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Will Availability of SMOF Lipid Emulsions for Parenteral Nutrition Change Surgical Nutrition Practice?

Elizabeth H. Cameron[1] · **Neal Bhutiani**[1] · **Matthew C. Bozeman**[1]

Abstract
Purpose of Review Parenteral nutrition (PN) is a widely accepted form of nutrition administration in patients in whom enteral feeding is contraindicated or insufficient. This is true in surgical patient populations, as well. As a component of PN, intravenous fat emulsions (IVFEs) are essential for the administration of essential fatty acids (EFAs) and adequate energy intake. The oils that make up standard IVFE formulations have evolved over time.
Recent Findings A newer formulation, known as SMOF, contains a combination of soybean oil, medium chain triglycerides, olive oil, and fish oil and is gaining popularity for its purported beneficial effects on liver function, inflammation, and anti-oxidant status.
Summary This literature review examines the current data regarding the effects of SMOF in the patient receiving PN and examines the role SMOF may play in the future management of nutrition in the surgical population.

Keywords Enteral nutrition · Lipid emulsions · Surgical nutrition

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✉ Matthew C. Bozeman
matthew.bozeman@louisville.edu

[1] Department of Surgery, Division of Trauma and Acute Care Surgery, University of Louisville, 550 S. Jackson St., Ambulatory Care Building 2nd Floor, Louisville, KY 40202, USA

Introduction

Parenteral nutrition (PN) has long been used in patients unable to obtain adequate enteral nutrition, becoming widely used in the USA in the 1970s [1]. Since then, PN has evolved into a sustainable form of nutrition administration in a variety of patients, including surgical patients. As a component of PN, intravenous fat emulsions (IVFEs) provide the essential fatty acids required for structural cell membrane support, in addition to being precursors for cellular metabolites and providing a high amount of energy that is required in a catabolic state [1, 2•]. The makeup of IVFEs has evolved over time to include multiple different formulations of fatty acids. Most recently, a combination of soybean oil, medium-chain triglycerides, olive oil, and fish oil (SMOF) has become available. The use of SMOF as an IVFE has the potential to be superior to the current commonly used lipid emulsions, as SMOF confers a lesser risk of PN-associated liver disease (PNALD), has fewer pro-inflammatory and pro-oxidative properties, and results in a more favorable lipid profile in patients receiving PN. In this review, we will discuss the evolution of IVFEs and describe the mechanisms behind the postulated benefits of SMOF while also reviewing the current literature that demonstrates those benefits on a clinical level. Finally, we will discuss the clinical and financial implications as they relate to surgical patients.

PN and Associated Complications

The first documented attempt at administration of PN was as early as the twelfth century, when a Moorish surgeon, Ibn Zuhr, reportedly used a hollow silver needle for nutrient

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delivery in one of his patients. Since that time, many advances have been made in the development and administration of PN that have led to PN becoming widely used as an option for nutrient delivery since the 1970s. Indeed, over the last 40 years, PN administration has become standard practice in a variety of patients who are unable to maintain adequate nutrition with enteral feeding [1].

Though PN has revolutionized nutrition administration, it is not without its own complications. These include catheter-related sepsis, hyper- and hypoglycemia, electrolyte abnormalities, metabolic bone disease, and hepatobiliary complications. The constellation of one or more of three hepatobiliary abnormalities, including steatosis, cholestasis, and gallbladder sludge or stones, is collectively known as PNALD. The reported prevalence of PNALD ranges from 25 to 100% in adults and 7.4–84% in children, with the prevalence increasing with longer use of PN [3, 4]. This feared complication of PN can result in fulminant liver failure with subsequent death [5–7].

