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Review Article

Various Diet on Immune and Nutrition of Gastrointestinal Surgical Patients

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Malnutrition is an important condition at the elective surgical patient. Malnutrition results in the dysfunction of immune system by impairing the function of neutrophils and lymphocytes. Following gastrointestinal surgical stress, patients experience some degree of immunosuppression, increasing their risk for acquired infectious morbidity and mortality. Immune and nutrition related with infection and hospital stay in elective gastrointestinal surgical patients. Several specific nutrients such as arginine, glutamine, omega-3 fatty acids, zinc, and vitamin D, influence immunological parameters in patients undergoing surgery in laboratory and clinical studies. In conclusion, immune and nutrition may decrease infectious complication rates. However, the treatment effect varies depending on the patient population and the intervention. Further research needs to define the underlying mechanism by which immune and nutrition may be harmful and to identify which products and which patients are associated with clinical benefit.

Key Words: Immune, Nutrition, Surgery

INTRODUCTION

Reduced food intake results in loss of fat, muscle, skin, and ultimately bone and viscera, with consequent weight loss and an increase in extracellular fluid volume.[1] Nutritional requirements fall as an individual's body mass decreases, probably reflecting more efficient utilization of ingested food and a reduction in work capacity at the cellular level. However, the combination of decreased tissue mass and reduction in work capacity impedes homeostatic responses to stressors such as surgery.[2] The surgical stress creates a hypermetabolic or catabolic state on the protein and energy requirements by. Macronutrients (fat, protein, and glycogen) are redistributed from the adipose tissue and skeletal muscle to more metabolically active tissues such as liver, bone, and visceral organs in the gastrointestinal surgical patients. The rate of development of malnutrition in these surgical patients is a function of their preexisting nutritional status and their degree of hypermetabolism.

Malnutrition causes lots of complications: infection, poor wound healing, pressure ulcers, overgrowth of bacteria in the gastrointestinal tract, and abnormal nutrient losses. Preoperative patients undergoing malnutrition have the risks of postoperative sepsis. Malnutrition is a severe condition at the patient undergoing elective surgery. Malnutrition leads to immune system dysfunction by impairing complement activation and production, bacterial opsonization, and the function of neutrophils, macrophages, and lymphocytes.[3]

Several specific nutrients such as arginine, glutamine, omega-3 fatty acids, zinc, and vitamin D, influence immunological parameters in patients

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undergoing surgery in the laboratory and clinical studies.[4-7] The purpose of this article is to systematically review the effects of various diet in the gastrointestinal surgical patients

NUTRITIONAL ISSUES SPECIFIC TO GASTROINTESTINAL SURGICAL PATIENTS

The patients who have undergone bowel surgery are at an immediate nutritional disadvantage since the optimal route of delivery of nutrients is believed to be the gut.[8] Of particular concern to patients undergoing surgery are the risks of postoperative sepsis and poor wound healing. Patients with protein energy malnutrition also have slower rates of wound healing. Some underfed patients had subnormal skin reactions to Candida and low levels of antibodies to various phytomitogens, suggesting that both humoral and cell mediated immunity are affected.[9]

Although a period of bowel rest may be appropriate in patients with disease that is severe enough to require gastrointestinal surgical intervention, the patients who are not able to take adequate oral nutrition and who have undernutrition or malnutrition should take several possible interventions. Earlier intervention may be important in patients who are malnourished at baseline, or who have a complicated postoperative course.

NUTRITIONAL ASSESSMENT IN THE GASTROINTESTINAL SURGICAL PATIENT

The nutritional assessment includes the past medical history, family history and social history: chronic medical illnesses (diabetes, inflammatory bowel disease), infections, recent hospitalizations, other past surgeries (particularly gastrointestinal surgery), use of substances (alcohol, tobacco, and other drugs), and current medications. Weight changes prior to the hospital stay should be assessed, as well as weight losses or gains during the hospitalization. In addition to vital signs and a general physical examination, the following specific areas and signs also should be assessed: height and weight, hair loss, xerosis, glossitis, bleeding or sores on the gums and oral mucosa, thyromegaly, edema, muscle wasting, peripheral neuropathy, ecchymoses, petechiae, pressure ulcers, assessment of gastrointestinal surgical wound healing, and signs of wound infection.

It is important to assess the protein status because of the close relationships between protein status and wound healing, and because of protein-calorie malnutrition in the gastrointestinal surgical patient. Protein status is affected by previous intake, muscle mass, duration of current illness, blood loss, wound healing, infections, and gastrointestinal absorption. Three serum measures (serum albumin, serum transferrin, serum prealbumin) of protein status are used for the patients with the current gastrointestinal surgical illness. These serum components are not directly associated with the nutritional status, but may rather reflect the degree of illness. The other laboratory tests which are glucose, BUN/creatinine, serum calcium, magnesium, and phosphorous may be helpful to assess overall clinical and volume status.

