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Introduction to Burn Injury and its Nutritional Management

Burn injuries remain a serious problem in the United States. Approximately 45,000 burn patients are hospitalized here annually, six percent of whom will die because of their wounds or the associated complications (1). Burn injuries have a very unique pathophysiology as compared to other types of traumas. Major burn trauma can cause severe systemic alterations. Among the most serious of these is depression of immune system function. Impaired defense and large areas of necrotic tissue make burn patients especially susceptible to infection. Indeed, this is the most common and serious complication associated with burn injury, and is responsible for the associated high mortality rate (2).

The wound healing which follows burn injury requires huge amounts of energy. Glycogen stores are rapidly depleted in this hypermetabolic state, and the body soon begins to oxidize its own proteins to generate ATP. This hypercatabolism of protein is another of the most serious effects of burn injury. It is associated with large losses of lean body mass and an accompanying decrease in skeletal muscle function, leading to prolonged recovery time (3).

Traditional nutritional care of burn patients has focused almost solely on providing enough protein and caloric content to meet this increased metabolic demand and prevent protein hypercatabolism. This was accomplished with high-protein, high-calorie diets, which are still the standard protocol for recovering burn patients (2) However, as understanding of the intricacies of burn pathophysiology has become more sophisticated, precise supplementation of certain compounds has been attempted and shown to be effective in helping the healing process. A few of the recent developments in the nutritional care of burn patients are discussed below.

Ornithine a-ketoglutarate supplementation

Ornithine a-ketoglutarate (OKG) is a biological molecule which has been the focus of much recent attention because of its beneficial effects in wound healing and infection prevention in patients following burn injury and other trauma. Before it was used clinically, a number of studies characterized the metabolic properties of this molecule in normal and various pathological situations, providing a theoretical basis for its later use in burn recovery. Studies in the 1980's showed that OKG administration helped raise plasma amino acid levels back to normal levels following burn injury and seemed to slow protein hypercatabolism (4,5) The same group that made these discoveries later showed that OKG is a precursor for glutamine and arginine in healthy subjects (6).

The first prospective study regarding OKG's effects on clinical outcome for burn patients was published in 1999 (7). Sixty burn patients were divided into control and experimental groups. The diets of patients in the experimental group were supplemented with OKG. Clinical outcomes assessed included infectious complications, quality of wound healing, quality of skin graft adherence, and quality of re-epithelialization of the donor site. Nitrogen balance was also measured. The data showed no significant difference in the

number of infectious occurrences between the groups. However, the experimental group showed significant improvements in wound healing, skin graft adherence, and re-epithelialization of the donor site. They also achieved positive nitrogen balance significantly faster.

These results sound promising, but Coudray-Lucas et al. note a number of criticisms of this study. Notably, the control and experimental diets contained different amounts of nitrogen and the diets were administered to different patients by either an oral or enteral route. Also, the study was not double-blind.⁸ Coudray Lucas et al. published their own clinical study regarding OKG supplementation in the diets of burn patients a year later (8). This study was double-blind, used a control diet isonitrogenous to the experimental diet, and used only nasogastric enteral feeding. The results of this study were significant for decreased healing time in the experimental group. Also, there was no significant difference in the occurrence of adverse side effects to the diets between the two groups.

It has, therefore, been established that OKG supplementation aids in the healing of burn patients. It is believed to accomplish this by both decreasing protein hypercatabolism and increasing immune function (9). Much research is now being conducted to try to discern the exact mechanisms of these effects.

Immunonutrition

The concept of immunonutrition has developed relatively recently as a result of the explosion of knowledge in the field of immunology. Its main premise is that certain dietary components provide an immune-enhancing effect when they are included in portions relatively larger than in a normal diet. Nutrients on which there has been considerable focus include arginine, glutamine, nucleotides, and certain omega-3 fatty acids (10). These nutrients were originally studied separately and are now included together in immune-enhancing diets, or IEDs.

Numerous studies have attempted to determine the efficacy of IEDs in the recovery of surgery patients and certain groups of trauma patients. The conclusions show clear benefits to IED administration, although some data reveal that IEDs may actually be harmful to certain types of critically ill patients (11).

Recovering burn patients would seem an ideal population in which to test IEDs, since infectious complication is the leading cause of mortality following major burns. It is surprising, then, that only a few studies have dealt with the effects of administering IEDs to burn patients. The first such study was conducted by Gottschlich et al.⁽¹²⁾ This study divided fifty burn patients into three groups which received one of three different feeding regimens. They report a significant decrease in wound infection in the group that had been on Shriner's formula, a modified immune-enhancing formula which contained omega-3 fatty acids. There were also nearly statistically significant decreases in occurrences of pneumonia and total infection. However, this study has since been criticized for a number of reasons. First, it lacked the statistical power necessary to analyze the number of outcome variables measured. Second, one of the non-IED groups

had a significantly higher occurrence of smoke inhalation prior to treatment than did the other two groups, possibly predisposing them to worse clinical outcomes (13).

