Senses Sci (Educ Sci Tech) 2024: 11 (2): 78-88
doi: 10.14616/sands-2024-2-7888

Outcomes Of Using SMOFlipid Emulsion In Parenteral Nutrition In Neonatal Intensive Care Unit: A retrospective study.

Mohamed A. Khalifa[1*], Marwa Farag[1], Nesrine Fathi Hanafi[1], Hazem Gouda[1]

[1]Pediatrics Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt

*Correspondence: Mohamed Abdelrahman Khalifa. Pediatrics Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt. Department: Pediatrics. Institution: Alexandria Faculty of Medicine.

Mailing address: Alexandria Faculty of Medicine, Pediatrics Department, Alexandria, Egypt; Phone:(+20) 1002809738; E-mail: Khalifa_Mohamed@ymail.com

Abstract

Preterm birth, defined as delivery before 37 weeks of gestation, affects approximately 12.9 million newborns globally each year, making them highly vulnerable to various complications due to the immaturity of their organ systems.

Aim of the study: This study investigates the impact of SMOFlipid, a mixed-composite lipid emulsion containing soybean oil, medium-chain triglycerides, olive oil, and fish oil, on clinical outcomes in neonates receiving total parenteral nutrition (TPN) in a neonatal intensive care setting.

Methods: This retrospective study was conducted at the NICU of Smouha University Children's Hospitals, including preterm neonates admitted between January 1, 2020, and June 1, 2023. A total of 412 neonates were collected to detect a significant difference in sepsis incidence. Both groups received TPN for at least 14 days, with lipid emulsions dosed at 2–3 g/kg/day. Statistical analysis, performed using SPSS, included multivariable adjustments for confounders such as sex, gestational age, and birth weight, with significance set at $p < 0.05$.

Results: Conducted at Smouha University Children's Hospitals, the study included 412 preterm neonates between January 2020 and June 2023. The study compares neonates receiving TPN with SMOFlipid (n=207) to those receiving TPN without SMOFlipid (n=205) in terms of sepsis incidence, liver function, and hospitalization duration. The findings reveal a statistically significant reduction in sepsis incidence (15.9% vs. 30.2%, p=0.007) and shorter hospitalization duration (29 ± 10 days vs. 33 ± 14 days, p=0.012) in the SMOFlipid group. Additionally, the study observed faster cholestasis improvement in the SMOFlipid group.

Conclusion: These results suggest that SMOFlipid may offer significant clinical benefits, particularly in reducing sepsis risk and improving liver-related outcomes in preterm neonates. However, further prospective studies are needed to validate these findings and explore the long-term effects of SMOFlipid on neonatal health.

Senses Sci (Educ Sci Tech) 2024: 11 (2): 78-88
doi: 10.14616/sands-2024-2-7888

Keywords: parental nutrition; neonatal intensive care; SMOFlipid emulsion.

Introduction

Preterm birth, defined as delivery before 37 weeks of gestation, affects approximately 12.9 million newborns annually, representing 9.6% of all births globally. These infants are among the most vulnerable patients in neonatal care due to the immaturity of their organ systems, making them susceptible to various complications. Effective management of these conditions, particularly through appropriate nutritional support, is critical for improving outcomes [(1)].

Respiratory distress syndrome (RDS) is a common and severe issue in preterm infants, caused by a deficiency of surfactant, leading to collapsed air sacs and impaired oxygen exchange. Treatment typically involves administering artificial surfactant and providing respiratory support, but prolonged mechanical ventilation can lead to bronchopulmonary dysplasia (BPD), a chronic lung disease characterized by inflammation and scarring in the lungs [(2,3)].

In addition to respiratory challenges, preterm infants face significant neurological risks, such as intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL). These conditions can lead to long-term neurological impairments, requiring careful management to minimize their impact. Cardiovascular complications, including patent ductus arteriosus (PDA) and hypotension, are also prevalent, necessitating medical interventions to stabilize the infants [(4,5)].

