

The Role of Metabolism and Nutrition Therapy in Burn Patients

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Abstract

Thermal injury elicits the greatest metabolic response, amongst all traumatic events, in critically ill patients. In order to ensure burns patients can meet the demands of their increased metabolic rate and energy expenditure, adequate nutritional support is essential. Burn injury results in a unique pathophysiology, involving alterations in endocrine, inflammatory, metabolic and immune pathways, and nutritional support needed during the inpatient stay varies depending on burn severity and idiosyncratic patient physiologic parameters. We review the effects of burn injury on nutritional requirements, and how this can be best supported in a healthcare setting.

Keywords: Metabolism; Nutrition; Burn

Background

Thermal injuries are responsible for generating the greatest metabolic response of any disease process in critically ill patients [1]. A number of alterations in inflammatory, immune, and endocrine pathways are initiated upon injury [2]. Immune cells are stimulated to secrete cytokines which can induce an unstable hypercatabolic state, which, if left unregulated, may lead to multiple organ failure and systematic inflammatory response syndrome [3]. Nutrition practice in burn injury requires a multifaceted approach aimed at providing metabolic support during a heightened inflammatory state, while accommodating surgical and medical needs of the patient. Nutritional assessment and determination of nutrient requirements is challenging, particularly given the metabolic disarray that frequently accompanies inflammation. Nutritional therapy requires careful decision making, regarding the safe use of enteral or parenteral nutrition and the aggressiveness of nutrient delivery given the severity of the patient's illness and response to treatment. Nutritional support, defined by provision of vital and ancillary nutrients to maintain or improve the patient's nutritional status and permit wound healing [4], is essential in the management of burns [5]. Treatment protocols are evidence-based, originating from clinical and laboratory data. Severely burned patient have much higher energy requirements due to the magnitude and duration of the hyper metabolic response as compared to non-burned critically ill patients [6]. The optimal dietary parameters, including amount, route and composition, are still unknown. The following review serves as a guideline for providing nutritional therapy to severely burned patients throughout their care.

Methods

PubMed, Embase and Web of Science databases were used to search for articles regarding nutrition and/or metabolism following burn injury. Articles published in English or German language were considered to be included in this review. There were no limitations regarding the year of publication.

Changes in metabolism and body composition following severe burn injury

Metabolic derangements secondary to major burn injuries are difficult to management [7]. Immediately after severe burn injury, plasma volume is depleted and insulin levels, lowered oxygen consumption, hypothermia and a decrease in overall metabolic rate [8]. This "ebb" phase is followed by an evolving "flow" phase [9] in weeks following injury. Enhanced secretion of catecholamines, glucagon, glucocorticoids, and dopamine are closely associated with the acute hypermetabolic response and the associated catabolic metabolism [10], resulting in tachycardia, hyperthermia, increased caloric consumption, proteolysis and neoglycogenesis [11]. Hyper-metabolism, which starts approximately on the fifth post-burn day and persists for up to twenty-four months [12]. Basal metabolic rate (BMR) can double and result in extreme loss of lean body mass [1]. Inability to meet the body's energy and protein demands can lead to impaired wound healing, inability to fight infection, organ dysfunction, and ultimately death [13]. The pathophysiology behind this response remains elusive, but involves a number of immune modulators including cytokines, platelet-activating factor, endotoxin, reactive oxygen species, nitric oxide, and complement cascade [14]. Additionally, acutely burned patients have increased intestinal permeability [15] and secondary immunodeficiency [16], making them more susceptible to secondary infections.

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Several studies, especially in pediatric patients, reported changes of body composition following burn injury [17-20]. The most common way to assess body composition in this and other patient populations is dual X-ray absorptiometry (DEXA). Cambiaso et al. reported a significant loss of lean mass in pediatric patients during their ICU stay, especially in the upper extremities. Furthermore, an increase of fat mass was noticed [17]. In long-term observations of pediatric burn patients, a progressive increase of lean mass was reported up to 36 months post-injury compared to discharge [18]. Furthermore, an impact of severe burn injury on the structure of bones with a decrease of bone mineral content and bone mineral density can be seen [20].

