PREOPERATIVE IMMUNONUTRITION IN GASTROINTESTINAL CANCER PATIENTS

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ABSTRACT

Surgical procedures due to gastrointestinal tumors are associated with increased risk of postoperative complications and mortality. This is a result of malnutrition and impairment of the immune system. Using nutritional treatment containing immunomodulatory components before surgery may improve the nutritional status of patients and also the immune system by stimulating the host’s immune response, improving the nitrogen balance and controlling the inflammatory response. The nutrients with immunomodulatory effect include: arginine, glutamine, ω-3 fatty acids, and nucleotides. Despite many clinical research the role of preoperative immunonutrition remains unambiguous. The optimal dose of using it is also unknown. The aim of this study was analysis of the impact of preoperative immunonutrition on postoperative complications in patients with gastrointestinal cancer treated surgically. The authors reviewed the literature of effect of preoperative immunonutrition on postoperative complications, mortality, and length of stay in hospital in gastrointestinal cancer patients. The studies including immunonutrients such as arginine, glutamine, ω-3 fatty acids and RNA (ribonucleic acid) were reviewed. Preoperative immunonutrition seems to be effective in the prevention of postoperative complications, both infectious and noninfectious, as well reduction of mortality and shorter length of stay in hospital. Patients with malnutrition are definitely benefit of this kind of support. Further studies are needed to assess the effect of preoperative immunonutrition in patients treated surgically due to gastrointestinal cancer.
astrointestinal cancer surgery is associated with higher postoperative infections, non-infective complications and mortality. It is a result of impairment immune function, perioperative stress and malnutrition in these patients. Malnutrition is common problem in preoperative gastrointestinal cancer patients. It is estimated in 65 – 85% patients with upper gastrointestinal cancer [1-3].

MALNUTRITION IN GASTROINTESTINAL CANCER PATIENTS

Nutritional status can be assessed by several methods both in the form and biochemical test. The most commonly and the simplest approach of assessing the nutritional status of patients in hospital is SGA (Subjective Global Assessment). It allows identification of patients at risk of malnutrition [4-6]. Another regularly used form is screening form for assessing the risk of malnutrition NRS 2002 (Nutritional Risk Screening). The occurrence of risk of malnutrition in patient with gastrointestinal cancer may be determined when one of the following criteria is found:

- Weight loss > 10% over the last 6 months
- BMI (body mass index) < 18.5 kg/m²
- Grade C on the SGA scale or result > 3 on the NRS 2002 scale
- Decreased plasma albumin level < 3 g/dl (excluding liver and kidney disease) [7].

In patients over the age 65, the diagnosis of malnutrition that requires nutritional intervention is diagnosed at BMI <24 kg/m² and when unintentional weight loss is > 5% in the last 6 months [8].

Unintentional weight loss is observed in 31 – 87 % of patients. The range of weight loss depends on the type of tumor location. Unintentional weight loss > 10% in the last 6 months is reported by approximately 15 % of patients with gastrointestinal cancer. Malnutrition is observed in up to 80% of patients with advanced stage of cancer [2, 3]. An extremely important issue is the co-occurrence of impairment of the immune system. There is a disturbance of the basic functions for example the defensive range, support of regenerative process or active tolerance. Malnutrition additionally affects the impairment of the immune system in proportion to its severity. One of the symptoms of failure of the immune system is a decrease in the number of lymphocytes [9, 10].

IMMUNONUTRITION

One way to remedy this situation is to improve the work of patient’s immune system by supplementing the nutrient deficiencies necessary for the proper functioning of the body. Thanks to this, conditions will be created for the progressive restoration of the immunocompetent cells’ efficiency. Participation in this is taken by nutrients that have ability to stimulate the host’s immune responses, improve the nitrogen balance and control of the inflammatory response. They also increase protein synthesis after surgery. These components include arginine, glutamine, ω-3 fatty acids, nucleotides (RNA) [11].

