The effect of preoperative standard enteral nutrition versus immune enhancing nutrition on the postoperative outcomes of the upper gastrointestinal cancer patients

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Abstract: The major concern regarding the value of nutritional support is improvement of patients' clinical outcomes. **Aim*:*** This is a quasi experimental study aimed to investigate the effect of preoperative standard enteral nutrition versus immune enhancing nutrition on the postoperative outcome of the upper gastrointestinal cancer patients. **Material and method** Convenient sample of (45) adults patient will be enrolled sequentially into three groups, each group consists of (15) patients. **Three tools** were utilized to collect data pertinent to the study. These tools were gastrointestinal cancer patient nutritional assessment sheet. **Tool II** included postoperative complications evaluation sheet for gastrointestinal cancer patient. It consisted of three parts: wound healing assessment, clinical sepsis indicators, nutritional risk index (NRI). ***Tool III*** was the preoperative feeding strategy. **Results:** - The main results revealed that there were a significant relationship between the type of nutritional regimen and length of hospital stay ($\chi 2$ = 15. 000, P = 0. 0001*). Also, there was a significant relationship between type of formula received and findings of postoperative wound culture and clinical sepsis *indicators*. Moreover, there were significant improvement in the criteria of wound healing among the patients receiving immune enhancing formula. Furthermore there were statistically significant association between pre operative DSH, degree of TIC depletion post nutritional regimen and post operative wound culture, clinical sepsis indicators and occurrence of wound healing complication in group (III) ($P \leq 0.05$) in group (III). **Conclusion and recommendation** Immune nutrition should be utilized in malnourished upper GI cancer patient under going surgery for 7-10 days preoperatively.

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1. Introduction

The major concern regarding the value of nutritional support is improvement of patients' clinical outcomes. Prevalence of malnutrition in gastrointestinal cancer patient has been reported to ranges from 42% to 87%. Gastrointestinal cancer Patients are particularly susceptible to nutritional deterioration for numerous reasons, including A) the presence of metabolic abnormalities associated with cancer, B) decreased dietary intake due to cancer-related symptom, and/or C) physical effects of the tumor in the digestive tract. Moreover, malnutrition is positively correlated with increased unintentional loss of weight (LOW). [(1-8)]

Moreover, malnutrition is one of the most important risk factors for postoperative complications. Malnutrition depresses both cellular and humoral immunity. In addition, complex surgical procedure and injury potentially lead to immunity suppression. Thus, infectious complications are frequent. In the presence of malnutrition, surgical wounds and anastomoses are less likely to heal, resulting in an increased risk of wound complications and anastomotic dehiscence. Furthermore, malnutrition results in gut smooth muscle atrophy and consequently an alteration in absorption of nutrient. [(9-18)]

Among the proposed strategies to reduce postoperative morbidity and its related costs, is artificial nutrition. Nowadays, there are several types of formulas. This includes standard enteral formula and standard enteral preparations that have been modified by the addition of immunonutrients such as arginine, glutamine, omega3fatty acids, nucleotides and others. These substrates have been shown to up-regulate host immune response, to control the inflammatory response and to improve nitrogen balance and protein synthesis after injury. [(19-22)]

Oncology critical care nurse play a key role in addressing the nutritional needs of the patient as well as the identification of patients at risk of developing malnutrition and providing effective nutritional care plan as apart of the overall plan of care. This will be done through dietary history, anthropometric measurement, laboratory and immune function data, diagnosis of preoperative and postoperative nutritional problems. This plays a crucial role in saving health care resources and cost by decreasing the postoperative complications particularly infectious complications and delayed wound healing. [14, 23]

Aim of the study:

The Aim of the study was to investigate the effect of preoperative standard enteral nutrition versus immune enhancing nutrition on the postoperative outcome of the upper gastrointestinal cancer patients.

Research hypothesis

A) There would be a relationship between the types of preoperative nutritional support and the postoperative outcome.

B) Standard enteral formula would have better or positive effect on the nutritional health state and postoperative outcome than the hospital formula.

C) Immune-enhancing enteral formula would have a positive effect on the nutritional health state and postoperative outcome than Standard enteral formula and hospital formula.

2. Material and methods

1- Design: - Quasi experimental study was utilized in this study.

2- Setting: - The study was conducted at the intensive care unit, surgery department at Tanta Cancer Center, Ministry of Health.

3-Subjects:

Convenience sample of (45) adults patient was enrolled sequentially into three groups, each group consists of (15) patients and the three groups received the formulas from day of admission until the 7th day preoperatively.

The three groups were as following:

***Group* (I)**: was the control group and received the hospital formula.

***Group* (II)**: was the quasi experimental group and received the standardized enteral formula

***Group* (III):** was the quasi experimental group and received the immune enhancing enteral formula

The subject selected according to the following Criteria:

Their age ranged from 18 to less than 60 years, confirmed diagnosis of carcinoma of the upper gastrointestinal system, upon admission until 7th day post operatively and scheduled for major elective surgery and malnourished according to modified Patient Generated-Subjective Global Assessment (PG – SGA) sheet.

Exclusion criteria are: Chronic diseases, receive recent immune suppressive therapy gastrointestinal diseases, Metastatic disease and past surgery of gastrointestinal tract.

Tools of the study:

Three tools were utilized to collect data pertinent to the study.

