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Effect of Immunonutrition on Postoperative Complications in Patients Undergoing Gastrointestinal Cancer Surgery

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Abstract

Background: Immunonutrition not only a nutritional supply for patients but it is a therapy which should be started as early as possible especially in expected malnutrition following gastrointestinal cancer surgery.

Objectives: To evaluate the effect of immunonutrition on postoperative complications in patients undergoing gastrointestinal cancer surgery.

Patient and Methods: A prospective randomized trial was carried out on 45 patients who were chosen and classified randomly into three groups each of them included 15 patients as the followings: Group I received total parenteral nutrition immediately postoperative for 7 days in the form of carbohydrate, protein, fat (Intralipid 20%), electrolytes, trace elements and glutamine intravenous in central venous catheter. Group II received nutrition like group one except that lipid was administered in a new formula containing soya bean oil, medium chain triglyceride, olive oil and fish oil. Group III received nutrition in the same formula of group II but it was started 7 days preoperative and continued for 7 days postoperative. Assessment parameters such as body weight and complications were recorded.

Results: No significant difference between three groups concerning age and sex. A significant effect of time on body weight collectively was proved. There was a significant group interaction between three groups. Body weight showed a significant drop both in group I and group III, but not in group II. Concerning postoperative complications there were no statistical significance between three groups. There was a decrease in the rate of respiratory tract infection/pneumonia in group III compared to other groups but the decrease was not statistically significant. Only one case of urinary tract infection was reported in group II and one case of intra-abdominal infection in group I.

Conclusion: There was a positive impact of parenteral immunonutrition on reduction of postoperative complications compared to basic caloric requirements (Intralipid postoperative). These findings suggest its use as a method of choice in patients undergoing gastrointestinal cancer surgery.

Key words: Immunonutrition, Postoperative Complications, Gastrointestinal Tract Cancer Surgery.

Introduction:

Malnutrition is a possible complication in patients with cancer and can be the first symptom to reveal the presence of the disease [1]. Malnourished patients have a significantly higher morbidity and mortality, a longer length of stay and increased hospital costs [2]. In addition, malnutrition is an independent risk factor for quality of life. Increasing evidence has been accumulated during recent years that nutritional screening and therapy are important adjuncts in modern surgical care since up to 40% of patients are at nutritional risk preoperatively [2].

Perioperative nutrition has been convincingly shown to improve clinical outcome in patients undergoing major gastrointestinal surgery and to reduce costs [2]. The mechanism of action seems to be not only an improved nutritional status by providing a higher

caloric intake, but primarily a reinforced immune response [3].

Immunonutrition contain pharmacologic doses of nutrients including arginine (Arg), ω-3 polyunsaturated fatty acids (ω-3 PUFA), glutamine (Glu) and ribonucleic acid (RNA), some clinical trials have been reported to affect the risk of postoperative infection and length of hospital stay in patients underwent operation [4].

Aim of the Study:

The present study aims to evaluate the effect of immunonutrition on postoperative complications in patients undergoing gastrointestinal cancer surgery.

Patients and Methods:

• *Study design:*

A prospective randomized, controlled study was conducted in South Egypt Cancer Institute, Assiut University during the period from September 2011 to September 2013. The patients who fulfilled the inclusion criteria were arranged randomly in the groups of study by sealed envelope technique.

• *Inclusion and exclusion criteria:*

The inclusion criteria included patients with good overall status aged between 18 and 70 years. Patients with organ failure (liver and renal insufficiency) and patients suffered from ongoing infections and/ or inflammatory bowel diseases were excluded.

• *Patient groups*:

A total of 45 patients met the inclusion criteria and underwent resectional surgery for gastrointestinal cancers were included in the study. The patients were divided into three groups:

Group I: consists of 15 patients and they received total parenteral nutrition immediately postoperative for 7 days, consists form carbohydrate, fat, protein with lipid emulsion in the form of Intralipid 20%, electrolytes, trace elements and glutamine intravenous was given to the patients in central venous catheter.

Group II: consists of 15 patients and they received total parenteral nutrition immediately postoperative for 7 days which was administered like group one except that fat emulsion administered in a new formula containing soya bean oil, medium chain triglyceride, olive oil, and fish oil (SMOF® - Fresenius Kabi).

