipid as a lipid emulsion in the PN of VLBW preterm infants was associated with a change in the prevalence of some neonatal comorbidities. The cases of cholestasis and severe BPD decreased markedly, but there was a significant increase in the number of cases of late sepsis when SMOFlipid was supplied for 1 week or more.

It is true that our study was performed in two different periods and that in those periods changes in work routines

Table 2 Average daily intake of nutrition during the first week of life

Characteristics	P1	P2	*p*-Value
Parenteral liquids (mL/kg/day)	102 (73.7–117.1)	102 (80.8– 116.1)	0.90
Enteral liquids (mL/kg/day)	12.5 (2.8–39.2)	14.5 (4.3–36.7)	0.59
Parenteral calories (kcal/kg/day)	55.4 (37.3–64.9)	59.1 (42.4–70.3)	0.18
Enteral calories (kcal/kg/day)	9.0 (2.0–32.8)	11.5 (2.6–32.5)	0.64
Parenteral proteins (g/kg/day)	2.28 (1.16–2.78)	2.51 (1.68–2.96)	0.09
Enteral proteins (g/kg/day)	0.20 (0.03–0.73)	0.17 (0.06–0.81)	0.98
Parenteral carbohydrates (g/kg/day)	9.17 (6.89–10.28)	9.50 (6.96–11.60)	0.23
Enteral carbohydrates (g/kg/day)	0.99 (0.22–3.07)	1.20 (0.27–3.20)	0.68
Parenteral fats (g/kg/day)	1.14 (0.44–1.57)	1.10 (0.66–1.42)	0.88
Enteral fats (g/kg/day)	0.47 (0.11–1.53)	0.60 (0.13–1.56)	0.67

Abbreviation: IQR, interquartile range.
Note: Median (IQR). Mann–Whitney *p* value for quantitative analyses.

Table 3 Analysis results for neonates with parenteral nutrition lasting >6 days

	P1	P2	OR (95% CI)	Adjusted *p*-Value
	n (%)	*n* (%)		
Cases (*n*)	56	47		
Mortality[a]	2 (3.6)	2 (4.3)	1.20 (0.16–8.86)	0.85
BPD[b]	26 (49.1)	21 (48.8)	2.14 (0.43–10.4)	0.34
Mild	7 (12.5)	10 (22.7)	2.25 (0.63–8.04)	0.20
Moderate	13 (23.2)	10 (22.7)	0.55 (0.14–2.18)	0.40
Severe	6 (10.7)	1 (2.3)		
NEC ≥ stage II[c]	5 (8.9)	11 (23.9)	1.96 (0.43–8.83)	0.37
NEC stage III[c]	2 (3.6)	1 (2.2)		
PDA[d]	13 (23.2)	12 (25.5)	0.58 (0.17–1.91)	0.37
IVH				
Grade I–II	9 (16.1)	7 (15.2)	0.93 (0.32–2.74)	0.90
Grade III–IV	2 (3.6)	1 (2.2)	1.66 (0.14–18.9)	0.68
ROP[e]	6 (6.7)	6 (13.3)	2.30 (0.55–9.48)	0.24
Late onset sepsis[c]	8 (14.3)	18 (38.3)	3.15 (1.12–8.86)	0.02
Cholestasis[f]	15 (27.3)	9 (19.1)	0.27 (0.07–1.05)	0.05

Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; PDA, Patent ductus arteriosus; ROP, retinopathy of prematurity.
*Median (IQR).
[a]Adjusted for IUGR and IVH.
[b]Adjusted for IUGR, late onset sepsis, oxygen support (h), and birth weight.
[c]Adjusted for central venous catheter (d), hospital stay (d), parenteral nutrition, and probiotics (d).
[d]Adjusted for IUGR, late onset sepsis, and birth weight.
[e]Adjusted for oxygen (d) and birth weight.
[f]Adjusted for late onset sepsis and parenteral nutrition (d).

may occur that may be a source of bias for our study. However, we want to point out that the analysis of the modifications of our work protocols and the periods in which they occurred indicate that the last modification was precisely the one that is the object of our study, that is, the introduction of SMOFlipid. Two changes were made to this nutritional practice in our neonatal unit. In April 2011 (prior to our study period), the first-day PN (early PN) began to be applied. This change, bringing our action protocols in line with international recommendations (ESPGHAN),[27] increased the newborns' caloric intake in the first week of life and, secondarily, enabled us to assess the energy repercussions more effectively. The second modification concerned the lipid emulsion used. In July 2016, SMOFlipid (Fresenius Kabi) was introduced, replacing Intralipid (Fresenius Kabi) as an emulsion commonly used in PN. The repercussions of this change with respect to energy intake are taken into account in our analysis of the results.

