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Nutrition in burns patient

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Abstract: *Burn injuries are a global public health problem, accounting for an estimated 265000 deaths annually. The majority of these occur in low- and middle-income countries and almost half occur in the WHO South-East Asia Region. The rate of child deaths from burns is currently over 7 times higher in low- and middle-income countries than in high-income countries. In India, over 100000 people are moderately or severely burnt every year. In many high-income countries,burn death rates have been decreasing due to improvements in treatment of burns, control of infection and advances in nutritional support. Non-fatal burn injuries are a leading cause of morbidity. Burns occur mainly in the home and workplace. Burns are preventable. Burns are among the leading causes of disability-adjusted life-years (DALYs) lost in low- and middle-income countries. Nutrition therapy is a cornerstone of burn care from the early resuscitation phase until the end of rehabilitation. While several aspects of nutrition therapy are similar in major burns and other critical care conditions,the patho-physiology of burn injury with its major endocrine, inflammatory, a metabolic and immune alteration requires some specific nutritional interventions.*

Keywords*: Burn injury, Thermal Burns, Nutritional support, Proteins, Carbohydrates, Substrate, critical care, Hypermetabolism, Hypercatabolism,*

I. Introduction

Burns patients typically have the hyper metabolism and negative catabolism. Nutritional support is an important step in the management of burns patients from the early phase of resuscitation to the final phase of rehabilitation. The patho-physiology of burn injury with its major endocrine, inflammatory, metabolic and immune alterations is similar to any other critical care situation. The route of administration and aggressiveness of the delivery of the nutrients depends on the severity of the patient's illness and the response of the particular patient. The plan of nutritional support to the patient during the whole period of stay in the hospital varies depending on the clinical condition of the patient. The treatment protocols are evidence based depending on the clinical and laboratory studies. Nutritional support is defined as the provision of nutrients and any necessary adjunctive therapeutic agents to improve or maintain the nutritional status of the patient for normal wound healing. Nutritional support is administered into the stomach or small intestine (enteral) and/or by intravenous infusion (parenteral)[1]. Most of the burn victims with lesser percentage of burns can be followed in the outpatient department. Less than 10% of the patients with burn injuries need in-patient treatment. Very few patients only require intensive care treatment. Patients with major burns are those with more than 20% total body surface area burn with or without inhalation injury.

Patients with major burns are characterized by

- Strong oxidative stress
- Intense inflammatory response
- Prolonged periods of hyper metabolic and catabolic response

These responses are proportionate to the extent and depth of the burns. Catecholamines, corticosteroids and inflammatory cytokines are the primary mediators of hyper metabolism following burn injury [2,,3]. During this phase the levels of Catecholamines and corticosteroids is increased by 10 to 20 fold and persists for a period of 12 months. These catabolic hormones result in increased lipolysis, proteolysis, and gluconeogenesis and energy expenditure.

II. Backgrounds and Aim

Burns management needs multidisciplinary approach with efforts from various specialties in the team. The dietitian in the burn team has a defined role in the care of the burn patients, from the acute phase followed through the rehabilitation. Their role in the assessment, treatment and management of nutritional requirements with or without inhalation injuries is followed in the unit. Patients with 25% burns are characterized by

- Metabolic rate is elevated to 118% to 210% in adults
- Resting metabolic rate elevated to approximately 180%

- Calorie needs may exceed 5000 Kcal/day
- Without nutritional support 40% burns patient lose 25% of pre admission weight in 3 weeks,
- Impaired immunity and delayed healing

This characteristic metabolic changes associated with burns indicates the need for a nutritional therapy program from the day of the injury.

2.1 Goals of nutritional management

- ✓ **Optimal wound healing and rapid recovery from burn injuries**
- ✓ Minimize complications including infection
- ✓ To attain and maintain normal nutritional status
- ✓ To minimize the metabolic disturbances during the treatment process.

2.2 Objectives of nutritional management:

- Provide nutrition via enteral route within 6-18 hours post burn injury
- Maintain weight within 5% -10% of pre-burn weight
- Prevent micronutrient deficiency
- Minimize hyperglycemia
- Minimize hypertriglyceridemia.

2.3 Timing of nutrition

There is a significant damage to the gut mucosa and translocation of the gut bacteria following major burn injuries. This leads to the decreased nutrient absorption. Enteral nutrition (EN) started earlier (within 24 hours of burn injury) results in good outcome for the patients [4,5]. With early institution of enteral nutrition there is a significant modulation of catecholamine levels and support of gut mucosal integrity[6]. With the early institution and by continuous enteral nutrition, by 3rd post-burn day there is an adequate supply of caloric requirements, reduction of plasma cortisol and glucagon levels and reduction of hyper metabolic response [7]. Post burn ileus affects the stomach and colon primarily.[8] Patients with major burn injuries can be fed through enteral tubes to the duodenum or jejunum as early as 6 hours post burn.[9]Early EN maintains gut integrity, motility and blood flow and helps to prevent intestinal hypo perfusion or ileus due to delays in resuscitation or reperfusion. The American burn association recommended early enteral nutrition during the acute phase of the burn within the 24 hours post burn. Peng et al. found markedly increased intestinal permeability in severely burnt patients by lactulose and mannitol measurements. Early enteral feedings reduces the excessive permeability and associated with lower levels of serum endotoxin and TNF-alpha compared to the delayed enteral fed patients.

III. Pathophysiology of Burn

Burn injuries result in changes in metabolic alterations, including malnutrition and Hypermetabolism [10].
The pathophysiological changes associated with the burn injuries are

- ✓ Activation of inflammatory mechanisms
- ✓ Disruption of cellular immunity
- ✓ Alterations in immune system mediators involving the activation of TNF-alpha, IL-1, IL-6 and IL-8.

These cytokines play an important roll in the inflammatory response and is ultimately connected to the mortality and morbidity in these patients [11]. Infection is one of the main causes of death in burn patients [12]. Infection control, early diagnosis and treatment of infections are crucial to the outcome of results. Burns management in relation to the nutritional, immunological and microbiological profile becomes inseparable components of patients hospitalized with burn diagnosis.

