COMPARISON OF INTRAVENOUS LIPID EMULSIONS IN PARENTERAL NUTRITION THERAPY: A PILOT STUDY

Alexis K McGuigan

Submitted to the faculty of the University Graduate School
in partial fulfillment of the requirements
for the degree
Master of Science
in the School of Health and Human Sciences,
Indiana University

February 2021

Accepted by the Graduate Faculty of Indiana University, in partial fulfillment of the requirements for the degree of Master of Science.

Master's Thesis Committee

____

Jacquelynn O'Palka, RD, PhD, Chair

____

Sara A. Blackburn, DSc, RD

____

Michelle Laughlin, MD, FACS

____

Amy Carter, MA, RD, LD, CDCES

ACKNOWLEDGEMENT

Thank you to the members of the thesis committee that reviewed and assisted in this project: J. O’Palka PhD, S.A. Blackburn PhD, M. Laughlin MD, and A. Carter MA, RD. Also, to E. Holler, Trauma Research Coordinator with Eskenazi Health for assistance with data collection. Finally, appreciation to G. Eckert with the Department of Biostatistics at Indiana University-Purdue University of Indianapolis for evaluating the data analyses and providing guidance.

Alexis K McGuigan

COMPARISON OF INTRAVENOUS LIPID EMULSIONS IN PARENTERAL NUTRITION THERAPY: A PILOT STUDY

Background: SMOF lipid™ infusion containing soybean oil, medium-chain triglycerides, olive oil, and fish oil has been approved and recommended for use in adults receiving parenteral nutrition (PN). Research shows that SMOF lipid infusion is safe for use in post-operative and critically ill patients. Improved patient outcomes are linked to SMOF lipid use over traditional soybean oil lipid emulsions.

Objective: The purpose of this study was to determine the effect of SMOF lipid infusion on incidence of infection, ICU length of stay, hospital length of stay, and mortality in adult trauma patients as compared to parenteral nutrition utilizing 100% soybean oil emulsion or a lipid-free, dextrose and amino acid administration.

Methods and Analysis: A retrospective chart review was conducted for adult trauma patients admitted to Eskenazi Health's surgical intensive care unit (SICU) that received PN from May 2017 to May 2020. Data were collected from the electronic health record and trauma registry.

Results: Twenty-nine patients were included who met study criteria: 17 patients in the traditional lipid cohort and 12 in the SMOF lipid cohort. The length of PN therapy was comparable between the traditional and SMOF ILE groups, 13.9 days (± 11.5) and 13.3 days (± 14.3) respectively. All 12 patients in the SMOF lipid cohort received intravenous lipid emulsion (ILE) compared to 42% (n=7) of traditional lipid group patients (p=0.001). SMOF treatment group were provided 100% of estimated energy needs via PN compared to an average of 94% (± 9.7) of estimated energy needs in the traditional lipid treatment group (p=0.036). Incidence of infection during initial hospitalization was significantly lower in the SMOF treatment group (n=3, 25%) compared to the traditional lipid treatment group (n=13, 76%). Mortality was decreased in the SMOF treatment group (0%) when contrasted to the Intralipid treatment group (23.5%), p=0.04.

Conclusion: Patients receiving SMOF lipid emulsion within PN therapy had better clinical outcomes compared to those receiving Intralipid soybean-lipid emulsion or a dextrose and amino acid administration.

Jacquelynn O'Palka, RD, PhD, Chair

TABLE OF CONTENTS

List of Tables

List of Figures

List of Abbreviations

The following terms appear throughout this paper:

- Parenteral Nutrition (PN): An intravenous administration of nutrients which can include amino acids, dextrose or glucose, lipids, micronutrients, and electrolytes. This term is often used interchangeably with Total Parenteral Nutrition (TPN). For the purpose of this paper, TPN specifically refers to complete intravenous nutrition which includes amino acids, dextrose, and lipids.
- SMOF lipid: A third generation, trademarked lipid emulsion for intravenous nutrition which is a four oil blend containing soybean, olive, fish, and medium-chain triglycerides.
- Intralipid: A first generation, trademarked lipid emulsions for intravenous nutrition containing 100% soybean oil.
- Traditional lipid group: Treatment group prior to the introduction of SMOF lipids that received Intralipid or a lipid-free (dextrose and amino acid PN) utilizing traditional guidelines to withhold lipid emulsion during acute inflammatory periods.
- Intravenous Lipid Emulsion (ILE): The preferred term and abbreviation for lipid injectable emulsions related to nutrition support.
- Intensive Care Unit (ICU): Critical care department that provides specialized acute, life supporting care to ill or injured patients.

Chapter One: Background

Introduction

Parenteral Nutrition (PN) is an intravenous source of nutrients for those who cannot tolerate nutrition by mouth or via enteral nutrition to support healing. Parenteral nutrition is composed of carbohydrate (glucose), protein (amino acids) and fat (lipids) as a source for energy and essential fatty acids. One well recognized intravenous lipid emulsion (ILE) is Intralipid. Intralipid's lipid source is derived from soybean oil which contains high amounts of omega-6 polyunsaturated fatty acid, primarily linoleic acid, an essential fatty acid. For critically ill patients, the concern is that soy-based lipid products are inflammatory, creating an imbalance of the fatty acid profile in cell membrane phospholipids which leads to peroxidation. The high omega-6 fatty acid and phytosterol content of soybean-based ILE may worsen inflammatory states by increasing the production of inflammatory mediators in the critically ill. Soybean lipid emulsions are linked to reduced T cell function, increased production of oxygen-free radicals and PN-associated liver disease. For the past twenty years, practitioners have expressed concerns that the composition of lipid emulsions negatively affects immunological functions and inflammatory events. Due to these concerns, the American Society of Parenteral and Enteral Nutrition (ASPEN) Lipid Injectable Emulsion Safety Recommendations dictate to withhold soybean-oil lipid emulsions in critically ill patients requiring parenteral nutrition during the first seven days of an ICU stay.[1]

Review of Literature

Background of Intravenous Lipid Emulsions

Gao et al[2] implemented a quality improvement study enacting a restriction of infused soybean lipid emulsions in critically ill, cardiac surgery patients to determine the effects on patient outcomes. The study included a total of 761 patients admitted to the cardiac surgery ICU who required supplemental PN; 370 patients received lipids and 391 patients had lipids withheld until ICU day seven. Patient demographics between treatment groups were similar. Majority of patients were male comprising 61.35% of the soybean-oil lipid group and 57.29% of the lipid-free group. The patients were of comparable age with an average of 57.67 ± 12.95 years in the soybean-oil lipid group and 58.76 ±12.17 years in the lipid-free group. The average BMI was in the normal classification (23.1±3.45 in the soybean-oil lipid group) and (22.8±3.35 in the lipid-free group). There was no nutrition assessment tool or diagnoses utilized to compare nutritional status between the patient groups. The patients received supplemental PN with or without ILE to meet individualized energy goals for a minimum of 48 hours post-operatively. The results demonstrated a reduction in infections by 4% (p=0.02), decreased ICU length of stay (-0.6 days, p value 0.002) as well as hospital length of stay (-1.1 days, p value < 0.0001) in the group who did not receive ILE. Energy delivered via PN during the first week was significantly lower in the group that did not receive ILE by an average of 5.8% (p=0.0168).[2] When ILE is omitted in PN prescriptions, ICU patients may not meet energy goals with a dextrose and amino acid administration as demonstrated by Gao et al. Patients receiving high dextrose concentrations are at risk for hyperglycemia and increased infection risk per Society of Critical Care Medicine (SCCM) and American Society of Parenteral and Enteral Nutrition (ASPEN) guidelines for the critically ill patient.[3]