Timing of nutritional support of the severely burned patient

Enteral nutrition (EN) is first advocated in the management of burns patients, however, the optimal form and chronology of nutrition is debated [21]. The American Burn Association practice guidelines state that EN should begin as soon as possible, there is no consensus among experts regarding the best time to initiate oral/enteral nutrition [22]. Most advocate initiating EN within 24 hours of injury [23], and research indicates starting EN 6 hours post injury is safe, effective, and can reverse the detrimental metabolic and hormonal shifts [7]. In human studies early EN can preserve blood levels of catecholamine's, cortisol, and glucagon and consequently preserve the intestinal mucosal integrity, as well as its motility, and blood flow [24-26].

In the acute post burn phase, patients experience a state of hemodynamic instability which inhibits intestinal motility and can trigger paralytic ileus, further contributing to impaired nutrition [27]. If some gastrointestinal function remains, EN is preferred over parenteral nutrition (PEN), with guidelines promoting the use of ED as soon as possible after resuscitation [22]. EN stimulates and directly nourishes the gastrointestinal tract and promotes release of intestinal hormones and growth factors [28]. In humans, EN can help preserve muscle mass and wound healing, and decrease time patients spend in intensive care [21]. Early EN dampens the hyper metabolic state and can reduce the occurrence of paralytic ileus [1]. It is advised that EN is initiated at a continuous low flow rate which is gradually increased to the goal volume at a rate tolerated by each patient [27]. Continuous EN is preferred over parenteral schedules, though data are limited and there is no conclusive evidence supporting the superiority of either schedule [7]. In the setting of prolonged ileus or intolerance of EN [12], however, PEN becomes necessary. Interestingly, reduced immune response, impairment of liver function, and increased mortality were observed when combining both enteral and parenteral feeding compared to enteral feeding alone [29].

Nutritional evaluation and energy requirements

Nutritional support post burn injury aims to supply additional calories required by patients in their hyper metabolic state while balancing the risk of overfeeding [7]. Without adequate nutrition patients are at risk of impaired immune function, delayed wound healing, increased risk of infection, prolonged dependency on mechanical ventilation, and heightened mortality risk [12]. Conversely, overfeeding can cause hyperglycemia, respiratory system overload, steatosis and hyperosmolarity [12]. Various equations have been developed to estimate nutritional requirements and caloric needs in burn patients using biochemical markers, biometrics, and anthropometry [30]. Body mass is considered the easiest indicator to assess nutritional status [31].

Based on the Curreri formula, adult patients should receive about

25 kcal/kg/day plus 40 kcal/%TBSA/day [6]. The requirement for children is 1800 kcal/day plus 2200 kcal/m² burn/day. Ideally this caloric intake should be via EN. The Harris-Benedict, Ireton-Jones, Toronto, Schofield and the American Society for Parenteral and Enteral Nutrition (ASPEN) have developed formulas to guide nutritional support in critically ill and burn patients [32]. The most widely used formulas in children are the Harris-Benedict, Mayes, and World Health Organization formulas in Table 1. These formulas only act as guides as energy expenditure fluctuates after burn, and strictly following these formulas can lead to underfeeding during the periods of highest energy utilization and overfeeding later during recovery injuries [33].

The current gold-standard for measuring energy expenditure is indirect calorimetry (IC) [34]. The volume of expired gas and the concentrations of oxygen and carbon dioxide in inhalation and exhalation are recorded [35]. This enables the carbon dioxide production (VCO₂) and oxygen consumption (VO₂), and therefore metabolic rate to be calculated [36]. The respiratory quotient (RQ) is the ratio of carbon dioxide produced to oxygen consumed (VCO₂/VO₂) [37], and is used to detect overfeeding or underfeeding. The normal metabolism of mixed substrates yields a RQ of 0.75-0.90. Overfeeding, characterized by the synthesis of fat from carbohydrate, results in a RQ of >1.0, while in unstressed starvation fat is utilized as a major energy source and the consequent RQ is under <0.7.