***Tool I* Gastrointestinal cancer patient nutritional assessment sheet.**

It was developed by the researcher according to review of relevant literature [24-34]. It consists of five parts:

Part (1) (Socio demographic and clinical data)

Part (2) (Patient generated subjective global assessment sheet)

It was developed by Detsky *et al.* (1987) and used for cancer patients. It also applied by Persson *et al.* 1999 on patient with gastrointestinal cancer. It was adopted by the researcher to identify the patient with high risk of malnutrition. [24-27]

Part (3) Anthropometric measurements: It included the measurement of the following [28-31]: Weight, Height, Body mass index (BMI), Triceps skin folds, mid arm circumferences.

Part (4) Laboratory studies

It included the measurement of serum protein, serum albumin, hemoglobin, total lymphocytic count, serum sodium and potassium, serum creatinine, blood urea, delayed skin hypersensitivity test and wound culture.

Part (5) Preoperative nutritional intake sheet

It was developed by the researcher after reviewing the relevant literatures. It was used to compare the daily nutritional intake by the three groups during the preoperative period. It includes the following items., amount and type of formula received, caloric content, actual calories received, ideal caloric needs, the energy provision provided for the patients was as following, carbohydrate provides 50% of energy needs, 20% in the form of lipid and 30% in the form of protein. Caloric needs were calculated based on patient's weight – based estimates. The total energy provision is 35 kcal/kg/day for patient within their ideal body weight, 30 kcal/kg/day for malnourished (mild-moderate) or below their ideal body weight, 25 kcal/ kg /day for severely malnourished patients and 20 kcal/ kg /day of adjusted body weight for obese persons, protein content, actual protein received, ideal protein needs: protein requirement will be 1. 5-2 g/kg/day of ideal body weight for malnourished or below their ideal body weight and for obese person 1. 5- 2 g/kg/day of adjusted body weight and date of the postoperative oral intake [32-34].

***Tool II*: Postoperative complications evaluation tool for gastrointestinal cancer patient.**

It was developed by the researcher after reviewing the related literatures [35-45] and it consists of three parts for the purpose of evaluation the effect of different nutritional therapy modalities on postoperative outcome for upper gastrointestinal cancer patients.

Part (1) Wound healing assessment.

It was developed by the researcher to assess wound healing and wound infection during the postoperative period for the upper gastrointestinal cancer patients. It included assessment of periwound skin area, wound margin; wound drainage, wound odor, signs and factors of delayed wound healing which included: delayed removal of suture, bleeding, dehiscence, anastomotic leak, and evisceration and wound infection. [35-38]

Part (2) Clinical sepsis indicators It includes one or more of the following clinical criteria. Fever > 38oC, hypotension (systolic blood pressure < 90 mmhg), oliguria (< 20 ml/h), WBcs count more than 11, 000 or les than 4000 u/L and positive wound culture. [39-41]

Part (3) Nutritional risk Index (NRI) [42-45]

Nutritional risk Index (NRI) it was developed by Buzby. et al, 1988 and used for patient undergoing gastrointestinal surgery. It was adopted by the researcher to predict the percent risk of operative complications related to the underlying nutritional state, the predictive equation is based on objective measurement of serum albumin and the ratio of current weight to usual weight. The risk index was calculated according to the following formula:

NRI=1. 59 x serum albumin level (g/L) +0. 417 x (current weight /usual weight) x 100

The results of the study were evaluated upon reference data. Low values correlate with increased risks of operative complications and it means that the patient is under the risk of surgical and septic complications. However, the results of NRI were divided into four groups: NRI score of > 100 indicates no risk; 97. 5 to 100, mild risk; 83. 5 to 97. 5, moderate risk, < 83. 5, severe risk.

***Tool (III)*: The preoperative feeding strategy.**

The calorie and protein needs were calculated individually according to patient weight. The patients received three services of formulas plus the hospital formula (1-standard enteral formula and (2- immune enhancing formula). These two formulas were administered from the first day of admission until 7th days preoperatively.

Methods

1- Official letters from the faculty of nursing were delivered to the appropriate authorities in the selected area to conduct the study.

2- Permission to conduct the study was obtained from the directors of the selected setting.

3- Oral consent was obtained from the patient to participate in the study.

4- The tools was developed by the researcher based on extensive review of related literature, and was tested for content validity by jury of expertise from the field of the study then evaluated and approved by a jury of 10 specialists and current thesis supervisors.

5- A pilot study was carried out on 10 patients to test the feasibility and applicability of the tools.

6- Reliability of the tool was tested by using Alpha Cronbach's and the reliability factor was =0. 852

7- The study was conducted from May 2010 to September 2011.

8- Every patient was interviewed on the first day of admission and followed up through seven days preoperatively, then in the first, the third postoperative day and finally after 7 days of surgery or until discharge.

- Anthropometric measures, laboratory studies and immunological tests it involved two tests which used to assess immune function and as a clinical indicator of malnutrition in nutritional assessment: Total lymphocytic count (TLC) and delayed skin hypersensitivity (DSH), was assessed twice. First time was on patient admission as abase line data. The second time was 7 days after the termination of preoperative nutritional therapy [28-31]
- **Nutritional intake sheet**

It was used during the preoperative period to identify the consumed calories and protein and compare it with the ideal calories and protein required by patients.

- **The Preoperative feeding strategy**

It was designed individually for the standard enteral nutrition group II and immune enhancing nutrition group III. It was used only during the preoperative period to identify the caloric and protein requirement for each patient and consequently the volume of formula recommended.