Arginine – it is consumed during the synthesis of proteins. It is essential substrate in many metabolic cycles. Deficiencies are observed in major injuries and cachexia. A beneficial effect on wound healing was observed [12]. Arginine administered orally or intravenously affects the immune system by stimulating the thymus to produce T lymphocytes and improving their efficiency, stimulating the function of macrophages, LAK cells (lymphokine-activated killer), NK cells (natural killer), allowing granulocytes phagocytosis. It also stimulates cancer cytotoxicity and has a protective effect during chemotherapy [13, 14].

Glutamine – it is the main source of nitrogen in the human body. It is particularly used by rapidly dividing cells. Glutamine administers to people with cancer appears to provide normal function of immune cells and intestinal epithelium. Polysaturated fatty acids ω-3 –in the human body they are present in phospholipids of cell membranes. They affect the process of cell growth and differentiation as well as participate in inflammatory and immunological processes. ω-3 fatty acids reduce the inflammatory reaction while ω-6 fatty acids have a strong proinflammatory effect.

Nucleotides – it is suggested that nucleotide supplementation has a beneficial effect on the regeneration of intestinal villi as well as improves immune function [9, 12].

The level of immunonutrients is compensated very slowly therefore the measurable benefits of immunizing are visible after the necessary time. In case of omitting this phase, it may be unexpected deterioration of patient’s condition [15-18]. Unfortunately, the legitimacy of preoperative immunonutrition in gastrointestinal cancer patients is unclear. The optimal duration of it is also unknown. According to current ESPEN (The European Society for Clinical Nutrition and Metabolism) guidelines, nutritional treatment containing immunologically active compounds should be used within 10-14 days in patients with cancer [20].

MATERIAL AND METHODS

The authors reviewed the literature of effect of preoperative immunonutrition on postoperative complications, mortality, and length of stay in hospital in gastrointestinal cancer patients. The studies including immunonutrients such as arginine, glutamine, ω-3 fatty acids and RNA were reviewed.

OUTCOMES IN GASTROINTESTINAL CANCER PATIENTS

Hennessey et al. conducted a study on 524 patients undergoing surgical treatment of the gastrointestinal tract. The albumin level was tested preoperatively. Patients with postoperative complications had hypoalbuminemia before surgery. The reduced pre-
operative albumin level also correlated positively with the length of stay in hospital after surgery [21].

In Albania there was a study carried out among 694 patients prepared for surgery due to gastrointestinal cancer admitted to the surgical ward and treated in ICU (Intensive Care Unit). The patients were divided into two groups – well-nourished and malnourished. Preoperative malnutrition was found in 65.3% of all patients including 84.9% of patients with malignant neoplasms of gastrointestinal tract. Patients were not received preoperative immunonutrition as it is recommended. Malnutrition is a significant problem in surgical patients, especially in patients with gastrointestinal tumor. This study point out that insufficient preoperative nutritional support is associated with an increased incidence of infections, postoperative complications, mortality and longer ICU stay [1].

Xu and co examined 60 patients with gastrointestinal cancer. Half of them received preoperative immunonutrition in form of IMPACT for 7 days before the operation. After the surgical treatment, it was noticed that in the group of patients receiving immunotherapy, the percentage of postoperative complications was significantly lower. Moreover there was a relevant reduction in length of hospital stay after surgery in this group. After analyzing the results, the authors found that enteral preoperative immunonutrition improves the nutritional status and immune response in patients with gastrointestinal cancer. It also reduces the incidence of postoperative infections and complications in these patients [22].

In Japan there was a study made up of 55 esophageal cancer patients before surgical treatment. Twenty six of them received preoperative immunonutrition treatment in form of an industrial product IMPACT for 5 days preoperatively in an amount of 750 ml per day. Control group consisted of 29 patients. Definitely less patients [4/26] from group receiving preoperative immunonutrition experienced postoperative complications compared to the group without immunonutrition [10/29]. In this group of patients no postoperative deaths were observed, as well as their length of stay in hospital was lower than patients from control group. The average 6-month survival was relatively higher in patients from group with preoperative immunonutrition (92%) than in group without receiving immunonutrition (72%). Preoperatively immunonutrition significantly improved the results of surgical treatment. The supply of immunostimulatory nutritional treatment before esophageal cancer surgery appears to be right strategy for reducing infectious complications, mortality and length of stay as well as short-term survival [23].