OUTCOMES WITH NUTRITIONAL INTERVENTION BY MACRONUTRIENTS

An early study suggested that parenteral nutrition

(PN) was beneficial in postoperative patients with upper gastrointestinal malignancies.[10-11] Several meta-analyses found that preoperative PN (13 randomized trials) decreased postoperative complications by 10 percent, while postoperative total parenteral nutrition (TPN) alone (8 randomized trials) resulted in a 10 percent increase in complication rates.[12] Another meta-analysis (26 randomized trials, although three were not in surgical patients) found that PN decreased hospital complications in studies where lipid-free solutions were used, and for patients who were malnourished.[13] Mortality and postoperative complications were decreased in a group of patients with gastrointestinal malignancies and weight loss who received ten days of preoperative TPN and nine days of postoperative TPN, compared to control patients who did not receive preoperative TPN and were only partially supplemented postoperatively.[14]

According to the randomized controlled trials of enteral nutrition (EN) in the perioperative period, there were no mortality differences among 3 groups: EN versus no artificial nutrition, EN versus PN, and volitional nutritional supplements (oral supplemental feeding) versus no artificial nutrition.[15] Compared to PN, EN recipients had fewer infections, fewer major complications, and shorter duration of hospitalization, but there was no significant impact on duration of hospitalization. Although they are the gastrointestinal surgical patients, EN is preferred to PN for meeting the nutritional needs of postoperative patients with functioning alimentary tracts.

IMMUNE AND NUTRITION

As the complex interactions between nutrition, mucosal barrier function, immunoregulation, and severe illness become clearer, unique forms of nutritional supplementation such as arginine, glutamine, omega-3 fatty acids, zinc, and vitamin D, might provide benefit for specific disease states. Meta-analyses have examined the benefits of supplementation with immune-enhancing nutrients in gastrointestinal surgical patients, and find some reduction in infectious complications and length of hospital stay, but find no benefit at the mortality.[16-17]

1. Arginine

Arginine acts on immunomodulatory actions by urea, ornithine which generates polyamines by the action of ornithine decarboxylase, and nitric oxide synthesis. Nitric oxide (NO) is synthesized from arginine in biologic systems is important in the maintenance of vascular tone, coagulation, the immune system, and the gastrointestinal tract.[18] NO is implicated as a factor in disease states as diverse as sepsis, hypertension, and cirrhosis. Sixty patients with gastrointestinal cancers were randomized to receive supplemental or standard diet via jejunostomy beginning on the first postoperative day (goal=25 kcal $\cdot kg^{-1} \cdot d^{-1}$) until hospital discharge.[19] Infectious wound complications occurred in 10% of the arginine 25 g/d supplemented group compared with 43% of the standard group. Arginine supplementation resulted in an enhanced response by peripheral blood lymphocytes to mitogens on the 7^{th} d after operation compared with the 1^{st} d, and was also associated with an increased number of circulating CD41 T cells. Arginine which stimulate the cellular defense system may reduce infectious complications in the elective surgical patient.[20] In contrast, the systemic inflammatory response may be deleterious in critically ill patients due to excess of nitric oxide, reactive oxygen species

(ROS), and excessive availability of lipid mediators.[20] The treatment effect of various nutrients will vary depending on the underlying pathophysiology of the host and whether the substrate influences cellular immune function and/or the synthesis of inflammatory mediators and/or the generation of ROS.

2. Glutamine

A randomized, double-blind controlled trial of glutamine (GLN) -supplemental PN in bone marrow transplant patients showed that fewer GLN-supplemented patients developed clinical infection and the incidence of microbial colonization was also significantly reduced.[21] Hospital stay was shortened in patients receiving glutamine supplementation compared with controls. In a study by van der Hulst et al.,[22] patients receiving GLN had maintained villus height and unchanged intestinal permeability. These effects on bowel mucosal growth and on bowel barrier function may greatly reduce the infections arising from the gut. T-cell DNA synthesis was increased in the GLN-supplemented patients when compared with preoperative values. However, GLN supplementation had no effect on IL-2, TNF, or IL-6 production. In another postoperative study, the GLN-fed patients revealed improved lymphocyte recovery by postoperative 6 days and enhanced polymorpholeukocytes cysteine-leukotriene levels when compared to controls.[23] The beneficial effects of GLN are to repair the epithelial layer and maintain bowel barrier function.