1-The hospital formula provided in the form of blenderized diet and parenteral nutrition in the form of glucose 25%, amino acids, intralipid 10%. Also, the protein, fat, Carbohydrates and total caloric content was analyzed daily for the three services of hospital formula to know the amount of caloric content provided daily by formula. Generally, the hospital formula content was estimated according to patient weight. The patient weighted 50-60 kg received meal provide 3000 cal and 100gm protein. The patient

weighted 60-70 kg received meal provides 3500 cal and 120gm protein. The patient weighted 70 kg or more received meal provides 4000 cal and 140gm protein.

2- Standard enteral nutrition formula included the following component; 37g Proteins /1000ml of formula, 32. 5g of fat/1000ml, 135. 7g Carbohydrates/1000ml, Caloric concentration provided one kcal/ml (ie 1000cal/1000ml), Non-protein- energy/ gN was 141:1, Total nitrogen was 5. 92(g/l) and Total energy/gN was166:1 (cal/gN). it was given orally three services daily. Each serving provided, 8. 5 g protein/230ml, 7. 5 g of fat/230ml, 31g of Carbohydrates/230 ml, Total nitrogen content was 1. 36 g/230ml and total caloric content was 230 cal per service. Also each services provided about 11. 5% of the total caloric needs per day; 230ml of formula*100/2000calorie per day. Consequently the three services provided; 690*100/2000=34. 5% of the total caloric needs per day. The rest of daily caloric need provided in the form of hospital diets. [46]

3- Immune enhancing nutrition formula included the following component; 52 g Proteins /1000ml of formula, 15. 5g of fat/1000ml, 89. 4g Carbohydrates/1000ml, 4. 32(g) L-Arginine, 6. 62(g) of Glutamic acid, 1. 55 g/l Omega-3 fatty acids, Caloric concentration provided 1. 1 kcal/ml, Non-protein-energy/ gN was 60:1, Total nitrogen was 8. 32 (g/l) and Total energy/gN was 85:1 (cal/gN). It was given orally three services daily. Each serving provided, 11. 96 g protein/230ml, 3. 6 g of fat/230ml, 20. 6 g of Carbohydrates/230 ml, Total nitrogen content was 2. 7(g/230ml). 0. 99 (g) L-Arginine /230ml, 1. 5(g) of Glutamic acid/230ml, 0. 36g/230 ml Omega-3 fatty, and total caloric content was 253 cal per service. Also each services provided about 11. 5% of the total caloric needs per day; 230ml of formula*100/2000calorie per day. Consequently the three services provided; 690*100/2000=34. 5% of the total caloric needs per day. the rest of daily caloric need provided in the form of hospital diets. [46,47]

Finally, the nutritional content of the hospital formula provided and analyzed by the researcher daily was added to nutritional content of the study formula (standard enteral formula and immune enhancing nutrition formula) to calculate the total caloric need provided by both formulas.

***Tool II*: - Postoperative complications evaluation sheet for gastrointestinal cancer patient which consisted of three parts**

***Part (1)* Wound healing assessment sheet** [35-38, 48-50]

It was used during the postoperative period according to the hospital policy in relation to the time of postoperative dressing for seven days postoperatively. The wound was assessed in relation to, ***1) Wound margin, 2) Wound drainage***, ***3) Wound odor***, ***4) peri wound skin area, 5) pain and 6) Surgical wound infection and Wound healing complications*** as delayed removal of suture, bleeding, dehiscence, anastomotic leak and evisceration.

Part (2) Clinical sepsis indicators [39-41]

It was done during the postoperative period for seven days. In relation to wound culture; it was done twice, at first dressing and after seven days.

Part (3) Nutritional risk Index (NRI) [42-45]

It was estimated before the beginning the preoperative nutritional therapy and after 7th day to identify the differences among the three nutritional regimens therapy in relation to percent risk of postoperative complications.

Statistical analysis:

The collected data were organized, tabulated and statistically analyzed using SPSS software statistical computer package version 13.

3. Results:

The age ranges from 29-60 years among the three groups, the mean values were found no significant difference among the control (hospital formula group) and study groups (standard enteral and immune enhancing formula groups) (51. 47 ± 7. 01, 54. 33 ± 17. 06 and 56. 20 ± 8. 82) respectively where (F = 1. 831, *P* = 0. 173). that the highest incidence of upper GIT cancer was among the age group of 45 to less than or equal 60 years old represented 86. 7%, 73. 3%, 60% among the control, standard enteral and immune enhancing formula groups respectively. In relation to patient's current diagnosis, it was found that the gastric cancer show high incidence among the control and study groups represented 33. 3%, 46. 7% and 66. 7% respectively followed by oral cancer represented 26. 7%, 33. 3% and 26. 7% among the control, enteral formula and immune enhancing formula groups respectively. Esophageal cancer showed lowest incidence among the control and study groups represented 40%, 20% and 6. 7% respectively.

Table (I):

Shows a significant relationship between the type of nutritional regimen and length of hospital stay (P = 0. 001*), where the mean length of hospital stay was 12. 20 ± 2. 42 days in G III compared to 17. 27± 2. 71 days in group I (*P* = 0. 0001*). Also, the mean length of hospital stay significantly lower in G II than G I by 3 days where (*P* = 0. 039*)

Table (II):

Subjective global – based assessment of nutritional condition showed that on admission to hospital the patients were moderately malnourished in majority of cases : in G I 60%, in group II 66. 7% and in group III 73. 3% Moderate malnutrition represented 66. 6% among the three groups. Moreover, the minority of patients represented mild degree of

malnutrition: in G I and G II 13. 3%, 13. 3 and no one had mild degree of malnutrition in group III. The patients with sever malnutrition constitutes only 24. 4% of the total cases of three groups. The findings showed that there were no statistically significant differences among the three groups.