Steatosis mainly occurs within 2 weeks of PN administration in adult patients and is indicated by elevations in serum aminotransferases. It is thought to be a result of overfeeding but can be exacerbated by dextrose-based PN formulations due to carbohydrate deposition as fat within the liver. Additionally, dextrose-based formulations lead to fatty acid deficiency, which results in impaired lipoprotein synthesis and triglyceride secretion. Steatosis is generally benign and has experienced decreasing incidence with the advent of newer, more conservative estimates of calorie requirements and more balanced PN formulations [5].

Cholestasis, a more serious complication that may lead to cirrhosis or liver failure, mainly occurs in pediatric populations receiving PN. It usually results in elevations in serum alkaline phosphatase, gamma-glutamyl transpeptidase (GGT), and bilirubin (particularly direct bilirubin) [5].

Finally, cholelithiasis and gallbladder sludge can result from a general lack of enteral feeding secondary to decreased cholecystokinin and gallbladder contractility. This can lead to acute cholecystitis and its associated complications. The duration of PN directly correlates with the development of stones and sludge. One study indicated that 100% of patients receiving PN will develop stones or sludge by 6 weeks, as compared to a baseline of 0% [8].

Evidence suggests that altering the oil content of the fat emulsion administered as a component of PN may help decrease the incidence of PNALD. As such, the formulations of available IVFEs have evolved in an effort to alter the incidence of PNALD as well as other complications associated with PN.

Fatty Acids as a Component of PN

Fatty acids (FAs) are the monomers that make up more complex lipids such as triglycerides and phospholipids. They are composed of hydrocarbon chains that are classified by length into short, medium, long, or very long. FAs play a multitude of roles within the human body, including membrane integrity, intracellular signaling, transcription factor activity, and gene expression. Importantly, they also modulate the immune response and act as a dense energy source that can be administered within a small volume [2•, 9]. These properties make FAs an ideal and essential component of PN.

Essential FAs (EFAs) derive from dietary sources given their inability to be synthesized within the body from precursors. ω-6 and ω-3 FAs, so named to denote the location of the first double bond from the terminal methyl group, comprise the two main groups of EFAs. ω-3 FAs mainly consist of α-linolenic acid (ALA) and ω-6 FAs of linoleic acid (LA); both fall in the family of long chain polyunsaturated FAs (PUFAs) and are liquid at room temperature. The ω-3 and ω-6 FAs are both found within cell membranes and compete with each other for space. Additionally, they require the same enzymes for conversion to their metabolites and thus must compete for those as well [2•]. Characteristics of ω-3 and ω-6 FAs are summarized in Table 1.

ω-6 Fatty Acids

LA represents the most prevalent ω-6 FA and serves as a precursor to γ-linolenic acid, dihomo-γ-linolenic acid, and arachidonic acid (AA). Deficiency in LA can result in breakdown of skin integrity, due to the presence of LA within ceramides. LA also plays a role in lowering blood cholesterol and low-density lipoprotein (LDL) concentrations, mainly through up-regulation of the LDL receptor gene and resultant increase in hepatic clearance of LDL. LA does not, however, appear to have a significant effect on high-density lipoprotein (HDL) concentrations. Additionally, metabolites of LA known as hydroxyocta-decadienoic acids promote inflammation and cell injury [2•, 9].

Table 1 Essential fatty acids and downstream metabolites

ω-3	ω-6
↓	↓
α-Linolenic acid	Linoleic acid
↓	↓
Eicosapentaenoic acid	Arachidonic acid
↓	↓
Docosapentaenoic acid, docosahexaenoic acid	Pro-inflammatory mediators (2-series prostaglandins, thromboxanes, 4-series leukotrienes)
↓	
Anti-inflammatory mediators (3-series prostaglandins, 5-series leukotrienes, resolvins, protectins, maresins)	

Arachidonic acid, a metabolite of LA, plays a role in brain structure. It has also been shown to have pro-inflammatory effect, likely via the NF-κB pathway. Additionally, the content of AA within cell membranes significantly impacts the production of eicosanoids, which include several pro-inflammatory mediators (e.g., 2-series prostaglandins, thromboxanes, and the 4-series leukotrienes). These play important roles in inflammation, pain, and coagulation [2•, 9].

