

## Nutritional Care to Prevent and Heal Pressure Ulcers

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### Abstract

Pressure sores are a well-recognized problem, with an etiology that is multifactorial and not solely a consequence of pressure itself. Malnutrition is one of the factors involved, namely low calorie and protein intake. Mainly elderly patients, patients after hip fracture, but also patients after trauma, burns or extended surgery require additional nutritional support to reduce the possibility of pressure ulcers developing. Evidence has shown the efficacy of percutaneous endoscopic gastrostomy in elderly patients with malnutrition and dementia. Nutritional support should include sufficient calories, protein, fat, carbohydrates, vitamins and minerals. Arginine is the main amino acid required and is essential for collagen deposition and wound healing. Vitamin A and zinc should be added to nutritional support.

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The relationship between nutritional status and the development of pressure ulcers has scarcely been investigated. A pressure sore occurs when injury, mainly pressure, destroys tissue integrity. In this wound, thousands of cells will die of physical disruption, desiccation on exposure to air, and exposure to non-physiologic solutions. Macrophages play a key role in the recognition of injury. In addition, local ischemia and hypoxia are always present in the center of the wound and induce the production of lactate, which stimulates cell growth in wounds. Structural elements like collagen and proteoglycans are synthesized in the wound. Wound nutrition, like any massive reconstruction, uses a combination of *in situ* and remote synthesis.

Recently, several randomized studies on the effect of nutrition on pressure evolution were conducted in high risk patients, namely, the elderly, patients in intensive care units, and patients with spinal cord injury. The aim of the present review is to summarize advances in the field, with special attention to the substrate, vitamin and trace mineral both *in situ* and remote from the wound, and to outline current recommendations for the use of nutrients in the treatment of pressure ulcers.

### Nutritional intake and development of pressure ulcers

In a study conducted in a large teaching hospital, Perneger et al. [1] found 247 new pressure sores among 2,373 admissions (5.7/1,000 person-days). The risk increased with older age, higher Norton Pressure Ulcer Prediction Score, presence of hip fracture, post-surgical care, and nasogastric tube or intravenous nutrition.

Breslow et al. [2] compared tube-fed patients with and without pressure sores and noted that the patients with pressure sores were in poorer nutritional condition, as assessed by albumin level, despite their higher caloric intake (32 vs. 26 kcal/kg) and protein intake (1.4 vs. 0.9 g/kg). Furthermore, pressure sore surface correlated negatively with body mass index.

One of the best studies on nutritional intake in the elderly was conducted by Bourdel-Marchasson and co-workers [3] in 672 severely ill elderly patients (age over 65 years) from several centers. The patients were divided by caloric intake into two groups: 377 received the regular diet of 1,800 kcal/day (controls), and 295 received the regular diet plus two daily supplements of 200 kcal (study group). The study group was sicker than the controls, had a lower serum albumin level (30.7 vs. 32.5 g/dl), a higher Norton score and a lower Kuntzman Care Requirements Scale score. The cumulative incidence of pressure ulcers at 15 days was 47.2% in the control group and 40.6% in the nutritional intervention group. On statistical analysis, the independent baseline risk factors for pressure ulcer development were a high Norton score, a low albumin level, presence of lower limb fracture (relative risk 2.68,  $P < 0.001$ ), and inclusion in the control group (relative risk 1.57,  $P < 0.04$ ).

Green et al. [4] investigated a community sample of 175 elderly patients and found that those with pressure ulcers had a lower calorie intake (mean difference 185 kcal/day) and lower protein intake (mean difference 6.7 g/day), and most required assistance with eating. The difficulty in feeding the elderly was further stressed by Hartgrink et al. [5]. These authors reported that of 62 (out of 129) patients randomized for tube feeding, 25 tolerated the tube for 1 week and only 16 for 2 weeks. Though energy and protein intake were higher in the tube-fed group, no difference was found in the prevalence of pressure ulcers.

Allman and colleagues [6] evaluated the risk factors among 286 hospitalized patients with activity limitation and age above 55 years. They found an increased incidence of pressure ulcers in patients older than 75 years, with dry skin, non-blanchable erythema, depleted triceps skinfold, lymphopenia, and decrease in body weight below 58 kg. Breslow and Bergstrom [7] reached the same conclusions in cross-sectional studies focusing on nutritional risk factors that predict pressure ulcers in hospital. Low weight, low triceps skinfold measurement, low serum albumin, and inadequate energy and protein intake were associated with pressure ulcers.