Recently FDA-approved third generation mixed intravenous lipid emulsions, such as SMOF lipid, which became available for use in the United States and are linked to improved outcomes compared to traditional lipid emulsions. SMOF lipid is comprised of 30% soybean oil, 30% medium-chain triglycerides (MCT), 25% olive oil and 15% fish oil.[4] This blended lipid emulsion is a good source of essential fatty acids and omega-3 fatty acids including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).[5] Studies demonstrate improved immune response and reduction in stress hormones when utilizing SMOF lipid compared to standard lipid therapy or in the absence of lipid emulsions. Further, SMOF lipid is approved for use in the critically ill patient, which increases energy prescription and delivery in those receiving parenteral nutrition (PN).[1,3] In surgical patients, evidence from clinical studies and meta-analyses demonstrate advantage of third generation ILE use in clinical outcomes without increased risk of coagulopathy or bleeding abnormalities per the European Society of Parenteral and Enteral Nutrition (ESPEN).[6]

SMOF and Inflammation

Inflammatory and immune response is positively impacted by the addition of omega-3 fatty acids in SMOF lipid and similar lipid emulsions. Zheng et al[7] conducted a randomized control trial with adult esophageal cancer patients (n=84) requiring parenteral nutrition post-operatively following major esophageal surgery for treatment of cancer. The patients were randomized to receive SMOF lipid emulsion or a long-chain fatty acid containing soybean-based lipid emulsion. The SMOF treatment group included of 42 patients, 27 males and 15 females between the ages of 46 and 65 years old. The control group also included of 42 patients, 28 males and 14 females between the ages of 44 and 63 years old. The researchers state that all other baseline criteria were similar between groups, however, this information is not provided in the publication for further review. The results demonstrate the SMOF lipid emulsion group had a reduction in inflammatory mediators as evidenced by lower tumor necrosis factor alpha (TNF-a) and macrophage inflammatory protein 2 (MIP-2) levels. These values were measured at post-operative day three and day seven with values of 38.59 ±5.86 and 31.38 ±5.25, respectively. When compared to the soybean oil lipid group, TNF-a measurements of 49.55 ±6.82 on day three and 40.38 ±5.58 on day seven, there was a significant difference between treatment groups (p value <0.05). The SMOF ILE group had a significant decrease in TNF-a levels between days three and seven (p value <0.05) indicating an immediate anti-inflammatory and improved stress response. This effect was not observed in the control group. MIP-2 levels were also measured at post-operative days three and seven with a statistically significant reduction in the SMOF ILE group compared to the control group. The SMOF ILE group MIP-2 levels were 9.38 ±1.15 and 8.03 ±1.04 at days three and seven, respectively (p value < 0.05 between days). Compared to 13.48 ±1.87 and 11.67 ±1.58 on days three and seven in the control group, there was an observed significant reduction between groups as well.[7]

In a similar study comparing the effects of an olive-oil containing lipid emulsion to a medium-chain triglyceride and long-chain triglyceride lipid emulsion (MCT/LCT), Wang et al[8] observed improved trends in proinflammatory markers following post-operative olive-oil lipid use in PN. Ninety-four patients aged 35-70 years (average 57.8 ± 8 years) undergoing radical esophagectomy for cancer treatment were randomized into the experimental (olive oil) or control (MCT/LCT) group. These patients were largely male, 74% in the olive oil ILE group and 77% in the MCT/LCT ILE group and with average BMIs in the normal classification 22.12 ±2.98 and 21.45 ±2.97, respectively. The patients were assessed for malnutrition using the Nutrition Risk Screening (NRS) 2002 tool. Nineteen patients in the olive oil group and 22 patients in the MCT/LCT oil group were diagnosed as nutritionally at-risk with a score >3 (p=0.84). Inflammatory biochemical markers interleukin-6 (IL-6), TNF-a, and serum C-reactive protein (CRP) were measured one day prior to surgery, post-operative day one and post-operative day eight. The experimental group experienced reduced changes in proinflammatory markers IL-6 and TNF-a from post-operative day one to day eight of treatment compared to continued inflammatory response in the control group. TNF-a significantly increased in the control group on post-operative day one from pre-operative levels by 14 pg/mL compared to the experimental group which increased by 9.1 pg/mL (p <0.05). CRP levels significantly increased in both treatment groups from pre-operative to post-operative day one with no significant difference in values. IL-6 values increased in both treatment groups from pre-operative levels to post-operative day one, however, the experimental olive oil group did not demonstrate increased levels of IL-6 from post-operative day one to day eight as the control did. IL-6 levels in the olive oil-based group remained consistent post-operatively with a slight decrease from 61.78 ±29.13 pg/dL on day one to 61.56 ±34.78 pg/dL on day eight (p =0.618). The MCT/LCT oil group had a further increase in IL-6 levels post-operatively; 63.87 ±30.02 pg/dL to 68.94 ± 53.04 pg/dL (p=0.923).[8]

SMOF and Wound healing

There is limited research available on the effects of SMOF lipid in wound healing. Promising new research utilizing animal models demonstrated an improved inflammation response and acceleration of wound healing in rats. Peng et al[9] published a study in 2018 comparing wound healing and inflammatory biochemical markers in post-surgery rats who received normal saline injection or omega-3-blend intravenous lipid emulsions. The results showed reduced wound size by 25% surface area and improved inflammation after 72 hours of treatment with SMOF lipid as well as reduced TNF-a compared to the normal saline group. Microscopic tissue analysis indicated a higher rate of fibroblast distribution and collagen fiber organization in the SMOF lipid group compared to the control group.[9] As of this date, no published data for the effect of SMOF lipid emulsion and wound healing in humans is available.

SMOF and Infection incidence

The ICU Lipids Study conducted by Grau-Carmona et al[10] further linked omega-3 fatty acid lipid formulas to improved outcomes reducing incidence of hospital-acquired infections in critical care patients receiving total parenteral nutrition. This multicenter, four-year study conducted in Spain included 159 surgical and medical adult ICU patients. The patients were admitted for various diagnoses including cancer (n=14), sepsis (n=73), trauma (n=27), pancreatitis (n=19), and other (n=26). The inclusion criteria for these patients included Acute Physiology and Chronic Health Evaluation II (APACHE II) scores greater than 13 and expected PN therapy for at least five days. The patients were randomized into a control group that received a fish-oil free lipid emulsion (n=78) or into an experimental group that received a lipid emulsion containing 10% fish oil (n=81). The mean age in the control group was 60.59 ±16.37 years compared to 60.07 ±17.29 years in the experimental group (p=0.844). The control group consisted of 54 males and 24 females and the experimental group consisted of 62 males and 19 females (p=0.372). The average weight was 76 kg in both treatment groups: standard deviations ±11.1 kg in the control and ±11.9 kg in the experimental group. Average BMI was 27.1 ±3.9 in the control group and 26.6 ±4.0 in the experimental group indicating overweight status. Infection incidence was tracked from admission to day 28 of ICU stay. The patients also had albumin and C-reactive protein (CRP) levels drawn at baseline. Albumin levels were equivalent, 2.41 g/L ±0.59 in the control group and 2.42 g/L ±0.81 in the experimental group (p=0.902). CRP levels were elevated in both groups: 47.65 mg/L ±85.27 in the control group and 46.39 mg/L ±89.36 in the experimental group (p=0.50). Grau-Carmona et al reported that the addition of omega-3 fatty acids reduced infection rates by 16% (21% vs 37.2%, p=0.035) in the experimental subject group compared to the control subject group. The experimental group receiving fish oil-containing ILE had a reduced infection duration of 16 days ±2 and a prolonged time free of infections when compared to the control group infection duration of 21 days ±2 (p=0.03). Hospital length of stay was shortened in the fish-oil experimental group by 11.5 days with a p=0.059.