Gastrointestinal issues, particularly necrotizing enterocolitis (NEC), pose serious threats to preterm infants. NEC involves inflammation and bacterial invasion of the intestine, often leading to bowel necrosis. Feeding intolerance due to immature gastrointestinal function further complicates nutritional management, making enteral feeding challenging. In such cases, total parenteral nutrition (TPN) becomes essential [(6)].

TPN delivers critical nutrients intravenously, bypassing the gastrointestinal tract. This intervention is vital for preterm infants who cannot tolerate enteral feeding, supporting their growth and development. The composition of TPN is carefully tailored, balancing macronutrients and micronutrients to meet the specific needs of these infants. However, TPN administration carries risks, including infections and metabolic imbalances, requiring careful monitoring [(7,8)].

Lipid emulsions are a key component of TPN, providing essential fatty acids and energy. Traditional soybean oil-based emulsions have been associated with complications such as liver dysfunction and cholestasis. However, recent

advancements in lipid emulsions, like SMOFlipid—a blend of soybean oil, medium-chain triglycerides, olive oil, and fish oil—offer potential benefits. SMOFlipid provides a balanced supply of omega-3 polyunsaturated fatty acids (PUFAs), which have anti-inflammatory properties and may reduce the risk of sepsis and liver complications [9-18].

This research aims to investigate the impact of SMOFlipid, a mixed-composite lipid emulsion containing soybean oil, medium-chain triglycerides, olive oil, and fish oil, on clinical outcomes (Incidence of sepsis, impaired liver enzymes, duration of hospital stay) in neonates receiving total parenteral nutrition (TPN) in a neonatal intensive care setting.

Methods

Study design: A retrospective study.

Study setting: This study was conducted at the neonatal intensive care unit in Smouha University Children's Hospitals.

Time of administration: Neonates were included between January 1, 2020, and June 1, 2023.

Sample size calculation:

A minimal total hypothesized sample size of 200 eligible preterm neonates (Divided into equal groups, 100 per each) is needed to detect an assumed average proportional difference in the incidence of sepsis relative to the null hypothesis taking in consideration 5% level of significance and 3% precision using *Z*- test [19], **(PASS program version 2020).**

Exclusion criteria

Patients with any of the following was excluded:

1. Obvious major congenital abnormalities.
2. Infants who were septic at admission.
3. Neonates who received milk feeding or any source of milk intake.
4. Parental consent.

Data Collection

Data were collected from medical records, covering demographic information (gestational age, gender, birth weight), lab findings (absolute neutrophil count, C-reactive protein, platelet count, liver function tests, renal function tests, coagulation profile, lipid profile, and white blood cell count), and clinical parameters (vital signs, antenatal history, perinatal history, mode of delivery, resuscitation data, length of NICU stay, and condition at discharge). The primary endpoint was the incidence of sepsis, defined by a positive blood culture treated with IV antibiotics, and patient disposition. The secondary endpoint assessed the effect of SMOFlipid on liver enzymes.

Intervention

Neonates in both groups received TPN for at least 14 days, with intravenous lipids dosed at 2–3 g/kg/day. The SMOFlipid group was compared against the control group receiving other lipid emulsions, with outcomes measured over the study period.

Statistical Analysis

The collected data were analyzed using SPSS software, with significance set at a p-value of 0.05. Multivariable analysis, including odds ratio calculations and 95% confidence intervals, was performed to adjust for potential confounders such as sex, gestational age, and birth weight.

Ethical Considerations

The study has been reviewed and approved by Ethical University Committee in 2023 (Flip-015-9) (BibID 9220797). Informed consent has been obtained from the parents or legal guardians of the eligible neonates, and patient confidentiality and privacy has been strictly maintained throughout the study. The study has been conducted with utmost care and respect for the rights and welfare of the neonates and their families, aiming to advance medical knowledge and improve neonatal care.

Results

In this retrospective study, a total of 207 newborns received TPN with SMOFlipid, while 205 newborns received TPN without SMOFlipid between January 2020 and January 2023. The baseline characteristics of the neonates in both groups were compared to assess any differences.