3.1 Metabolic response to burns injury

The patient essentially exhibits two phases: the first is referred to the ebb stage, in which the patient shows a deficit in plasma volume and insulin levels, initial signs of shock, hypothermia, lowered oxygen consumption and a decrease in overall metabolic rate. After this, the ebb phase evolves to the flow phase. This stage is characterized by an increased concentration of catabolic hormones regulating the metabolic response. An increase in heart rate, body temperature, calorie consumption, and proteolysis and neo- glycogenesis is observed [13]. These reactions result of metabolic events aimed at wound healing [14].

3.2 Excess energy demands
- Marked increase in energy demand due to increased metabolic rate
- Abnormal and inefficient processing of Nutrients (Carbohydrate and fat)
- Hyperthermia
- Excessive gluconeogenesis
- Decreased use of fat

3.3 Catabolism induced complications are
- ✓ Erosion of the lean body mass due to marked catabolism
- ✓ Net loss of protein due to utilization of amino acids in excess, instead of fat for energy.

3.4 Mortality and Morbidity in relation to Loss of Lean Body Mass

Percent loss of Lean mass	Complications	Mortality
10%	Impaired immunity Increased infection	10%
20%	Decreased wound healing, Weakness, infection	30%
30%	Too week, Pressure ulcer, Pneumonia	50%
40%	Death commonly due to pneumonia	100%

IV. Nutritional assessment

4.1 Nutritional assessment in adults

In burn patients there is poor correlation between serum levels of pre-albumin, retinol binding protein or transferrin and nitrogen balance. These are affected not only by the nutritional status but also due to age, burn wound size, post-burn day and nitrogen intake. Albumin levels correlate poorly with nitrogen balance. The loss of nitrogen through the burn wound could not be measured correctly. Use of total urinary nitrogen is a better indicator of nitrogen balance calculation. A baseline nutritional assessment must be recorded. Assessment regarding the pre-burn height and weight, number of days post burn, post-burn care and associated complications are important. Patients with malnutrition and at risk of re-feeding syndrome must be identified [15,16]

- ➢ Serial body composition can be measured by dual energy x-ray absorptiometry.
- ➢ REE(resting energy expenditure) is measured using indirect calorimetry. REE can now can be measured by using hand-held instruments.

4.2 Nutritional status assessment is based mainly on
- Dietary and fluid intake
- Clinical assessment
- Anthropometry and
- Biochemistry

Medical status can be assessed based on the extent and depth of burn, functional status of organs, and presence of pre-existing diseases like diabetes mellitus, presence of sepsis, hydration and the medications like inotropes. Anthropometric measurements may be difficult due to burn injuries with bandages, catheters, intravenous line and posture of critically ill patients. Measuring the Bed length, knee height and arm may help in height measurement. From the calculated BMI, the percentage of weight loss and percentage of height loss may be calculated.

4.3 Nutritional assessment includes
- ❖ Height and pre-burn weight
- ❖ Details of previous nutritional status
- ❖ Percentage of burn
- ❖ Gastrointestinal function
- ❖ Pain control
- ❖ Pre-existing medical conditions
- ❖ Usual diet and any specific dietary needs

Nutritional assessment history taking is in relation to
- ➢ Poor per oral intake,
- ➢ Poor wound healing,
- ➢ Weakness - malaise,

- Weight change over 1 month and 6 months (%)
- Dietary intake change (duration, type)
- GI symptoms > 2 weeks (nausea, vomiting, diarrhea, anorexia)
- Functional capacity (duration, type).
- Physical examination must assess > 10% (Ideal Body Weight) weight loss leading to malnutrition, muscle wasting, decreased strength (muscle function tests), ankle edema, sacral edema, ascites, triceps skin fold, mid-arm circumference measurements and height index.

4.4 Laboratory

- Albumin (t1/2: 18-21 days): normal > 3.5-4.0 g/dl; mild depletion → 3.0-3.5 g/dl, moderate depletion → 2.5-3.0 g/dl, severe depletion → < 2.5 g/dl.
- Total Lymphocyte Count: normal > 2000-2200 cells/mm3; mild depletion → 1500-2000 /mm3, moderate depletion → 1000-1500 /mm3, severe depletion → < 1000 /mm3
- Transferrin (t1/2: 7-8 days): normal →200-340 mg/dl (2.0-3.4 g/l); mild depletion → 150-200 mg/dl, moderate depletion →100-150 mg/dl, severe depletion < 100 mg/dl
- Prealbumin (t1/2: 2 days): normal → 16-32 mg/dl
- Antigen Panels - Delayed Cutaneous Hypersensitivity (Candida, Mumps, Trichophyton, Streptokinase - Streptodarnase)
  Nitrogen Balance (24 hours) = (g Protein Intake)/6.25* - (UUN + 4) [monitor weekly] *Note 6.25 g of protein = 1 g of nitrogen
- Ideal Body Weight (IBW) Estimation Men → 48 kg + (2.7 x each inch over 5 feet); Women -> 45 kg + (2.3 x each inch over 5 feet)

4.1.2 Nutritional assessment in children

Children with burn injuries have unique nutritional assessment and treatment protocols. Special considerations in children are multi-factorial

- Physiology of fluid and electrolyte
- Special energy requirements
- Differences in various body proportions.
- Children have nearly three times the body surface area (BSA) to body mass ratio of adults
- Greater fluid loss
- Risk of hypothermia
- Children younger than two years lose more water and heat because of the very thin layer of skin.
- Non-shivering thermogesis in children increase the metabolic rate, oxygen consumption and lactate production.
- Difficulty in assessment of depth of burn in children.

4.1.3 Curreri junior formula

0-1 year	BMR + 15 Kcal/% burn
1-3 years	BMR + 25 Kcal/% burns
4-15 years	BMR + 40 Kcal/% burn

- SBI - Galveston revised formula (1-11 Years): Daily calorie requirement: 1800 Kcal/m2+1300 Kcal/m2 BSAB.
- Matsuda et al have suggested children with more than 10 % burn should be under a dietary regimen with non-protein to nitrogen ratio of 100:1 to achieve a positive nitrogen balance. This has a protein intake 20% carbohydrate provides 48% of total calories and fat provides the rest of the requirement.
- A child with burn injury needs twice the energy and protein compared to normal children.
- Requirements of Vitamins A, C and B group, and Iron, Zinc and copper are also increased and needs supplementation for children with greater than 15% burns

4.1.4 Common nutritional issues in children

- Pain
- Sedation
- Disruptions in normal feeding patterns
- Amount of time asleep
- Change /unfamiliar environment
- Burn injury to mouth and hands
- Fussy eating

4.1.5 Referral criteria to the dietitian

- Children with 10 % TBSA
- Burn to child < 1 year
- Burns involving the hands and mouth

4.1.6 Oral intake

- High energy food products
- Small and frequent amounts of high protein and high-energy food and drinks at regular intervals must be encouraged in children who can tolerate oral feeds.