Nakamura et al. conducted a study in esophageal cancer patients assessing the optimal amount of preoperative immunonutrition. Patients were divided into two groups, one of them consumed 500 ml of industrial immunonutrition IMPACT while second group were fed with 1000 ml of the product. Patients consuming a larger amount of immunonutrition developed diarrhea and loss of appetite. The study suggests that 500 ml dose of IMPACT is optimal for patients with esophageal cancer [24].

Fujitani et al. examined 244 well-nourished patients with early gastric cancer before complete gastrectomy. Patients were divided into two groups, first group was fed by immunostimulating substances 5 days before surgery while the second group was control. In group of patients received immunonutrition there was no reduction in the incidence of postoperative complications. Five-day preoperative immunonutrition did not protect well-nourished patients from postoperative complications [25].

Fukuda and co. carried out research among 800 patients with gastric cancer before surgical treatment. The risk of malnutrition was determined by means of unintentional weight loss > 10% within 6 months, BMI < 18.5 kg/m², grade C on the SGA scale, reduced level of albumin < 3.0 g/dl. Patients were divided into 4 groups: I Group – didn’t received preoperative immunonutrition, groups II, III, IV were fed respectively 1-9, 10-13 and ≥ 14 days. Adequate nutrition was assessed as an intake of > 25 kcal/kg/day. In 19 % patients malnutrition was observed. Postoperative complications were significantly higher in malnutrition patients. Patients with malnutrition, but fed adequately had less postoperative complications than malnourished patients without nutritional support or with duration < 10 days. Based on the study authors concluded that proper preoperative nutrition support reduces the occurrence of postoperative complications in malnourished patients with gastric cancer after surgery [26].

The study involved 67 patients with colorectal cancer without malnutrition before planned surgery. Patients were divided into two groups- first group (n=33) were fed with preoperative immunonutrition within 5 days before the operation. Second group was made up of patients without any nutritional treatment. In patients receiving nutritional support no postoperative complications were noticed. Preoperative enteral immunonutrition may be effective in the prevention of postoperative complications in patients with colorectal cancer without malnutrition [27].

In Switzerland, a prospective, randomized, double-blind, placebo-controlled were conducted in patients with gastrointestinal cancer before surgery. Only well-nourished patients were include in the study. Patients received preoperative immunonutrition in form of IMPACT or placebo. Nutritional support was used for 3 days before planned surgery. There was no significant improvement in the incidence of postoperative complications and infectivity between two groups. There was also no relevant difference in perioperative mortality and length of stay in hospital. Preoperative immunonutrition applied 3 days before planned surgery in well-nourished patients did not affect the improvement of postoperative complications [28].

CONCLUSIONS

To sum up there are more and more studies suggesting the appropriateness of preoperative immunonutrition nowadays. It seems to be effective in the prevention of as well postoperative complications, both infectious and noninfectious, reduction of mortality as length of stay in hospital. The patients diagnosed with malnutrition before planned surgical treatment can definitely benefit from
such nutritional support. Unfortunately, despite the suggestions, the optimal time of using immunonutrition is not determined. Further studies are needed to confirm the appropriateness of preoperative immunonutrition in patients with gastrointestinal cancer.

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ABBREVIATIONS
BMI – body mass index
ESFEN – The European Society for Clinical Nutrition and Metabolism
ICU – Intensive Care Unit
LAK – lymphokine-activated killer
NK – natural killers
NRS – Nutritional Risk Screening
RNA – ribonucleic acid
SGA – Subjective Global Assessment

REFERENCES