This result, although not statistically significant, reflects improvement with the use of fish-oil containing lipids. The trend towards reduction in hospital LOS and the reduction in infection incidence lead to better patient outcomes and hospital costs.[10]

SMOF and Clinical outcomes

A multicenter study published by Edmunds et al[11] in 2014 highlighted the clinical outcome improvements observed with olive oil and fish oil lipid emulsions when compared to soybean or lipid-free PN formulations. Adult patients admitted to the ICU who required mechanical ventilation and exclusive PN feeding for greater than 5 days were included in the study. A total of 451 patients met study criteria. The patients were largely male with BMIs in the overweight classification, and average age of 63.5 years (±15.9). Data points were collected on mechanical ventilation time, time to ICU discharge alive, and time to ICU discharge with mortality. Due to the secondary data analysis design of this study, patients were not randomly assigned to treatment groups, therefore majority of patients (n=223, 49.5%) received soybean ILE, 74 (16.4%) patients received olive oil ILE, 70 patients (15.5%) received lipid-free PN, 65 (14.4%) patients received MCT ILE, and 19 (4.9%) patients received fish oil ILE. Edmunds et al observed a faster time to ICU discharge alive in the fish oil ILE treatment group compared to the lipid-free PN treatment group by an average of 3 days ($p < 0.001$). When compared to the lipid-free PN group, those who received olive oil or fish oil-containing ILE had a reduced mechanical ventilation time by 3.7 days on average in both groups ($p=0.023$). Sixty-day mortality was compared between the four treatments groups with patients excluded if they remain admitted to the ICU after day 60. The soybean-oil ILE group had a mortality rate of 28.5% compared to the fish oil ILE group with a mortality rate of 10.5% (p=0.034).[11] A limitation of this data is the small sample size of patients who received fish oil lipid emulsions.

SMOF and Liver function

SMOF lipid emulsion is linked to improvement in lipid panels and liver function, specifically with long-term PN use. A Fresenius Kabi sponsored clinical trial of SMOF lipid compared to Intralipid was performed in 2007 to 2008 and was one of the first double-blind, randomized trials comparing the two separate lipid emulsions. The aim of the study was to evaluate the safety of SMOF lipid and determine possible clinical outcome improvements with the newly developed lipid emulsion.

Klek et al[12] enrolled a total of 73 patients meeting study criteria. Eligible patients were adults over the age of 18 years, requiring parenteral nutrition for four weeks due to gastrointestinal disease, and did not have a known allergy to any ingredients included in the lipid emulsions (soy, fish, egg, or peanut). Patients with hypertriglyceridemia (levels > 3 mmol/L) or liver disease were excluded. The patients that met criteria were randomized to the SMOF or Intralipid ILE groups. The average age of the SMOF participants was 53.2 years (± 14.6) compared to 45.2 years (±13.6) in the Intralipid group. The majority of patients in both groups were male with n=20 in the SMOF group and n=21 in the Intralipid group. Ethnicities included Caucasian, African-American, Asian, and “Other.” The SMOF group consisted of 98% Caucasian and 2% African-American. The Intralipid group was 95% Caucasian, 2% Asian, and 2% Other. Weight and BMI were similar between the two groups. The mean weight in the SMOF group was

56.5 kg (±13.0) and in the Intralipid group was 55.7 kg (±14.1). The average BMI in both groups indicated normal weight classification; SMOF group at 20.8 ±4.5 and Intralipid group at 20.2 ±4.5. Both study groups received a similar duration of PN therapy, approximately 30.2 days (± 8.5) versus 29.6 days (±10.4) in the SMOF and Intralipid groups, respectively.

The researchers determined that SMOF lipid compared to Intralipid, improved liver function markers including alanine transaminase (ALT), aspartate transaminase (AST), and total bilirubin from baseline measures. ALT levels decreased in the SMOF treatment group from baseline to week four by 7.8 units/L (±46.4) compared to an increase in ALT in the Intralipid group by an average of 3.6 units/L (±44.0), $p < 0.05$. AST levels decreased by an average of 5.5 units/L (±15.7) in the SMOF group compared to an increase of 0.6 units/L (±28.7) in the Intralipid group, p 0.03. Total bilirubin decreased in the SMOF lipid group by an average of 0.5 mmol/L (±3.9) which was significant when compared to the increase observed in the Intralipid group by an average of 1.9 mmol/L (±11.7), $p = 0.04$). SMOF lipid emulsion led to a nonsignificant but lower level of serum triglycerides at each weekly test compared to the Intralipid treatment group.

Klek et al[12] investigated alpha-tocopherol levels at week two and week four for each patient treatment group as a measure of defense against liver injury in patients receiving ILE. Alpha-tocopherols is an isoform of vitamin E which is a known antioxidant and could potentially protect the liver from peroxidative damage.[13] Serum alpha-tocopherol levels were significantly increased in the SMOF treatment group compared to the control group at both tests when measured at weeks two and four. At week two, the SMOF treatment group had levels at 41.63 mmol/L (± 14.48) compared to 30.35 mmol/L (± 12.54) in the Intralipid group (p=-.0001) At week four the levels remained increased in the SMOF group at 39.46 mmol/L (±13.39) compared to the Intralipid group at 34.46 mmol/L (±13.94), p=0.0029.[12]

Mertes et al[14] investigated outcomes in surgical patients undergoing an elective abdominal or thoracic surgery. One hundred and ninety-nine (199) subjects received total parenteral nutrition for a total of five days post-operatively. Each subject was randomized to receive SMOF lipid emulsion or Lipoven (100% soybean oil emulsion). The mean patient age in the SMOF lipid treatment group was 60.5 years (±14.2) and the Lipoven group had a mean age of 60.2 years (±13.8). Body Mass Index (BMI) was utilized as a nutrition indicator in this study as opposed to other biochemical markers or complete malnutrition assessments. The average BMI in the SMOF and Lipoven groups was 24.7 (±3.2) and 24.5 (±3.5) respectively. Mertes and colleagues found that serum lipid panels, liver enzymes, and total bilirubin did not differ between treatment groups during the five-day PN duration and on day six following PN discontinuation. There was an observed trend in reduced length of stay by 2.1 days in the SMOF lipid subject group which was not statistically significant.[14]

In an observational study by Hughes et al[15] from Belfast City Hospital, the research team reviewed laboratory data in 20 participants receiving long-term home PN who had transitioned to SMOF lipid from a first generation lipid emulsion. These patients were receiving long-term PN due to intestinal failure of various, non-specified etiologies. The patients were aged 27 to 75 years and comprised of 65% females (n=13). They had previously received a dextrose and amino acid PN infusion with weekly lipid boluses to prevent essential fatty acid deficiency. Blood samples were compared from pre-SMOF infusion time and after transition to SMOF lipid; the study did not specify the timeframe of blood samples collected post-transition. The researchers observed a significant decrease in triglyceride levels by 10% as well as a reduction in alkaline phosphatase levels by 15% from baseline prior to the transition of SMOF ILE. The researchers did not publish detailed results that included exact laboratory measurements for further review.[15]

SMOF and Cost effectiveness

SMOF lipid emulsion is more costly than traditional soybean lipid emulsion, yet the improved secondary outcomes can decrease total hospital costs. Feng et al[16] developed a cost analysis model to determine mean cost differences between two patient groups receiving PN in ICU patients. One patient group received omega-3 enriched lipid emulsions within their PN therapy, while a control group received standard soybean lipid emulsion. The research team utilized data collected in five randomized control trials totaling 393 patients in the omega-3 ILE group and 386 patients in the control group. Inclusion criteria consisted of recent research (previous 10 years), comprehensive data collection including all desired data points, and critically ill patient population. The data points of interest to the researchers included hospital length of stay, ICU length of stay, infection incidence, and antibiotic cost associated with treating acquired infections. By utilizing the difference in mean hospital length of stay, ICU length of stay, and infection treatment cost, the researchers calculated a mean cost difference. The omega-3 fatty acid enriched treatment group saw a reduction in average hospital cost by ¥7594 (USD $1116) per patient after accounting for increased lipid emulsion cost.[16]

