DOI: 10.4274/MMJ.galenos.2022.83548
Medeni Med J 2022;37:240-247

Original Article

Effects of Fish Oil (SMOFlipid®) and Olive Oil Lipid (ClinOleic®) on Neonatal Morbidities in Preterm Infants

Balık Yağı (SMOFlipid®) ve Zeytinyağı Lipidi (Clinoleic®) İçeren Lipidlerin Erken Doğmuş Bebeklerde Neonatal Morbiditeler Üzerine Etkileri

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ABSTRACT

Objective: Total parenteral nutrition (TPN) is very important for providing optimal nutrition during the critical developmental period of preterm newborns. Thus, there is a need to optimize TPN solutions to reduce morbidities. This study aimed to examine the effects of olive oil (ClinOleic®) and fish oil (SMOFlipid®) therapies on the frequencies of neonatal morbidities.

Methods: Premature newborns hospitalized in the neonatal intensive care unit and receiving TPN for at least 14 days were included in the study. Newborns who were hospitalized and received olive oil-based lipid (ClinOleic®) were included in the olive oil group, and those who received omega-3 containing multi-lipid (SMOFlipid®) were included in the SMOFlipid group.

Results: This study enrolled a total of 222 very-low-birth-weight premature newborns. The breastfeeding rate in the olive oil group was significantly lower than that in the SMOFlipid group ($p<0.05$). The rate of necrotizing entercolitis (NEC) in the olive oil group was significantly higher than that in the SMOFlipid group ($p<0.05$). The rate of bronchopulmonary dysplasia (BPD) in the SMOFlipid group was lower than that in the olive oil group ($p<0.05$).

Conclusions: The rates of BPD and NEC were lower in the fish oil group. In this situation, fish oil therapy may provide protection against the development of BPD and NEC. Prospective studies are needed to determine whether this is caused by lipid therapy or an effect of breast milk.

Keywords: Lipid emulsions, parenteral nutrition, premature newborns, morbidities

ÖZ

Amaç: Uzun süreli total parenteral beslenme (TPN), erken doğan yenidoğanların kritik bir gelişim aşamasında optimal beslenmeyi sağlamaları için çok önemlidir. Morbiditeleri azaltmak için TPN çözümlerini optimize etmeye ihtiyaç vardır. Bu çalışma, zeytinyağı (ClinOleic®) ve balık yağı (SMOFlipid®) tedavilerinin neonatal morbidite sıklıkları üzerine etkilerini araştırmayı amaçlamıştır.

Yöntemler: Yenidoğan yoğun bakım ünitesinde yatan ve en az 14 gün total parenteral beslenme alan prematüre yenidoğanlar çalışmaya dahil edildi. Hastaneye yatırılan ve zeytinyağı bazlı lipid (ClinOleic®) verilen yenidoğanlar zeytinyağı grubuna, hastaneye yatırılan ve multi-lipid içeren omega 3 (SMOFlipid®) verilen yenidoğanlar SMOF lipid grubuna alındı.

Bulgular: Bu çalışmaya toplam 222 çok düşük doğum ağırlıklı prematüre yenidoğan kaydedildi. Zeytinyağı tedavisi gören yenidoğanlarda emzirme oranı diğer gruba göre anlamlı derecede düşüktü ($p<0,05$). Zeytinyağı tedavisi alan yenidoğanlarda nekrotizan enterokolit (NEK) oranı diğer gruba göre anlamlı derecede yüksekti. SMOFlipid grubu alan yenidoğanlarda bronkopulmoner displazi (BPD) oranı zeytinyağı tedavisi alan yenidoğanlara göre daha düşüktü ($p<0,05$).