Group III: consists of 15 patients and they received total parenteral nutrition in the same formula of group II but in this group of patients the nutrition started 7 days preoperative and continued for 7 days postoperative.

Normal caloric requirements were calculated by nomograms based on Harris Bendict equation [5]. this equation is used to predict the basal energy expenditure (BEE) which is the basal metabolic rate in the resting and fasting states, corrected by considering both activity and stress factors (+45%) provided that the patients were not feverish, and accordingly macronutrients (proteins and fats) and micronutrients (vitamins, trace elements and electrolytes) was calculated and supplied.

This equation depends on the age, sex, height, ideal body weight.

Male's BEE (kcal/day) = 66+ (13.7 × body weight in kg) + (5×height in cm) – (6.7× age in years)

Females BEE (kcal/day) = 655+ (9.6×body weight in kg) + (1.8× height in cm) – (4.7×age in years)

These predictive equations (with adjustments for the degree of stress) overestimate the daily energy needs by 20-60%. Therefore, they are only a guide in the Intensive Care Unit. All patients provided routine perioperative care with antibiotic prophylaxis, multimodal analgesia, deep venous thrombosis prophylaxis and early mobilization.

• *Index of assessment:*

Each patient in the first two groups was followed up for 7 days postoperatively but in the third group follow up was started 7 days preoperative and continued for 7 days postoperative. All patients were monitored for: bodyweight and major postoperative complications such as: fistula, wound infection, respiratory tract infection/pneumonia, urinary tract infection and intra-abdominal infection.

As regard body weight it was assessed by digital scale. In each patient it was measured four times in the morning, the first time in group I and II was twenty four hours before surgery, in group III it was seven days before surgery, the next measure was twenty four hours after surgery in all patients. The time interval between the second and third measures and between the third and fourth measures was forty eight hours and ninety six hours, respectively.

Rigid objective criteria were established defining each complication to avoid subjective bias. Fistulae were radiographically documented. Pneumonia/ respiratory tract infection was documented by positive sputum culture of clear clinical and radiographic evidence of consolidation. The presence of a wound infection was defined by culture and operative or spontaneous drainage of purulent materials. Urinary tract infection was defined by urine culture. Intra-abdominal infection was defined by culture or abdominal collection of pus with operative drainage.

• *Ethical considerations:*

The study was carried out after the approval of the Ethical Committee of the South Egypt Cancer Institute, Assiut University. Administrative approval of the Dean of the Institute was obtained. Patient participation was voluntary. Written informed consent was obtained from each respondent. The aim of the study was explained to the participants. The participants were informed that

their non-compliance would not in any way influence their clinical services or treatment.

• *Statistical analysis:*

SPSS version 18 was used for data analysis. The differences in proportions among the groups were assessed using the Chi square test. Continuous data were studied using the ANOVA to compare the preoperative and postoperative mean weight of the studied groups. The differences are statistically significant at $p < 0.05$.

Results:

The present study included 45 patients 16 were males and 29 were females with aged ranged from 35 to 69 years old. As shown in Table (1), there were no statistically significant differences in demographic data as regards age and sex of the three studied groups ($p > 0.05$). Table (2) and Figure (1) show the differences between the body weight of the studied groups pre-operatively and 1, 3 and 7 days post-operative which revealed a significant effect of time on body weight collectively. This effect was not found for the three groups (evident by significant group interaction, $p< 0.001$). Body weight showed a significant drop in both group I ($p=0.009$) and group III ($p < 0.001$), but not in group II ($p = 0.63$). In group I significant drop in body weight was only one day after operation but not afterwards, $p = 0.03$. In group III highly significant drop in body weight was one day after operation and continued up to seventh day.