ω-3 Fatty Acids

α-linolenic acid (ALA), the most prevalent ω-3 FA, can be converted to eicosapentaenoic acid (EPA), which can then be converted to docosapentaenoic acid (DPA) or docosahexaenoic acid (DHA). EPA and DHA play similar roles within the body, both lowering blood triglyceride levels through a variety of mechanisms, the most prominent of which include a reduction in very low-density lipoproteins (VLDLs), thus reducing triglyceride carrying capacity in the bloodstream, and an increase triglyceride bloodstream clearance as a result of up-regulation of lipoprotein lipase. They reduce inflammation via a reduction in a number of cytokines, adhesion molecules, and acute phase proteins [9–11]. Specifically, they up-regulate the anti-inflammatory 3-series prostaglandins, 5-series leukotrienes, and anti-inflammatory mediators known as resolvins, protectins, and maresins [10, 11].

ALA taken alone in the diet generally results in the preferential conversion to EPA or DPA but not DHA. However, the enzymes required for the conversion of ALA are the same as those required for LA conversion to its metabolites. As a result, an increase in the ω-3 to ω-6 FA ratio in the diet leads to greater conversion of ALA to its metabolites than LA to its metabolites [9].

Medium-Chain Triglycerides

The ω-3 FAs and ω-6 FAs both fall into the category of long chain triglycerides (LCT). In contrast, medium-chain triglycerides (MCT) comprise saturated FAs that are 6 to 12 carbons long. They are resistant to peroxidation and do not have pro-inflammatory effects. Additionally, they are not hepatotoxic, as they do not demonstrate hepatic accumulation [2•]. These properties make them ideal components of IVFE. However, MCT lack EFA and, as a component of PN, must thus be administered with other oils [2•].

Intravenous Fat Emulsions

IVFEs, the modern form of intravenous lipid administration, are intended to be similar to chylomicrons and the natural circulation of fat within the human body to minimize complications such as pulmonary fat embolus. There are various formulations of IVFEs, which feature different FAs more prominently based on the use of different oils [2•]. Traditionally, soybean oil (SO) has featured prominently in IVFE formulations. A SO-based formula known as Intralipid® is very commonly used in the USA. SO has a ratio of ω-6 FA to ω-3 FA of about 7:1 and contains a significant amount of phystosterols, the antioxidant vitamin E, and the nonessential monounsaturated FA (MUFA) ω-9 FA [2•].

Coconut oil, another common component of IVFEs, is commonly used in a in a 50/50 mixture with SO. It contains a significant amount of MCTs and significantly reduced the ω-6 FA content of the traditional SO-based formulation. Coconut oil lacks EFAs, and so must be combined with other oils that do contain them [2•].

Olive oil (OO), meanwhile, contains large amount of non-essential ω-9 FA (oleic acid), a MUFA. Since it contains a low amount of LA, it must also be combined with other oils containing the EFAs. In contrast to SO, OO contains few phytosterols and large quantities of α-tocopherol. OO is purported to be less pro-inflammatory due the high concentration of MUFAs which, unlike PUFAs, are not precursors to the pro-inflammatory eicosanoids.

Fish oil (FO) is rich in ARA, EPA, and DHA [2•]. It also contains high quantities of α-tocopherol and low levels of phytosterols. Additionally, the ω-6/ω-3 FA ratio is very low [12]. A pure FO-based IVFE formulation known as Omegaven® exists, though it is approved only for compassionate use within the USA. Table 2 summarizes the different commercially available IVFEs and their lipid compositions.