Table (III):

Shows a significant relationship between type of nutritional regimen and percent of body weight change (P = 0. 0001) the majority of subjects (93. 3%) received hospital formula had severe weight loss post nutritional regimen, on the other hand only 6. 7% of subjects received immune enhancing formula had severe weight loss post nutritional regimen. Also 60% of subjects received enteral formula had significant weight loss and more than one third of the subjects received immune enhancing formula had no weight change post nutritional regimen. In addition findings showed statistically significant difference between group I and group II (Z=3, 592, P = 0. 0001). Also group I and group III (Z=4. 356, P = 0. 0001). There were no significant differences between G II and group III (z=0. 926, P = 0. 345).

Table (IV):

This table describes the effect of the three therapeutic nutritional regimens on laboratory study of the control and study groups with upper gastrointestinal cancer. The mean value of ***hemoglobin*** post nutritional regimen not statistically significantly different from the pre nutritional regimen among the patient of three groups where F = 1. 535, P = 0. 227) and (F = 1. 476, P = 0. 245) respectively. ***Regarding serum protein,*** the mean value increased post nutritional regimen in group II and group III but this increased were not statistically significant where P > 0. 05) In contrary the mean value of serum protein decreased post nutritional regimen in group I by 5. 26 ± 0. 55 from that pre nutritional regimen 5. 63± 0. 53, with no significant difference between the two nutritional interval.

Concerning serum albumin, there were statistically significant differences among the three groups in relation to mean value of serum albumin post nutritional regimen where the mean value decreased significantly by 2. 24 ± 0. 45 post nutritional regimen in group I where (p= 0. 011*). On the other hand, this value increased significantly to 2. 85 ± 0. 23 post nutritional regimen in group III where (P = 0. 019*).

Table (V):

Shows that the mean value of ***delayed skin hypersensitivity test*** increased significantly post nutritional regimen by 4. 566 ± 1. 412 from 3. 746 ± 1. 253 pre nutritional regimen for group (III). Where (P = 0. 0001). Also there were statistically significant differences between G I versus G III, G II versus G III where P < 0. 01 ***Concerning total lymphocytic count***, the mean values of total lymphocytic count in the three groups were less than normal range per and post nutritional regimen. The subject received immune enhancing formula, the mean value of total lymphocytic count increased to 1120. 40± 183. 45 post nutritional regimen but not statistically significant (P = 0. 102). More over the findings showed that there were statistically significant difference between group I and group II, group I versus group III, group II versus group III and among the three groups post nutritional regimen where P < 0. 01.

Represents the relationship between degree of malnutrition assessed by serum albumin and total lymphocytic count and the three therapeutic nutritional regimens of the control and study groups. ***Regarding serum albumin*** there were no statistical significant difference between the pre and post nutritional regimen and degree of malnutrition for the three groups where (P >0. 05) but there were significant relationship between type of formula received and degree of malnutrition where (($\chi 2$ = 18. 29, P = 0. 001*). ***As regards total lymphocytic count*** There were statistically significant differences between the pre and post nutritional regimens for patients received immune-enhancing formula where($\chi 2$ =8. 27, p=0. 016*). Also There were statistically significant relationship between types of formula received and total lymphocytic count where(p≤0. 05*).

Table (VI):

Shows There were no statistically significant differences between results of pre and post nutritional regimen of delayed skin hypersensitivity test for group I and II where (P = 0. 226), (P = 0. 494) respectively. On contrary, there was a significant improvement in the result of delayed skin hypersensitivity test for group III after receiving immune enhancing formula where (P = 0. 0001*). Also, there were a statistical significant differences among the three groups pre and post nutritional regimen where (P=0. 006*), (P = 0. 032*) respectively.

Table (VII):

Shows that, the patients in group I who were negative for wound infection on third day post operatively representing (80%) significantly decreased to (26. 7%) on the 7th day post operative day. On the other hand, the number of patients in group II, III who were negative wound infection on the 3rd post operative day decreased from (86. 7%) to (53. 3%) and (100%) to (66. 7) respectively on the 7th postoperative day. There were no statistically significant differences between the 3rd and 7th post operative day for group II and III where (P >0. 05). In addition the were significant differences among the three groups on the 7th post operative day where (P = 0. 041*).

Table (VIII):

Shows statistically significant association observed between type of nutritional regimen received and risk degree of post operative complications where (*P* = 0. 018*). Also there were no statistically significant differences between the pre and post nutritional regimen in group II and III while group I showed significant differences between the pre and post nutritional regimen. More than half of the patients in hospital formula group (53. 3%) had moderate risk of post operative complication (moderate malnutrition) post nutritional regimen. While this percentage decreased to (46. 7%, 26. 7%) in enteral formula and immune enhancing group patients respectively post nutritional regimen. At the same time no one had severe risk of post operative complication in immune enhancing formula group patients if compared to group I and group II (33. 3%, 6. 7%) respectively who had severe risk of post operative complication post nutritional regimen.

Table (1): Distribution of the control and study groups with upper gastrointestinal cancer according to risk of malnutrition using modified patient generated subjective global assessment sheet (MPG-SGA).

