Effect of intravenous Glutamine supplementation in severely burn critically ill patient receiving enteral nutrition study protocol: a prospective, blinded, randomized, placebo controlled clinical trial

Thesis
Submitted in the Partial Fulfillment of the
MD Degree in Anesthesiology

By
Hanan Ibrahim EL Tartoushy
MB,BCh; MSc. Anesthesia

Supervised by

Prof. Dr. Abdel Rahman Fathalla
Professor of Anesthesiology
Faculty of Medicine, Cairo University

Prof. Dr. Ahmed Helmy
Professor of Anesthesiology
Faculty of Medicine, Cairo University

Ass. Prof. Nashwa Nabil
Assistant Professor of Anesthesiology
Faculty of Medicine, Cairo University

Cairo University
2015

Acknowledgement

First praise is to **Allah**, the Almighty, on whom ultimately we depend for sustenance and guidance.

Second, my sincere appreciation goes to **Prof. Dr.** ***Abdel Rahman Fathalla***, Professor of Anesthesiology Faculty of Medicine Cairo University, whose guidance, careful reading and constructive comments were valuable. I express my sincerest appreciation for his assistance in any way that I may have asked. I really owe him much for his support and encouragement, during conducting this work.

I am also deeply indebted to **Prof. Dr.** ***Ahmed Helmi*** Professor of Anesthesiology Faculty of Medicine Cairo University, for his valuable advice and supervision during this work. I could hardly find the words to express my thanks. His timely and efficient contribution helped me shape this into its final form.

I am also deeply indebted to **Dr. Nashwa Nabil** *Assistant* Professor of Anesthesiology Faculty of Medicine Cairo University, for his valuable advice and supervision during this work. I could hardly find the words to express my thanks. His timely and efficient contribution helped me shape this into its final form.

Finally no words can express the warmth of my feelings to my family and my husband to whom I am forever indebted for their patience, support and help.

Key Words : intravenous glutamine**.....** ، severe burn..... ، ...Infection**...** ، **...**

Abstract

This study was done to determine whether providing intravenous alanyl-glutamine (0.5 g/kg/day)will be associated with improved clinical outcomes in the term of reduced severity of organ dysfunction, length of stay in ICU, length of stay in hospital, number of days on mechanical ventilation, number of days of antibiotic use during ICU stay, in hospital mortality in compared with placebo in critically ill burn patient.

Contents ***Page***

List of Abbreviations:

TBSA: Total **B**ody **S**urface **A**rea.

Gy: Gre**y (SI** unit of absorbed radiation).

rhGH: recombinant **h**uman **G**rowth **F**actor.

SIRS: Systemic **I**nflamatory **R**esponse **S**yndrome.

MSSA: Methicillin **S**ensitive **S**taph **A**ureus.

MRSA: Methicillin **R**esistant **S**taph **A**ureus.

ARDS: Adult **R**espiratory **D**istress **S**yndrome.

BAL: Broncho **A**lveolar **L**avage.

ETA: Endo**T**racheal **A**spiration.

PBB: Protected **B**ronchial **B**rush.

ESBL: Extended **B**eta **L**actamase.

GS: Glutamine **S**ynthetase.

HSP: Heat **S**hock **P**rotiens.

HSE: Heat **S**hock **E**lement.

NF: Nuclear **F**actor.

ALI: Acute **L**ung **I**njury.

CIP: Clinical **I**llness **P**olyneuropathy.

MODS: Multiple **O**rgan **D**ysfunction **S**yndrome.

REDOX: REducing **D**eaths due to **Ox**idative Stress.

SOFA: Sequential **O**rgan **F**ailure **A**ssessement.

CAUTI: Catheter **A**ssociated **U**rinary **T**ract **I**nfection.

CDC: Center for **D**isease **C**ontrol and Prevention.

CLABSI: Central **L**ine **A**ssociated **B**lood **S**tream **I**nfection.

VAP: Ventilator **A**ssociated **P**neumonia.