4.1.7 Enteral feeding in children

Early enteral feeding is indicated in burn children with < 10 % of burns and cannot fulfill their nutritional requirements and in children with >15% of burns. Enteral feeding must be started within the first 24-48 hours of burn injury. Nasogastric feeds can be used for short term feeding. If the children do not tolerate the nasogastric tube, nasojejunal feeding may be considered. Feeding may be continuous using enteral feeding pump or as boluses during the day. PEG feeds are used for long term feeding and in severe burn injuries. Feeding should be continued until the child is able to take adequately or till the wounds are healed. The children are weighed twice weekly without wet dressings with the same scale to check the nutritional support is adequate. It is important to address to the psychological problems and some older children may need counseling to enable them to overcome the burn trauma and early return to school. Milk, traditionally an isocaloric-isoprotein, but a high fat diet, consisting of 44% fat, 42% carbohydrate and 14% protein, became standard of care for the pediatric burned patient. Although it was well tolerated, fat did not serve as the optimal energy source for these patients. There was continued protein degradation, and lean body mass gains paled in comparison with high carbohydrate diets – consisting of 3% fat, 15% protein and 82% carbohydrate.

The high carbohydrate diet helps in

- ✓ increased protein synthesis,
- ✓ increased effective endogenous insulin production and
- ✓ Improved lean body mass.

V. Mode of nutrition support

5.1 Enteral nutrition

Early Enteral Feeding (within the first 24-48 hours) is the preferred mode of artificial feeding over total parenteral nutrition (TPN), and should be maintained while patients remain in the flow or catabolic phase of their injury regardless of their state of oral intake.

Indicators of the flow phase include

- Tachycardia
- Hypertension
- Hyperventilation

5.2 Parenteral nutrition

- ✓ Peripheral
- ✓ Central
- ✓ Dual feeding

The following criteria are followed in Burn Nutrition

-Enteral/parenteral

-Enteral/oral

-Peri and intra-operative nutrition support in adults

-Post-operative nutritional support

-Immune-nutrition.

5.3 Peripheral Parenteral Nutrition

Indications: Patients who Require < 10 days of nutritional supplementation and who can't consume these calories via oral or enteral route. This can be used as bridge to maintain adequate caloric intake while advancing enteral or oral feeds.

Components: IV Dextrose - up to D10 final concentration; (Note - 42 mls/hr. → 1 liter/day, 84 mls/ hr. → 2 liters/day, 125 mls/hr. → 3 liters/day

Protein - up to 3.5% amino acid concentration

Fat - up to 20% Intralipids, provides higher % of caloric intake

Maximum milliosmols permitted is 900. Thrombophlebitis can be prevented with Heparin 1000 units/liter and Hydrocortisone 5-10 mg/liter.

VI. Nutritional supplement

Various enteral supplements have been used to maintain nutritional status in patients with severe burn injuries. Standard polymeric feedings remain common practice in severe burns help

- wound healing and
- Lean body mass when energy and protein intakes are sufficient.
- cost
- they are well tolerated

6.1. **Essential Amino acids**: The Gut is recognized as an immune regulating organ, several key nutrients given enterally alter the physiological processes in response to injury in a favorable direction. Most specialty formulas that are of interest in burn nutrition have wound healing and/or immune enhancing properties. Essential amino acids glutamine and arginine are two important constituents of nutritional supplement formulas. Glutamine with two amine groups functions as a nitrogen shuttle, carrying nitrogen for purine and pyrimidine synthesis. Glutamine serves as a primary oxidative fuel source for rapidly dividing cells, including the enterocyte. As a precursor to glutathione, a potent antioxidant, glutamine participates in reducing oxidative damage [17]. Glutamine supplementation in burn injury has shown moderate benefit. The effect of glutamine supplementation (0.6 g/kg) on protein economy showed that a glutamine-enriched diet had a similar effect on protein turnover and breakdown as a mixture of essential amino acids [18]. Glutamine supplementation resulted in decreased muscle protein breakdown (as indicated by 3-methyl-histidine) and improved wound healing when fed enterally. Other clinical benefits of glutamine supplementation in burn patients include reductions in infection rate, length of stay, cost, and mortality[19,20]. Glutamine supplementation is relatively safe, making it a reasonable consideration for practice in this population

Treatment with alanyl-glutamine (0.35 g/kg/day) Zhou et al, 2003

- Restores plasma glutamine concentration
- Reduces gut permeability
- Depressed plasma endotoxin level
- Reduction in the length of hospitalization and
- Lower costs.

Stress-induced depletion of arginine in tissue pools suggests that it is semi-essential after burn. Increased extra hepatic uptake of arginine contributes to accelerated urea production in burn patients further exacerbating its losses from the body. This is concerning given arginine's role in wound healing (as a stimulant to growth hormone) and immunity through the nitric oxide pathway [21]. Unfortunately, uncontrolled production of nitric oxide can also be detrimental, and may have contributed to adverse clinical outcomes particularly in patients who are septic [22]. Conversely, the possible benefit of arginine in wound healing can especially be realized in malnourished patients, or patients who are not metabolically stressed, suggesting a role in the burn population.[23] Further studies are needed to determine safe dosing for the more critically ill patient.

For short-term (<10 days) parenteral nutrition (PN) withhold entirely from using lipid emulsions.[24] For patients needing longer PN periods (>10 days) use 0.5–1 g fat/kg/d, withholding administration to once or twice weekly based on individual assessment of benefits and safety.[25]. A non-dietary fat calorie is also considered.