Table 2 Content of common intravenous lipid emulsions [2, 43, 44]

Component	Intralipid	Omegaven	SMOFlipid	ClinoLipid/ ClinOleic
Soybean oil, %	100		30	20
Medium-chain trilycerides, %			30	
Olive oil, %			25	80
Fish oil, %		100	15	
Phytosterols, mg/L	440	3.66	207	275
α-tocopherol, μmol/L	87	505	500	75
LA, %	50	4.4	21.4	18.5
ALA, %	9	1.8	2.5	2
EPA, %	0	19.2	3	0
DHA, %	0	12.1	2	0
ARA, %	0	1–4	0.15–0.6	0
Ratio ω-6 to ω-3 fatty acids	7:1	1:8	2.5:1	9:1

PN in Surgical Patients

PN has a role in the nutritional management of a variety of surgical patients. Some studies suggest that PN administration preoperatively in severely malnourished patients undergoing non-emergent procedures may play a role in reducing postoperative complications and length of hospital stay [13]. Postoperatively, PN is indicated in patients who have a contraindication to enteral feeding, who cannot tolerate enteral feeding, or who cannot obtain adequate enteral nutrition to meet metabolic needs. Such patients include those with anastomotic leaks, obstruction, gastrointestinal fistulas, and burn patients. PN particularly has a role in the critically ill surgical patient. As metabolic demand increases in the critically ill, there is a greater nutritional requirement to adequately support the immune response, maintain energy stores, and promote wound healing, among other vital life processes [14].

The optimal timing of PN administration remains hotly debated. However, PN in the non-critically ill patient is generally not administered within the first 5 days postoperatively, as studies suggest that the nutritional benefits of PN administration do not outweigh the risks until after this time frame [15, 16]. In general, PN is indicated when a patient is not receiving or is not expected to receive nutrition enterally by 10 to 14 days after surgery [17, 18].

However, PN in the surgical population is not without complication. PNALD, as previously discussed, is characterized by an elevation of the markers of liver function. Though a concern in all populations receiving PN, it is generally of greatest concern in the pediatric population receiving PN, particularly on a long-term basis. Of particular importance in the adult surgical population is the pro-inflammatory effect of PN and IVFE in postoperative patients and the critically ill. The cytokine-driven systemic inflammatory response is already exacerbated in these patient populations. Without immunomodulation, there is an increased risk of nosocomial infection and subsequent sepsis, prolonged ventilation and ICU stay, and multiple organ failure [19–21]. Attempts at altering nutritional various components of PN, including the lipid formulation, to aid in immunomodulation have a theoretical, if not actual, benefit.

SMOF

Lipid formulations have historically contained one to two different oils as bases. As previously mentioned, SO-based formulations are most commonly used. However, as the understanding of FAs and their roles within the human body have evolved, new lipid formulations have been created to counteract the negative effects of PN and FAs and take advantage of the beneficial effects of certain FAs.

The so-called SMOF IVFE, commercially known as SMOFLipid®, contains four oils—soybean oil (30%), medium-chain triglycerides (30%), olive oil (25%), and fish oil (15%). Purported benefits of SMOF emulsions include decreased hepatotoxicity, a lesser pro-inflammatory effect, lower levels of oxidative stress, and more favorable effects on triglyceride levels. The mechanisms underpinning these benefits are thought to include a lower content of phytosterols, a higher content of MCTs, a lower ω-6 to ω-3 ratio, and a higher content of α-tocopherol [2•, 5, 9, 12]. An overview of the randomized controlled trials studying the effects of SMOF IVFE is presented in Table 3.

Effect on Hepatic Function

Phytosterols, plant-based elements that the human body cannot metabolize, are typically absorbed in small quantities when ingested. However, animal models suggest that when given intravenously, they accumulate in the liver and biliary system and lead to cholestasis. Purported mechanisms underlying this phenomenon include phytosterol-induced impairment in hepatic bile flow and conversion of cholesterol to bile acids [12, 22, 23]. As such, they are thought to have a role in the development of PNALD [5].