3. Omega-3 fatty acids

The omega-3 fatty acids diminish inflammatory and vascular responses because of their effects on cytokines and eicosanoid production. However, prospective randomized placebo-controlled clinical trials have not always been consistent and have not always shown the anticipated effect. These inconsistencies may have occurred because of interactions with concurrent but uncontrolled drug therapy, non-comparable groups, the amount and type of lipid given, or selection of inappropriate placebos.[16] Seven published randomized placebo controlled studies in which surgical patients have been treated with complete immunonutrient diets, have shown reduction in wound infections and complications of 50-75% and a reduction in hospital stay of approximately 20%.[6] The eicosanoids have significant effects on intracellular signaling as well as a variety of inflammatory, cell development, growth, and differentiation. In well-controlled clinical studies, dietary intervention with increased amounts of the omega-3 fatty acids, often along with decreased total fat in the diet, will alter the development of cardiovascular disease, inflammatory processes, autoimmune disorders, infection, allograft rejection, and renal disease.[24] The amount and type of dietary fat will alter cellular responses, but they don't act alone, and their effect, while potent, is significantly influenced by other nutrients (e.g., arginine, glutamine, vitamins E, A, and C) as well as drugs which might influence intracellular signaling.

4. Zinc

The trace element zinc is essential for growth and development of all organisms and the high rate of proliferation and differentiation of immune cells. Although overdosing zinc supplementation can have a negative impact on immune efficiency, zinc is generally regarded as a non-toxic essential metal. Zinc supplementation does not just promote the immune

response; it rather normalizes immune function on the cellular level. A lot of hospitalized surgical subjects might have the high prevalence of zinc deficiency. Zinc deficiency effects on hypoplasia of lymphoid tissues, and reductions in T-helper cell numbers, NK cell activity, antibody production, cell mediated immunity, and phagocytosis.[25] Zinc supplementation (45 mg elemental zinc as gluconate vs. placebo) to a group of elderly surgical patients significantly reduced the incidence of postoperative infections.[26] Erythrocyte zinc was inversely correlated with granulocyte phagocytic capacity and serum zinc with the concentration of CRP.[27] The correlation between zinc status and immune function surely justifies zinc supplementation to these patients to normalize zinc levels.

5. Vitamin D

Vitamin D 'insufficiency' is defined by serum levels of $25OHD_3$ that are sub-optimal (<75 nM) but not necessarily rachitic (<20 nM).[28] Individuals with vitamin D-insufficiency are less able to support macrophage induction of cathelicidin[29] which is the antibiotic protein known to be transcriptionally regulated by $1,25(OH)_2D_3$, and may therefore be at greater risk of infection. Expression of vitamin D-receptor by T- and B-cells was only immunologically functional in the proliferating cells, suggesting an antiproliferative role of $1,25(OH)_2D_3$ on these cells.[29] $1,25(OH)_2D_3$ acts to the inhibition on the expression of Th1 cytokines (IL-2, IFNγ, tumor necrosis factor alpha)[30], while promoting Th2 cytokines (IL-3, IL-4, IL-5, IL-10)[31]. The ability of $1,25(OH)_2D_3$ to suppress B-cell proliferation and immunoglobulin production was initially considered to be an indirect effect mediated via helper T-cells.[32]

CONCLUSION

Immune and nutrition was related with the infectious complications and the length of hospital stay in elective gastrointestinal surgical patients. The effect of immune and nutrition in elective gastrointestinal surgical patients may be systematically different from the treatment effect in critically ill patients. Perhaps these differences are due to differences in underlying pathophysiology, populations studied, other cointerventions, or outcomes. Generally, elective gastrointestinal surgical patients are at a much lower risk of adverse outcomes (complications or death) than critically ill patients. Following gastrointestinal surgical stress, patients experience some degree of immunosuppression, increasing their risk for acquired infectious morbidity and mortality. We might suggest that the results of studies of elective gastrointestinal surgical patients should not be generalized to critically ill patients.

In conclusion, immune and nutrition may decrease infectious complication rates. However, the treatment effect varies depending on the patient population and the intervention. Further research needs to define the underlying mechanism by which immune and nutrition may be harmful and to identify which products and which patients are associated with clinical benefit.

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Peer Reviewers' Commentary

The purpose of this article is to systematically review the effects of various diet in gastrointestinal surgical patients. Immune and nutrition may decrease infectious complication rates. However, the treatment effect varies depending on the patient population and the intervention. In this paper, the nutritional approach of gastrointestinal surgical patients is thought to be beneficial.

(정리: 편집위원회)