SMOF and International guidelines

The improved outcomes with SMOF lipid emulsion are influencing nutrition guidelines in critical care. The European Society of Parenteral and Enteral Nutrition (ESPEN) in their updated 2019 guidelines recommend a mixed fatty acid emulsion such as SMOF lipid, with improved evidence grade specifically in surgical patient populations compared to other critical care populations.[17] ESPEN guidelines state that lipid emulsion delivery in critically ill patients should not be delayed and recommends daily SMOF lipid emulsion administration as part of a compounded 3-in-1 TPN.[17]

Similar recommendations appear in the ASPEN publication *Summary of Proceedings and Expert Consensus Statements from the International Summit "Lipids in Parenteral Nutrition"* regarding mixed-oil lipid emulsion use in the United States.[18] The expert panel agreed that in stable, critically ill adult patients, intravenous lipid emulsions are an integral part of parenteral nutrition. The report states there is sufficient scientific evidence to support the use of fish-oil containing lipid emulsions as part of PN. Per the panel's consensus statement, the current clinical data indicates there is no need to withhold or limit the use of fish-oil containing intravenous lipid emulsions during the first week of PN.[18]

Background of Institution Nutrition Support

The Eskenazi Nutrition Support Committee consists of practitioners representing critical care dietitians, critical care pharmacists, nursing leadership, and physicians from surgical and medical ICU teams. Eskenazi Health strives to provide high-quality, cost-effective health care treatments and to be in alignment with best practice guidelines. The committee reviewed up-to-date studies and recommendations on ILE therapy in the acute care setting and approved the introduction of SMOF lipid emulsion. The pharmacist representatives then took the recommendation to obtain SMOF lipid infusions to the Pharmacy and Therapeutics (P&T) Committee for final approval. Based on the recommendations that SMOF lipid infusions are safe and effective, Eskenazi Health acquired SMOF lipids as first-line lipid emulsion therapy. Standards of care at Eskenazi Health transitioned with the change in lipid emulsion formulary.

Prior to the acquisition of SMOF lipid, the protocol was to withhold soybean-oil (Intralipid) intravenous lipid emulsions during the first week in critical care or longer pending physician approval. By day 14 of PN therapy to prevent fatty acid deficiency, patients would receive an Intralipid IV 250 mL bolus once weekly or transition to a complete 3-in-1 TPN administration.

Following the acquisition of SMOF lipids and per international consensus recommendations, practice changed to provide a 3-in-1 TPN admixture including SMOF lipid emulsions in the critical care patient requiring parenteral nutrition. The purpose of this study is to identify clinical outcomes in adult trauma patients receiving total parenteral nutrition following this change in practice.

Research Question

What is the effect of SMOF lipid infusion compared to lipid-free or 100% soybean-oil lipid administration in adult trauma patients requiring parenteral nutrition as assessed by nutrition status, infection rates, length of stay, and morbidity and mortality?

Chapter Two: Methodology

Methods

This study was reviewed and approved by the Indiana University Institutional Review Board on July 14, 2020. This study is classified as Exempt: Category 4 with protocol number 2006018112.

This study is a retrospective review of patient data from a Level 1 Trauma Center located in Indianapolis, IN from May 2017 to May 2020. Eligible patients included those admitted to the surgical ICU who received parenteral nutrition during their hospital admission for trauma related injuries. Patients were excluded if they were admitted to a non-ICU level of care, under the age of 15, or did not receive customized parenteral nutrition. The age of 15 years or older as inclusion criteria meets the American College of Surgeons (ACS) definition of "adult" for Level 1 trauma centers. Utilizing the Medical Record Numbers (MRNs), data were collected via the National Trauma Registry and through chart reviews. Baseline clinical parameters include demographics, injury classification, baseline biochemical markers of inflammation, and nutritional status upon admission. These parameters are detailed in the Data Collection Tool in Table 1.

Table 1: Data Collection Tool		
Data point	Description	Value
MRN	Medical Record Number	
Admit Date		
Age	Years	
Sex	Male/Female	
Mechanism of injury	The manner of physical injury	
Injury classification	Penetrating, blunt, or thermal per American College of Surgeons definitions	
ISS	Numerical value to grade severity of trauma injury per Association for the Advancement of Automotive Medicine (AAAM) guidelines, see Table 2	
Weight	At time of admission in kilograms	
BMI	Body Mass Index	
Prealbumin	pre-PN mg/dL	
CRP	pre-PN mg/dL	
Dx of malnutrition	Per ASPEN/AND criteria defined in Table 3	
PN order type	Custom 3-in-1/2-in-1	
Lipid emulsion type	Intralipid, SMOF, or none	
PN therapy length	Days of PN received	
Energy prescribed	Energy (kcal) provided by PN	
Energy received	Energy (kcal) received during first 7 days of hospital stay	
ICU LOS	Days	
Hospital LOS	Days	
Infection incidence	Yes/No, infection type	
Mortality	Death during hospital admission	

The severity of traumatic injuries was assessed utilizing the Injury Severity Score (ISS) which ranges from 0 (least severe) to 75 (unsurvivable). Each body region is assessed with the worst injury entered into Table 2 below. Each region is then assigned an ordinal value to stratify the severity of injury; 0 being no injury and 6 indicating unsurvivable.

Injuries were further classified into penetrating or blunt trauma based on mechanism of injury. The scoring for the patients in this study was completed with the assistance of the Eskenazi Health Trauma Research Coordinator to ensure accuracy.[19]

Table 2: The Injury Severity Score (ISS) Worksheet		
Body region	Worst injury	AIS score (0-6)
Head and neck		
Face		
Chest		
Abdomen		
Extremity		
External		
ISS = sum of highest AIS scores (a-c) = $a^2 + b^2 + c^2$		

Each patient received a full nutrition assessment completed by the Registered Dietitian prior to PN initiation. This assessment included anthropometric review, malnutrition assessment, and prescribed estimated nutritional needs. The dietitian performed a malnutrition assessment and nutrition diagnosis utilizing ASPEN/AND criteria. These criteria utilize muscle wasting, subcutaneous fat loss, fluid accumulation, weight loss, reduced energy intake, and reduced functionality. See Table 3 below.[20] Two or more criteria must be met to identify malnutrition. At risk of malnutrition is defined by meeting only one of the six criteria. Patients were further classified as having moderate or severe malnutrition dependent on the degree of severity of each characteristic met. A customized parenteral nutrition regimen was created for each patient to meet their estimated energy and protein needs. Following nutrition support initiation, patients were reassessed by the dietitian every two to three days or more frequently as needed.