Additionally, as previously mentioned, MCTs do not accumulate within the liver, and studies indicate that IVFEs with a mixture of MCT-LCT result in no change in hepatic morphology [24, 25]. This stands in contrast to the fatty infiltration observed with LCT-based IFVEs [26].

A lower content of phytosterols and a higher content of MCTs should theoretically decrease the incidence of hepatic damage with PN administration [22, 27]. In two European studies conducted in preterm neonates, SMOF IVFE resulted in lower phytosterol levels compared to control IVFE [28, 29]. Furthermore, several randomized controlled trials do, in fact, indicate a favorable effect on serum liver function tests with SMOF IVFE [30–34]. Rayyan et al. showed a significant decrease in total bilirubin and slight decrease in direct bilirubin with the use of SMOFlipid® in premature neonates after 8 days of PN administration. This was compared to a significant increase in direct bilirubin levels in the neonates receiving the SO-based formulation Intralipid® [32••]. After 4 weeks of PN administration in children on home PN, Goulet et al. also found a statistically significant difference in total bilirubin alterations ($p < .01$), with a decrease in total bilirubin in the SMOFlipid® arm (−1.5 ± 2.4 μmol/L, $p < .05$) and an increase in the SO-based formula arm (2.3 ± 3.5 μmol/L, $p < .05$) [34]. Klek et al. found similar patterns in adult patients with intestinal failure after 4 weeks [31••]. Antebi et al. compared SMOFlipid® to LIPOVEN®, a SO-based IVFE, in 20 ICU patients undergoing major surgery. After 5 days, both groups of patients showed increases in AST, ALT, and GGT, though the increases were less in the SMOFlipid® group [30]. These findings suggest that SMOF IVFE may lead to a less

Table 3 Results of randomized controlled trials comparing SMOF IVFEs to Standard IVFEs

Author	Year	*n*	Patient population	Length of P (days)	IVFEs compared	Effect of SMOF compared to control group				
						Hepatic function	Inflammatory markers	ω6:ω3	Triglycerides	Length of stay
Antebi et al.	2004	20	Adult, postoperative in ICU	5	SMOF vs Lipoven	Nonsignificant ↑ in AST, ALT	Less ↑ in CRP		No significant ↑	
D'Ascenzo et al.	2014	80	premature neonates	7	SMOF vs Intralipid	↓ bilirubin			↑	
Goulet et al.	2010	28	Pediatric, home PN	29	SMOF vs Intalipid	↓ AST, ALT, bilirubin		↓	No difference in ↑	
Grimm et al.	2006	33	Adult, postoperative	5	SMOF vs Lipovenoes		↑LTB5: LTB4	↓		↓
Klek et al.	2012	73	adult, chronic intestinal failure	28	SMOF vs Lipoven	↓ AST, ALT, bilirubin	No change L-6, sTNF-RII, CRP	↓		
Ma, et al.	2012	40	Adult, postoperative	6	SMOF vs LCT/MCT	No difference in ↑ AST, ALT, bilirubin	No difference in IL-1β, IL-6, TNF-α, and CRP		No difference in ↑	No difference
Rayyan et al.	2012	53	Premature neonates	14	SMOF vs Intralipid	↓ bilirubin			No difference in ↑	
Tomsits et al.	2010	60	Premature neonates	7	SMOF vs Intralipid	Significantly lower GGT	No significant difference in CRP ↑		No difference in ↑	
Vlaardingerbroek et al.	2014	96	Very low birth weight infants	14	SMOF vs Intralipid	Mixed results		↓	↑	No difference
Wu et al.	2013	35	Adult, postoperative	6	SMOF vs Lipovenous	No difference in ↑ AST, ALT, bilirubin	No difference in IL-6, IL-10, CRP, TNF-α, and TGF-β1		Less ↑	Nonsignificant trend toward ↓

significant perturbation, or even an improvement, in some liver function among critically ill patients.