Propofol is used as a Patient-controlled sedation and analgesia. Propofol affects the total amount of fat calories administered in a given day. A 1% propofol solution has the same caloric value of a 10% intralipid emulsion (1.1 kcal/mL, 440 kcal in a 400-mL infusion) and may lead to significant metabolic alterations. Serum triglyceride concentrations should be monitored in patients receiving such infusions and caloric intake corrected accordingly. One should also consider the types of dietary fat administered, as these are potentially as important as their amounts. The use of diets enriched with nutrients such as Use of arginine and ω-3 fatty acids has been found to be beneficial in patients with >30% TBSA third-degree burns.[26] Fatty acids are metabolized to proinflammatory cytokines, which may facilitate inflammation, diets high in ω-3 fatty acids have been associated with improved outcomes, attenuated inflammatory response, and reduced incidence of hyperglycemia.[27,28,29]

Patients with burn injuries develop marked energy deficits and suffer nutritional related complications within 7 to 10 days of burn injury. Also burn injury is associated with an obligatory lean body mass turnover which cannot be reversed with excessive caloric support. Hart et al found resting energy expenditure (REE) correlated directly with burn size, sepsis, and ventilator support and muscle protein catabolism. Noordenbos et al. concluded that even early excision and grafting of the burn wound, coupled with aggressive enteral nutrition

with a high protein diet failed to prevent the hyper metabolism associated with thermal injury. At the same time overfeeding put a burden on the respiratory system, higher rate of systemic infection, steatosis of the liver and an increase in total body fat.

Numerous reports have documented a wide range of energy expenditures in hyper metabolic burn patients, rendering use of standardized formulas to determine energy needs of limited value. Dickerson et al. evaluated the bias and precision of 46 standardized formulas published from 1953 to 2000 for estimating resting energy expenditure (REE) of thermally injured patients. The pre-1980s methods more frequently over-predicted MEE compared with the 1990 to 2000 studies.

The most precise unbiased methods for estimating MEE are
1. Milner (1994), at a mean error of 16 percent (CI of 10 to 22 percent):6(BMR x 24 x BSA) x (0.274 + 0.0079 x BSAB - 0.004 x DPB) + (BMR x 24 x BSA)
2. Zawacki (1970) with a mean error of 16 percent (CI of 9 to 23 percent):7(1440 kcal/m2/day)
3. Xie (1993) at a mean error of 18 percent (CI of 12 to 24 percent):8(1000 kcal/m2/day) + 25 x BSAB)
Where:

BMR	=	basal	metabolic	rate	in	kcal/meter	squared/hour			
BSA	=	body	surface	area	in	meters	squared			
BSAB	=	percent	body	surface	area	burn				
DPB	=	post	burn	days						
CI	= confidence interval									

Thermally injured patients are with variable hyper metabolic state and their energy requirements should be based on frequent measurements of the REE using indirect calorimetry. REE can be easily measured using hand-held, self-calibrating indirect calorimeters. Two hand-held devices are currently commercially available:

- The MedGem by Healthetech
- The ReeVue by Korr. The formulas above should only be utilized only if indirect calorimetry is not available.

6.2 Substrate Requirements

6.2.1 Carbohydrates:

The major energy source for burn patients should be carbohydrates which

- serve as fuel for wound healing,
- provide glucose for metabolic pathways,
- spare the amino acids needed for catabolic burn patients and
- Are helpful in wound healing and has a protein-sparing effect.

Minimum baseline adult requirements of carbohydrates is 2 g/kg/d [30] and the maximum rate at which glucose can be assimilated in severely burned patients is up-to 7 g/kg/d [31,32,33]. Severely burned patients may very well have greater needs than those that can safely be supplied. Inadequate carbohydrate delivery that fails to meet the increased demands of burned patients may lead to uncontrolled protein catabolism, whereas supplementation in excess of utilization leads to hyperglycemia, conversion of glucose into fat, glycosuria, polyuria, dehydration, and respiratory problems. Insulin therapy in burned patients stimulates muscle protein synthesis, increases lean body mass, and is associated with improved wound healing, without increasing hepatic triglyceride production[34,35]. Severely burned patients demonstrate improved donor site wound healing after receiving 7 days of continuous infusion of insulin and glucose titrated to maintain euglycemia and plasma insulin concentrations of 400–900 μU/m[36] .In addition, patients receiving a high-carbohydrate, high-protein enteral formula and insulin infused at 1.5 μU/kg/min to maintain blood glucose levels between 100 and 140 mg/dL significantly improved lean body mass, bone mineral density, and decreased length of stay during the acute hospitalization[37].Administration of carbohydrates should be closely monitored as hypoglycemia can quickly lead to increased morbidity and mortality.

6.2.2 Estimation of protein needs

Proteolysis is another hallmark of the hyper metabolic response after severe burn injury. Protein catabolism in burn patients can exceed 150 grams/day, or almost a half-pound of skeletal muscle Protein deficiency occurs in severe burns due to loss of amino acids from muscle to accommodate amino acid needs for

- Tissue repair
- Acute-phase protein production
- Cellular immunity

- Gluconeogenesis [38]

There is a need to provide sufficient quantity and quality of amino acids in the diet to avoid depletion of skeletal muscle amino acid and provide for sufficient proteins synthesis for optimal wound healing and immune function. Protein dynamic studies provide the actual rates of both protein synthesis and protein breakdown [39].

6.2.3 Fats

The hyper metabolic, catabolic response to severe burns suppresses lipolysis and limits the extent to which lipids can be utilized for energy. Thus, fat should comprise no more than about 30% of non-protein calories, or about 1 gm/kg/day of intravenous lipids in TPN. The composition of administered fat is more important than the quantity. Most common lipid sources contain omega-6 free fatty acids (ω-6 FFA's) such as linoleic acid which are metabolized through synthesis of arachidonic acid, a precursor of pro-inflammatory cytokines such as Prostaglandin E2. Omega-3 fatty acids (ω-3 FFA's) are metabolized without provoking pro-inflammatory compounds. Diets high in ω-3 FFA's have been associated with an improved inflammatory response, improved outcomes, and reduced incidences of hyperglycemia.