Table 4 Etiology of the late sepsis observed

	P1	P2
Candida albicans	1	1
Candida parapsilosis	0	1
Klebsiella pneumoniae	1	1
Klebsiella oxytoca	0	1
Staphilococcus epidermidis	2	10
Staphilococcus aureus	2	0
Staphilococcus warneri	0	1
Pseudomona aeruginosa	1	0
Clinical sepsis (blood culture)	1	3
Total	8	18

Lipid emulsions based on fish oil have been shown to be effective in reducing the levels of triglycerides, conjugated bilirubin and liver enzymes, compared with emulsions based on soybean oil.[28] Our results show a tendency to decrease the cases of cholestasis during P2, which differs with that reported in a systematic review by Kapoor et al[29] who do not observe differences in the prevalence of cholestasis after the use of emulsions based on fish or soybean oil.

Hsiao et al[30] observe a significant decrease of BPD after the use of lipid emulsions with fish oil in PN. Our results do not show a significant decrease in cases of BPD although there seems to be a trend toward a decrease in the number of cases of severe BPD. We think that the anti-inflammatory effect derived from the high content of ω-3 VLC-PUFAs or the higher content of vitamin E in SMOFlipid could explain this finding.

Freeman et al[31] reported that 56% of all cases of nosocomial infection, especially those due to coagulase-negative staphylococci, could be attributed to the administration of lipids. Our results show a higher prevalence of late sepsis

during P2 mainly due to *S. epidermidis*. Other authors,[14] refer that when fish oil emulsions were included in the PN of VLBW preterm infants, the level of EPA rose and that of AA fell. Unfortunately, we have not made AA determinations in our patients. On the contrary, Vlaardingerbroek et al in a study published in 2012[6] and in another, 2 years later,[32] reported finding fewer episodes of late sepsis after lipid emulsions based on fish oil were used in PN although in no case were statistically significant differences observed. The meta-analysis by Kapoor et al[29] did not reveal any differences in the prevalence of late sepsis after the use of lipid emulsions based on fish or soybean oil, which corroborated other studies[33–35] that had observed no significant decrease in the prevalence of late sepsis with the use of fish oil emulsions.

Most studies[33,35] show no association between the administration of parenteral lipids and the development of NEC nor decrease in its prevalence after the administration of fish oil emulsions. Although we did not observe statistical significance, we observed an increasing tendency of NEC cases in P2, without concordance with the cases of late sepsis observed. The use of probiotics in P2 was 11.4% lower than in P1, we think that this circumstance could explain our results. Our observations differ with those reported by Zhang et al,[15] who observed a tendency to decrease NEC after lipid emulsion supplementation of ω-3 LCPUFAs in PN.

Although we are aware of the limitations of our study, as it is a retroactive observational study, we conjecture that the use of lipid emulsions with fish oil can modify the balance between eicosanoids (derived from AA) and resolvins (derived from DHA).[5] In this sense, in our sample we have observed a tendency to decrease cholestasis and severe forms of BPD although we observe more episodes of late sepsis by Gram-positive bacteria.

Conclusion

The results obtained in the present study corroborate previous research findings that PN with lipid emulsions supplying soybean oil (30%), MCT (30%), olive oil (25%), and fish oil (15%) (SMOFlipid), with a ω-6:ω-3 ratio of 5:2 and higher vitamin E content, can discreetly improve the prevalence of cholestasis or BPD. However, we observe in our sample an increased risk of late sepsis.

Authors' Contributions

All authors have read and approved the final manuscript. J.U. designed the research study and drafted the manuscript. S.J.M., M.M.O., P.N.G., and E.N.L. coordinated and prepared the database and analyzed the data.

Ethical Approval

The protocol was approved by the ethics committee of the hospital and all current regulations regarding data confidentiality were complied with.

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None.

Conflict of Interest

None declared.

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