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The Role of Alternative Lipid Emulsions in Critically Ill Patients: What the Evidence Shows

Lipid emulsions (LEs) are a component of parenteral nutrition (PN) providing a dense source of energy and essential fatty acids.¹ In critically ill patients, commonly used LEs have been rich in long-chain triglycerides (LCTs) providing a high percentage of linoleic acid (ω -6 polyunsaturated fatty acids [ω -6 PUFA] 18:2 ω -6). The current literature suggests that intravenous (IV) soybean-oil (SO) and safflower-based LEs are able to promote production of pro-inflammatory prostanooids and leukotrienes and therefore increase oxidative stress and systemic inflammation in the critically ill.^{2,3} In 2006, it was suggested that inclusion of ω -6-based LEs might be detrimental, which is more probable in the most seriously ill patients.⁴ Withholding lipid emulsion high in SO has been recommended in patients who tolerate some EN and who require short term PN (< 10 days).⁵

Over the last decade, different LEs reducing the load of omega-6 fatty acids (also named “soybean-sparing” strategies, or “omega-6 reducing” strategies) have been evaluated in several experimental studies and clinical trials. Among these strategies, fish oil (FO) based LEs, which contain the omega-3 fatty acids eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA), olive oil-based LEs and medium-chain triglycerides (MCTs) based LEs, have been developed.

Within the last year, we published two systematic reviews and meta-analyses on SO-sparing LEs in the critically ill. Firstly, we demonstrated that FO-containing LEs either in the context of patients receiving PN or EN⁶ may be able to decrease mortality (risk ratio [RR], 0.71; 95% confidence interval [CI], 0.49–1.04; $P = 0.08$; heterogeneity $I^2 = 0\%$) and ventilation days (weighted mean difference in days [WMD], -1.41 ; 95% CI, -3.43 to 0.61 ; $P = 0.17$) in the critically ill. More recently, our second meta-analyses⁷ combined all RCTs that examined the effect of soy bean emulsion strategies and demonstrated that after aggregating 12 RCTs, SO-sparing strategies were associated with clinically important reductions in mortality (RR 0.83; 95 % CI 0.62, 1.11; $P = 0.20$), in duration of ventilation (WMD -2.57 ; 95 % CI -5.51 , 0.37 ; $P = 0.09$), and in ICU length of stay (WMD -2.31 ; 95 % CI -5.28 , 0.66 ; $P = 0.13$) but none of these differences were statistically significant.

Given the paucity of data from RCTs, we explored the association between SO-sparing LE and clinical outcomes in a large observational database.⁸ Using appropriate statistics that adjust for confounding variables, when compared to SO based LEs in PN, patients who received olive oil or FO had a reduced time to extubation alive and a reduced ICU LOS alive. No significant difference was seen with respect to hospital LOS. The cumulative hazard curve for discharge from the ICU alive comparing lipid-free emulsions versus SO, MCT oil, olive oil and FO is shown in **Figure 1**.

On the basis of the updated literature, the 2013 Canadian Clinical Practice Guidelines⁵ consider that there are insufficient data to make a recommendation on the specific type of omega-6 fatty acid reducing strategy in critically ill patients who require PN. Notwithstanding, when indicated, IV lipids that reduce the overall load of omega-6 fatty acids should be considered in ICU patients. Having said that, we believe that two additional comments and final recommendations should be addressed:

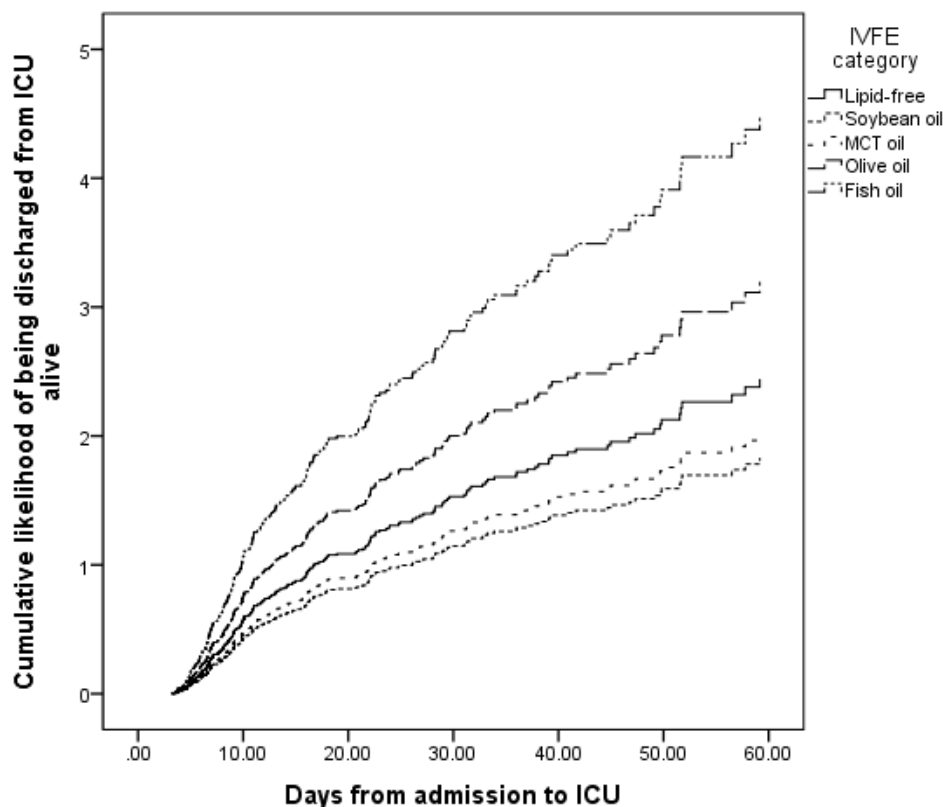
1. When a patient requires PN, is it necessary to start nutrition therapy using an alternative LE as a source of lipids?

According to the 2013 Canadian Clinical Practice Guidelines, there is weak evidence to support the withholding of lipids high in soybean oil in critically ill patients who are not malnourished, are tolerating some EN, or when parenteral nutrition is indicated for short term use (< 10 days). There are insufficient data to make a conclusive recommendation about withholding lipids high in SO in malnourished critically ill patients or in those who require long term PN⁵. However, **when LEs are indicated, lipids that reduce the overall load of omega-6 fatty acids should be utilized.**

2. Based on our data, are we able to define the best alternative LEs in the critically ill?

So far, there is no randomized trial comparing head-to-head the types of lipids (i.e. omega-3, omega-9, or MCT emulsions) to each other. Therefore, **we were unable to recommend the best type of omega-6 sparing strategy.**

Figure 1. Cumulative hazard curve of the likelihood of patients being discharged from ICU alive ($p < 0.001$) (Revised and published with permission from C. Edmunds⁹)



Unfortunately, current literature on the clinical effect of alternative oil-based LEs is still inconclusive. However, these strategies have been demonstrated to be safe and effective in reducing the overall load of omega-6 FA and could have potential clinical benefits. Large, multicenter, multi-country, well designed, randomized trials are required to elucidate the efficacy and define the best alternative LE to be used in the critically ill.

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