MPG-SGA for assessing malnutrition risk	G1 Hospital formula(control) (n=15)		G2 Enteral formula (n=15)		G3 Immune enhancing formula (n=15)		χ^2	*P*
	N	%	n	%	n	%		
●Grading:								
Mild(2-3)	2	13. 3	2	13. 3	0	0	2. 382	0. 666
Moderate(4-8)	9	60. 0	10	66. 7	11	73. 3		
Severe(≥9)	4	26. 7	3	20. 0	4	26. 7		
●Scoring:								
Range	2-12		3-11		6-15			
Mean±SD	6. 87±2. 69		7. 07±2. 49		8. 87±2. 42			
F-test	2. 827							
P	0. 070							

***Significant (*P*<0. 05)**

Table (2): Relationship between percent of body weight change of the control and study groups with upper gastrointestinal cancer and nutritional regimen.

Body weight change %	The studied upper gastrointestinal cancer patients (n=45)						Kruskal Wallis test (χ^2)	*P*
	G1 Hospital(control) formula (n=15)		G2 Enteral formula (n=15)		G3 Immune enhancing formula (n=15)			
	N	%	n	%	n	%		
-No change	1	6. 7	2	13. 3	6	40. 0		
-Significant weight loss (1%-2%)	0	0	9	60. 0	8	53. 3		
-Severe weight loss (>2%)	14	93. 3	4	26. 7	1	6. 7		
χ^2	27. 886							
P	0. 0001*							
Range	-10. 20-0. 00		-4. 60-3. 30		-1. 60-3. 10		22. 034	0. 0001*
Mean±SD	-4. 39±2. 53		-0. 83±1. 94		-1. 00±1. 29			
Mann-Whitney test (Z)	I vs II, Z=3. 592, P=0. 0001*							
	I vs III, Z=4. 356, P=0. 0001*							
P	II vs III, Z=0. 926, P=0. 354							

***Significant (P<0. 05)**

Table (3): Effect of the three therapeutic nutritional regimens on laboratory studies of the control and study groups with upper gastrointestinal cancer.

Findings of laboratory studies	The studied upper gastrointestinal cancer patients (n=45)						F-test P	
	G1 Hospital formula (control) (n=15)		G2 Enteral formula (n=15)		G3 Immune enhancing formula (n=15)			
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
HB (g/dL):								
Range	7. 80-13. 00	9. 00-12. 00	7. 50-13. 50	9. 00-12. 60	7. 80-11. 00	9. 00-11. 00	1. 476	1. 535
Mean±SD	10. 40±1. 52	10. 39±0. 79	10. 26±1. 66	10. 34±0. 99	9. 56±1. 06	10. 06±0. 57	0. 240	0. 227
t-test	0. 015		0. 160		1. 607			
P	0. 988		0. 874		0. 119			
Serum protein (g/dL):								
Range	4. 80-6. 50	4. 30-6. 00	4. 40-6. 70	4. 90-6. 40	4. 20-6. 00	4. 30-6. 40	1. 322	2. 517
Mean±SD	5. 63±0. 53	5. 26±0. 55	5. 65±0. 62	5. 71±0. 49	5. 33±0. 69	5. 55±0. 64	0. 278	0. 093
t-test	1. 902		0. 294		0. 933			
P	0. 067		0. 771		0. 359			
Serum albumin (g/dL):								
Range	2. 00-3. 40	1. 50-3. 00	1. 80-3. 60	2. 10-3. 50	1. 90-3. 20	2. 40-3. 30	2. 474	13. 685
Mean±SD	2. 68±0. 44	2. 24±0. 45	2. 90±0. 52	2. 85±0. 39	2. 52±0. 45	2. 85±0. 23	0. 096	0. 0001*
t-test	2. 729		0. 278		2. 494			
P	0. 011*		0. 783		0. 019*			

***Significant (P<0. 05)**

Table (4): Effect of the three therapeutic nutritional regimens on immune assay of the control and study groups with upper gastrointestinal cancer.

Delayed skin hypersensitivity (DSH)	G1 Hospital formula (control) (n=15)		G2 Enteral formula (n=15)		G3 Immune enhancing formula (n=15)		F Test P value	
	Pre *ns*	Post *ns*	Pre *ns*	Post *ns*	Pre *ns*	Post *ns*	Pre *ns*	Post *ns*
Mean ± SD	5. 38± 0. 771	2. 32± 1. 834	4. 02± 1. 162	3. 613± 1. 954	3. 746± 1. 253	4. 566± 1. 412	9. 54 0. 0003	6. 12 0. 0046
T test	1. 64		0. 69		5. 96			
P	0. 112		0. 495		0. 0001			
Tukey HDS test	**HDS[0. 05] =0. 98 G1 vs G2 p non significant G1 vs G3 p <0. 01 G2 vs G3 p <0. 01**							
Total lymphocytes count (/mm^3):								
Range	655-1300	750-1160	749-1290	790-1300	646-1198	745-1350	0. 564	4. 362
Mean± SD	1004. 93± 198. 74	943. 67± 150. 72	1068. 60± 174. 40	1068. 80± 169. 81	1009. 00± 177. 28	1120. 40± 183. 45	0. 573	0. 019*
t-test	0. 502		0. 003		1. 691			
P	0. 350		0. 997		0. 102			
Tukey HDS test	**HDS[0. 05] =1. 64 G1 vs G2 p <0. 01 G1 vs G3 p <0. 01 G2 vs G3 p <0. 01**							

Significant P≤ 0. 05

Table (5): Relationship between degrees of malnutrition assessed by serum albumin and total lymphocytic count and the three therapeutic nutritional regimens of the control and study groups with upper gastrointestinal cancer.