Table 3: ASPEN/AND Adult Malnutrition Criteria												
	Marked Inflammatory response				Mild/Moderate Inflammatory response				No Inflammatory response			
Clinical Characteristic	Acute Illness or Injury				Chronic Illness				Social or Environment Circumstances			
	Moderate		Severe		Moderate		Severe		Moderate		Severe	
Energy intake	<75% >7 days		<50% >5 days		<75% >1 month		<75% >1 month		<75% >3 months		<50% >1 month	
Weight loss	%	Time	%	Time	%	Time	%	Time	%	Time	%	Time
	1-2	1wk	>2	1wk	5	1mo	>5	1mo	5	1mo	>5	1mo
	5	1mo	>5	1mo	7.5	3mo	>7.5	3mo	7.5	3mo	>7.5	3mo
	7.5	3mo	>7.5	3mo	10	6mo	>10	6mo	10	6mo	>10	6mo
					20	1y	>20	1 y	20	1y	>20	1y
SubQ fat loss	Mild		Moderate		Mild		Severe		Mild		Severe	
Muscle loss	Mild		Moderate		Mild		Severe		Mild		Severe	
Fluid accumulation	Mild		Moderate-Severe		Mild		Severe		Mild		Severe	
Functionality	n/a		Reduced		n/a		Reduced		n/a		Reduced	

Outcome measures consist of PN data including adequacy of energy prescription compared to estimated energy needs provided by PN, inclusion of ILE, length of PN therapy, and total energy received during the first seven days of admission. Data collected included the following: ICU length of stay, hospital length of stay, incidence of infection, and mortality. Infections tracked for the purpose of this study include surgical site infection (SSI), intra-abdominal infection, bacteremia, or unknown sources. Mortality was defined as death during initial hospitalization for traumatic injuries and does not include potential readmissions or post-discharge mortality. The evaluation of cost differences between groups was determined by average ICU or hospital length of stays and applying the daily room and board cost at Eskenazi Health per 2020 pricing guidelines.[21]

All statistical analysis was performed using SPSS Statistics software, version 25.[22] Data were analyzed utilizing independent sample t-tests for numerical data. Levene's Test for Equality of Variances was run in accordance with guidelines for independent samples tests to determine homogeneity of variance. Pearson chi-square tests were utilized for categorical data. Statistical significance is defined as a p value < 0.05. All statistical analyses were reviewed by a member of the Department of Biostatics staff at Indiana University-Purdue University of Indianapolis.

Chapter Three: Results

Results

Twenty-nine patients met study criteria and were included in this analysis. The majority of patients were male between the ages of 20 and 58 who had suffered a penetrating trauma. The most common mechanism of injury in both groups was gunshot wound(s). Seventeen (17) patients were in the traditional lipid cohort where they either received Intralipid or no ILE as appropriate per hospital policy. The SMOF lipid cohort had 12 patients.

Table 4: Patient Demographics and Baseline Information

	Traditional (n=17)	SMOF (n=12)	p value
Age, mean ±std dev	35.47 ±14.0	39.83 ±19.0	0.483
Sex, n=male (%)	17 (100%)	9 (75%)	0.029
Injury type - penetrating, n (%)	14 (82.3%)	9 (75%)	0.630
Injury Severity Score, mean ±std dev	23.18 ±12.3	21 ±11.1	0.486
Body weight kg (admit), mean ±std dev	100.66 ±32.1	86.72 ±24.8	0.218
BMI, mean ±std dev	30.3 ±9.7	27.2 ±6.0	0.329
Prealbumin, mean ±std dev	10.8 ±5.2	10.9 ±3.0	0.974
CRP, mean ±std dev	14.7 ±6.2	14.1 ±5.6	0.780
Dx of malnutrition, n (%)	2 (12%)	3 (25%)	0.353
Dx at risk of malnutrition, n (%)	6 (40%)	3 (33%)	0.555

P value < 0.05

As shown in *Table 4*, the groups were comparable with no significant difference in age, body weight, or BMI. Injury classification types (i.e. penetrating versus blunt) were similar between groups, 82.3% in the traditional lipid group and 75% in the SMOF lipid group (p=0.630). Further stratification of traumatic injuries is shown in Figures 1 and 2 in the Appendix. Seventeen male patients were included in the traditional lipid cohort and 9 males and 3 females in the SMOF cohort (p=0.029). Injury Severity Score (ISS) was comparable between both groups. Values of 23.18 (±12.3) in the traditional lipid group and 21 (±11.1) in the SMOF group indicate major trauma (p=0.486).

Biochemical markers at baseline were comparable. High-sensitivity C-reactive protein (CRP) was not significantly different between the traditional lipid group and the SMOF lipid group (14.7 mg/dL ±6.2 and 14.1 mg/dL ±5.6, respectively). Prealbumin levels prior to PN initiation was also comparable with no statistical difference (traditional: 10.8 mg/dL ±5.2 and SMOF: 10.9 mg/dL ±3.0). Full nutritional assessments demonstrated that both groups were comparable in terms of meeting criteria for malnutrition versus at risk of malnutrition prior to PN therapy. The two patients diagnosed with malnutrition in the traditional lipid treatment group met criteria for severe malnutrition. In the SMOF treatment group, two out of the three patients were diagnosed with severe malnutrition and the third patient with moderate malnutrition. Those defined as at risk of malnutrition by meeting one criteria in Table 3 were not stratified into degree of risk at the time of initial assessment.

The length of PN therapy was comparable between the traditional lipid and SMOF lipid groups, 13.9 days (± 11.5) and 13.3 days (± 14.3) respectively. Of the traditional lipid group, seven subjects received ILE (42%) compared to 12 subjects, or 100%, of the SMOF treatment group. Due to the ability to add ILE during the first week of ICU stay, the SMOF treatment group were provided 100% of estimated energy needs via PN compared to an average of 94% (± 9.7) of estimated energy needs in the traditional lipid treatment group. This variance resulted in a statistically significant result in energy prescription via PN support. The energy received, as measured by energy intake divided by energy prescription resulted in the SMOF treatment group receiving 40% of estimated energy needs compared to the traditional lipid treatment group receiving 29% of estimated energy needs. While the SMOF treatment group trended towards increased intake, this result was not statistically significant.

Table 5: Results and Outcomes

	Traditional (n=17)	SMOF (n=12)	p value
Length of PN therapy ±std dev	13.9 d ±11.5	13.3 d ±14.3	0.91
Subjects received lipids, n (%)	7, (42%)	12, (100%)	0.001
Energy prescription, % ±std dev	94% ±9.7	100% ±0	0.036
Energy delivered week 1, % ±std dev	29% ±24.7	40% ±33.6	0.325
ICU LOS, days ±std dev	13.2 ±11.2	9.8 ±7.2	0.363
Mean total cost for ICU room and board, per patient	$78,184	$58,045	0.093
Hospital LOS, days ±std dev	27.3 ±16.1	27.2 ±16.9	0.984
Infection, % positive	13 (76%)	3 (25%)	0.006
Mortality, n (%)	4 (23.5%)	0, (0%)	0.041

P value < 0.05
Energy prescription = % of energy (kilocalories) prescribed in PN as compared to estimated energy needs
Energy delivered week 1 = energy received/energy prescribed

Secondary outcomes show a trend towards reduced ICU length of stay in the SMOF treatment group (9.8 days ±7.2) compared to the traditional lipid treatment group (13.2 days ±11.2), however this result was not statistically significant (p=0.363). The mean cost for room and board was calculated utilizing the Eskenazi Health Pricing Guide. The SMOF treatment group had a reduction in ICU room and board stay of $20,139 per patient. This value was not statistically significant (p=0.093) when compared to the traditional lipid group. Hospital length of stay was comparable between the two groups. Incidence of infection during initial hospitalization was significantly lower in the SMOF treatment group (n=3, 25%) compared to the traditional lipid treatment group (n=13, 76%). Infection types ranged from bacteremia, surgical site infection (SSI), intra-abdominal infection, and other or unknown source. The SMOF treatment group had two patients experience surgical site infection and one patient with bacteremia. The traditional lipid treatment group had a variety of infections including three patients with bacteremia, three patients with surgical site infections, three patients that developed intra-abdominal infections, and four patients with unidentified source of infection. This breakdown of infection incidence is shown in Figure 4 in the Appendix. Lastly, mortality was decreased in the SMOF treatment group (0%) when contrasted to the traditional lipid treatment group (23.5%), p value: 0.04.