SSI: Surgical **S**ite **I**nfection.

VFD: Ventilator **F**ree **D**ays.

BMI: Body **M**ass **I**ndex.

PN: Parenteral **N**utrition.

List of Figures:

Page

List of tables

page

Introduction

Severe burn injury represents a significant problem worldwide. More than 1 million burn injuries occur annually in the United States. Although most of these burn injuries are minor, approximately 10% of patients with burns require admission to a hospital or major burn center for appropriate treatment every year.(1)

Advances in therapeutic strategies, including advances in resuscitation, wound coverage, better support of hypermetabolic response to injury, more appropriate infection control, and improved treatment of inhalation injury, have further improved the clinical outcome of this unique patient population over the past years. However, severe burns remain a devastating injury affecting nearly every organ system and leading to significant morbidity and mortality.(2)

Severe burns covering more than 40% total body surface area (TBSA) are typically followed by a period of stress, inflammation, and hyper metabolism, characterized by a hyper dynamic circulatory response with increased body temperature, glycolysis, proteolysis, lipolysis, and futile substrate cycling. (3-4)

All trauma, surgical, or critically ill patients, almost have the same reactions but the severity, length, and magnitude are unique for patients with burns. (2,5) Marked and sustained increases in catecholamine, glucocorticoid, glucagons, and dopamine secretion are believed to initiate the cascade of events leading to the acute hyper metabolic response with its ensuing catabolic state.(6)

The response is characterized by supraphysiologic metabolic rates, constitutive muscle and bone catabolism, growth retardation, insulin resistance, and increased risk for infection.(3-4)

Loss of lean body mass during critical illness is considered a major clinical problem that delays wound healing and recovery. In parallel, there is a depletion of glutamine levels in muscle. (6)

Although glutamine production is increased in critically ill patients, it is not sufficient to maintain intracellular levels of glutamine in muscle.(7) Determinants of successful initial burn treatment include early aggressive resuscitation (including nutrition), control of infection, and early closure of the burn wound. Aggressive, early enteral feeding improves outcomes in the burned patient by mitigating the degree and extent of catabolism.(8)

Attempting to overcompensate by providing excess calories and/or protein is ineffective and likely to increase such complications as hyperglycemia, CO_2 retention, and azotemia. Thus, the primary goal of nutritional support in patients with burns is to satisfy acute, burn-specific requirements, and not to over feed. Under stress and catabolic conditions such as major surgery,(9)burn injury(10 , 11)and multiple trauma,(12 ,13) there is a severe depletion of glutamine levels in plasma. It has been reported that a low plasma glutamine level at intensive-care unit (ICU) admission is an independent risk factor for mortality.(14)

Aim of the work

The aim of this study is to determine whether providing intravenous alanyl-glutamine (0.5 g/kg/day)will be associated with improved clinical outcomes in the term of reduced severity of organ dysfunction, length of stay in ICU, length of stay in hospital, number of days on mechanical ventilation, number of days of antibiotic use during ICU stay, in hospital mortality in comparison with placebo in critically ill burn patient.

Burn

A **burn** is a type of injury to flesh or skin caused by heat, electricity, chemicals, friction, or radiation.[15] Burns that affect only the superficial skin are known as superficial or first-degree burns. When damage penetrates into some of the underlying layers, it is a partial-thickness or second-degree burn. In a full-thickness or third-degree burn, the injury extends to all layers of the skin. A fourth-degree burn additionally involves injury to deeper tissues, such as muscle or bone.

The treatment required depends on the severity of the burn. Superficial burns may be managed with little more than simple anelgesics, while major burns may require prolonged treatment in specialized burn centers. Cooling with tap water may help to relieve pain. Partial-thickness burns may require cleaning with soap and water, followed by dressings and try to leave the blisters intact. Full-thickness burns usually require surgical treatments, such as skin grafting. Extensive burns often require large amounts of intravenous fluid, because the subsequent inflammatory response causes significant capillary fluid leakage and edema. The most common complications of burns involve infection.