degree of Malnutrition	G1 Hospital formula(control) (n=15)				G2 Enteral formula (n=15)				G3 Immune enhancing formula (n=15)				χ^2 P	
	Pre		Post		Pre		Post		Pre		Post		Pre	Post
	n	%	n	%	n	%	n	%	n	%	n	%		
•Seum albumin (g/dL):														
-Mild (2. 8-3. 5 g/dl)	8	53. 3	2	13. 3	12	80. 0	10	66. 7	6	40. 0	10	66. 7	5. 42	18. 29
-Moderate (2. 1-<2. 8 g/dl)	4	26. 7	7	46. 7	1	6. 7	5	33. 3	5	33. 3	5	33. 3	0. 247	0. 001*
-Severe (<2. 1 g/dl)	3	20. 0	6	40. 0	2	13. 3	0	0	4	26. 7	0	0		
χ^2 P	5. 42 0. 066				4. 85 0. 088				5. 00 0. 082					
•Total Lymphocytic count (/mm3):														
-Mild (1200-1500)	2	13. 3	0	0	2	13. 3	3	20. 0	0	0	6	40. 0	2. 38	9. 60
-Moderate (800-<1200)	9	60. 0	11	73. 3	10	66. 7	11	73. 3	11	73. 3	8	53. 3	0. 666	0. 048*
-Severe (<800)	4	26. 7	4	26. 7	3	20. 0	1	6. 7	4	26. 7	1	6. 7		
χ^2 P	2. 20 0. 333				1. 25 0. 536				8. 27 0. 016*					

*Significant (P<0. 05)

Table (6): Effect of the three therapeutic nutritional regimens on the preoperative delayed skin hypersensitivity (DSH) pre and post nutritional regimen of the control and study groups with upper gastrointestinal cancer.

Delayed skin hypersensitivity classes (mm)	G1 Hospital formula (control) (n=15)				G2 Enteral formula (n=15)				G3 Immune enhancing formula (n=15)				χ^2 P	
	Pre ns		Post ns		Pre ns		Post ns		Pre ns		Post ns		Pre	Post
	n	%	n	%	n	%	n	%	n	%	n	%		
Anergic (No reaction)	2	13. 3	2	13. 3	3	20. 0	0	0	5	33. 3	0	0	14. 400	10. 557
Hypoergic (< 5 mm)	3	20. 0	12	80. 0	9	60. 0	9	60. 0	9	60. 0	7	46. 7	0. 006*	0. 032*
Normoergic (≥5 mm)	10	66. 7	1	6. 7	3	20. 0	6	40. 0	1	6. 7	8	53. 3		
Range	0-5. 70		0-5. 00		0-5. 50		2. 10-5. 30		0-5. 00		2. 10-7. 00			
Mean± SD	4. 27±1. 89		3. 73±1. 58		3. 61±1. 95		4. 02±1. 16		2. 32±1. 83		4. 81±1. 25			
t-test P	1. 238 0. 226				0. 693 0. 494				4. 347 0. 0001*					

*Significant (P<0. 05)

Table (7): Relationship between wound culture findings and types of nutritional regimen of the control and study groups with upper gastrointestinal cancer at 3rd and seventh post-operative day.

Findings of post-operative wound culture	G1 Hospital formula(control) (n=15)				G2 Enteral formula (n=15)				G3 Immune enhancing formula (n=15)				χ^2 P	
	3rd day		7th day		3rd day		7th day		3rd day		7th day		3rd day	7th day
	n	%	n	%	n	%	n	%	n	%	n	%		
•-ve infection	12	80. 0	4	26. 7	13	86. 7	8	53. 3	15	100	10	66. 7	10. 35	16. 12
•+ve infection	3	20. 0	11	73. 3	2	13. 3	7	46. 7	0	0	5	33. 3	0. 111	0. 041*
-Gram positive cocci	2	13. 3	0	0	0	0	3	20. 0	0	0	2	13. 3		
-Gram negative cocci	0	0	2	13. 3	2	13. 3	3	20. 0	0	0	1	6. 7		
-Gram positive bacilli	1	6. 7	4	26. 7	0	0	0	0	0	0	1	6. 7		
-Gram negative bacilli	0	0	5	33. 3	0	0	1	6. 7	0	0	1	6. 7		
χ^2 P	14. 80 0. 005				5. 39 0. 145				6. 00 0. 199					

**Significant (P<0. 05)

Table (8): Effect of the three therapeutic nutritional regimens of the control and study groups with upper gastrointestinal cancer on risk degree of post-operative complications.

Risk degree of post-operative complications. / Preoperative nutritional risk index(NRI)	G1 Hospital formula (n=15)				G2 Enteral formula (n=15)				G3 Immune enhancing formula (n=15)				χ^2 P	
	Pre		Post		Pre		Post		Pre		Post		Pre	Post
	n	%	N	%	n	%	n	%	n	%	n	%		
No risk (>100)	2	13. 3	0	0	0	0	1	6. 7	2	13. 3	3	20. 0	13. 01	15. 368
Mild (97. 5-100)	10	66. 7	2	13. 3	4	26. 7	6	40. 0	3	20. 0	8	53. 3	0. 043*	0. 018*
Moderate (83. 5-<97. 5)	3	20. 0	8	53. 3	8	53. 3	7	46. 7	6	40. 0	4	26. 7		
Severe (<83. 5	0	0	5	33. 3	3	20. 0	1	6. 7	4	26. 7	0	0		
χ^2 P	14. 61 0. 002*				2. 47 0. 481				6. 87 0. 076					

***Significant (*P*<0. 05)**

4. Discussion:

As regards to length of hospital stay, the present study revealed that there was found significantly relationship between type of nutritional regimen and length of hospitality where the length of hospital stay decreased significantly by 5 days in group III and 3 days in group II than group I who received the hospital diet. This is in the same line with other researchers; they reported a significant reduction in the length of hospital stay in immunonutrients group compared to the control groups. [51, 52]

In addition, many authors [53-60] had proven that preoperative nutrition improve postoperative outcome by helping to reduce postoperative morbidity and mortality, shorter hospital stay and decreasing postoperative complications. ***Braga. et. al; (2002), Braga and Rocchettis (2006)*** [61, 62] conclude that administration of immune – enhancing diets before surgery appears to be the key factor in improving outcomes in patient undergoing elective GI surgery. In both malnourished and well nourished patients, preoperative immuno- nutrition has demonstrated improved postoperative metabolic response and significantly reduced post operative infection rates and length of hospital stay.

