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Trust Guideline for the Management of: Clinical Guideline for Use of SMOFlipid in Neonatal and Paediatric Patients at Risk of Intestinal Failure Associated Liver Disease

A clinical guideline

For Use in:	Jenny Lind Children's Hospital
By:	Registered Paediatric Nurses, Medical Staff, Paediatric Dietitians and Paediatric Pharmacists
For:	Infants, children and adolescents with or at risk of developing, intestinal failure associated liver disease (IFALD).
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Glossary

BIFS	British Intestinal Failure Survey
IFALD	Intestinal failure-associated liver disease
LFTs	Liver function tests PN Parenteral Nutrition
SMOFlipid®	Emulsion of soya, MCT, olive and fish oils
TPN	Total Parenteral Nutrition

1. Objectives

To provide a consistent management to infants, children and adolescents with or at risk of developing, intestinal failure-associated liver disease (IFALD).

2. Introduction

The first line lipid component of parenteral nutrition (PN) for paediatric use is currently 20% Intralipid®. Its use is required primarily in preterm neonates and in patients with intestinal failure (IF) which is defined as gastrointestinal problems resulting in dependence on PN for some or all nutrition for 27 or more days, consecutively or in total. One of the most significant complications of long term PN is intestinal failure-associated liver disease (IFALD) which occurs in up to 50% of children after 6-12 weeks on PN (1). Possible mechanisms include lack of enteral feeding, reduced gut hormones secretions, reduction of bile flow and biliary stasis leading to the development of cholestasis, biliary sludge and gallstones, which exacerbate hepatic dysfunction (2). Premature infants, infants born small for dates, those with congenital gut anomalies and severe acquired conditions resulting in short gut syndrome or in gut dysmotility are most at risk.

The pro-inflammatory properties of soyabased lipids (e.g. Intralipid®) are widely considered to have a causative role in inducing IFALD. There is now increasing evidence that change to a lipid preparation containing fish oils can reverse liver disease over a 4-6 week period (3,4,5,6,7,10, 11,12). One such preparation comprises soya, medium chain triglycerides, olive oil and fish oil (SMOFlipid®; Fresenius Kabi, Bad Homburg, Germany). SMOFlipid contains 30% soybean oil, 30% medium-chain triglycerides (as coconut oil), 25% olive oil and 15%

fish oil.[8] Relative to Intralipid, SMOFlipid provides higher concentrations of arachidonic acid (ARA) and docosahexaenoic acid (DHA) as well as the n-3 fatty acid eicosapentaenoic acid with an ARA:DHA ratio of 1.0:3.5.

Two randomised controlled trials have shown SMOF to decrease plasma bilirubin and gamma-glutamyl transpeptidase (GGT) levels in comparison to the levels seen with traditional soybean lipids. SMOFlipid® has also been shown to increase omega 3 fatty acids and alpha tocopherol without changing lipid peroxidation. This is thought to protect premature infants from increased levels of oxidative stress and may benefit their cognitive development and visual capacity.(8)

The use of a multi-lipid emulsion is advised as one of the preventative and/or treatment strategies but further studies are required to establish whether SMOFlipid® can reverse PN-associated liver disease (PNALD) .

SMOFlipid® is now used by intestinal failure units including Great Ormond Street Hospital and Birmingham Children's Hospital. A survey of further 32 paediatric centres shows SMOFlipid® to be the preferred lipid for patients who develop signs of liver dysfunction on Intralipid® (9). The British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) recommend the consideration of SMOFlipid® in children with IFALD. Many neonatal units across the USA, Canada, Europe and Asia are now using SMOFlipid®as a first line lipid in highrisk infants (13). However the evidence to support routine use in neonates is not established. ESPGHAN guideline (14) published in 2018 include a consensus recommendation that for PN lasting longer than a few days, pure soy emulsion should be replaced by composite ILEs with or without fish oils.

NICE 2020 (15) supports change from pure soy emulsions to composite lipid in babies with PNALD but felt the published evidence in preterm infants was weak and concluded that it could be trialled because these babies are at risk of developing progressive liver disease and liver failure. They did not make any specific recommendations for infants with surgical conditions or infants at risk of, but without evidence of, PNALD.

3. Safety and efficacy

Studies have demonstrated the safety of SMOF but evidence of superiority in all infants is less clear. Current ESPGHAN current guidance is to use composite with or without fish oil as first choice for PN use which will last more than a few days (14). NICE guideline (2020) comments that it is reasonable to choose SMOF despite evidence of efficacy not being compelling, because of the risk in the high risk babies, i.e. reasonable to use on a prophylaxis basis (15). Frazer & Martin in their 2021 review come out against routine SMOF pending better evidence of superiority/safety over Intralipid (16).

Pending further data this guideline does not therefore recommended routine use in all infants outside the EEPGN guidelines.

4. Indication

The East of England Paediatric Gastroenterology Network (EEPGN) recommends that SMOFlipid® is considered for the following paediatric patients:

1. PN-dependant for over 27 days (even if LFTs normal).
2. Patients at high risk of needing PN for >27 days.
3. Significant liver dysfunction before 27 days on PN (conjugated bilirubin >50 mmol/l or ultrasound evidence of splenomegaly).
4. Patients transferred into units who are established on SMOFlipid® already.
    - Paediatric patients meeting the criteria for use of SMOFlipid® should be discussed with a consultant in paediatric gastroenterology or consultant neonatologist.
    - Typically SMOFlipid®use will be for the duration of inpatient PN.

5. Clinical audit standards

1. SMOFlipid® considered for patients reaching criteria (100%).
2. Patients meeting the criteria for SMOFlipid® for whom SMOF is not used should have documented discussion with neonatal and paediatrics gastroenterology consultants explaining reason for deviation (100%).

6. Summary of development and consultation process undertaken before registration and dissemination

This guideline has been developed by the East of England Paediatric Gastroenterology Network. This document has been updated after literature search of recent SMOFlipid®-related studies. During its development it has been circulated for comment to: Paediatric Nutritional group in Norfolk and Norwich University Hospital. This was reviewed in August 2018 and the requirement to log patients onto National database deleted as this is no longer active. In 2018 literature review revealed only reference 10 to be added. 2022 update included minor text revision in sections 2 and 3 with additional references 11-16.

7. Distribution list/ dissemination method

Trust Intranet.

8. References/ source documents

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