Sonuçlar: Balık yağı grubunda BPD ve NEK oranlarımız daha düşük bulundu. Bu durumda balık yağı tedavisi BPD ve NEK gelişimine karşı koruyucu olabilir. Bunun kullanılan lipid tedavisinin sonucundan mı yoksa anne sütünün etkisinden mi kaynaklandığını belirlemek için ileriye dönük çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Lipid emülsiyonları, parenteral beslenme, prematüre yenidoğanlar, morbiditeler

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Received: 13 June 2022
Accepted: 30 July 2022
Online First: 06 September 2022

Cite as: Kilicbay F, Keskin A, Gunlemez A. Effects of Fish Oil (SMOFlipid®) and Olive Oil Lipid (ClinOleic®) on Neonatal Morbidities in Preterm Infants. Medeni Med J 2022;37:240-247

INTRODUCTION

Postnatal growth restriction due to feeding intolerance and necrotizing enterocolitis (NEC) in high-risk newborns is a very important issue. Long-term total parenteral nutrition (TPN) is very important in these infants to ensure optimal postnatal growth[1]. Lipid emulsion (LE) is an essential component of TPN because it contains essential fatty acids, a concentrated source of energy, and long-chain polyunsaturated fatty acids (LC-PUFAs) with limited endogenous synthesis[2].

Although soybean oil (SO)-based LEs are frequently used today, the frequency of use of olive oil-based LEs has increased recently in many neonatal intensive care units[3,4]. SO emulsion is high in omega-6 PUFAs, which have lipid peroxidation and inflammation-promoting properties, such as linoleic acid (LA). Olive oil emulsions are high in monounsaturated fatty acids (MUFAs) and have a higher omega-6/omega-3 ratio because of their lower omega-3 PUFA content (9:1), which is not ideal for the developing newborn[5,6].

"SMOFlipid," a new LE, is based on a mixture of SO (30%), medium-chain triglycerides (MCTs) (30%), olive oil (25%), and SMOFlipid (15%). It is a great source of energy, MUFAs, and omega-3 fatty acids. In addition, its antioxidant property is supported by α-tocopherol (200 mg/L), and it has a small omega-6 to omega-3 ratio (2.5:1)[7,8]. The benefit of the new lipid-based emulsion products is the reduction of cholestasis as a result of rapid lipid clearance, less oxidative stress, less lipid peroxidation, appropriate amount of antioxidant α-tocopherol and MUFAs, necessary LC-PUFAs that have a crucial role in neurodevelopment, and optimum visual function. SMOFlipid has an omega-6 to omega-3 ratio, which decreases immune activity, and has an anti-inflammatory effect because it contains omega-3 PUFAs[8,9].

Premature birth, immature immune system, and low birth weight (SGA) leave newborns vulnerable to oxidative stress damage, which facilitates the development of intraventricular hemorrhage (IVH), NEC, and chronic lung disease [bronchopulmonary dysplasia (BPD)], and retinopathy of prematurity (ROP)[10]. As LC-PUFAs such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) in preterm babies pass from the mother to the fetus during the third trimester, fatty acid deficiency occurs[11]. These fatty acids are very important for the improvement of vision and cognition and decreased thrombotic and inflammatory responses[12]. The use of lipid preparations consisting of SO, MCTs, olive oil, and fish oil (SMOFlipid) has increased in recent years. SO provides both LA and alpha-LA. Olive oil is rich in MUFAs that are less sensitive to lipid peroxidation than PUFAs influencing hepatobiliary function. The metabolic clearance of lipid preparations containing fish oil is faster than olive oil[13]. Some studies have shown improvement in ROP and neonatal cholestasis in newborns receiving SMOFlipid therapy[14].

We hypothesized that due to increased omega-3 LC-PUFA levels, SMOFlipid therapy could reduce the prevalence of neonatal morbidities, including ROP, NEC, and BPD, and the duration of hospitalization in high-risk preterm newborns dependent on TPN support compared with olive oil LE therapy. Despite studies regarding the positive effects of SMOFlipid on the liver, we conducted this study because of the limited number of studies on premature babies. Thus, this study aimed to investigate the effects of olive oil lipid (ClinOleic®) and fish oil (SMOFlipid®) on the frequency of neonatal morbidities, including ROP, IVH, patent ductus arteriosus (PDA), NEC, BPD, late-onset neonatal sepsis, cholestasis, and length of stay.