The present study showed that, the majority of the three groups were moderately malnourished according to ***patient generated subjective global assessment of nutritional condition***. ***Gupta et. al, (2006)*** [62] emphasize that the nurses should assess the nutritional status of patients with gastrointestinal cancer as part of the their nursing assessment. While there is no "gold standard" method for nutritional assessment, Subjective global assessment (SGA) could play an important role in the nutritional assessment in oncology patients. The study done by ***Wu et. al, (2010)*** [63] which used SGA tool in assessing nutritional status of Chinese patients with gastrointestinal cancer concluded that the purpose of nutritional assessment for GIT cancer patients is to discover mild or moderate stated of malnutrition before the patient has become overtly wasted to be able to attempt to prevent further deterioration and to improve the quality of care. .

The present study agreed with the study done by ***Segura et al.*** [64] which showed that 52% of patients were moderately malnourished and the study done by ***Bauer et. al, (2002)***[65] which documented that only 25% of the patients were well nourished and that 75% were malnourished (59% moderately malnourished and 16% severely malnourished). More over other studies concluded that 42. 2% of the patients with gastrointestinal cancer (GIT) were mildly to moderately and 3. 2% were severely malnourished according to SGA and this is in the same line with the present study. [66]

The body weight, among anthropometric measures, is a basic consideration used in the evaluation of total body component and is a parameter in body mass index (BMI) assessment. Body weight is considered to be normal for an individual when body mass index (BMI) is the range of 20. 0 kg /m^2 to 24. 9 kg/m^2 BMI is useful in the evaluation of protein energy malnutrition. BMI has been shown to be lower in digestive system cancers (esophagus, stomach, colon and rectum). [67] Also ***many researchers***. [68-72] showed in the review done to discuss the importance of nutritional screening in treatment of cancer related weight loss that, many factors contribute to weight loss in patient with GIT cancer. This include a physiological abnormalities associated with tumor (such as malabsorption, obstruction, diarrhea, vomiting etc), the host response to the tumor (causing anorexia and altered metabolism) and the side effects of anticancer treatment

The finding of the present study demonstrated that a significant decline of the mean value of serum

albumin post nutritional regimen in group I compared to pre nutritional regimen, this decline may indicate in adequate nutritional support. On the other hand, this value increased significantly post nutritional regimen in group III. Moreover significant differences among the three groups were observed in relation to mean value of serum albumin post nutritional regimen these finding reveals a strong relationship between type of nutritional regimen and improvement of serum albumin. Where this improvement were more noticeable in group III who received the immune enhancing formula. The present study was in consistent with ***Erdem and Coworker (2001)*** [73] who showed a significant decrease of serum albumin in the 8th preoperative day in the study groups after oral supplement with immunonutrients in gastrointestinal cancer patient. Also ***Page and OO (2002)***[74] showed no significant differences between the study and control groups after receiving two types of feeding protocol (intravenous hydration versus enteral feeding post esophagectomy.

In addition, the patients who had specific degree of malnutrition pre nutritional regimen according to their serum albumin level had increased their degree of malnutrition after nutritional regimen in group I (i. e the patients who had moderate and sever depletion increased their percentage post nutritional regimen in group I). On the other hand, the patients who had mild depletion of serum, albumin in group III increased their percentage post nutritional regimen on contrary the patient who had severe depletion of serum albumin pre nutritional regimen decreased their percentage to none of patient had severe depletion post nutritional regimen in group II and III. These findings reveals a significant relationship between type of formula received and degree of malnutrition reflects the positive effect of immune enhancing formula on patients nutritional status than the other types of formula and also the effect of nutritional deficiencies on this parameter, the catabolic effect of disease and stress for patients in group I.

In the same aspect ***Gupta and Ihmaidat (2003)*** [75] mention that, the relationship between serum proteins and nutritional well being has long been recognized. Also they showed that plasma levels of proteins are affected by changes in energy intake and correlated highly with all other commonly used method of assessing nutritional state. Moreover, low serum albumin correlated with a reduced intake. In addition, they emphasizing on the use of albumin alone as a marker with extreme caution.