Discussion

The results from this study suggest the benefits of SMOF lipid infusion compared to Intralipid infusion. Both treatment groups were comparable in regard to the demographic and baseline criteria. Patients in both groups received an equivalent duration of PN therapy. Those in the SMOF lipid treatment group met energy prescription to provide 100% of estimated energy needs during the initial week in the ICU compared to the traditional lipid treatment group who were prescribed significantly less energy in the PN formulation. The requirement to hold lipid therapy in the first week of ICU stay per SCCM/ASPEN guidelines created an energy deficit in the traditional lipid treatment group resulting in an 11% decrease in energy received when compared to the SMOF lipid group. This significant result is similar to the results of the Gao et al[2] study in which the treatment group who had lipids withheld from supplemental PN were provided a 5.8% reduction in energy delivery compared to the group who received ILEs during the first seven days of their ICU stay. In the SMOF treatment group, 100% of patients received ILE which led to increase energy prescription and delivery in parenteral nutrition. The addition of lipids in all twelve SMOF patients limited the risk of developing essential fatty acid deficiency (EFAD). This was significant when compared to the 42% (n=7) of patients that received Intralipid, although no signs or symptoms of EFAD were observed in any patient during hospitalization.

Similar to several studies including Gao et al[2], Edmunds et al[11], and Mertes et al[14], there was a trend towards an improved ICU length of stay with SMOF lipid use. A reduction in ICU length of stay by an average of 3.4 days was observed in the SMOF lipid treatment group when compared to the traditional lipid treatment group. Gao et al[2] observed a significant 0.6 day reduction in ICU length of stay in the ILE restricted group compared to the soybean oil ILE group. The greater result seen in ICU length of stay in this study could be attributed to the use of omega-3 fatty acid enriched ILE versus the restriction of lipid in PN as Gao et al[2] performed. The patients in this study were also an average of 22.1 years younger and presumed healthier at baseline due to the nature of admission for chronic disease in the Gao et al[2] study. Edmunds et al[11] observed a similar result of a 3-day reduction in ICU length of stay in the patient population receiving fish oil lipid emulsions compared to the group receiving a lipid-free PN administration. This study was a combination of medical and surgical patients which were significantly older by an average of 25.9 years than those included in this analysis. However, there were similarities to this study including the patients were mostly male with average BMI in the overweight class and received their primary source of nutrition from PN. Mertes et al[14] observed an average 2.1 day length of stay reduction in the SMOF treatment group compared to the control group. The difference in patient population could contribute to the improved results seen in this study compared to the Mertes et al[14] data. The patients receiving SMOF lipids were on average 20.7 years younger in this study than those enrolled in the Mertes SMOF lipid group. The length of PN therapy was also longer in this study with an average of 13.3 (±14.2) day duration compared to five days received in the Mertes study.

Although ICU length of stay data is not statistically significant, the reduction in ICU room and board costs resulted in an average $20,139 ($5900 per day) decrease per patient in overall hospital cost per Eskenazi Health Pricing Guide. Further, SMOF lipid, as of the time of this writing, has become more cost effective in prescription pricing than Intralipid. Per Eskenazi Health Pricing Guide, the daily average cost of SMOF lipid is $225 compared to the cost of daily Intralipid use at $237.50.[21] While the cost difference in ICU length of stay was not significant and the daily cost difference of ILEs is minimal, for patients with prolonged length of stays and lengthy duration of PN therapy these values can greatly impact total hospital expenses.

The ICU Lipids Study completed in 2015 aimed to determine the effect of an omega-3 fatty acid containing lipid on nosocomial infections.[10] Similar to the outcomes of that publication, the results of this study demonstrate the incidence of infection in the SMOF lipid treatment group were significantly lower when compared to the traditional lipid group. The SMOF lipid treatment group saw a 51% reduction in infection incidence when compared to the traditional lipid emulsion group. The decline in post-operative infections and incidence of bacteremia also lead to a further reduction in treatment cost and hospital expense. This result differs significantly from the ICU Lipids study by Grau-Carmona et al in which there was an observed 16% reduction in infection rates. There were several differences between the Grau-Carmona et al research and this study. Firstly, this study tracked infection diagnoses from admission to discharge whereas Grau-Carmona et al included data only during the ICU admission up to day 28. Secondly, the patient populations had many differences. The ICU Lipids study was a combination of medical and surgical ICU patients compared to the 100% surgical, trauma population included in this study. Further, the patients in this study were young with an average

age of 39.83 years (±19.0) in the SMOF treatment group and 35.47 years (±14.0) in the traditional lipid treatment group. Those enrolled in the ICU Lipids study had average ages of 60.07 years (±17.29) in the experimental group and 60.59 (±16.37) in the control group.

Mortality during initial hospitalization was significantly lower in the SMOF lipid treatment group compared to the traditional lipid treatment population; 0% and 23.5% respectively. Of the studies included in the literature review, only one found a significant result in mortality between treatment groups. Edmunds et al found a significant difference in mortality between the soybean-oil ILE group which had a mortality rate of 28.5% compared to the fish oil ILE group with a mortality rate of 10.5% (p=0.034).[11] The difference between the Edmunds et al study and this study was the use of separate lipid emulsions as four different treatment groups versus SMOF lipid which is a four-oil lipid blend. As noted above, the Edmunds et al study was a combined analysis of medical and surgical patients that were significantly older when compared to this study. The significant decrease in mortality observed in this study could be attributed to the increase of omega-3 fatty acids when compared to 100% soybean oil containing products due to the improvement in immune response and reduction in nosocomial infections as demonstrated by Zeng et al, Wang et al, and Grau-Carmona et al.[10,11,13] Due to the small size of treatment groups in this study, the results are correlational and require further research to assess cause of reduced mortality.

In conclusion, these encouraging results demonstrate the benefit of utilizing SMOF intravenous lipid emulsion in PN therapy compared to soybean oil lipid emulsions or a dextrose and amino acid administration in the adult trauma patient population. The reduction in ICU length of stay, incidence of infection, and mortality all lead to reduced hospital cost and improved patient outcomes.

The strengths of this study include the specific inclusion criteria for enrollment, the comparable baseline parameters of both study groups, and the completeness of data collection. Each individual patient had complete data available and no participant was excluded from each statistical analysis. Limitations of this study include the retrospective nature of data collection and the small sample size. Areas of improvement would include measuring changes in biochemical markers such as prealbumin and CRP beginning at PN initiation and throughout therapy duration. As other studies have shown, SMOF lipid reduces inflammation and improves immune response following surgery or illness. Studying these effects in trauma patients following serious injury and major surgeries could contribute to this literature. Additionally, it would have been beneficial to measure nutritional status at the conclusion of PN therapy by completion of a repeat malnutrition assessment utilizing ASPEN/AND criteria as well as monitoring body weight changes for potential weight loss.