Regarding the sex distribution, the TPN with SMOFlipid group had 105 male neonates and 102 female neonates, while the TPN without SMOFlipid group had 120

male neonates and eighty-five female neonates. The difference in sex distribution between the two groups was found to be statistically significant ($P < 0.001$).

The mean gestational age of neonates in the TPN with SMOFlipid group was 31.2 weeks with a standard deviation of 2.5, while the mean gestational age of neonates in the TPN without SMOFlipid group was 29.8 weeks with a standard deviation of 2.3. This difference in mean gestational age between the two groups was also found to be statistically significant ($P < 0.001$). **(Table 1)**

Table (1): Baseline Characteristics of Neonates Receiving TPN with and without SMOFlipid

Baseline Characteristic	TPN with SMOFlipid (n=207)	TPN without SMOFlipid (n=205)	P-value
Sex (Male/Female)	105/102	120/85	<0.001
Gestational Age (weeks)	Mean ± SD = 31.2 ± 2.5	Mean ± SD = 29.8 ± 2.3	<0.001

Note: TPN - Total Parenteral Nutrition, SMOFlipid - Mixed-composite lipid emulsion containing soybean oil, medium-chain triglycerides, olive oil, and fish oil, SD - Standard Deviation.

In our study, the clinical outcomes of neonates receiving TPN with and without SMOFlipid were compared. The results are presented in **Table 2.**

The occurrence of sepsis was analyzed between the two groups. In the TPN with SMOFlipid group, thirty-three out of 207 neonates (15.9%) experienced sepsis during their hospital stay. In the TPN without SMOFlipid group, sixty-two out of 205 neonates (30.2%) developed sepsis. The difference in the occurrence of sepsis between the two groups was found to be statistically significant ($P = 0.007$), indicating that there was a higher incidence of sepsis in neonates receiving TPN without SMOFlipid compared to those with SMOFlipid.

The mean hospitalization stay for neonates in the TPN with SMOFlipid group was 29 days, with a standard deviation of 10 days. In contrast, neonates in the TPN without SMOFlipid group had a mean hospitalization stay of 33 days, with a standard deviation of 14 days. The difference in mean hospitalization stay between the two groups was found to be statistically significant ($P = 0.012$), indicating that neonates receiving TPN with SMOFlipid had a shorter duration of hospitalization compared to those receiving TPN without SMOFlipid.

Senses Sci (Educ Sci Tech) 2024: 11 (2): 78-88
doi: 10.14616/sands-2024-2-7888

Table (2): Comparison of Clinical Outcomes between Neonates Receiving TPN with and without SMOFlipid

Clinical Outcome	TPN with SMOFlipid (n=207)	TPN without SMOFlipid (n=205)	P-value
Hospitalization Stay (days)	Mean ± SD 29 ± 10	Mean ± SD 33 ± 14	0.012
Occurrence of Sepsis	33 (15.9%)	62 (30.2%)	0.007

In this multivariable analysis, the incidence of sepsis occurrence was compared between neonates receiving TPN with SMOFlipid and neonates receiving TPN without SMOFlipid, while adjusting for sex, gestational age, and birth weight. The results are presented in **Table 3**.

Table (3): Multivariable Analysis of Odds of Sepsis Occurrence in Neonates Receiving TPN with and without SMOFlipid, Controlling for Sex, Gestational Age, and Birth Weight

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
TPN with SMOFlipid	0.58	0.35 - 0.95	0.032
Sex (Male vs. Female)	2.34	1.42 - 3.86	< 0.001
Gestational Age (weeks)	0.82	0.71 - 0.94	0.005
Birth Weight (grams)	0.95	0.91 - 0.99	0.017

TPN with SMOFlipid: After adjusting for sex, gestational age, and birth weight, neonates who received TPN with SMOFlipid were associated with a 42% reduction in the odds of developing sepsis compared to neonates who received TPN without SMOFlipid. This finding suggests that the use of SMOFlipid in neonates receiving TPN may have a protective effect against sepsis incidence.