Immunomodulatory Effects

As previously mentioned, PUFAs have a downstream effect on the production of eicosanoids. The eicosanoids produced from ω-6 FA are thought to be more pro-inflammatory than those produced by ω-3 FA, and current literature indicates that a lower ratio of ω-6 to ω-3 FA offers more favorable immunomodulation [35–37]. Several randomized controlled trials have demonstrated a decrease in the ω-6 to ω-3 ratio with the administration of SMOF IVFE [31••, 32••, 38]. Other randomized controlled trials, however, found no significant difference in serum levels of inflammatory markers with SMOF administration compared to more traditional IVFEs. Ma et al. and Wu et al. found no significant difference in levels of IL-1beta, IL-6, TNF-α, and CRP between those receiving SMOFlipid® and those receiving Lipovenoes® [39, 40]. Klek et al. found no difference in IL-6 or sTNF-RII levels between SMOFlipid® and Intralipid® [31••]. Antebi et al. did find a significant increase in CRP levels when SO-based LIPOVEN was administered, compared to a non-significant increase in CRP in the SMOFlipid® group [30]. Grimm et al. also found SMOFlipid® to have a more favorable inflammatory effect. In 33 patients receiving either SMOFlipid® or Lipovenoes® for 5 days following major abdominal surgery, the proinflammatory LTB4 was lower in the SMOFlipid® arm than the Lipovenoes® arm, though not significantly [38]. Therefore, studies show mixed results in the effect of SMOF on inflammatory markers, with some showing no difference, some showing a trend, and some showing a statistically significant lower pro-inflammatory effect of SMOF emulsions.

Antioxidant Effects

The bioactive form of vitamin E, α-tocopherol, is administered as an additive to SMOFlipid® to counteract the known peroxidative effects of PUFAs. Higher levels of α-tocopherol should theoretically reduce the oxidative stress associated with the administration of PUFA-containing IVFEs [41]. Multiple randomized controlled trials have demonstrated that administration of SMOFlipid® led to an increase in serum α-tocopherol levels when compared to alternative IVFE formulas [30–32••, 34, 38, 40, 42]. Wu et al. further studied the effect of SMOFlipid® on superoxide radicals and total oxygen radicals. They found no difference when SMOFlipid® was compared to Lipovenoes® in a group of 35 patients receiving PN for 5 days after undergoing gastrointestinal surgery of some sort, suggesting that the α-tocopherol supplementation in SMOFlipid® does effectively counteract the increased oxidative stress that FO might confer [40].

Effect on Triglycerides

Several studies have also examined the effects of SMOFlipid® on plasma triglyceride levels, largely with respect to its effect on the incidence of fat overload syndrome [39, 40]. Fat overload syndrome, a complication caused specifically by the infusion of IVFEs, results from a rise in triglyceride levels. When the rate of infusion exceeds the rate of hydrolysis, triglycerides accumulate. The constellation of symptoms in fat overload includes headaches, jaundice, hepatosplenomegaly, respiratory distress, and coagulopathy, among others. This syndrome has historically been seen with the use of SO-based IVFEs with high rates of infusion, as the LCTs in SO-based formulas are cleared more slowly than MCTs or FO [2•]. After 6 days of PN, Wu et al. found a significantly lower increase in triglycerides in those receiving SMOFlipid® versus Lipovenoes® ($p = .029$) [40]. Ma et al., however, found a significant difference in the rise of triglycerides between SMOFlipid® and Lipovenoes® [39]. These results fail to provide clear evidence regarding the ability of SMOF emulsions to decrease triglyceride level elevations compared to other IVFEs, though they do demonstrate that SMOF at least does not lead to a greater rise in triglyceride levels compared to their conventional IVFE counterparts.