MATERIALS and METHODS

Premature newborns hospitalized in Kocaeli University Faculty of Medicine Neonatal Intensive Care Unit with a very low birth weight (VLBW, birth weight ≤1,500 g) and who received TPN for at least 14 days were included in the study. Newborn files were scanned retrospectively. Newborns hospitalized between 01.1.2009, and 02.1.2012, who received olive oil-based lipid (ClinOleic®) were assigned to TPN group 1. Newborns hospitalized between February 2, 2012, and November 30, 2012, who received omega-3 containing multi-lipid (SMOFlipid®) preparation are assigned to TPN group 2.

The newborns included in the study received two types of LEs: olive oil (20% ClinOleic® Baxter, S.A. Belgium) or SMOFlipid (20% SMOFlipid Fresenius Kabi, Pymble, Australia) (Table 1).

This study enrolled a total of 273 newborns. Of the study population, 51 were excluded because of incomplete data recording due to the workload of the neonatology service and low transition time to full oral feeding to follow-up. Of the newborns who were enrolled in the study, 106 were in the olive oil group, and 116 were in the SMOFlipid group. The exclusion criteria were as follows: Unconjugated hyperbilirubinemia (requiring exchange transfusion); early neonatal sepsis with blood culture growth; thrombocytopenia in the hemogram (platelet count <150×109 cells/L); postnatal age >3 d; metabolic problems, including lactic acidosis

Table 1. Clinical characteristics of newborns in olive oil and SMOFlipid groups.			
	Olive oil (n=106)	**SMOFlipid (n=116)**	**p-values**
Gestational age (w)*	29 (27-30)	29 (27-30)	0.733
Birth weight (g)*	1025 (810-1173)	1010 (850-1160)	0.760
Sex			
Male	52 (49.1%)	46 (39.7%)	0.117
Female	54 (50.9%)	70 (60.3%)	
SGA	69 (65.1%)	76 (65.5%)	0.947
Duration of TPN therapy (d)*	34 (23-44)	30 (21-44)	0.137
Duration of lipid therapy (d)*	24 (15-33)	25 (15-35)	0.525
Transition time to full oral feeding (d)*	36 (28-50)	34 (26-47)	0.251
Feeding style			
Breast milk	64 (60.4%)	94 (81%)	0.001
Formula	18 (17%)	4 (3.5%)	
Mixed	24 (22.6%)	18 (15.5%)	
*Data were expressed as median with interquartile range. SGA: Small for gestational age, TPN: Total parenteral nutrition			

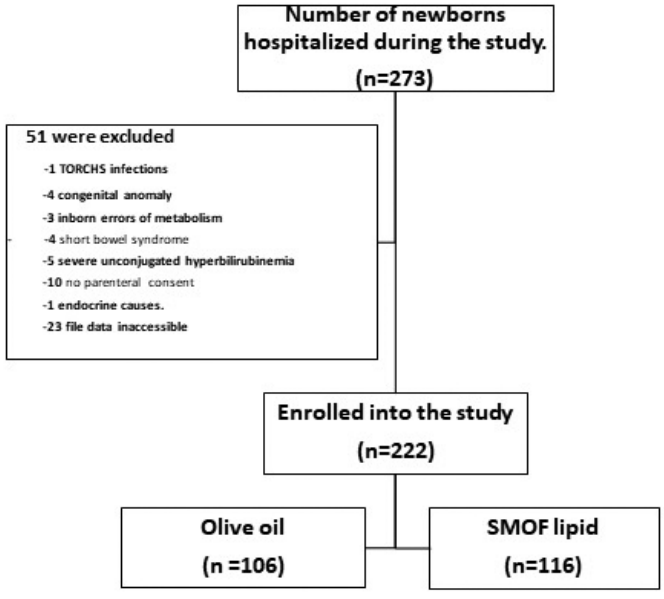

Figure 1. Flow diagram of the study.

and/or noncompensated administration of intravenous lipid infusion before the study; newborns with a bleeding disorder; and parental consent not given (Figure 1).

All patients, sex, gestational week, birth weight, small for gestational age (SGA) according to gestational week, length of stay, TPN duration, lipid duration, time to full oral feeding ratio, nutritional information, and problems accompanying prematurity such as late-onset neonatal sepsis, cholestasis, ROP, IVH, NEC, PDA, and BPD were evaluated during the TPN therapy.