While large burns can be fatal, modern treatments developed since 1960 have significantly improved the outcomes, especially in children and young adults.[16] Globally, about 11 million people seek medical treatment, and 300,000 die from burns each year.[17] In the United States, approximately 4% of those admitted to a burn center die from their injuries.[18] The long-term outcome is primarily related to the size of burn and the age of the person affected.

Fig(1): Second degree burn of the hand

Signs and symptoms

The characteristics of a burn depend upon its depth. Superficial burns cause pain lasting two or three days, followed by peeling of the skin over the next few days.[19,20] Individuals suffering from more severe burns may indicate discomfort or complain of feeling pressure rather than pain. Full-thickness burns may be entirely insensitive to light touch or puncture.[20] While superficial burns are typically red in color, severe burns may be pink, white or black.[20] Burns around the mouth or singed hair inside the nose may indicate that burns to the airways have occurred, but these findings are not definitive.[21] More worrisome signs include: shortness of breath, hoarseness, and stridor or wheezing.[21] Itchiness is common during the healing process, occurring in up to 90% of adults and nearly all children.[22] Numbness or tingling may persist for a prolonged period of time after an electrical injury.[23] Burns may also produce emotional and psychological distress.

Table (1): Types of burn[(24)]

Type[24]	**Layers involved**	**Appearance**	**Texture**	**Sensation**	**Healing Time**	**Prognosis**	**Example**
Superficial (1st-degree)	Epidermis [19]	Red without blisters [24]	Dry	Painful[24]	5-10 days (24,25)	Heals well;[24] Repeated sunburns increase the risk of skin cancer later in life[26]	
Superficial partial thickness (2nd-degree)	Extends into superficial (papillary) dermis[24]	Redness with clear blister. Blanches with pressure. [24]	Moist[24]	Very painful[24]	<2–3 weeks (20,24)	Local infection/ cellulitis but no scarring typically[20]	
Deep partial thickness (Second-degree)	Extends into deep (reticular) dermis[24]	Yellow or white. Less blanching. May be blistering.[24]	Fairly dry[20]	Pressure and discomfort [20]	3 to 8 weeks [24]	Scarring, contractures (may require excision and skin grafting)[20]	
Full thickness (3rd-degree)	Extends through entire dermis[24]	Stiff and white/ brown[24] No blanching [20]	Leathery [24]	Painless [24]	Prolonged (months) and incomplete [24]	Scarring, contractures, amputation (early excision recommended) [20]	

4th-degree	Extends through entire skin, and into underlying fat, muscle and bone[24]	Black; charred with eschar	Dry	Painless	Requires excision[24]	Amputation, significant functional impairment, and, in some cases, death.[24]	

Cause

Burns are caused by a variety of external sources classified as thermal (heat-related), chemical, electrical, and radiation.[27] In the United States, the most common causes of burns are: fire or flame (44%), scalds (33%), hot objects (9%), electricity (4%), and chemicals (3%).[28] Most (69%) burn injuries occur at home or at work (9%),[18] and most are accidental, with 2% due to assault by another, and 1-2% resulting from a suicide attempt.[17] These sources can cause inhalation injury to the airway and/or lungs, occurring in about 6%.[29]

Burn injuries occur more commonly in the poor. Smoking is a risk factor, although alcohol use is not. Fire-related burns are generally more common in colder climates.[17] Specific risk factors in the developing world include cooking with open fires or on the floor[15] as well as developmental disabilities in children and chronic diseases in adults.[30]

Thermal

In the United States, fire and hot liquids are the most common causes of burns.[29] Of house fires that result in death, smoking causes 25% and heating devices cause 22%.[15] Almost half of injuries are due to efforts to fight a fire.[15] Scalding is caused by hot liquids or gases and most commonly occurs from exposure to hot drinks, high temperature tap water in baths or showers, hot