Immediately following burn injury

- There is an increase in peripheral fat breakdown
- Increase in utilization of fat by the liver
- During hyper metabolic response, only 30% of the available free fatty acid undergoes degradation. The remaining undergoes reesterification with accumulation in the liver [40].

6.2.4 Micronutrient requirements

Patients with major burns have increased micronutrients requirements (i.e. trace elements and vitamins) due to their hyper metabolic response, to their wound healing requirements and to the important cutaneous exudative losses which characterize burns with open wounds. An intense oxidative stress is associated with burn injury which in combination with the intense inflammatory response contributes to the exhaustion of the endogenous antioxidant defenses which are highly dependent on micronutrients[41] The delivery of standard micronutrient intakes invariably results in clinical deficiency syndromes that become clinically visible by the end of the first month with delayed wound healing and infectious complications. The biological deficits are detectable by the end of the first week itself. The industrial enteral feeding solutions or the parenteral multivitamin and multi-trace element solutions are insufficient to cover the elevated major burn patients' requirements. The substitution of the losses and the increased nutritional requirements cannot be covered by the enteral route (due to absorption antagonism and competition between trace elements delivered in supra-nutritional doses).Regarding vitamin requirements, the clinical studies have mainly investigated vitamin B, C, E and D[42]. Additional thiamin intake normalizes lactate and pyruvate metabolism.[43] Clinical benefits have been shown with reduction of oxidative stress, and improved wound healing using doses of vitamin C and E 1.5 to 3 times higher than recommended daily intakes in children and adults.[44] The results are not as clear with vitamin D, which is deficient and contributes to the development of osteoporosis in patients with major burns. Standard intakes are obviously insufficient. 400 IU/day of vitamin D2 does not improve bone density [45].The nutritional requirements for vitamin C have been shown to remain elevated during the entire acute phase (0.5 to 1 g/day). Recently Vitamin C administered at very high early doses (0.66 mg/kg/h for 24 h) has been proved to stabilize the endothelium,thereby reducing the capillary leak and reduce the fluid resuscitation requirements by about 30 %[46]. This serves as an adjunctive therapy to resuscitation.

Trace elements: Copper (Cu), selenium (Se) and zinc (Zn) have been shown to be particularly important in immunity and wound healing of both adult and pediatric burn casualties. Copper (Cu), selenium (Se) and zinc (Zn) are lost in large quantities with the exudative losses, the losses persisting as long as the burns wound are not closed[47]. The duration for elevated substitution requirements is therefore determined by the burn surface area as follows : 7 to 8 days for burns involving 20 to 40%, 2 weeks with burns 40 to 60% and 30 days for burns > 60% TBSA. The early admission is associated with reduction of lipid peroxidation, improved antioxidant defenses, improved immunity with lower incidence of infectious complications, improved wound healing and shorter ICU stay[48,49] Competition between Cu and Zn for intestinal absorption (metallothionein transporter) makes the administration of enteral substitution doses inefficient. The same considerations apply to children using substitution doses calculated at the prorate of their body weight or body surface [50].Copper is important for maturation of collagen. Selenium is essential for glutathione peroxidase activity and Zinc for immunity and cell replication. Decreased levels of Vitamins A, C, and D, iron, zinc, and selenium have been implicated in decreased wound healing and immune dysfunction post severe burn injury.

6.3 Probiotics:

The concept of probiotics was introduced by Metchnikoff (Russian Scientist). FAO/WHO defines Probiotics as Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host.

6 .4 "Immune-enhancing" diets (IEDs)

Immune-enhancing diets (IEDs) are aimed at improving outcomes in patients suffering trauma and infection. IED enhanced with omega-3 fatty acids, arginine, and RNA are used. Feedings were begun within 48 hours of injury, and continued until patients supported themselves with oral intake. Administration of an IED has no clear advantages over the use of less expensive high-protein enteral nutrition in burn patients.

6.5 Fat in the nutrition support

The optimal amount and type of fat in the nutrition support of burned patients have not been determined. Low-fat nutritional solutions, with or without fish oil, shows very little difference compared to the conventional fat formulae on protein metabolism, morbidity, and length of care in severely burned adults. Low-fat with fish oil was given for 30 days. Nitrogen balance, urinary 3-methylhistidine excretion, urinary cortisol, and clinical status were measured daily. Corticosteroid-binding globulin and total and free serum cortisol were measured every 3 days. The following observations were made

- Patients on low-fat support had fewer complications of pneumonia, better respiratory and nutrition status, and shorter time to healing of burn wounds.
- There was no difference in nitrogen balance , 3-methylhistidine excretion was higher and serum free cortisol level was found to be lower in low-fat-fed patients
- Low-fat nutrition support decreases infectious morbidity and shortens length of hospital stay in burn patients.
- Fish oil does not seem to add clinical benefit to low-fat solutions.
- Nutritional intervention modulates cortisol-binding globulin and the concentration of free circulating cortisol after a severe stress [51]

VII. Non-nutritional management of hyper metabolism

In addition to the various nutritional support, marked benefits have been recorded with the Non-Nutritional measures in the management of Burn patients which include

- ✓ Maintenance of nursing environment at 28-30 degree C
- ✓ Early excision and coverage of deep wounds
- ✓ Agents to stimulate protein synthesis (non-selective beta-blockers,oxandrolone especially in children)
- ✓ Pain control
- ✓ Early exercise therapy
- ✓ Propranolol used in a dose to reduce the basal heart rate by 20% decreases the cytokines or stress hormones release
- ✓ Oxandrolone[52,53] administered at 10mg/12h in adults and at 0.1mg/kg/12h in children has the following effects

  Decrease in mortality
  Reduced length of hospital stay
  Positive beneficial effects on weight loss, protein catabolism, healing time and on bone metabolism

The drugs can be administered at the end of resuscitation phase. Propranolol is administered at the end of one week and oxandrolone after 10 days post-burn.

7.1 Pharmacologic Modalities

7.1.1 Insulin-like Growth Factor 1 is also called Somatomedin C or IGF-1. It is a growth factor which is very closely related to insulin. It is an important factor in childhood growth and is highly anabolic in adults and highly anti-catabolic. It also

- Promotes growth of new muscle cell
- Increases connective tissue production
- Improves collagen formation
- bone production and repair
- aids in cartilage repair.