ROP Requiring Treatment: All newborn routine screening and examination findings were categorized by the International Classification of Retinopathy of Prematurity[15]. The diagnosis of ROP requiring treatment was made according to the Early Treatment for Retinopathy of Prematurity criteria[16].

PDA: Echocardiography was performed on all newborns 24-48 h after birth. Medical PDA treatment was given to patients who were found to have medium and large PDA. The characteristics of hemodynamically significant PDA are as follows: ductus diameter >1.5 mm and observed on Doppler echocardiography; left atrium-to-aortic-root ratio ≥1.4; holodiastolic inverse flow in the descending aorta; enlargement of the left ventricle; additional respiratory support; and signs of left ventricular failure and/or hepatomegaly. Surgical ligation was applied to patients who did not respond to medical treatment[17].

NEC: Patients with abdominal distention, feeding intolerance, increased gastric residues, vomiting bile, and palpable stretched bowel loops on physical examination were evaluated as having NEC. The Bell classification was used for clinical staging[18].

Intracranial Hemorrhage: All patients underwent transfontanel ultrasonography for periventricular/intraventricular hemorrhage (PV/IVH) within the first 3 days of their hospitalization. Papile classification was used for the PV/IVC classification[19].

BPD: The definition of BPD was made for newborns who received oxygen for at least 28 days. BPD

classification was made according to the need for oxygen and respiratory support at the 36th gestational week[20].

Late-onset Neonatal Sepsis: Newborns diagnosed according to clinical findings of sepsis on days 4-30 of life after birth were defined as late neonatal sepsis. The presence of clinical and laboratory findings and pathogenic microorganisms in cultures taken from the sterile field was defined as "proven sepsis"[21].

Lipid Infusion Dosages and Therapy

The lipid dose protocol (20% ClinOleic® or 20% SMOFlipid) to be applied during TPN was 1 g/kg for day 1 and 2 g/kg for day 2. It was applied at 3 g/kg from day 3 onward. The lipid dose protocol was continued by the neonatologist for newborns who required TPN support for at least 14 days. LEs were administered via peripheral or central lines intravenously with an infusion pump in a light-shielded set and syringe.

Routine Management

Daily care and treatment protocols were common for all newborns included in the study. Minimal enteral feeding was initiated early, followed by a standard enteral feeding schedule. All newborns included in the study received initial total TPN solutions including 10% glucose and amino acids (Primene, Baxter Health Care, Old Toongabbie, Australia), and lipids were added according to the study protocol. Newborns were given standard trace elements and vitamins (Cernevit Baxter/ Clintec Parenteral, Montargis, France) in parenteral nutrition according to the unit policy.

Outcomes

The primary outcomes included the rates of ROP, IVH, PDA, NEC, and BPD developed during TPN therapy, late-onset neonatal sepsis, cholestasis, and length of hospital stay.

Ethical Approval

Approval for the study was granted by the use of data for extraction. Institutional Ethics Committee approval (Department of Pediatrics, Kocaeli University Faculty of Medicine: Kocaeli KAEK: 2015/107).

Statistical Analysis

IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Data were evaluated with descriptive statistical methods. The normality of numeric variables was tested with the Shapiro-Wilk test. Non-parametric tests were applied to the data that did not conform to a normal distribution. Descriptive measures were expressed as numbers and percentages for categorical variables and as median and minimum-maximum values for data that did not show normal distribution. The Mann-Whitney U, Wilcoxon, and chi-square tests were used as non-parametric tests in the comparisons of data that did not show normal distribution. A value of $p<0.05$ was considered significant.

RESULTS

This study enrolled a total of 273 newborns. Of the study population, 51 were excluded because of incomplete data recording due to the workload of the neonatology service or were lost to follow-up. Of the enrolled newborns, 106 were assigned to the olive oil group and 116 were placed in the SMOFlipid group.

Table 1 displays the clinical characteristics of newborns by study groups. No significant differences were found between the olive oil and SMOFlipid groups regarding the rates of gestational age, birth weight, sex, SGA, duration of TPN and lipid therapy, and transition time to full oral feeding ($p>0.05$). Moreover, 60.4% (n=55) and 81% (n=79) of the newborns in the olive oil group and SMOFlipid group were breastfed. The breastfeeding rate in the olive oil group was significantly lower than that in the SMOFlipid group ($p<0.05$).