Critically ill patients may be subject to pressure ulcers despite good nutritional support. Body mass loss seems to play a major

role in patients with spinal cord injury whose body mass index is one standard deviation below the mean, increasing the incidence of pressure ulcer to 33% [8]. In a study of 148 trauma patients, Watts et al. [9] found that 20% developed pressure ulcers, which were usually positional but also close to the cervical collar or the endotracheal tube. The risk was further increased in smokers and in patients with changes in collagen metabolism [10]. More than good nutrition, in critically ill patients, factors that affect ulcer development include norepinephrine infusion (odds 8.11), high severity score (odds 3.4), fecal incontinence, anemia, and prolonged hospital stay (odds 2.7) [11]. The best predictive tool for pressure sores in the intensive care unit is the Braden Scale [12].

### **Nutritional intake and healing of pressure ulcers**

Many factors related to the specific condition of the patient affect wound healing. Radiotherapy or chemotherapy in cancer patients may interfere with nutritional status, as can renal failure and the use of hemodialysis. Diabetes mellitus, inadequate tissue perfusion, impaired oxygen delivery, and edema due to systemic inflammatory response syndrome are also important factors that adversely affect the wound healing rate. Nevertheless, successful wound healing can be achieved in these patients, and is based, at least in part, on their intake of adequate proteins, nitric oxide, carbohydrates, fats, vitamins and minerals. This is possible only after the acute catabolic phase. During that acute phase, muscle atrophy is severe and seems to be secondary to increased proteolysis induced by the ATP-dependent ubiquitin-proteasome pathway [13]. Increased levels of ubiquitin-conjugated proteins, increases in mRNA levels for polyubiquitin, certain proteasome subunits and E2 14K are features found in most atrophying muscles studied so far [14]. When this process terminates, arginine administration is a significant factor for nitrogen retention.

### **Proteins**

The importance of protein in the healing process of pressure ulcers was emphasized by Breslow et al. [15]. In their study, 28 malnourished patients with a total of 33 truncal pressure ulcers were randomized to receive 24% protein or 14% protein liquid nutritional formulas. Patients who received the 24% protein formula exhibited a decrease in the pressure ulcer surface area ( $-4.2 \text{ cm}^2$ ,  $P < 0.02$ ). In contrast, in patients who received only 14% protein formula, the decrease in the pressure ulcer surface area was not significant. The change in total ulcer area correlated strongly with dietary protein intake and caloric intake. Therefore, the authors concluded that a high protein diet may enhance the healing process of pressure ulcers in malnourished patients.

Amino acids are essential for healing [16]. Methionine and cysteine improve the rate of fibroplasia and collagen synthesis. Arginine increases collagen deposition [17] and, as a precursor of proline and hydroxyproline, is necessary for the secretion of growth hormone [18]. It is a non-essential amino acid that may become conditionally essential during stress. Arginine is important for wound healing, as a substrate of the immune system, and is the precursor for nitric oxide synthesis. Nitric oxide regulates the flow through several important organs such as the liver, the gut, the

kidney and the heart especially during the periods of stress. Arginine is mainly synthesized in the kidney. In ischemia reperfusion injury, arginine reduces the injury and improves survival. In patients with burns it stimulates wound healing and improves immunologic function, and is therefore included as an "immunonutrient."

In a situation of stress, new pathways consume specific amino acids. Immune activation *increases* the demand for glutamine and arginine, acute phase protein synthesis affects the need for aromatic and sulphur amino acids, and peroxidative defenses require cysteine. The body protein mass becomes a source of substrate for healing. The liver has a major role as the supplier that converts the protein mass into glucose. Sustained synthesis, particularly during infection, requires a huge amount of energy. The mismatch between the altered needs and the available supply underlies the predisposition of the stressed patient to muscle protein loss and eventual malnutrition. Supplementation should prevent the early changes in metabolism and the later stages.

Nitric oxide derived from the oxidation of arginine and catalyzed by three nitric oxide synthetases triggers vasodilatation, angiogenesis and melanogenesis. The selective regulation of gene expression by NO may make the difference between successful healing and continued or uncontrolled inflammation [19]. Defects in NO synthesis have been found to be associated with hyperproliferative and inflammatory skin disease [20]. Stallmeyer et al. [21] studied the temporal expression of NO synthetase activity in acute wound healing with the use of polyvinylalcohol sponges. NO production reached a peak after 1–2 days, during the intense inflammation phases [21].