IC also allows the REE to be calculated using the Harris-Benedict equation. Compared to an isocaloric-isoprotein high fat enteral diet, a high carbohydrate diet with 82% carbohydrate, 15% protein and 3% fat, stimulates protein synthesis by increasing endogenous insulin production, resulting in improved lean body mass accretion [38]. In pediatric burn patients, 1.4 times the REE (in kcal/m²/day) is needed to maintain body weight [23]. Few clinicians have access to IC due to its high cost and the training required, and IC is therefore mainly performed for research.

Requirements of macronutrients

Metabolism of carbohydrates, proteins, and lipids provides energy via different pathways [39]. Carbohydrates are needed in abundance by burn patients to provide the glucose required for many metabolic pathways, promote wound healing, and spare the use of amino acids as an alternative fuel source [7,40]. A randomized study of 14 severely burned children found that high-carbohydrate diets resulted in significantly less muscle protein degradation than high-fat diet [41]. The glucose requirement in severely burned patients, however, may exceed the amount of glucose that can be safely administered. Severely burned patients oxidize glucose at a maximum rate of 7 g/kg/day [1], and un-metabolized excess glucose can result in hyperglycemia, glycosuria, dehydration, respiratory failure, or the conversion of glucose to fat [23]. In addition, acute injury can result in hormonal changes which lead to insulin resistance. Supplementary insulin can promote wound healing and muscle protein synthesis in burns patients [42]. When used in combination with a high-carbohydrate, insulin infusion and high-protein diet in severely burned patients improve donor site healing, lean body mass, bone mineral density, and decrease length of stay [43,44].

Fat, in small quantities, can improve glucose tolerance, reduce the volume of total carbohydrates required [40], and prevent essential fatty acid deficiency. Fat, however, is recommended only in limited amounts [45]. Lipolysis is suppressed as part of the hyper metabolic and catabolic response to severe burns, limiting the degree to which lipids can be utilized for energy; only 30% of available free fatty acids are degraded,

Formula	Patients	Formula
Harris & Benedict	Male Female	Estimated Energy Requirements: BMR x Activity factor x Injury factor 66 + (13.7 x weight in kg) + (5 x height in cm) - (6.8 x age) 665 + (9.6 x weight in kg) + (1.8 x height in cm) - (4.7 x age) Activity factor Confined to bed: 1.2 Minimal ambulation: 1.3 Injury factor < 20% TBSA: 1.5 20-40% TBSA: 1.6 > 40% TBSA: 1.7
Ireton-Jones	spontaneously breathing Ventilated-Dependent	Estimated Energy Requirements: 629 - (11 x yrs) + (25 x w) - (609 x O) 1784 - (11 x yrs) + (25 x w) + (244 x S) + (239 x t) + (804 x B)
Toronto	For all patients	Estimated Energy Requirements: [- 4343 + (10.5 x %TBSA) + (0.23 x kcals) + (0.84 x Harris Benedict) + (114 x T (°C)) - (4.5 x days post-burn)] x Activity Factors Activity factors non-ventilated: Confined to bed: 1.2 Minimal ambulation: 1.3 Moderate act, 1.4 Ventilated-Dependent: 1.2
Schofield (modified)	Men 10-18 years 18-30 years 30-60 years > 60 years Women 10-18 years 18-30 years 30-60 years > 60 years	Estimated Energy Requirements: BMR x Injury factor (0.074 x w) + 2.754 (0.063 x w) + 2.896 (0.048 x w) + 3.653 (0.049 x w) + 2.459 (0.056 x w) + 2.898 (0.062 x w) + 2.036 (0.034 x w) + 3.538 (0.038 x w) + 2.755 Injury Factors: < 10% TBSA = 1.2 11-20% TBSA = 1.3 21-30% TBSA = 1.5 31-50% TBSA = 1.8 > 50% TBSA = 2.0
ASPEN	For all patients	25 a 35 kcal/kg/day
Mayes	For Children Male & Female < 3 years 3 to 10 years	Estimated Energy Requirements: 108 + (68 x weight in kg) + (3.9 x %TBSA) 818 + (37.4 x weight in kg) + (9.3 x %TBSA)
WHO	For Children Male < 3 years 3 - 10 years Female < 3 years 3 - 10 years	(60.9 x weight in kg) - 54 (22.7 x weight in kg) + 495 (61.0 x weight in kg) - 51 (22.5 x weight in kg) + 499
Galveston	For Children Male & Female 0 - 1 year 1 - 11 years 12 - 18 years	2100 (BSA) + 1000 (BSA x TBSA) 1800 (BSA) + 1300 (BSA x TBSA) 1500 (BSA) + 1500 (BSA x TBSA)