Table 2 displays the rates of morbidities in newborns in the study groups. No significant differences were found between the olive oil and SMOFlipid groups regarding the rates of ROP, IVH, PDA, late-onset neonatal sepsis, cholestasis, and length of stay ($p>0.05$). The rate of NEC in the olive oil group was significantly higher than that in the SMOFlipid group ($p<0.05$). Moreover, while 61 (57.5%) newborns in the olive oil group and 31 (25.9%) newborns in the SMOFlipid group received medical treatment, only one newborn received surgical treatment in the olive oil group. The BPD rate in the SMOFlipid group was lower than those in the olive oil group ($p<0.05$). No significant difference was found in BPD staging between the two treatment groups ($p>0.05$).

DISCUSSION

Intravenous lipid solutions have a considerably important place in the feeding of preterm newborns because of their high energy needs. Lipids are the most important source of non-protein energy. Lipids are critical for growth, development, vision, and cognitive functions[22].

Specific lipids have a robust biological effect, especially on inflammatory and immunomodulatory processes. SO-based lipids were commonly the first

Table 2. Rates of morbidities in newborns in the olive oil and SMOFlipid groups.			
	Olive oil (n=106)	**SMOFlipid (n=116)**	**p-values**
ROP (requiring treatment)			
Yes	4 (3.8%)	7 (6%)	0.641
No	102 (96.2%)	109 (94%)	
Intraventricular hemorrhage			
No	62 (58.5%)	81 (69.8%)	0.282
Grade 1	24 (22.6%)	22 (19%)	
Grade 2	8 (7.5%)	8 (6.9%)	
Grade 3	7 (6.6%)	3 (2.6%)	
Grade 4	5 (4.7%)	2 (1.7%)	
PDA			
No	60 (56.6%)	72 (62.1%)	0.181
Requiring medical treatment	41 (38.7%)	42 (36.2%)	
Requiring surgical treatment	5 (4.7%)	2 (1.7%)	
NEC	61 (57.5%)	31 (25.9%)	0.001
BPD	63 (59.4%)	51 (44%)	0.021
BPD stage			
Mild BPD	33 (31.1%)	24 (20.7%)	0.074
Moderate BPD	19 (17.9%)	13 (11.2%)	
Severe BPD	11 (10.4%)	14 (12.1%)	
Late-onset neonatal sepsis			
No	42 (39.6%)	43 (37.1%)	0.439
Clinical sepsis	49 (46.2%)	62 (53.4%)	
Proven sepsis	15 (14.2%)	11 (9.5%)	
Cholestasis	22 (20.8%)	18 (15.5%)	0.401
Length of stay (day)*	57 (41-72)	51 (36-74)	0.231

*Data were expressed as median with interquartile range. ROP: Retinopathy of prematurity, NEC: Necrotizing enterocolitis, BPD: Bronchopulmonary dysplasia

lipid preparation used, and they contain high amounts of omega-6 PUFAs. The increased amount of LA taken with omega-6 PUFA is converted into arachidonic acid, the precursor of proinflammatory and thrombogenic eicosanoids. Alpha-linolenic acid taken with omega-3 PUFA is the precursor of EPA and DHA. EPA is believed to have anti-inflammatory and anti-thrombogenic effects. SMOFlipid is the primary source of omega-3 PUFA in oral non-nourishment and TPN therapy[23].

In a Cochrane meta-analysis comparing SMOFlipid with SO-based LE in preterm newborns and including seven studies (total participants =469), no significant difference was found in major neonatal morbidities such as mortality, BPD, nosocomial infections, NEC, and severe ROP[14]. Another Cochrane meta-analysis conducted in 2019 included 29 studies (total participants =2,037) that compared SMOF-lipid, SO-based lipid, and alternative-lipid LEs [e.g., MCT-SO LE (MS-LE), olive-SO LE, and borage oil-based LE] in newborns and have not reported any significant differences in major neonatal morbidities such as mortality, BPD, nosocomial infections, NEC, severe ROP, and IVH (grades III-IV)[24]. In our study, the baseline clinical characteristics of newborns who received olive oil and SMOFlipid therapies, including the gestational age, birth weight, sex, SGA, duration of TPN and lipid therapy, and rates of PDA, IVH, and cholestasis were comparable (p>0.05).