7.1.2 Recombinant human growth hormone

Recombinant human growth hormone is not recommended in adult burn patients because of the adverse effect of hyperglycemia. In burn children it is a good substitute for GH deficiency with growth impairment. It is

administered at a dose of 0.05-0.2 mg/kg/day for a period of one year has good donor site healing, reduces hyper metabolism and growth deficit is corrected. [54]

7.1.3 Propranolol is administered orally with a dose of 1mg/kg/day in divided doses and adjusted to decrease the resting heart rate by 20% of the baseline value.

- Propranolol decreases energy expenditure
- Decreases muscle protein catabolism
- Improves healing process and decrease wound-healing time

7.1.4 Oxandrolone; Burn-induced catabolism is characterized by accelerated protein breakdown and decreased protein synthesis. Oxandrolone at a dose of 0.1mg/kg by mouth twice daily has been proved to increased efficiency on protein synthesis.

VIII. Attenuation Of Hyperglycemia In Post-Burn Patients

8.1 Methods to reduce hyper metabolism in burns patients:

- ✓ Insulin
- ✓ Metformin
- ✓ Glucagon-Like-Peptide (GLP)-1 and PPAR- agonists (e.g., pioglitazone, thioglitazones) or the combination of various anti-diabetic drugs. PPAR- agonists, such as fenofibrate, have been shown to improve insulin sensitivity in patients with diabetes.

8.1.1.propranolol: Hart et al, concluded propranolol was a strongly anabolic drug during the early, hyper catabolic period after burns. With or without growth hormones propranolol had effect on tachycardia, energy expenditure and improved the net balance of muscle protein synthesis and breakdown in children with over 40% TBSA burn. Morio et al, concluded that propranolol reduces the rate of hepatic fat accumulation.

8.1.2 Insulin: Thomas et al. administered continuous infusions of insulin to maintain blood glucose between 100 and 140 mg/dL in a randomized controlled clinical trial of 18 children with major burns. They found insulin-treated patients had improved lean body mass, less muscle wasting, and reduced length of hospital stay, compared to controls. Van den Berghe et al, confirmed the importance of close control of blood glucose level by use of insulin to minimize the septic complications

8.1.3 Anabolic Steroids: Testosterone and analogs like oxandrolone, have demonstrated limited benefits in the burn patient.

IX. Nutrition assessment tools

9.1 Nutrition assessment tools

commonly used tools for screening are

- Malnutrition Universal Screening Tool (MUST),
- Subjective Global Assessment (SGA),
- Mini Nutritional Assessment (MNA),
- Malnutrition Screening Tool (MST).
- Nutritional Risks Screening 2002 (NRS-2002),
- Nutrition Risk Index (NRI) and the
- Short Nutritional Assessment Questionnaire (SNAQ).

The tool selected must be validated for the type of population and the type of care setting for the selected screening [55]

X. Nutritional, immunological and microbiological profiles of burn patients

10.1.1. Patient Monitoring

- ✓ Fluid Balance
- ✓ Blood Glucose Levels
- ✓ Observations (T/RR/HR/BP)
- ✓ Gastric Residuals
- ✓ Bowels
- ✓ Healing rate
- ✓ Functional parameters
- ✓ Nutrient intake (enteral, parenteral &oral)

- ✓ Weight measurement every week (without dressings)

10.1.2. Parameter Suggested Frequency
- ➢ Fluid Balance Daily during Acute phase and then PRN
- ➢ Blood Glucose Levels Daily while Acute then PRN
- ➢ Monitor vitals (T/RR/HR/BP) Daily while Acute then PRN
- ➢ Gastric Residuals Daily while Acute then PRN
- ➢ Bowels Daily while Acute then PRN
- ➢ Healing rate Daily while Acute then PRN
- ➢ Functional parameters Daily while Acute then PRN
- ➢ Nutrient intake (enteral, parenteral & oral)
- ➢ Daily while Acute then PRN
- ➢ Weight Weekly (without dressings)

10.1.3 Biochemical Monitoring: Parameter Suggested Frequency
- ✓ Urea & Electrolytes Daily
- ✓ Serum Ca, PO4, Mg Every second Day
- ✓ ABG's Every second Day
- ✓ Nutritional Markers- ie pre-albumin Twice Weekly
- ✓ Inflammatory markers (CRP) Twice Weekly
- ✓ LFT's Twice Weekly
- ✓ Definitive guidelines for the monitoring of serum Copper, Zinc & Selenium have not been determined. For BSA > 20% the UK Burns interest group recommend monitoring plasma levels at days 7,14,21.

10.2.1 Gastric residual volume is always used together with clinical assessments. With GRV (gastric residual volume) > 500 ml Withhold feeds and reassess the patient's tolerance.With GRV between 200–500 ml maintain feeding and Careful bedside evaluation is a must .With GRV < 200 ml maintain feeding. (Gonzalez et al 2008) [56,57] Estimation of various negative and positive phase proteins are crucial to the estimation of nutritional status. Negative acute phase proteins are albumin; transferrin, pre-albumin and retinol-binding protein (RBP) and positive acute phase proteins are C-reactive protein (CRP), ceruloplasmin and various others [58]. Nitrogen balance assessment is the only biochemical parameter that truly reflects visceral and somatic protein pools.[59].

10.2.2 Albumin is a poor indicator of nutritional status in critically ill patients. It is a sensitive indicator of mortality and morbidity and length of hospitalization [60, 61] Albumin can be used as a marker of injury and metabolic stress during the acute phase response. In trauma patients an albumin of ≤ 26 g/L is a significant independent predictor of mortality and morbidity. Combination of a low albumin level and increased age was the most predictive of infection and mortality.[62].