The next study regarding this topic was conducted by Saffle et al. (14) This study compared a number of outcome variables in two groups of recovering burn patients. The control group was fed Replete, a standard high-protein diet, while the experimental group received Impact, and IED enhanced with omega-3 fatty acids, arginine, and RNA. The groups were stratified according to total body surface area burn. The results showed no difference between the groups in occurrence of infection, length of hospitalization, mortality, number of days on ventilation, or hospital charges. The authors conclude that there is no advantage to administering burn patients an IED, especially since these diets are much more expensive than the standard high-protein diets traditionally given to burn patients. However, Martindale et al. noted a number of criticisms of this paper as well (13). Most significantly, analysis of the nutrient content of the two feeding formulas used shows that both have significant omega-3 fatty acid content, even though Impact does have more arginine and RNA than Replete. This could account for the lack of difference in outcomes reported among the two groups.

Supplementation of Trace Elements

There is increasing evidence, mostly coming from a team of researchers in Switzerland, to suggest that supplementing the diets of burn patients with certain trace elements can improve clinical outcome as well. It has long been noted that that thermal injury leads to abnormal metabolism of trace elements. Berger et al. first showed that large cutaneous losses of copper, selenium, and zinc occur in burn patients in the first week after their injuries (15,16). They were also the first group to study how supplementation of these elements in the diets of burn patients would affect recovery. Their most recent clinical study divided twenty burn patients into two groups (17). Both groups received a high-energy, high-protein enteral formula as well as standard amounts of trace elements. The experimental group also received additional supplements of copper, selenium, and zinc for 8 days following their injuries. Clinical outcome measures included length of stay in the burn unit and number of infectious complications.

The total number of infectious episodes was significantly lower for the supplement group. The difference was most striking with regard to pulmonary infections, of which the control group had fifteen and the supplement group had only three. The authors note that the decrease in pulmonary infection rate is of great significance clinically, since pneumonia is the most common infection in burn patients. Average hospital stay was almost two weeks shorter for the supplement group, although this result was not statistically significant. It is notable, however, that the supplement group, which had a greater mean total body area burn, required, on average, a shorter hospital stay than the control group. The decrease in length of stay in the ICU for patients who received the supplementation was statistically significant when the size of the burns were taken into account.

Research regarding the roles of selenium, copper, and zinc in immunity provides possible explanations for why supplementation of these elements helps in healing and defense against infection (17). Also, selenium is essential for the function of glutathione peroxidase, an enzyme which protects against oxidative damage by catalyzing the conversion of harmful peroxides into alcohols (18). Such anti-oxidant activity would be especially important in burn patients, who are producing many more free-radicals than normal in their hypermetabolic state.

The Future of Nutritional Care for Burn Patients

It is clear that there is much overlap among the actions of the various types of supplementation discussed above. For example, although selenium, copper, and zinc are not usually included in what are considered IEDs, the help they provide in promoting the healing of burn patients is due to an immune-enhancing effect. Also, OKG likely works at least in part by providing the body with glutamine and arginine, two compounds that have been determined to be immune-enhancing and are therefore included in many IEDs (3).

Traditional nutritional care for burn patients has focused mainly on providing for their energy and protein needs. However, it seems that in the future, their nutritional care will also be aimed at enhancing their bodies' own defense mechanisms and preventing the decline in immune function seen after burn injury. Additional research will have to be conducted before this is the case, though. First, questions regarding the efficacy of presently available IEDs in the burn population could be answered with a large, multi-centered study that uses a high-calorie, high-protein control diet. Because of evidence from animal models and other trauma populations, researchers are reservedly hopeful that such a study would show that present IEDs are beneficial for burn patients (13). Second, the potential roles of copper, zinc, and selenium in future IEDs should be evaluated, as there now seems to be solid evidence for their immune-enhancing effect. Further study with larger study sizes may need to precede such an evaluation, though. Third, a study should evaluate the efficacy of OKG supplementation versus glutamine/arginine supplementation. This would allow us to begin to understand whether OKG's beneficial effects are due to its conversion into these amino acids in the body or by some other unknown mechanism. The cost-effectiveness of all of these supplements would need to be thoroughly evaluated as well.

So then, while great progress has been made recently in this area, there is still much work to do. Also, it is certain that more potential ways to use nutrition as a means of improving the clinical outcome of burn patients will be hypothesized as we continue to broaden our understanding of the incredibly complex pathophysiology of burn.

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