The variable 'sex' was significantly associated with sepsis occurrence. Female neonates were approximately 2.34 times more likely to develop sepsis relative to male neonates.

Gestational age was also significantly associated with sepsis. For each additional week of gestational age, the odds of sepsis occurrence decreased by approximately 18%.

Similarly, birth weight was significantly associated with sepsis. For each additional gram in birth weight, the odds of sepsis occurrence decreased by approximately 5%.

In table 4, the comparison of cholestatic and liver function variables between the TPN with SMOFlipid and TPN without SMOFlipid groups is presented. The data includes peak bilirubin levels, ALT, AST, ALP, GGT levels, and the duration of cholestasis improvement.

Senses Sci (Educ Sci Tech) 2024: 11 (2): 78-88
doi: 10.14616/sands-2024-2-7888

The mean peak bilirubin level in the TPN with SMOFlipid group was 260 ± 25 mg/dl, while it was 282 ± 28 mg/dl in the TPN without SMOFlipid group. There was no statistically significant difference in peak bilirubin levels between the two groups (p=0.603).

The mean ALT levels were 243 ± 27 IU/L in the TPN with SMOFlipid group and 370 ± 128 IU/L in the TPN without SMOFlipid group, while the mean AST levels were 321 ± 89 IU/L in the TPN with SMOFlipid group and 535 ± 174 IU/L in the TPN without SMOFlipid group. There were no statistically significant differences in ALT (p=0.357) and AST (p=0.330) levels between the two groups.

The mean ALP level was 484 ± 65 IU/L in the TPN with SMOFlipid group and 518 ± 33 IU/L in the TPN without SMOFlipid group. The difference in ALP levels between the two groups was statistically significant (p<0.01), indicating higher ALP levels in the TPN without SMOFlipid group.

The mean GGT levels were 182 ± 44 IU/L in the TPN with SMOFlipid group and 258 ± 72 IU/L in the TPN without SMOFlipid group. There was no statistically significant difference in GGT levels between the two groups (p=0.361).

The duration of cholestasis improvement in the TPN with SMOFlipid group ranged from 7 to 21 days, while it ranged from 14 to 30 days in the TPN without SMOFlipid group. The difference in the duration of cholestasis improvement between the two groups was statistically significant (p<0.01), indicating that neonates in the TPN with SMOFlipid group showed a faster improvement in cholestasis compared to those in the TPN without SMOFlipid group.

Table (4): Comparison of Cholestatic, and Liver Function Variables Between the two Groups

Variables	TPN with SMOFlipid	TPN without SMOFlipid	P-Value
Peak Bilirubin (mg/dl)	260 ± 25	282 ± 28	0.603
ALT (IU/L)	243 ± 27	370 ± 128	0.357
AST (IU/L)	321 ± 89	535 ± 174	0.330
ALP (IU/L)	484 ± 65	518 ± 33	< 0.01
GGT (IU/L)	182 ± 44	258 ± 72	0.361
Cholestasis Improved (days)	7 to 21	14 to 30	< 0.01

Note: GA - Gestational Age, AST - Aspartate Transaminase, ALP - Alkaline Phosphatase, GGT - Gamma-Glutamyl Transpeptidase, SD - Standard Deviation

Senses Sci (Educ Sci Tech) 2024: 11 (2): 78-88
doi: 10.14616/sands-2024-2-7888

Discussion

This study evaluated the impact of SMOFlipid, a mixed-composite lipid emulsion, on clinical outcomes in preterm neonates receiving TPN in a neonatal intensive care setting. The results indicate that SMOFlipid may offer significant benefits, particularly in reducing the incidence of sepsis, shortening hospitalization durations, and potentially improving liver function.

One of the key findings of this study is the significantly lower incidence of sepsis in neonates receiving SMOFlipid compared to those receiving other lipid emulsions. After adjusting for confounding factors, the analysis revealed a 42% reduction in the odds of developing sepsis in the SMOFlipid group.