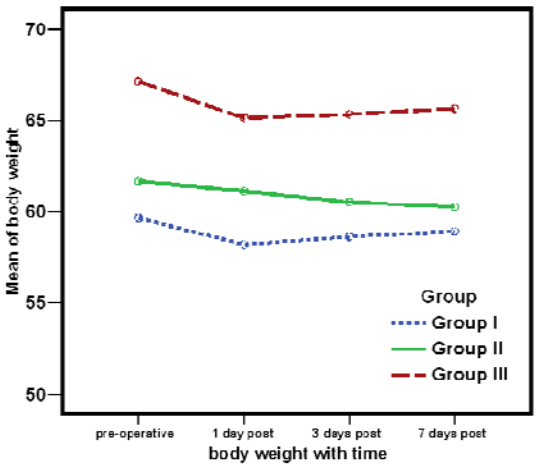

Figure (1): Body weight pre-operatively and 1, 3 and 7 days post-operative of the studied groups

Table (1): Personal characteristics of the studied groups

	Group I (n= 15)		Group II (n= 15)		Group III (n= 15)		P-value
	No.	**%**	**No.**	**%**	**No.**	**%**	
Sex:							
• Male	5	33.3	8	53.3	3	20.0	0.158
• Female	10	66.7	7	46.7	12	80.0	
Age: (years)							
• Mean ± SD	53.60 ± 8.35		50.67 ± 6.22		52.40 ± 7.44		0.118
• Range	35.0 – 64.0		40.0 – 62.0		42.0 – 69.0		

Table (2): Body weight pre-operatively and 1, 3 and 7 days post-operative of the studied groups

Time in days	**Group I**		**Group II**		**Group III**		**P-value group interaction**
	Mean	SD	Mean	SD	Mean	SD	
Pre-operative	59.67	7.43	61.67	8.16	67.13	8.55	< 0.001
Day1 post	58.20	7.26	61.13	7.99	65.13	8.37	
Day3 post	58.63	6.97	60.53	7.99	65.33	8.34	
Day7 post	58.93	6.97	60.27	7.90	65.67	8.25	
P value for time effect in each group	0.009		0.63		< 0.001		
P value for overall Time effect	< 0.001						

Concerning postoperative complications there were no statistically significant differences among three groups ($p > 0.05$). There was a decrease in the rate of respiratory tract infection/pneumonia in group III compared to other groups. But the decrease was not statistically significant. In group I, there were 4 patients (26.7%) had fistula, also 4 patients (26.7%) had wound infection, 2 patients (13.3%) had respiratory tract infection/pneumonia and one patient (6.7%) had intra-abdominal infection. In group II, there were 3 patients (20%) had fistula, 5 patients (33.3%) had wound infection, 3 patients (20%) had respiratory tract infection/pneumonia and one patient (6.7%) had urinary tract infection. In group III, there were 5 patients (33.3) had fistula, 4 patients (26.7%) had wound infection and one patient (6.7%) had respiratory tract infection/pneumonia (Table 3).

Table (3): Postoperative complications among the studied groups

Complications	Group I (n= 15)		Group II (n= 15)		Group III (n= 15)		P-value
	No.	%	No.	%	No.	%	
Fistula	4	26.7	3	20.0	5	33.3	0.711
Wound infection	4	26.7	5	33.3	4	26.7	0.897
Respiratory tract infection /pneumonia	2	13.3	3	20.0	1	6.7	0.562
Urinary tract infection	0	0.0	1	6.7	0	0.0	0.360
Intra-abdominal infection	1	6.7	0	0.0	0	0.0	0.360

Discussion:

The place of pre- and postoperative nutrition is no longer in question; particularly since it has been confirmed that, in severely malnourished individuals scheduled for major gastrointestinal surgery, it was advantageous to postpone surgery for up to 10–14 days and to administer nutritional support, preferably with enteral diets. From the surgical point of view, it was not enough to stop there; for over 10 years the focus has been on understanding immunologic and inflammatory responses, so as to enhance host defense mechanisms and improve clinical course [6].These activities led to the idea of immunonutrition, a type of pharmaconutrition that has been described as nutritional intervention, not only able to provide essential nutrients to maintain basic organ functions, but also to augment the immune system. [7].

In the present study, the early administration of nutritional support using micro and macro nutrients was tailored to complement the primary treatment (surgery).The purpose was to improve the clinical outcome. We found that there was a decrease in the rate of complications (wound infection, respiratory tract infection/pneumonia, urinary tract infection, and intra-abdominal infection) in the immune enhanced diet group SMOF either peri or postoperative groups to the group who received only basic caloric requirements (Intralipid postoperative). The decrease was not statistically significant but that could be attributed to the sample size and the duration of immunonutrition as it could have been not long enough.