### **Carbohydrates and fat**

Carbohydrates provide energy for leukocytes and fibroblasts. Fibroblasts need glucose or fat to synthesize messenger RNA and DNA for replication and to form the high energy bonds required for amino acid transfer and protein synthesis. Fibroblasts, as well as epithelial and endothelial cells, migrate with this provision of energy. However, glycemia has to be controlled since persistent hyperglycemia impairs wound healing. Fat is also a source of energy: omega-6 fatty acids induce a stronger prostaglandin response whereas omega-3 fatty acids have a detrimental effect on wound healing [22].

### **Vitamins and trace elements**

Vitamin deficiency is common in critically ill and elderly patients, but the precise requirement is unknown. Vitamin A deficiency impairs epithelialization, the rate of collagen synthesis, the cross-linking of collagen, and humoral and cell-mediated immunity [23]. Vitamin A supplementation may prevent delayed wound healing in patients receiving steroids [24]. It seems to increase the number of macrophages in the wound and to stimulate epithelial cells [25].

Vitamin E, via its antioxidant and anti-inflammatory actions, may protect cells from free radical injury. However, no studies have investigated the benefits of vitamin E supplementation. In animals,

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NO = nitric oxide

vitamin E has been found to retard collagen synthesis, decrease wound tensile strength, and reduce the number of fibroblasts by inhibiting the inflammatory response [26,27].

Vitamin C is needed for hydroxylation of proline and lysine in collagen synthesis [28]. Supplementation is required for patients deficient in this vitamin [29]. In one study, 10 of 22 elderly patients with femoral neck fracture developed pressure ulcer. A comparison of the two groups yielded similar levels of zinc, albumin, hemoglobin and vitamins A and E, but lower concentrations of leukocyte vitamin C in the patients with ulcers [30]. In another study, 88 patients with pressure ulcers from 11 nursing homes were randomized to receive 1 g of vitamin C or 10 mg of ascorbic acid over 12 weeks. No differences in healing rates or wound survival were noted [31].

Finally, with regard to the trace elements, zinc is a co-factor for enzymes involved in the synthesis of DNA, RNA and proteins, and is required by all proliferating cells, including inflammatory cells, epithelial cells and fibroblasts. It is therefore assumed to be mandatory for the wound-healing process [32]. Low values are associated with delayed wound closure, decreased wound tensile strength, and suppressed inflammatory response. However, there are no studies indicating that zinc supplementation improves healing.

#### Modulators of nutrition

Growth factors, too, have recently gained much interest in the study of wound healing. Robson et al. [33] showed that the administration of most cytokines, but mainly platelet-derived growth factors, was very effective in healing small or moderate-sized pressure ulcers, thereby decreasing both the duration and cost of hospitalization. Further studies are required, however, to determine the role of these growth factors together with nutrients in the treatment of pressure sores.

#### Discussion

Pressure ulcers are a common finding in older persons and in acutely ill patients. Complications associated with pressure sores may include severe infection and even death. With the primary factor being pressure together with shearing forces, friction and moisture as well as immobility, a significant risk factor is nutritional status. The greater the protein calorie deficit, the higher the risk for developing pressure ulcer. Accordingly, prospective studies have shown that additional caloric and protein intake increases the prevention of pressure ulcer. When pressure ulcers do develop, the treatment should include adequate nutrition with a high protein diet, sufficient caloric intake according to Harris Benedict equations, as well as vitamin and trace element supplementation.

Many of the high risk patients are elderly patients hospitalized in nursing homes, and sometimes suffering from dementia. The introduction of a nasogastric tube for feeding poses an ethical dilemma. No prospective randomized study has demonstrated an advantage for nasogastric feeding in terms of reducing the incidence of aspiration, infection or pressure ulcer in these patients [34]. Moreover, Abuksis and associates [35] showed an increase in morbidity and mortality after percutaneous endoscopic gastro-

stomy in hospitalized patients with dementia as compared to residents of a nursing home. Clearly therefore, caution should be taken when considering this intervention.

#### Conclusion

Nutritional supplementation, including carbohydrates, fats and protein, may decrease the incidence of pressure ulcers in high risk patients. Arginine and vitamin A are also important in the wound-healing process. The modulation of nitric oxide, together with growth factors, may serve as a key therapy.

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