Kcals: Calorie intake in past 24 hours; Harris Benedict: Casal requirements in calories using the Harris Benedict formula with no stress factors or activity factors; T: Body temperature in degree Celsius; Days post burn: The number of days after the burn injury is sustained using the day itself as day zero; W: Weight in kg; TBSA: Total body surface area; BSA: Body surface area

Note: Specific formulas developed for critically ill and burn patients include the Harris-Benedict, Ireton-Jones, Toronto, Schofield and the American Society for Parenteral and Enteral Nutrition (ASPEN) recommendations [28]. The most widely used formulas in children include the Harris-Benedict, Mayes and World Health Organization formulas.

Table 1: Formulas for calculating nutritional needs in burn cases.

while the remainder undergo re-esterification and accumulate in the liver (steatosis). Fats should, therefore, comprise a maximum of 30% of non-protein calories, or 1 mg/kg/day of intravenous lipids in total parental nutrition (TPN). Various studies have also suggested that increased fat intake impairs immune function [46,47]. Resultantly, several low-fat enteral formulas have been created [48]. The composition of fat in the diet of burn patients is also an important consideration. Omega-6 fatty acids (ω -6 FFA's), like linoleic acid, are

metabolized through the synthesis of arachidonic acid, a precursor of pro-inflammatory cytokines such as Prostaglandin E2. Omega-3 fatty acids (ω -3 FFA's), on the other hand, are metabolized without generating pro-inflammatory molecules. ω -3 FFA-rich diets in burns victims are associated with a reduced incidence of hyperglycemia, improved inflammatory response, and improved outcomes in general [49]. Resultantly, immune-enhancing diets have a ω 6: ω 3 ratio closer to 1:1, while most enteral formulas have a ratio between 2.5:1 and 6:1.

The ideal composition and amount of fat in nutritional support for burn patients warrants further investigation and remains a topic of controversy.

Protein supplementation is essential to meet the ongoing demands, maintain lean body mass, and to supply a substrate for immune function and wound healing. Increased proteolysis is a hallmark of the hyper metabolic response to severe burn resulting in degradation of a half pound of skeletal muscle per day [50]. Healthy individuals require 1 g/kg/day of protein [51], and based on *in vivo* kinetics measuring oxidation rates of essential and non-essential amino acids, burn patients are calculated to use 50% more protein per day than healthy individuals in the fasting state [6,23,52]. Currently, protein requirements are estimated at 1.5-2.0 g/kg/day for burned adults, and 2.5-4.0 g/kg/day for burned children [53]. Several amino acids are essential to recovery following burn injury [54]. Glutamine, alanine, and arginine efflux from skeletal muscle and solid organs following a burn injury [55], and provide a source of energy for the liver and help in wound healing [56,57]. Glutamine helps to maintain the integrity of the small bowel and to preserve the immune function of the gut by and directly fueling lymphocytes and enterocytes [58]. Glutamine also increases the synthesis heat shock proteins and is as a precursor of glutathione, a critical antioxidant, which can help to protect cells under stress [59]. Administration of 25 g/kg/day of glutamine can reduce mortality and length of hospitalization in burn patients [60]. Evidence also supports supplementation of burns patients with arginine [61], which is associated with promotion of wound healing and immune function. Arginine acts to stimulate T-lymphocytes, augment the function of natural killer cells, and accelerate the synthesis of nitric oxide [62]. Data from non-burn critically ill patients, however, suggest that arginine can be harmful [63] and further study is warranted before its use can be recommended.