The result of our study was in agreement with a prospective randomized studies done by Nabeya in 2006 which showed that giving preoperative immunonutrition in esophageal cancer patients decreased significantly the incidence of infectious complications in study group versus patients in the control group who received normal diet [8].Nineteen randomized controlled trials done by Zhang et al. 2012 in which the results showed significantly decreased morbidity of postoperative infectious and non-infectious complication in perioperative immunonutrition in comparison with standard diet [9].Wu and his colleagues conducted a study on 468 elective moderately or severely malnourished surgical patients with gastric or colorectal cancers, they concluded that perioperative nutrition support is beneficial for moderately or severely malnourished gastrointestinal cancer patients and can reduce surgical complications [10].

Also our result was in agreement with a study done by Braga et al. in 2002, focused on patients with weight loss of >10% of body weight over the preceding 6 months they found that the group receiving immunonutrition both before and after surgery had fewer complications than those fed control solution postoperatively. Although the statistical analysis did not confirm this, they concluded that perioperative immunonutrition seems to be the best approach to support malnourished patients with cancer [11]. A prospective clinical trial in 2005 done by Kłek et al. of a group of 105 patients operated for gastric carcinoma. They found that there was decrease in the rate of postoperative infectious complications in groups who received parenteral immunonutrition versus group of standard parenteral nutrition but this result was not statistically significant [12]. In 2014 Metry et al. conducted a prospective randomized double-blinded study was designed to compare between two groups of

postsurgical ICU patients. Both groups were given total parenteral nutrition for not less than 7 days postoperatively. Group I was given Intralipid as a source of fat, and Group II was given SMOF in substitution of Intralipid. In this study, they found that there was decrease in postoperative infectious complications in the group received SMOF [13].

In 2012 Pradelli et al. found that ω-3 PUFA-enriched emulsions are associated with a statistically and clinically significant reduction in the infection rate in surgical and ICU patients receiving parenteral nutrition. Pooled data indicate important and significant positive effects of ω -3 PUFA-enriched parenteral regimens over a wide range of outcomes in the selected patient populations. [14]. One study done by Gianotti et al. in 2002 compared the effects of preoperative immunonutrition, pre and post-operative immunonutrition with no nutrition support in 305 patients scheduled for elective GI cancer surgery in patients with <10% weight loss. The investigators reported a significant reduction in postoperative infections in both immunonutrition groups either preoperative or pre and post-operative immmunonutrition compared to those who did not receive nutrition support [15].

On the other hand, a study was done by Helminen et al. in 2007 on one hundred patients with a planned elective operation for benign or malignant gastrointestinal illness they found that no significant decrease in rate of postoperative infectious complication in IN group. The investigator found that routine perioperative immunonutrition to the patients undergoing major gastrointestinal surgery was not beneficial [16]. This study was done on benign and malignant GIT surgeries ours was done on cancer patients only; cancer has unique effect on immune and inflammatory responses different from any other disease which affect infection rate in cancer patients. Another study has compared IN versus no nutrition support in patients receiving surgery for GI cancer. The authors reported no difference in infections between the two groups [17]. In their study the patients received only part of their nutritional needs from immunonutrition, but in our study the patients received all the nutrition needs from immunonutrition which may lead to decrease in the rate of post-operative infectious complications.

Some limitations are present in this study, including lack of follow up of patients after discharge from ICU and from the institute and small number of patients studied, limiting the generalizability of our findings.

Conclusion and Recommendations:

There was a positive impact of parenteral immunonutrition on reduction of postoperative complications compared to basic caloric requirements (Intralipid postoperative). These findings suggest its use as a method of choice in patients undergoing gastrointestinal cancer surgery.We recommend that the results of this study raising attention about using immunonutrition in cancer surgical patients especially in gastrointestinal tract cancer consequently decreasing the incidence of postoperative complications.

List of Abbreviations:

BEE	:	Basal Energy Expenditure
GIT	:	Gastrointestinal tract
ICU	:	Intensive Care Unit
PUFA	:	Poly Unsaturated long-chain Fatty Acids
SMOF	:	Soya bean oil, Medium chain triglyceride, Olive oil, and Fish oil

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