Effect of changing lipid formulation in Parenteral Nutrition in the Newborn
Experimental Pathology BSc
Abstract

Analysis of data of newborns receiving Intralipid-based TPN in 2009 revealed presence of high incidence of liver dysfunction during an audit at the Royal London Hospital, Whitechapel. (unpublished data). The hospital clinical practice was changed in 2010 and SMOFlipid-based preparation was used for TPN in babies with indications of liver disease. Criteria for commencing SMOFlipid was total bilirubin >100µmol/L or conjugated bilirubin >50µmol/L.

Several studies report clinical benefits of fish-oil based intravenous lipid emulsions (IVLE) for use in total parenteral nutrition (TPN) showing a lower incidence of parenteral nutrition associated liver disease (PNALD). However, to our knowledge, this benefit is yet to be proven by evidence in biochemical results.

Liver function tests from neonatal patients on long-term TPN for more than 28 days and whose bilirubin levels rose over 100µmol/L or conjugated bilirubin rose over 50µmol/L were used in this study. In 2010, the lipid emulsion was changed to SMOFlipid when bilirubin levels rose over 100µmol/L or conjugated bilirubin rose over 50µmol/L. All infants receiving TPN for more than 28 days who were eligible for SMOFlipid were used in the study.

Results showed some improvements in total bilirubin levels and CRP in neonatal patients receiving SMOFlipid-based IVLE compared to those with Intralipid emulsions in their TPN. Other modalities showed insignificant or nonsensical results due to confounding factors. There was a significant reduction in the rates of sepsis from 2009 to 2010 when the lipid preparations were changed from Intralipid to SMOFlipid. This project highlights some biochemical evidence to support hepatic advantages of SMOFlipid based emulsions, but not all results were conclusive. It highlights the need for a larger secondary study so that more reliable results can be obtained.
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**Introduction**

Parenteral nutrition (PN) is a method of delivering protein, energy, nutrients and metabolic requirements intravenously directly into the bloodstream, bypassing the gastrointestinal tract. It is a method of providing the required energy to patients incapable of oral or enteral feeding for various reasons. It is invasive and is only to be used when there is no alternative method of feeding available due to its associated complications.(1)

There are two types; peripheral and total parenteral nutrition. Peripheral parenteral nutrition is given through a cannula in a peripheral vein. It can supply some nutritional components for patients who cannot meet all their nutritional requirements. These patients have some oral intake (or assisted enteral feeding), however it may be insufficient or they may have problems digesting and/or absorbing all they need. Therefore it is given to supplement the diet rather than replace it. Peripheral parenteral nutrition can be used only as a short term option. It is preferred over total parenteral feeding as the maintenance of at least some gastrointestinal activity prevents villous atrophy, which is a major problem in those receiving total parenteral nutrition.(2)

Total parenteral nutrition is designed to replace enteral intake entirely. It is relatively new in patient care and it involves the insertion of a large central vein catheter (central line) into the upper chest or neck to terminate in the superior vena cava or the subclavian vein. This allows for all daily nutritional requirements to be given to a patient. Large volumes of nutrients such as protein (as amino acids), carbohydrate or energy (as glucose), lipids (as triglycerides), vitamins and minerals enter the bloodstream directly. The feed is connected to a pump which regulates the volume of nutrients and the speed at which it is administered.(2)

TPN is most widely used in neonatal medicine compared to any other specialty.(3) It is indicated if it is anticipated that an infant will not receive enteral feeds for 2-3 days and adequate nutrition cannot be achieved, or should begin immediately in medical
conditions where enteral feeding is contraindicated. This is most frequently encountered in the treatment of premature infants, who have the inability to tolerate enteral feeding well due to their small stomachs and under-developed gastrointestinal tracts. Gastric emptying and intestinal transit times are also shown to be significantly delayed compared to term babies.(4) These babies also have a higher nutritional need, as well as very minimal caloric reserves. TPN is also essential as an energy source for the growth of neonates with conditions such as short bowel syndrome, necrotizing enterocolitis and intestinal failure.(5) Without this option, most would not survive due to complications of malnutrition or starvation.

There is no doubt that TPN has many great benefits, but there are also risks associated with its prolonged use. Glucose and electrolyte imbalance is associated with feeds that enter the bloodstream directly and bypass normal regulation by the bowel and other mechanisms. Catheter-associated infection is another major problem with this form of treatment. The nutritional property of these solutions combined with its iso-osmotic properties provides an ideal environment for microorganisms to grow in, hence the use of aseptic techniques during its preparation and administration is of utmost importance.(6) However, the most significant complication associated with TPN is cholestatic parenteral nutrition associated liver disease, which can advance to irreversible cirrhosis and liver failure if PN use is not arrested and enteral feeding resumed.(7) Although re-establishing the use of enteral nutrition can possibly reverse the cholestasis, the risk of malnutrition is high when the patient’s natural absorptive processes are not yet fully functioning so this is not always possible.(8) Without successful weaning off TPN or failure to receive a liver/small bowel transplant, the mortality rate within one year of diagnosis of TPN-associated liver disease approaches 100% for these infants.(9)

The use of TPN for longer than a two week period increases the risk of PNALD. Though the aetiology remains unknown, recent evidence has shown that a major causative risk factor is the composition of the intravenous lipid emulsions used in TPN.(10) TPN must contain lipid emulsions to provide a non-protein or glucose energy source and essential fatty acids for cellular growth and development. The first non-toxic lipid emulsion was called ‘Intralipid’, and was developed in 1961 by the
Swedish scientist Arvid Wretlind. The safe method of delivery through a central vein was only suggested in 1968 by the American, Dudrick et al. These combined discoveries allowed for the delivery of a more complete nutritional package to patients intravenously.

Intralipid was the first commercially available lipid emulsion and its content was made entirely of soybean oil. These lipid emulsions provide a good source of non-protein calories and are an alternative to dextrose to prevent hyperglycaemia that occurred in cases of over feeding from the glucose and amino acid admixtures. These emulsions also provide essential fatty acids which are not produced endogenously and must be taken through the diet. Essential fatty acids enhance the immune system, improving the cellular structure and function as they are a vital component of cell membranes and also positively influence inflammatory mediator production.(11) The traditional IVLEs that are still used today, mimic chylomicrons and are composed of soybean oil or safflower oil, which provides long chain triglycerides (LCTs) and egg-derived phospholipids. They are a concentrated source of energy, essential fatty acids and lipid soluble vitamins. Soybean based IVLEs are available in different concentrations; 10%, 20% and 30% (weight/volume), which respectively contains 1.0, 2.0 and 3.0 kcal/mL of energy. These emulsions contain the polyunsaturated fatty acid linoleic acid, which accounts for as much as 50% of the total composition.(12)

Although Intralipid has an important role in providing essential fatty acids there have been issues regarding its concentration of omega 6 polyunsaturated fatty acid. An increased level of linoleic acid is associated with hepatobiliary dysfunction and increased oxidative stress.(13) Several clinical and in vitro studies have also demonstrated immunosuppressive and pro-inflammatory effects of soybean based emulsions, which may be linked to poorer outcomes for patients.(14)(15) The use of soybean oil lipid emulsions has been shown to cause unfavourable derangements in lipid profiles such as hypertriglyceridemia, hypercholesterolemia, reduced high density lipoprotein (HDL) concentrations and increased low density lipoprotein (LDL) concentrations.(16)(17) Children on long-term PN containing soybean oil based lipid emulsions were found to develop PN associated cholestasis.(18)