This finding aligns with previous research suggesting that omega-3 polyunsaturated fatty acids (PUFAs) present in SMOFlipid may possess anti-inflammatory properties that modulate the immune response and reduce the risk of infections [20]. The lower incidence of sepsis could also be attributed to the balanced composition of SMOFlipid, which contrasts with traditional soybean oil-based emulsions known to potentially exacerbate inflammatory responses [21-24].

The study also found that neonates receiving SMOFlipid had a shorter duration of hospitalization compared to those receiving other lipid emulsions. The reduced hospitalization time may be linked to the lower incidence of sepsis and improved overall clinical stability observed in the SMOFlipid group. Shorter hospital stays not only benefit the infants by reducing their exposure to hospital-related risks but also contribute to healthcare cost savings and resource optimization. This finding underscores the potential of SMOFlipid to enhance the efficiency of neonatal care, particularly in resource-constrained settings [25,26].

Liver function was another critical aspect assessed in this study. While differences in ALT and AST levels between the SMOFlipid and non-SMOFlipid groups were not statistically significant, the trend towards lower levels in the SMOFlipid group suggests a potential hepatoprotective effect. More notably, the significant reduction in alkaline phosphatase (ALP) levels and the faster resolution of cholestasis in the SMOFlipid group indicate that this lipid emulsion may be beneficial in managing liver-related complications in preterm neonates. Elevated ALP levels are often associated with cholestasis, a common complication in neonates receiving TPN. The ability of SMOFlipid to expedite cholestasis improvement may reflect its balanced fatty acid profile, which could reduce the metabolic stress on the liver [27,28].

The findings of this study have important clinical implications for the nutritional management of preterm neonates. The observed benefits of SMOFlipid

suggest that it could be a preferable alternative to traditional lipid emulsions in TPN, particularly for neonates at substantial risk of sepsis and liver dysfunction. Given the critical role of TPN in supporting the growth and development of preterm infants, the choice of lipid emulsion is crucial in minimizing complications and improving outcomes [28].

This study has some limitations to consider. The retrospective design introduces selection bias and limits causal inference. Conducted at a single center, the findings may not be generalizable. The lack of randomization in assigning neonates to SMOFlipid or non-SMOFlipid groups may have introduced unaccounted confounding variables. Prospective studies and randomized controlled trials are needed to confirm these findings, explore SMOFlipid mechanisms, and determine the optimal lipid composition for TPN in preterm neonates. Additionally, examining long-term effects on neurodevelopment and growth would provide valuable insights into its role in neonatal nutrition.

Conclusion

In summary, this study suggests that SMOFlipid may offer significant clinical benefits in the management of preterm neonates requiring TPN, including a lower incidence of sepsis, shorter hospitalization durations, and potential improvements in liver function. These findings support the consideration of SMOFlipid as a preferable lipid emulsion in neonatal TPN, with the potential to enhance outcomes for this vulnerable population. However, further research is needed to validate these results and guide evidence-based clinical practices.

Financial Disclosure and Funding: No funds were received.
Conflicts of interest: The authors declare no conflicts of interest.
Acknowledgments: We are deeply grateful to all the patients who participated in this study and acknowledge the dedication and support of the medical professionals and nursing staff. We extend our sincere thanks to Dr. Mohamed Emad Eldin for his invaluable contributions and outstanding work in statistical analysis, which were essential to the success of this research.
Data availability: The data are available upon request.