10.2.3 Pre-albumin correlates with short term changes in PEM and is a marker of protein intake. Pre-albumin does not respond sensitively to nutrition support particularly during the early period. It is a good marker of the systemic inflammatory response of the acute phase response due to the delayed return to anabolic status [63]. Only in the presence of stable inflammatory parameters does pre-albumin reflect adequacy of nutrition support [64] . The same difficulties emerged in interpretation of study on retinol-binding protein [65].Measurement of pre-albumin and acute phase response protein on a bi-weekly basis provides information about metabolic status [66]. Pro-calcitonin is an indicator of infections, SIRS, sepsis and MOF. Insulin-like growth factor (IGF) is particularly sensitive to protein intake, responds rapidly to protein energy status [67]. The disadvantage is that it is very expensive. The most commonly used somatic protein status indicators include urinary creatinine, the creatinine-height index. Creatinine derived from dietary sources can not be distinguished from endogenously produced creatinine and 3-methylhistidine excretion. The body's somatic protein pool is directly proportional to the amount of creatinine excreted. 3-Methylhistidine assessment is a labor intensive procedure and it is difficult to assess the amount supplied by the diet.

XI. Overfeeding

The overfeeding of severely burned patients can lead to major complications. Overfeeding with carbohydrates results in
- ✓ elevated respiratory quotients
- ✓ increased fat synthesis
- ✓ Increased CO2 elimination
- ✓ Ventilated patients become more difficult to manage and difficult to wean from ventilator support.

- ✓ Excess carbohydrate or fat can also lead to fat deposition in the liver.

Excess protein replacement leads to elevated blood urea nitrogen (BUN), which could lead to acute renal failure, increased propensity to sepsis, and death. Overfeeding can lead to hyperglycemia, which is already present in up to 90% of all critically ill patients, leading to increased morbidity and mortality. This iatrogenic hyperglycemia is even harder to treat as both endogenous and exogenous insulin effects are often countered by the surge of catabolic hormones. These complications are not specific to parenteral or enteral feedings, but are manifestations of attempts to over-compensate for the tremendous losses suffered by severely burned patients. Positive changes in body weight are among the best predictors of overall nutritional status. Significant weight loss, particularly rapid and unplanned, is a predictor of mortality. However, it should be noted that resuscitation and maintenance fluid increases may mask ongoing loss of lean body mass so that patients can suffer significant inanition and still weigh more than they did at the time of admission. In addition, fluid shifts associated with infections, ventilator support, hypoptroteinemia, and elevations in aldosterone and antidiuretic hormone lead to wide fluctuations in weight that have little to do with nutritional status. Judicious monitoring of long-term trends is paramount in the clinical management of severely burned patients. Determination of nitrogen balance, serum proteins, and abnormalities of immune function will also aid the assessment of nutritional supplementation post-burn. No single laboratory test is fully reliable in nutritional monitoring. So regular metabolic assessment is paramount in the ever-evolving physiologic response post-burn.

11.1 Over feeding in the burn patient causes
A) Hyperglycemia
B) Fatty liver
C) Respiratory insufficiency [68].

11.2 Excessive carbohydrate feeding leads to
- ➢ increased O2 Production
- ➢ Hyperglycemia
- ➢ Fatty liver

11.3 Excessive protein leads to
- ➢ Uremia
- ➢ Dehydration
- ➢ Metabolic acidosis

11.4. Excessive feeding with fat results in
- ✓ hypertriglyceridemia
- ✓ Compromised immunity [69].
- ✓ Hart et al concluded intakes beyond 1.2 times resting energy expenditure results in increased fat mass without changes in lean body mass.[70].

XII. Refeeding syndrome

12.1 Refeeding syndrome is characterized by
- Hypophosphatemia
- Abnormal fluid and sodium balance
- Thiamin deficiency
- Hypokalemia
- Hypomagnesaemia [71]
- Changes in blood glucose, protein and fat metabolism.

XIII. Early enteral feeding

13.1 Energy and macronutrient support

Energy need is calculated as 5 calories per kilogram in adults and 25 calories per kilogram plus 40 calories per each percent of burn area. For children 1800 calories plus 2200 calories per m2 of burn area. Nutrition assessment is made for patients with more than 20%TBSA burns as they need individualized nutritional support.

13.2 High protein and high carbohydrate diet
- ➢ Patient must be hemodynamically stable (for prevention of bowel ischemia)
- ➢ Duodenal route is tolerated better

- TPN is not indicated since it does not prevent the catabolic response to burns Impairs immunity and impaired liver function.

High-carbohydrate, low-fat diets results in less proteolysis and improvement in lean body mass. High-carbohydrate diet has the complication of hyperglycemia. Insulin resistance is common part of hyper metabolic response that needs to be treated with insulin drip. Protein and fluid needs must also be considered carefully. Protein oxidation rates are 50% higher in burn patients, and protein needs are 1.5 to 2.0 grams/kg. Water loss can be as much as 4 liters/m2/day, and fluids must be administered in the range of 30 to 50 ml/hour depending on urine output.

13.3. Micronutrient Support

Vitamin A and E and carotenoids: Vitamin E treatment reduces lipid peroxide levels in burn patients. Vitamin D allowance of 400 IU per day is required. With major burns trace elements Zinc and Selenium and copper also suffer acute deficiencies, partly because of large exudative losses through the burned areas. [72] A lack of selenium and zinc can exacerbate poor immunity, and burns are the second–leading cause of immunodeficiency, after HIV infection. Although a role for free radicals and lipid peroxides in burn trauma has been established [73] Little research has been done on the effects of antioxidant supplements in human burn injury. Addition of selenium, zinc, and copper to a standard trace element formula and enteral nutrition is associated with a significant decrease in the number of bronchopneumonia infections and with a shorter hospital stay.

XIV. Formulas for Nutritional Management

Formulas must be the guidelines and reassessment must be done on a regular basis. The hyper metabolic phase can last for three weeks. The nutrition has to be adjusted according to the requirement to avoid overfeeding. The following factors are considered to calculate the requirements

- ✧ use of ideal body weight
- ✧ reassessing as wounds are closed and healed
- ✧ ensuring at least twice weekly re-evaluation
- ✧ consider graft mesh size
- ✧ Consider the changes of physiotherapy and occupational therapy using the activity factors.

14.1 Toronto Formula:

The **Toronto Formula** is useful in the acute stages of burn injury. This must be assessed and adjusted with changes in the clinical parameters.

For all patients: REE (kcal) = - 4343 + (10.5 x TBSA burned) + (0.23 x kcals) + (0.84 x Harris Benedict) + (114 x T (degree C)) - (4.5 x days post-burn)

TBSA = total body surface area burned;

Kcals = calorie intake in past 24 hours;

Harris Benedict = basal requirements in calories using the Harris Benedict equation with no stress factors or activity factors;

T = body temperature in degrees Celsius;

Days post-burn = the number of days after the burn injury is sustained using the day itself as day zero.