The main LC-PUFAs are v6FA and v3FA; they have a strong negative effect on the same enzymes through a complex system required for membrane synthesis and inheritance by competing in the same metabolic pathway with dietary substrates[25]. In conclusion, active v3FAs interfere with the metabolism of v6FA arachidonic acid, leading to the downregulation of inflammatory eicosanoids[25]. Therefore, the v6FA to v3FA ratio (n6:n3 ratio) is a key factor in regulating inflammation. For

immunomodulation, it is recommended that the optimal n6:n3 ratio be between 1:1 and 4:1[26,27].

The ROP study conducted by Beken et al.[28] was the only randomized control trial. As with this study, they compared SMOF- and SO-based lipids and included VLBW infants with a gestational age of <32 weeks. They found that severe ROP rates requiring treatment revealed no significant difference among the groups, with only one newborn requiring therapy in each group. However, a significant increase in ROP at all stages in the SO-based LE group (n=80, odds ratio: 9.1, 95% confidence interval: 1.9-43.8, p=0.004) against SMOF-based LE was observed. DHA, which is abundant in fish oil, can provide protection against the development of ROP because of its anti-inflammatory or oxidative effects on stress reduction[29]. In the Cochrane meta-analysis, 27 studies comparing SMOF and SO LEs did not show any difference in the incidence of ROP and IVH[14]. Nevertheless, in the study by Collins et al.[30], enteral DHA supplementation in infants born before 29 gestational weeks yielded similar findings on IVH, BPD, ROP, and death. In this study, the rates of ROP in both groups were comparable.

SMOFlipid is recommended depending on the composition of its constituents. The increase in the amount of omega-3 fatty acids, MUFAs, and DHA in the LE helps increase immunity and platelet function, increase neurodevelopment, and reduce inflammation[10]. Therefore, we speculated that the inflammation-/immune-related morbidities associated with premature birth could be altered with the use of SMOFlipid LE instead of olive oil LE. We have not identified changes in early and late-onset neonatal sepsis, BPD, IVH, BPD, PDA, or treated ROP in infants who received SMOFlipid LE. We observed a reduction in any stage ROP in the SMOFlipid LE group, indicating a possible effect on early retinal vascular growth. Similarly, in the study conducted by Torgalkar et al.[10] on extremely low preterm newborns, they did not find a significant difference in neonatal morbidity between the intralipid and SMOFlipid groups. Recently, Najm et al.[31] compared SMOFlipid and ClinOleic LEs and observed no difference in morbidity (ROP, BPD, and PDA) and growth.

In a prospective study conducted by Skouroliakou et al.[32] in infants weighing <2,500 g, the type of lipid affects the frequency of BPD in infants with VLBW. A low rate of BPD was detected in patients with VLBW receiving SMOFlipid than in those receiving SO-based lipids. As discussed about cholestasis, SMOFlipid is rich in omega-3 because of its lipid content in fish oil, its immunomodulatory effect is higher thanks to MUFAs, it is more resistant to oxygen radicals thanks to MCT, and its anti-inflammatory effect is higher. SMOFlipid may have reduced the development of BPD with these anti-inflammatory effects. However, randomized controlled prospective studies on this subject are needed[32]. The results of our study revealed that BPD developed less in SMOFlipid areas. In the present study, the BPD rate in the SMOFlipid group was lower than those in the olive oil group ($p<0.05$). In our study, the BPD rate was higher in newborns with cholestasis. This is why newborns with cholestasis have more severe conditions and complications, and they require higher and longer ventilation; consequently, BPD is more common. Although no significant difference was found in mechanical ventilator settings between 2009 and 2014 covering the entire working period, the fact that BPD was observed less in SMOFlipid areas suggests that SMOFlipid has positive effects on BPD. Some randomized controlled trials have also found no difference in BPD between SMOFlipid and SO-based LEs[33]. However, Collins et al.[30] and Qian et al.[33] reported their fish oil supplement trial in premature infants was associated with a significantly greater risk of BPD. Recently, a meta-analysis study indicated that no specific LE with or without fish oil was superior to another LE in preventing ROP, BPD, cholestasis, growth, mortality, and other neonatal outcomes. There is currently insufficient evidence from randomized studies to determine if fish oil LE has an advantage in the prevention or resolution of any clinical outcomes[14,24].