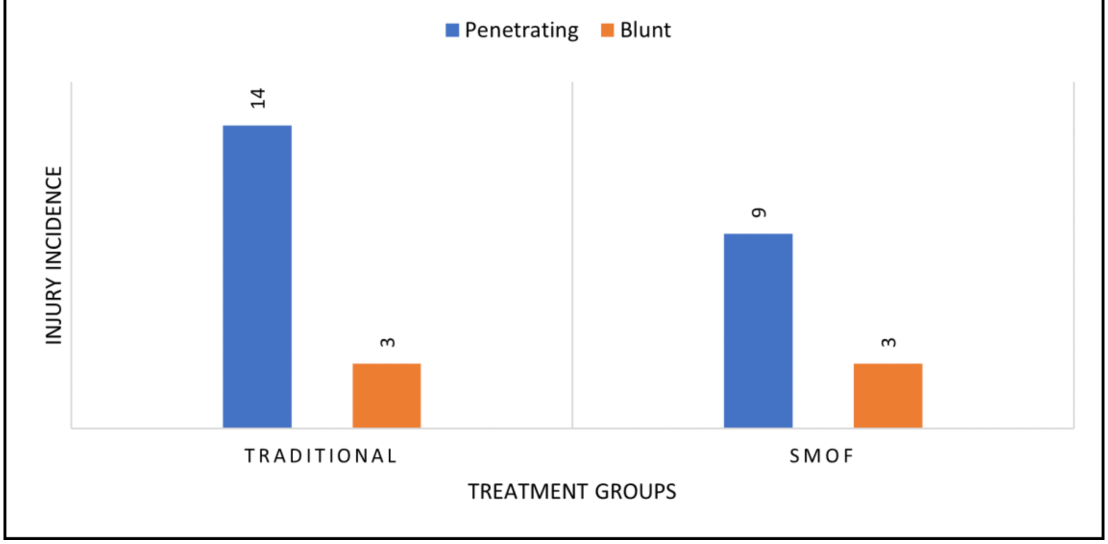
Future Directions

Further research into the effects of SMOF lipid emulsions, or other omega-3 enriched ILEs, need to account for other nutritional impacts in order to make conclusions on the cause of improved patient outcomes. For example, the amount of protein (amino acids) may also contribute to nutritional status in parenterally fed patients as well as biochemical markers and improved outcomes. Protein provision provided to each patient should be controlled with a consistent set of parameters for prescription. Additional studies should explore the changes in wound healing in humans. As Peng et al[9] demonstrated, omega-3 fatty acid containing lipid emulsions led to improved wound healing in rats when compared to a normal saline control. In the adult trauma patient population this could be accomplished by tracking changes in exploratory laparotomy midline incision size and granulation or use of negative-pressure wound therapy.

Appendices

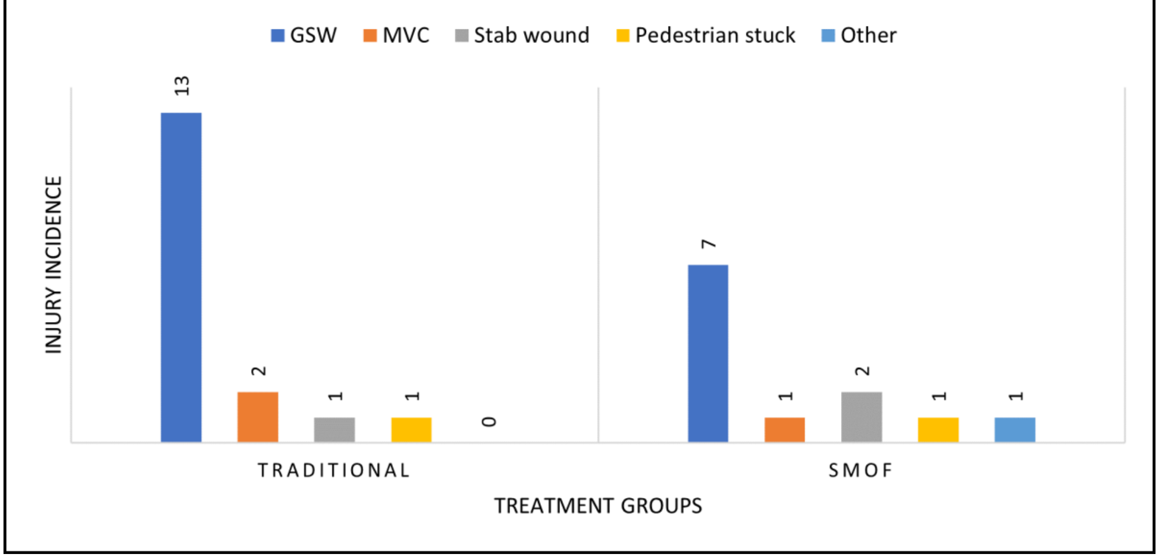
Appendix A

FIGURE 1: INJURY TYPE BY TREATMENT GROUP

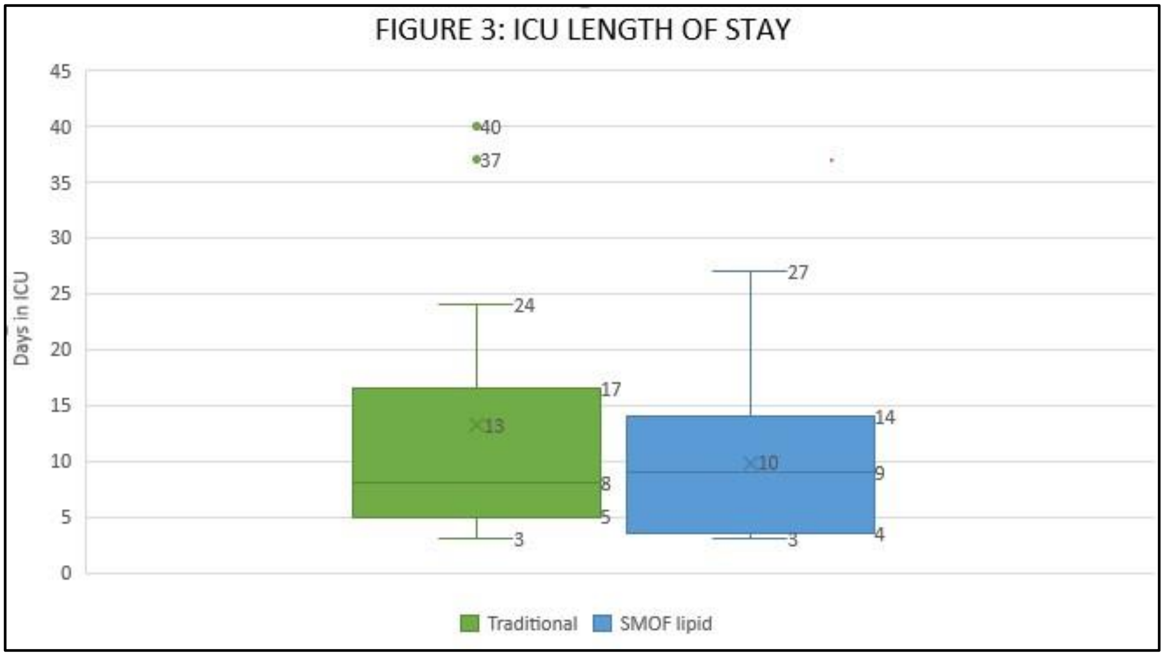


Appendix B

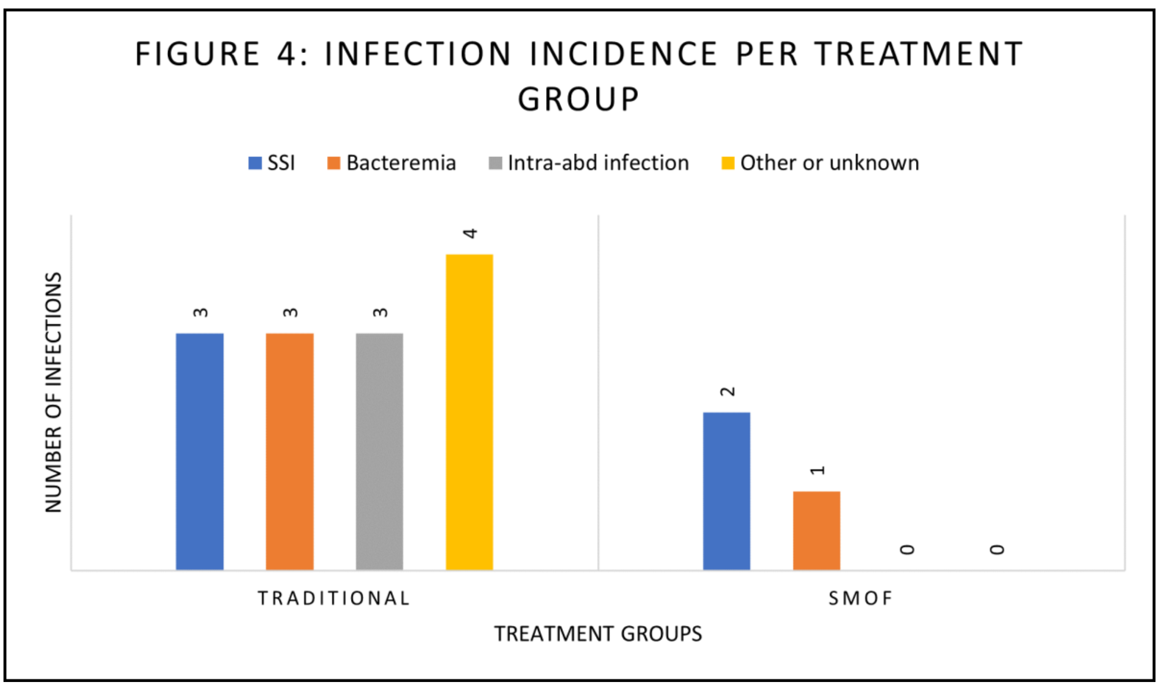
FIGURE 2: DETAILED INJURY MECHANISM BY TREATMENT GROUP