There are no activity factors for non-ventilated patients.

14.2 Modified Harris Benedict Equation:

The **Modified Harris Benedict** and **Modified Schofield [74]** have also been used with patients with burn injury. Ongoing monitoring and assessment are still required.

Male: BEE (kJ) = 278 + (57.5 x kg Wt.) + (20.9 x cm Ht) – (28.3 x age)

Female: BEE (kJ) = 2741 + (40 x kg Wt.) + (7.7 x cm Ht) – (19.6 x age)

EER = BEE x IF

Injury Factor (IF):

% Burn	**<10**	**11-20**	**21-30**	**31-50**	**50+**
1.1.1.1.1.1	**1.2**	1.3	1.5	1.8	2.0

These are the injury factors commonly used in the hospitals of the NSW Severe Burns Hospital.

14.3 Modified Schofield Equation:

FEMALE Kcal/d BMR		Male Kcal/d BMR	
15-18 years	13.3W + 690	15-18 years	17.6+656
18-30 years	14.8W + 485	18-30 years	15.0W+690
30-60 years	8.1W + 842	30-60 years	11.4W+870
Over 60 years	9.0W + 656	Over 60 years	11.7W + 585

W = weight in kg

EER = BMR x IF x AF
Injury Factor (IF)
Up to 10% burn 1.0-1.1
10-25% 1.1-1.3
25-90% 1.2-1.7 these injury factors appear to be based on expert opinion or consensus only.

Activity Factor (AF) – including diet induced thermogenesis
Bed bound immobile : 1.1
Bed bound mobile/ sitting : 1.15-1.2
Mobile onward : 1.25

14.4 Ireton-Jones Equation is used in the Intensive Care setting

For spontaneously breathing patients:
EEE (kcal) = 629 – 11(A) + 25(W) – 609(O)
Where EEE = estimated energy expenditure;
A = age in yrs.,
W = weight in kg,
O = presence of obesity > 30% above IBW: 0 = absent; 1 = present

Ventilator-dependent patients:
EEE (kcal) = 1784 – 11A + 5W + 244G + 239T + 804B
Where A = age in yrs.,
W = weight in kg,
G = gender: 0=female, 1=male,
T = diagnosis of trauma: 0=absent; 1=present,
B=diagnosis of burn: 0=absent, 1=present.

14.5 The Curreri Formula [75] is well known to overestimate requirements. This may be due to advances in the medical management of burns which have reduced the hyper metabolism associated with a burn injury, e.g. early excision and grafting, wound dressings and environmental temperature control.

Curreri Formula: For all patients: **25kcal/kg actual BW + 40kcal/%TBSA burn.**

XV. Discussion

Using the GRADE methodology (Grade of Recommendation, Assessment, Development and Evaluation) to evaluate human burn clinical trials between 1979 and 2011 the following recommendations were made.

- Early enteral feeding,
- The elevated protein requirements (1.5-2 g/kg in adults, 3 g/kg in children),
- The limitation of glucose delivery to a maximum of 55% of energy and 5 mg/kg/h associated with moderate blood glucose (target ≤ 8 mmol/l) control by means of continuous infusion with insulin.
- To associate trace element and vitamin substitution early on, and
- To use non-nutritional strategies to attenuate hyper metabolism by pharmacological (propranolol, oxandrolone) and physical tools (early surgery and thermo-neutral room) during the first weeks after Injury.

Suggestion were made in the absence of indirect calorimetry, to use of the Toronto equation (Schoffield in children) for energy requirement determination (risk of overfeeding), and to maintain fat administration ≤ 30% of total energy delivery.

Manning recommends that "nutritional assessment should be repeated frequently in patients requiring prolonged nutritional support, to assess the adequacy of the support provided and to guide adjustments to the nutritional regimen"[76]. A recommendation can be made for the relative superiority of pre-albumin as a marker for the adequacy of nutritional support, there certainly are no data to suggest how often this laboratory parameter should be repeated and adjustments to the nutritional regimen based on the pre-albumin level or any other monitoring tool will improve in future.

XVI. Future Investigation

Much work remains to be done in the field of nutrition monitoring. Serum protein markers, due to their simplicity, ready availability, and relatively low cost, will likely remain the mainstay of nutritional monitoring tests in the future. Prospective randomized studies are needed to identify the optimal serum protein marker and the frequency with which it should be assayed. Most importantly, prospective studies are needed to determine whether changes in the nutritional prescription based on routine nutritional monitoring actually improve patient outcomes.

XVII. Conclusion

Severely burned patients have profound nutritional requirements secondary to the prolonged post-burn hyper metabolic, hyper catabolic response. Enteral nutritional support should be initiated early to optimize total burn care and decrease long-term morbidity. Early enteral feeding within the first 12 hours after injury, is an integral part of initial resuscitation of burn management. Nutritional requirement are higher than those of other critically ill patients. Weight-based formula are not accurate, as the requirements are changing constantly .Trace elements are lost early in the cutaneous exudative phase. Major Burn patients require a supra-nutritional amounts of Zinc, Copper and selenium. Non-nutritional therapies are essential to reduce the hyper metabolism and hyper catabolism. Neither non-pharmacologic nor pharmacologic strategies are sufficient to abate completely the catabolic response to severe burn injury. All therapeutic strategies have contributed to some extent to the improvements in morbidity and mortality. Early enteral nutrition has contributed to the significant decline in lean body mass loss of severely catabolic patients. Modulation of the hyper metabolic response is paramount in the optimal restoration of structure and function of severely burned patients and remains an elusive factor in the nutritional management. Despite the significant advances made in this area in the past few decade this remains to be still an incompletely fulfilled goal. Burn care and nutrition involves a teamwork involving various specialties. Patients and care providers must be educated continuously throughout all phases of recovery from admission. Updating knowledge on burn management and the dynamically changing nutritional care is essential for complete patient care. Infection control practices are essential for optimal results in patient recovery. Dietitian must attempt to identify the psychosocial factors, which impact the outcome of treatment of burn patients.

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