Efficacy and safety of combined omega-6 and 3 versus omega-6 fat containing lipid emulsion in intensive care patients following digestive surgery

Thesis

Submitted for Partial Fulfillment of MD in Intensive Care Medicine

By

Faten Farid El-sayed Ahmed Awd Alla
M.B.B.Ch., M.Sc. of Intensive Care

Under Supervision of

Prof. Dr. Baha El din Ewiss Hassan
Professor of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University

Prof.Dr. Mohamed Ismail El saidy
Professor of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University

Dr. Ahmed Najah El-Shaer
Assistant Professor of Anesthesia and Intensive Care
Faculty of Medicine- Ain Shams University

Dr. Noha El sayed Hussien
Lecturer of Anesthesia and Intensive Care
Faculty of Medicine-Ain Shams University

Ain Shams University
Cairo, Egypt
(2012)

فعالية وامان استخدام محاليل الدهون الوريدية المحتوية على الاحماض الدهنية اوميجا٣ واوميجا ٦ مقارنه بتلك المحتوية على الاحماض الدهنيةاوميجا ٦ فى مرضى الرعاية المركزة بعد عمليات الجهاز الهضمى

رسالة مقدمة من

الطبيبة / فاتن فريد السيد احمد

بكالوريوس الطب والجراحة . ماجستير الرعاية المركزة

توطئة للحصول على درجة الدكتوراة فى الرعاية المركزة

تحت اشراف

الاستاذ الدكتور/ بهاء الدين عويس حسن

أستاذ التخدير والرعاية المركزة بكلية الطب - جامعة عين شمس

الاستاذ الدكتور/محمد اسماعيل الصعيدى

أستاذ التخدير والرعاية المركزة بكلية الطب - جامعة عين شمس

الدكتور/احمد نجاح الشاعر

أستاذ مساعد التخدير والرعاية المركزة بكلية الطب - جامعة عين شمس

الدكتورة/نهى السيد حسين

مدرس التخدير والرعاية المركزة بكلية الطب - جامعة عين شمس

Ain Shams University
Cairo, Egypt
(2012)

ACKNOWLEDGEMENTS

First of all thanks to ***ALLAH*** for helping me to achieve this work. I would like to express my deepest gratitude and sincere thanks to ***Prof. Dr. Baha El dien Ewiss,*** professor of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University who initiated and designed the subject of this thesis, for his continuous supervision, helpful criticism and support during the whole work.

Also I would like to express my deepest gratitude to ***Prof. Dr. Mohamed Ismail***, professor of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University for his through supervision of this work and close observation.

I wish to express my profound gratitude and deep appreciation to ***Dr.Ahmed Najah El-Shaer,*** assistant professors of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University for his continuous thinking, working, advising and following up of this work to be on the correct way.

wish to express my profound thanks and deep appreciation to ***Dr.Noha El sayed,*** assistant professors of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University for her kidness, continous working, advising and following up of this work to be on the correct way.

