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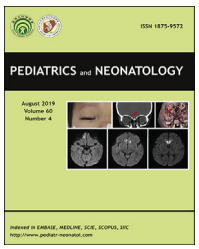

Editorial

Selection of lipid emulsions for protection against parenteral nutrition-associated liver disease

In the past decades, considerable progress has been made in intensive care and survival rate of premature infants. Administration of parenteral nutrition (PN) has improved the nutritional status of premature infants in their early life, especially for infants with extremely low birth weight. Lipid emulsions (LEs) are recognized as essential components of non-protein energy supplement of PN. In addition to their high caloric value and low osmolality, the use of LE prevents the complications of using glucose as sole non-protein energy source; these complications include fatty acid deficiency, hyperglycemia, and hepatic steatosis.[1] With the widespread usage of PN, PN-associated liver disease (PNALD) has been considered as one of the most frequent complications of PN.

PNALD is defined as cholestasis occurring in the setting of PN considering that other specific causes of liver injury have been excluded.[2] Risk factors for PNALD are related to numerous factors. In previous research, young gestational age, low birth weight, high frequency sepsis episodes, and long duration of PN usage are significant risk factors for PNALD.[3] With the improvement of clinical understanding and technological advancement, the constituents of PN, such as deficiencies, excesses, and toxicity, are studied and considered as possible risk factors for PNALD. Various mechanisms, including modulation of oxidative stress and inflammation, have been proposed for the possible role of LE in PNALD.[2] The possible toxicity of LE is a focus of concern. Growing evidence shows that different sources of lipid in LE may result in different effects on liver injury development. Long-chain triglyceride/soybean oil (SO), medium-chain triglyceride/SO (MCT/SO), olive oil/SO (OO/SO) with polyunsaturated fatty acid (PUFA), and fish oil (FO)-based lipids are examples of LE components. In this issue of *Pediatrics and Neonatology*, Yildizdas et al. compared the effects of two different LEs on antioxidant status, lipid peroxidation, and PNALD in premature infants.[4] The two LEs included OO/SO-based lipid (with high levels of α-tocopherol, ω-9, and ω-6 PUFA) (ClinOleic®, Baxter, Lessines, Belgium) and lipid consisting of FO, MCT, OO, and SO (FMOS; with high levels of α-tocopherol and low level of phytosterol) (SMOFlipid®, Fresenius Kabi, Pymble, Australia). A total of 67 premature infants with gestational age $\leq$32 weeks and/or birth weight $\leq$1500 g were included in the randomized-controlled study, with 33 receiving OO/SO LE and 34 being administrated with FMOS LE. Under similar clinical parameter conditions, compared with the OO/SO group, cholestasis was significantly lower, and neonates in the FMOS LE group regained birth weight earlier.[4] Savini et al. (2013)[5] and other studies have reported the lack of differences in the incidence of cholestasis and makers of liver integrity when comparing the usage of different LEs. Varying clinical conditions might have contributed to the morbidity. However, research also showed lower plasma phytosterol, increased eicosapentaenoic acid (EPA), and docosapentaenoic acid (DHA) in premature infants receiving FMOS LE.[5,6] The blood concentration of phytosterol is closely associated with cholestasis in children and adults.[2] Experimental research on PNALD animal model showed that phytosterols promote liver injury and Kupffer cell activation. Therefore, low plasma phytosterol levels might reduce the risk of cholestasis. EPA has been shown to modulate inflammatory pathways by decreasing the production of pro-inflammatory cytokines and increasing the secretion of anti-inflammatory interleukin-10.[2] DHA is important for neurodevelopment and visual function. Premature infants experience a large deficit in DHA. FO is a rich source of DHA and EPA. Therefore, FMOS LE features the theoretical advantage of supporting premature infants.

Oxidative stress is proposed to be one of the processes that leads to several diseases of prematurity as premature

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infants have limited antioxidant system and are exposed to more oxygen, ventilations, and infections.[4] LE components may contribute to lipid peroxidation under certain clinical conditions. The antioxidant status and lipid peroxidation, including anti-oxienzyme activities and thiobarbituric acid-reactive substances, were evaluated in the research of Yildizdas et al. but yielded no promising results.[4] However, other researchers reported the high total antioxidant capacity measured in premature infants receiving SMOFlipid after 7 days.[7] The antioxidant status and lipid peroxidation could be affected by an individual's clinical conditions, such as oxygen usage, ventilation support, and other inflammatory status. The results could be different due to different methodology.

In conclusion, FMOS LE is a new generation of LEs. FO containing high levels of DHA and EPA and zero phytosterol exhibits the theoretical advantage of supporting premature infants requiring PN. Yildizdas et al. has shown some evidence.[4] With knowledge and technological advancements, more studies will provide additional evidence to support our conclusion.

Conflict of interest

I have nothing to disclose.

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