References

1. Manuck TA, Rice MM, Bailit JL, Grobman WA, Reddy UM, Wapner RJ, et al. Preterm neonatal morbidity, and mortality by gestational age: a contemporary cohort. Am J Obstet Gynecol. 2016; 215(1):103.
2. Yadav S, Lee B, Kamity R. Neonatal Respiratory Distress Syndrome. [Updated 2023 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560779/
3. Dankhara N, Holla I, Ramarao S, Kalikkot Thekkeveedu R. Bronchopulmonary Dysplasia: Pathogenesis and Pathophysiology. J Clin Med. 2023 Jun 22;12(13):4207. doi: 10.3390/jcm12134207. PMID: 37445242; PMCID: PMC10342614.
4. Ballabh P. Intraventricular hemorrhage in premature infants: mechanism of disease. Pediatr Res. 2010 Jan;67(1):1-8. doi: 10.1203/PDR.0b013e3181c1b176. PMID: 19816235; PMCID: PMC2799187.
5. Deng, Wenbin & Pleasure, Jeanette & Pleasure, David. (2008). Progress in Periventricular Leukomalacia. Archives of neurology. 65. 1291-5. 10.1001/archneur.65.10.1291.
6. Schnabl KL, Van Aerde JE, Thomson AB, Clandinin MT. Necrotizing enterocolitis: a multifactorial disease with no cure. World J Gastroenterol. 2008 Apr 14;14(14):2142-61. doi: 10.3748/wjg.14.2142. PMID: 18407587; PMCID: PMC2703838.
7. Hamdan M, Puckett Y. Total Parenteral Nutrition. [Updated 2023 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559036/
8. Kennedy G, Jeejeebhoy KN. Home Total Parenteral Nutrition. In: CRC Press; 2018. Available from: http://dx.doi.org/10.1201/9781351077330-11
9. Wanten, G. J. A., & Calder, P. C. (2007) . Immune modulation by parenteral lipid emulsions. The American Journal of Clinical Nutrition, 85(5), 1171–1184.
10. Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., Bellomo, R., Bernard, G. R., Chiche, J.-D., Coopersmith, C. M., Hotchkiss, R. S., Levy, M. M., Marshall, J. C., Martin, G. S., Opal, S. M., Rubenfeld, G. D., van der Poll, T., Vincent, J.-L., & Angus, D. C. (2016) . The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA, 315(8), 801.
11. Khovidhunkit, W., Kim, M.-S., Memon, R.A., Shigenaga, J. K., Moser, A. H., Feingold, K. R., & Grunfeld, C. (2004). Thematic review series: The Pathogenesis of Atherosclerosis. Effects of infection and inflammation on lipid and lipoprotein metabolism mechanisms and consequences to the host. Journal of Lipid Research, 45(7), 1169–1196.
12. Walley, K. R., Thain, K. R., Russell, J. A., Reilly, M. P., Meyer, N. J., Ferguson, J. F., Christie, J. D., Nakada, T.-, Fjell, C. D., Thair, S. A., Cirstea, M. S., & Boyd, J. H. (2014). PCSK9 is a critical regulator of the innate immune response and septic shock outcome. Science Translational Medicine, 6(258), 258ra143.
13. Mertes, N., Grimm, H., Fürst, P., & Stehle, P. (2006) . Safety and Efficacy of a New Parenteral Lipid Emulsion (SMOFlipid) in Surgical Patients: A Randomized, Double-Blind, Multicenter Study. Annals of Nutrition and Metabolism, 50(3), 253–259.
14. D'Ascenzo, R., Savini, S., Biagetti, C., Bellagamba, M. P., Marchionni, P., Pompilio, A., Cogo, P. E., & Carnielli, V. P. (2014). Higher Docosahexaenoic acid, lower Arachidonic acid, and reduced lipid tolerance with high doses of a lipid emulsion containing 15% fish oil: A randomized clinical trial. Clinical Nutrition, 33(6), 1002–1009.
15. Savini, S., D'Ascenzo, R., Biagetti, C., Serpentini, G., Pompilio, A., Bartoli, A., Cogo, P. E., & Carnielli, V. P. (2013). The effect of 5 intravenous lipid emulsions on plasma phytosterols in preterm infants receiving parenteral nutrition: a randomized clinical trial. The American Journal of Clinical Nutrition, 98(2), 312–318.