List of abbreviation

ALA……..... *α-linolenic acid*

ALP……..……. *Alkaline phosphatase*

ALT……..……. *Alanine Transferase*

APACHE II….. *Acute Physiology and Chronic Health Evaluation*

AST…..……..... *Aspartate Transferase*

BEE…….. *Basal energy expenditure*

BIL…….... *Bilirubin*

BMI…..…….... *body mass index*

BUN……..….... *blood urea nitrogen*

CRP……...….... *C-reactive protein*

CVC…….…….. *central venous catheters*

DHA…….…….... *docosahexaenoic acid*

EEE……..…….. *Estimated energy expenditure*

EFA……..….. *Essential fatty acid*

EPA……..….. *eicosapentaenoic acid*

ESR.. …….... *erythrocyte sedimentation rate*

FA…….. *Fatty acids*

FO…….. *Fish oil-*

GGT…….. *γ-Glutamyl Transferase*

IBW……..….. *Ideal body weight*

ICU……..….. *Intensive care unit-*

IFALD…….. *intestinal failure–associated liver disease*

IV……..…….. *Intravenous*

IVFE…….. *Intravenous fat emulsion*

LCT……..….. *long chain triglycerides*

LPL…….. ***Lipoprotein lipase***

MAP…….. ***Mean arterial pressure***

MCT…….. ***Medium-chain triglycerides***

MPS…….. ***the mononuclear phagocyte system***

MUFA…….. ***Monounsaturated fatty acids***

OO…….….. ***Olive oil***

ω-3 FA…….. ***Omega-3 fatty acids***

ω-6 FA…….. ***Omega-6 fatty acids***

ω-9 FA…….. ***Omega-9 fatty acids***

PLT…….. ***platelet count -***

PN…… ***parental nutrition***

PUFA…….. ***polyunsaturated fatty acids***

REE…… ***Resting metabolic rate***

SD…….….. ***Standard of deviation***

SIRS…… ***Systemic inflammatory response***

SO…….….. ***soy bean oil***

SPSS…… ***Statistical Package of Social Science***

TG…….….. ***triglycerides level***

TLC…….. ***total leucocytic count***

TPN…….. ***Total parental nutrition***

List of Contents

List of Figures

List of Tables

Efficacy and safety of combined omega-6 and 3 versus omega-6 fat containing lipid emulsion in intensive care patients following digestive surgery

Bahaa EL-Din Ewiss, Mohammed I Elsaedy, Ahmed N Al-shaear , Noha Sayed Hussien, Faten Farid

Abstract

***OBJECTIVES*:** evaluate plasma elimination as well as systemic and local tolerance of fish oil based lipid emulsion (contains omega 3 and 6 fatty acids) in comparison to standard soybean based lipid emulsion (contain ω-6 fatty acids) in intensive care patients following digestive surgery

***PATIENTS AND METHODS*:** The studies included 60critically ill patients (newly admitted to the ICU for post operative care after major abdominal surgery necessitating TPN)(20-60 years old)were randomly chosen to be enrolled in this study. All patients received the same standard total parenteral nutrition started 24 hours after the operation except for lipid emulsion. Where **Group A contains 30** patients received standard parenteral nutrition but with the use of soybean based lipid emulsion. **Group B contains 30** patients received standard parenteral nutrition but with the use with the use of omega-3 fat based lipid emulsion. The study period lasted for 5 days. Parenteral nutrition began 24 hours after the operation. Laboratory parameters were recorded on 1st post operative day before the beginning of parenteral nutrition then on 3rd day, and 5th day after starting parenteral nutrition.

***RESULTS*:** The results showed that there was statistical significant increase in parameters of cholestasis , lipid profile and parameters of systemic inflammatory response.

CONCLUSION: The present study show better tolerance for omega 3 fatty acids based lipid emulsion than soybean based lipid emulsion in post gastrointestinal operations.

Introduction

Nutritional support has become a routine part of the care of the critically ill patient. It is an adjunctive therapy, the main goal of which is to attenuate the development of malnutrition, yet the effectiveness of nutritional support is often affected by an underlying metabolic response. This requires that these metabolic changes be taken into consideration when designing nutritional regimens for such patients **(Ziegler, 2009).**

Patients who have undergone a major operation or severe trauma may develop a posttraumatic dysregulation of their host defense, which is characterized by the suppression of specific and non specific immune functions and an enhanced susceptibility towards microbial infections. The increased susceptibility to infection results from a multitude of metabolic or immunologic imbalances due to trauma, tissue ischemia, and operation injury, length of surgery and anesthesia, loss of blood and associated illness. However, the mechanisms of the pathophysiological alterations are complex. The interaction of various factors such as the traumatic insult, microbial pathogenicity factors or mediators of the neuroendocrine axis leads to adverse host reactions, which are driven by excessive production of inflammatory mediators (e.g. proinflammatory cytokines or proinflammatory lipid mediators such as the leukotrienes) and may result finally in systemic inflammatory reactions **(Bessey, 2002).**