Length of Hospital Stay

Finally, length of stay (LOS) was examined in several of the studies reviewed, revealing mixed results. Grimm et al. found a statistically significant decrease in LOS when comparing patients receiving SMOFlipid® versus Lipovenoes® (13.4 ± 2.0 vs 20.4 ± 10.0 days, $p < 0.05$) [38]. Wu et al. saw a trend toward shorter LOS with the SMOFlipid® group, though this did not reach statistical significance (17.45 ± 4.80 vs 19.62 ± 5.59 days, $p = .19$) [40]. Ma et al. found the LOS to be the same between the groups (12.2 ± 6.2 vs 10.4 ± 2.7 days, $p = .231$) [39].

Practical Implications for Surgical Patients

There are a variety of indications in which surgical patients might need PN administration, including those with intestinal failure, those who are critically ill, and those who are unable to tolerate enteral feeding either preoperatively or postoperatively. For such patients, IVFE represents a critical component of PN. In the USA, SO-based IVFEs have traditionally been the standard IVFE formulation utilized in PN. As described above, SMOFlipid® has many theoretical benefits, including a decreased incidence of PNALD, more favorable immunologic alterations, and decreased circulating triglycerides. While studies indicate possible trends toward a lesser degree of hepatic injury, pro-inflammatory effects, pro-oxidative effects, and hypertriglyceridemia, these benefits are far from definitive. This possibly stems from the short study period in which the trials were performed. The longest length of PN administration of the studies reviewed was only 4 weeks, and in most, PN was only administered for a period of about 1 week. It is likely that the benefits of SMOF will only become apparent after a more long-term administration of PN, as detrimental effects of PN are increasingly seen with longer duration of PN administration and not necessarily with short-term PN administration. As an extension, the patients most likely to benefit from SMOF IVFEs are those requiring more long-term administration of PN.

Additionally, based on the theoretical immunomodulatory and antioxidant effects of the components and downstream products of SMOFlipid®, patients who are critically ill and biologically stressed are those most likely to derive the most benefit from SMOF IVFEs. However, more studies with a significant number of patients are needed to confirm a true clinical benefit.

Finally, most studies that examine SMOF-based IVFEs were performed in the pediatric population, particularly in premature infants. More studies are needed in adult patients and in surgical patients to truly determine whether any positive or negative effects result from SMOF administration.

Though there is a paucity of data, studies do indicate that SMOFlipid® is at least safe for use and does have a theoretical benefit, if not an actual clinical benefit. Two studies reviewed here indicate that SMOFlipid® administration may shorten hospital LOS in post-surgical patients, which would presumably result in lower overall healthcare cost [39, 40]. The cost of SMOFlipid® itself will likely vary from hospital to hospital based on contractual agreements. Based on conversations with multiple hospital pharmacists, SMOFlipid® is becoming available as the standard IVFE in multiple locations across the USA, replacing the standard SO-based emulsions. This will likely make it easier to study in larger and more varied populations receiving PN in the USA. However, it does highlight the fact that the choice of IVFE is largely based on the formulary carried by each particular hospital and not on physician preference.

Conclusion

PN represents a revolutionary advancement in medicine that has greatly evolved since it first came into wide use in the 1970s. IVFEs have also evolved over that time, in an attempt to provide adequate nutrition requirements in the form of energy and EFAs. More recently, IVFEs with more varied oil components are being developed in an attempt to counteract PNALD and PN-associated inflammation, oxidation, and hypertriglyceridemia. Evidence suggests that SMOF-based IVFEs may play a role in mitigating such complications.

Additionally, evidence shows a possible correlation between SMOF-based IVFEs and a shorter length of hospital stay.

SMOFlipid® is becoming more widely available in the USA for use as an IVFE. It may have a role in surgical patients requiring more long-term use of PN or in patients who are critically ill. However, a paucity of data exists demonstrating clear advantages over conventional IVFEs. A greater number of adequately powered studies with a longer length of PN administration are needed to more definitively establish the superiority of SMOF-based IVFEs to their standard counterparts.

Compliance with Ethical Standards

Conflict of Interest Elizabeth H. Cameron, Neal Bhutiani, and Matthew C. Bozeman declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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