Requirements of micronutrients

A number of vitamins and micronutrients can help to facilitate wound healing and immune function following burn [4]. Severe burns lead to intense oxidative stress combined with substantial inflammatory response, which accelerates the depletion of endogenous antioxidant defenses [7]. Levels of vitamins A, C, D, iron, zinc, selenium and calcium can also drop following burns injury, which has resultant detrimental effects on wound healing, the immune system and skeletal muscle function [64]. Vitamin A is required for wound healing and epithelial growth. Vitamin C is needed for collagen production and cross-linking. Vitamin D is essential in the prevention of further bone catabolism post-burn, though its exact role and optimal dose after severe burn remains to be determined [65]. Pediatric burn patients often have altered calcium and vitamin D homeostasis [66] as well as osteoblast apoptosis, bone resorption and urinary calcium wasting [67]. Additionally, burned skins can no longer function to activate vitamin D3. One study in the pediatric burns population found that multivitamins containing 400 IU of vitamin D2 did not correct vitamin D insufficiency [67]. Methods to combat calcium and vitamin D deficiency need further investigation.

The trace elements Iron (Fe), copper (Cu), selenium (Se), and Zinc (Zn) play an important roles in cellular and humoral immunity, but are lost in large quantities during burn wound exudation [68]. Se is important cell-mediated immunity; Fe is a cofactor for oxygen-carrying proteins [7]. Zn is critical for protein synthesis, wound healing, DNA replication, and lymphocyte function [69]. Cu deficiency has been implicated in arrhythmias, decreased immunity, and worse outcomes

after burn [7]. Supplementing these micronutrients can improvement morbidity for severely burned patients.

Pharmacologic modalities

Current methods of nutritional support, although perceived to be effective, may fail to replenish all nutritional deficiencies. Pharmacological nutrition is the concept whereby nutritional support is “tailor made” for the specific disease and/or organ involved and involves administration of two to seven times the usual amounts of selected normal dietary constituents with reduction of the remaining components to avoid overfeeding. Dietary supplementation with pharmacological levels of specific amino acids and fatty acids, alone or in combination, can improve immunologic function, reduce the intensity and number of infections, stimulate the proliferation of ileal and colonic mucosa, thereby also improving their barrier functions, and maintain muscle anabolism and nitrogen balance. Pharmacological nutrition can thus significantly altering the clinical course of critically ill patients [16]. According to Häusinger’s hypothesis, pharmacological nutrition regulates cell hydration [70]. Among the nutritional supplements most frequently used in pharmacological nutrition for burn patients are glutamine, arginine and (ω -3) fatty acids [16].

Conclusion

Effective assessment and management of nutritional status optimizes wound healing and decreases complications and mortality. With each change in clinical status, reassessment of nutrient requirement is necessary. Early enteral nutrition builds the basis of nutritional support, and ideally nutritional support is individualized and continually adjusted throughout recovery according to changing needs to achieve predetermined nutritional endpoints.

Declarations

Ethics approval and consent to participate

Ethical approval was not required for this study.

Consent for publication

Not applicable.

Availability of data and material

Please contact author for data requests.

Competing interests

The content of this article was expressly written by the authors listed. MS, MRB, ZNM, SR, MPC, CCS, DD, CT, LKB, CW, BB, ML, FS and KSH have no potential conflicts of interest, affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed herein.

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