Lipid emulsions provide energy and essential fatty acids to patients requiring parenteral nutrition. Recently, the important role of some fatty acids and lipid-soluble vitamins to modulate key metabolic functions was recognized.Conventional emulsions derived from soybean oil contain a high share of omega-6 polyunsaturated fatty acids, mainly linoleic acid and low amounts of antioxidants. Their infusion may lead to an unbalanced fatty acid profile in cell membrane phospholipids and an augmentation of peroxidation. This could adversely affect immunologic functions and inflammatory events. To avoid undesirable effects of excessive linoleic acid intake, substitution of part of the soybean oil in a lipid emulsion by other lipids is strongly recommended **(Laviano A, Fanelli F., 2010).**

Chapter 1
Nutrition support intensive care unit

The provision of specialized nutrition support to the patient in intensive care unit (ICU) is a complex task. Nutrition support benefits the critically ill patient by facilitating wound healing, ameliorating the maladaptive response to injury, and decrease the overall morbidity. Although nutrition support can prevent mortality and morbidity associated with prolonged malnutrition, its use can cause infectious, metabolic and mechanical comlications. Clinicians providing nutrition support do so with the goals of improving the patient outcomes **(Brak et al., 2002)**.

1)Physiological changes post operatively (Table1):-

The metabolic response to critical illness or injury is grouped into two phases. It is based on their temporal relation to the injury or insult. The **Ebb phase** is the early phase of the response to injury. And the following phase is the **Flow phase (Bessey, 2002).**

***Table1: Metabolic Stages* (Bessey, 2002).**

Day	Phase	Characteristics
1-2	Ebb (or Shock)	Low metabolism
2-25	Catabolic flow	high metabolism high nitrogen consumption Redirection of protein synthesis
25+	Anabolic Flow	Lower metabolism normal protein synthesis

a)Protein metabolism:-

Protein loss is accelerated by increases in proteolysis even in the critical care setting, where protein and nonprotein substrates

are provided; negative nitrogen balance can be an expected result. Urinary nitrogen excretion can exceed 15–20 g/day. The excessive protein catabolism occurs because of not only gluconeogenesis, but also thermogenesis, immune function, acute phase protein synthesis and tissue repair. These processes may result in a substantial loss of body protein within a relatively short duration of ongoing critical illness. Body composition studies in critical illness have revealed that a majority of these losses occur in skeletal muscle. Most experts recommend that protein be given as amino acids at a rate of at least 1.5-2.0 g/kg/day **(McClave and Mallampalli, 2001).**

b)Carbohydrate Metabolism:-

Glucose is a primary source of fuel for the brain. It also provides energy for immune function, red blood cells, bone marrow, and for the healing wound. Hyperglycemia is highly prevalent among critically ill patients, which occurs because of resistance in peripheral muscle to the effects of insulin despite increased insulin secretion in concert with increased rates of gluconeogenesis and increases in counterregulatory hormones. The catabolism of protein is a major source of the glucose produced in critical illness. Administering exogenous carbohydrate to these patients does not suppress the gluconeogenesis as it does in healthy patients, and it may further exacerbate hyperglycemia. The degree and control of

hyperglycemia in the ICU are being revealed as increasingly important to predicting outcomes related to critical illness. The maximum rate of glucose oxidation in critically ill patients is about 5 mg/kg/minute. Administering glucose in excess of this rate leads to lipogenesis, hepatic steatosis, and hyperglycemia **(Btaiche and Khalidi, 2004).**

c)Lipid Metabolism:-

Lipid metabolism also is altered in critical illness; lipolysis is accelerated because of increased adrenergic stimulation. This increase in lipolysis is not suppressed by hypercaloric carbohydrate administration. The rate of turnover of glycerol and free fatty acids increases and reflects the degree of acceleration in lipolysis because of stress. The concentrations observed indicate increases in re-esterification of free fatty acids to triglyceride concentrations and increased lipolysis of triglyceride concentrations to free fatty acids. The contribution of fat oxidation to energy production is increased in critically ill patients. The fatty acids liberated by lipolysis are oxidized as a primary source of adenosine triphosphate during stress. In patients fed parenterally, lipid emulsion must be provided to prevent the development of essential fatty acid deficiency **(Woodcock, et al., 2001).**

d)Fluid Changes:-

Fluid and electrolyte changes are a constant challenge to critical care practitioners. Critical illness predictably results in