NEC is a severe gastrointestinal system disease commonly seen in preterm infants. In its treatment, enteral nutrition should be reduced and stopped. This situation leads to the prolongation of PN and thus to prolonged PN complications. In our study, the rate of NEC in the olive oil group was significantly higher than that in the other group ($p<0.05$). Yildizdas et al.[34] compared fish oil, olive oil, and SO in newborns aged <32 weeks of gestation and found no difference between them in terms of neonatal morbidities. The incidence of NEC was less in newborns receiving SMOFlipid[34]. In recent years, we think that the use of ibuprofen instead of indomethacin for the treatment of PDA is effective in this case. Ibuprofen was predominantly used in PDA medical treatment during SMOFlipid treatment in our patients who were scanned cross-sectionally, retrospectively, because it was reported to have less risk of NEC compared to indomethacin, which had major side effects of disrupting gastrointestinal perfusion and NEC.

The breastfeeding rate in the olive oil group was significantly lower than that in the SMOFlipid group ($p<0.05$). In addition, in our study, the NEC and BPD rates were lower in the breastfeeding group. The lower

rate of NEC and BPD in the SMOFlipid group can be explained by the effect of the lipid used and excessive breastfeeding. Human milk has various antioxidants that can eliminate free radicals and thereby limit the damage caused by oxidative stress. These compounds consist of α-tocopherol, β-carotene, cysteine, ascorbic acid, catalase, and glutathione peroxidase[35]. OS-LE (ClinOleic®) has been reported to have a fatty acid composition like that of breast milk and increase the level of α-tocopherol levels in preterm newborns when compared with S-LE (Intralipid®)[36]. In a multicenter study conducted by Hair et al.[37] in 1,587 on extremely premature infants, the rates of NEC, BPD, late-onset sepsis, ROP, and mortality were significantly lower in the breastfed group. The shortcoming of our study was related to its periodic design and the rate of breastfeeding between the two groups was higher in the SMOFlipid group during the SMOFlipid treatment period. Prospective studies are needed to determine whether this is the result of lipid therapy or the effect of breast milk.

In our study, both LEs were safe to use and well-tolerated without any significant side effects. No significant change was found in the renal and hematological functions of the newborn babies analyzed. Many observational studies have demonstrated the beneficial outcomes of SMOFlipid LEs in the treatment of newborns receiving long-term TPN[23,38]. The main limitations of our study are the retrospective design, periodic differences, and different rates of breast milk intake between the two groups.

CONCLUSION

Given that olive oil and fish oil treatments provide very similar results in newborns, both of them could be used in neonatology practice. In our retrospective cohort study, the change in practice in the routine use of SMOF-based therapy rather than olive oil therapy has not been associated with changes in severe ROP, IVH, PDA, nosocomial infection, and cholestasis. The two treatment methods give comparable results in terms of lipid tolerance. Our BPD and NEC rates were lower in the fish oil group. In this situation, fish oil therapy may provide protection against BPD and NEC development. Prospective studies are needed to determine whether this is caused by lipid therapy or the effect of breast milk.

Ethics

Ethics Committee Approval: Approval for the study was granted by the use of data for extraction. Institutional Ethics Committee approval (Department of Pediatrics, Kocaeli University Faculty of Medicine: Kocaeli KAEK: 2015/107).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Author Contributions

Surgical and Medical Practices: F.K., A.G., Concept: F.K., A.G., Design: F.K., A.K., A.G., Data Collection and/or Processing: F.K., A.K., A.G., Analysis and/or Interpretation: F.K., A.G., Literature Search: F.K., A.K., A.G., Writing: F.K., A.G.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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