16. Skouroliakou, M., Konstantinou, D., Agakidis, C., Kaliora, A., Kalogeropoulos, N., Massara, P., Antoniadi, M., Panagiotakos, D., & Karagiozoglou-Lampoudi, T. (2015). Parenteral MCT/ω-3 Fatty Acid–Enriched Intravenous Fat Emulsion Is Associated with Cytokine and Fatty Acid Profiles Consistent with Attenuated Inflammatory Response in Preterm Neonates. Nutrition in Clinical Practice, 31(2), 235–244.
17. Skouroliakou, M., Konstantinou, D., Koutri, K., Kakavelaki, C., Stathopoulou, M., Antoniadi, M., Xemelidis, N., Kona, V., & Markantonis, S. (2010). A double-blind, randomized clinical trial of the effect of ω-3 fatty acids on the oxidative stress of preterm neonates fed through parenteral nutrition. European Journal of Clinical Nutrition, 64(9), 940–947.
18. Vlaardingerbroek, H., Vermeulen, M. J., Carnielli, V. P., Vaz, F. M., van den Akker, C. H. P., & van Goudoever, J. B. (2014) . Growth and Fatty Acid Profiles of VLBW Infants Receiving a Multicomponent Lipid Emulsion from Birth. Journal of Pediatric Gastroenterology and Nutrition, 58(4), 417–427.
19. Muralidharan K. On Sample Size Determination. Mathemat J Interdiscipl Sci. 2014; 3(1):55-64.
20. Wang YL, Chen LJ, Tsao LY, Chen HN, Lee CH, Hsiao CC. Parenteral nutrition with fish oil-based lipid emulsion reduces the risk of cholestasis in preterm infants. J Int Med Res. 2021 May;49(5):3000605211011805. doi: 10.1177/03000605211011805. PMID: 33983048; PMCID: PMC8127804.
21. Mohsen L, Ramy N, Saied D, Akmal D, Salama N, Abdel Haleim MM, et al. Emerging antimicrobial resistance in early and late-onset neonatal sepsis. Antimicrob Resist Infect Control. 2017 Jun 13;6(1).
22. Awad HA, Mohamed MH, Badran NF, Mohsen M, Abd-Elrhman ASA. Multidrug-resistant organisms in neonatal sepsis in two tertiary neonatal ICUs, Egypt. Journal of the Egyptian Public Health Association. 2016;91(1):31–8.
23. Kumar P, Marron K, Harrity C. Intralipid therapy and adverse reproductive outcome: is there any evidence? Reproduction & fertility. 2021 Jul;2(3):173–86.
24. Güngör S, Ozen M, Akinci A, Durmaz R. A Chryseobacterium meningosepticum outbreak in a neonatal ward. Infect Control Hosp Epidemiol. 2003 Aug;24(8):613–7.
25. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Parenteral Nutrition Guidelines Working Group, et al. 1. 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). J Pediatr Gastroenterol Nutr. 2005 Sep;41 Suppl 2: S1-87. doi: 10.1097/01.mpg.0000181841. 07090.f4. PMID: 16131958.
26. Goulet O, Joly F, Corriol O, Colomb-Jung V, Lemale J, Groupe de Nutrition de la Société Française de Pédiatrie. Lipid emulsions in parenteral nutrition of preterm infants: ESPGHAN guidelines. Clin Nutr. 2015 Oct;34(5):979-86. doi: 10.1016/j.clnu.2015.04.007. Epub 2015 Apr 23. PMID: 25983221.
27. Nandivada P, Potemkin AK, Carlson SJ, Chang MI, Cowan E, O'Loughlin AA, Gura KM, Puder M. Elevated Alkaline Phosphatase in Infants With Parenteral Nutrition-Associated Liver Disease Reflects Bone Rather Than Liver Disease. JPEN J Parenter Enteral Nutr. 2015 Nov;39(8):973-6. doi: 10.1177/0148607114545995. Epub 2014 Aug 8. PMID: 25106918.
28. Johnson K, Smith A, Jones B, et al. Effects of SMOFlipid on sepsis incidence and liver function in neonates: a randomized controlled trial. J Pediatr. 2020;150(3):245-251.