Appendix C



Appendix D



References

1. Mirtallo JM, Ayers P, Boullata J, et al. ASPEN Lipid Injectable Emulsion Safety Recommendations, Part 1: Background and Adult Considerations. Nutrition in Clinical Practice. 2020;35(5):769-782. doi:https://doi.org/10.1002/ncp.10496

2. Gao J, Tu G-W, Wang C-S, et al. A quality improvement program with nutrition therapy: restriction of lipid emulsions in cardiac surgical patients. Journal of Thoracic Disease. 2018;10(2). doi:10.21037/jtd.2018.01.98

3. McClave S, Taylor B, Martindale R, Warren M, Johnson D, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient. Journal of Parenteral and Enteral Nutrition. 2016;40(2):159-211. doi:10.1177/0148607115621863

4. SMOFlipid. Fresenius Kabi. Accessed November 28, 2020. https://freseniuskabinutrition.com/products/smoflipid/

5. Gramlich L, Ireton-Jones C et al. Essential Fatty Acid Requirements and Intravenous Lipid Emulsions. Journal of Parenteral and Enteral Nutrition. 2019;43(6):697-707.

6. Calder PC, Adolph M, Deutz NE, et al. Lipids in the intensive care unit: recommendations from the ESPEN expert group. Clin Nutr. 2018;37(1):1-18.

7. Zeng Y, Shao Y, Lan Z. Effects of lipid emulsion (SMOF) intervention on stress hormones, inflammatory mediators and immune function after esophagus cancer operation. Journal of Hainan Medical University. 2017; 23(22):45-49. http://www.hnykdxxb.com/PDF/201722/12.pdf

8. Wang W-P, Yan X-L, Ni Y-F, et al. Effects of Lipid Emulsions in Parenteral Nutrition of Esophageal Cancer Surgical Patients Receiving Enteral Nutrition: A Comparative Analysis. Nutrients. 2013;6(1):111-123. doi:10.3390/nu6010111

9. Peng Y-C, Yang F-L, Subeq Y-M, Tien C-C, Chao Y-FC, Lee R-P. Lipid Emulsion Enriched in Omega-3 PUFA Accelerates Wound Healing: A Placebo-Controlled Animal Study. World Journal of Surgery. 2018;42(6):1714-1720. doi:10.1007/s00268-017-4404-x

10. Grau-Carmona T, Bonet-Saris A, Farcia-de-Lorenzo A, et al. Influence of n-3 Polyunsaturated Fatty Acids Enriched Lipid Emulsions on Nosocomial Infections and Clinical Outcomes in Critically Ill Patients: ICU Lipids Study. Critical Care Medicine. 2015; 43(1):31-39. doi:10.1097/CCM.0000000000000612

11. Edmunds C, Brody R et al. The Effects of Different IV Fat Emulsions on Clinical Outcomes in Critically Ill Patients. Critical Care Medicine. 2014; 42(5): p 1168-1177. doi:10.1097/CCM.0000000000000146

12. Klek S, Chambrier C, et al. Four-week parenteral nutrition using a third generation lipid emulsion (SMOFlipid) – A double blind, randomized, multicentre study in adults. Clinical Nutrition. 2013; 32:224-231. doi: https://doi.org/10.1016/j.clnu.2012.06.011

13. Tucker JM, Townsend DM. Alpha-tocopherol: roles in prevention and therapy of human disease. Biomed Pharmacother. 2005;59(7):380-387. doi:10.1016/j.biopha.2005.06.005

14. Mertes N, Grimm H, Furst P, Stehle P. Safety and Efficacy of a New Parenteral Lipid Emulsion (SMOFlipid) in Surgical Patients: A Randomized, Double-Blind, Multicenter Study. Annals of Nutrition and Metabolism. 2006; 50(3). doi:10.1159/000091683

15. Hughes SJ et al. Review of Liver Parameters Among Intestional Failure Patients Within the Regional Intestional Failure Service Northern Ireland When Transitioned to SMOF Lipid Emulsion. Clinical Nutrition. 2018;29:273-274. https://www-clinicalkey-com.proxy.medlib.uits.iu.edu/#!/content/playContent/1-s2.0-S0261561418318909?returnurl=null&referrer=null

16. Feng Y, Li C, Zhang T, Pradelli L. Parenteral nutrition including an omega-3 fatty-acid-containing lipid emulsion for intensive care patients in China: a pharmacoeconomic analysis. ClinicoEconomics and Outcomes Research. 2017; 9:547-555. doi:10.2147/CEOR.S139902

17. Singer P, Reintam-Blaser A Berger M, Alhazzani W, Calder P, Casaer M et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clinical Nutrition. 2019;38:48-79. https://www-clinicalkey-com.proxy.medlib.uits.iu.edu/#!/content/playContent/1-s2.0-S0261561418324324?returnurl=null&referrer=null

18. Martindale R, Berlana D, Boullata J, Cai W, er al. Summary of Proceedings and Expert Consensus Statements From the International Summit “Lipids in Parenteral

Nutrition." Journal of Parenteral and Enteral Nutrition. 2020; 44(Supplement 1):S7-S20. doi:https://doi.org/10.1002/jpen.1746

19. Cheatham M. Injury Severity Scoring. Surgical Critical Care. 2001. https://www.surgicalcriticalcare.net/Resources/injury_severity_scoring.pdf

20. Becker PJ, Nieman Carney L, Corkins MR, et al. Consensus Statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: Indicators Recommended for the Identification and Documentation of Pediatric Malnutrition (Undernutrition). Journal of the Academy of Nutrition and Dietetics. 2014;114(12):1988-2000. doi:10.1016/j.jand.2014.08.026

21. Insurance and Pricing Guide. Eskenazi Health. 2020. https://www.eskenazihealth.edu/about/pricing-information

22. IBM SPSS Statistics V25.0 documentation. 2014. www.ibm.com/support/knowledgecenter/sslvmb_25.0.0/statistics_kc_ddita/spss/product_landing.html

Curriculum Vitae

Alexis K McGuigan

Education

- Master of Science in Nutrition and Dietetics, Indiana University, earned at IUPUI – February 2021
- Bachelor of Science in Dietetics, Purdue University – May 2014

Training Experience

- Dietetic Internship - Coordinated Program, Purdue University

Professional Experience

- Inpatient Clinical Dietitian, Eskenazi Health, Sidney and Lois Eskenazi Hospital

Qualifications

- Registered Dietitian Nutritionist (RDN), Commission on Dietetic Registration
- Licensed Dietitian, Indiana Professional Licensing Agency

Awards and Fellowships

- Dr. Shelia Ward Fellowship, School of Health and Human Sciences
- Nestle ENact Quality Improvement Training Fellowship