Preoperative serum albumin levels were documented by a number of trials to be an important predictor of postoperative complications, correlated with the incidence of major complications, including anastomotic leak, wound dehiscence, intra-abdominal abscess … etc. An inverse relationship existed between preoperative serum albumin and complications rate, with a low rate of about 8% in patients having a preoperative serum albumin level of 4. 25g/d L or higher, but increasing to a complication rate of over 50% when the albumin level was 1. 75 g/d L or lower and this is in the same line with the present study [76, 77]

As regard hemoglobin, it was found from the present study that the mean value of Hg level among the three groups was below normal level. Hemoglobin reflects oxygen carrying power of blood. When its level is reduced, oxygenation is reduced and tissue repair is altered resulting delayed healing. A decline of Hg value in this study may have many etiological factors including blood loss from tumor site, nutritional deficiencies, pharmacological agent and suppression of red blood cell production by the previous cancer therapy. According to literature, the healing process is affected by many factors. Of these, the most important factors include nutrition, oxygenation, and the blood supply to the wound area. [78 - 80]

The effect of nutritional therapy on immune competence was estimated in ***the present study*** by calculation of the total lymphocyte count (TLC) and delayed skin hypersensitivity test which are a useful indicator of nutritional status. This depend on the fact that changes in immune response can occur early in nutritional deficiency so they are considered as an early indicator of nutritional status and an index of response to nutritional therapy or support.

A significant relationship exists between type of nutritional regimen and total lymphocyte count (TLC) post nutritional regimens. Where a significant decrease in the mean total lymphocyte count was found in group I compared to group II and group III. Also group II showed significant decrease in TLC compared to group III post nutritional regimens. Hence, it was found that the mean value of TLC in the three groups was less than normal range pre and post nutritional regimens.

The study was done by ***Games. KV and Maio. R (2012)***[81] to determine the association between nutritional status and systemic inflammatory response in patient with GIT cancer showed that a number of patient exhibited immune deficiency based on TLC, which was related to both nutritional status and inflammatory response. ***Roxburgh et. al, (2009)***[82] found that the systemic inflammatory response in patients with GIT cancer was associated with a reduced TLC as well as increased white blood cell and neutronphile counts. Also it indicated that immune system deficiency in GIT cancer is multifactorial due to the tumor itself, cachexia, poor dietary intake, surgical trauma and treatment. Malnutrition is a factor that can affect the TLC, thereby compromising immunological status. However lymphocyte count can increase in the presence of bacterial infection.

Moreover there were significant relation between types of formula received and degree of malnutrition as assessed by TLC, this indicate significant improvement t in TLC for patient receiving immune-enhancing formula. This result consistent with the fact of nutritional deficiency affects the TLC or patients immune competence. ***Hudgens et. al, (2004)*** [83] mention that immune function is impaired in malnourished individual and can be used to indirectly assess nutritional status. ***Other authors*** [84, 86] mention that, malnutrition especially that resulting from inadequate intake of calories and protein, decrease the total number of lymphocytes. This is in the same line of ***Braga and Coworker (2003)*** [87] who demonstrated significant improvement in immunological markers (TLC and skin test) in patients given an immune-enhancing diets before surgery versus control. ***Micelle (2002)*** [88] mention that, there are other factors affecting TLC besides the nutritional states includes cancer disease, inflammation, infection, stress, pain, anesthesia and immunosuppressant drugs.

As regards delayed skin hypersensitivity test, the present study reveals that the mean value of delayed skin hyper sensitivity test increased significantly post nutritional regimen (7 days of nutritional therapy preoperatively) for the subject group who received immune nutrition On contrary this mean value deceased after nutritional therapy for group I and II. Moreover group III showed significant improvement in the mean value of delayed skin hypersensitivity response than group I and II. This reflects the positive effect of immune enhancing formula on immune status of patient consequently enhanced cell mediated immunity reflected in delayed skin hypersensitivity (DSH) response.

This is in the same line as the study done by ***Erdem et. al, (2001)*** [61] who studied preoperative oral supplement with immunonutrients in GIT cancer patient. He observed that patients given immunonutrients preoperatively 7 days had improved immunological measurements as TLC and delayed skin hypersensitivity (DSH) response and developed no postoperative complications. Also other researchers reported an improvement in delayed hypersensitivity test after 12 day of preoperative nutritional therapy and enhancement of immunological parameters. These results suggested the idea that the key point in elective surgery cancer patients is to provide immunonutrients before surgery [74, 90, 91, and 92].

Griffin et al. (2007) [92] concluded that delayed cutaneous hypersensitivity response was often restored by an aggressive nutritional support. The consequences of malnutrition on immunity described by ***Moulias (2002)*** [93] which characterized by decreased in cell – mediated immunity with reduction of T cells and cytokine production. ***Keusch (2003)*** [94] also noted that malnutrition could impair cell-mediated immunity and diminish antibody responses to protein antigens dependent on T. cell help.

The present finding support research hypothesis that immune enhancing formula had appositive effect on postoperative out come than hospital and standard enteral formula. ***Christou et al.*** [95] in a study of (19) reactive response of (DSH) and (26) anergic patient before and after elective surgery, the incidence of major postoperative infections episodes was 0% in the reactive group but 25% in the anergic group

In the same context the studies done by ***Braga et al. and Senkal et al. (2003)*** [87] demonstrated that cancer patient fed before surgery with immune enhancing diets, had a significant reduction of both post operative infections and shorter length of hospital stay (LOS) when compared to patients fed with a standard enteral formula. This reduction found in the supplemented group in both studies reflects the immunological and metabolic advantages of immunonutrition.

In fact, preoperative administration of immunonutrition reduced post operative infection rate regardless of the baseline nutritional states of patients (i-e malnourished patients and sub groups of well – nourished patients in whom an impairment of the host defense mechanisms has been reported after surgery. Also preoperative administration of immunonutrition improved metabolic postoperative response and significantly reduced post operative infection rate and length of hospital stay [61]. ***Seness et. al, (2008)*** [96] concluded that preoperative oral immunonutrition is associated with a 50% decrease in post operative complication for patient with GIT cancer.

The finding of present study showed statistically significant association was found between type of nutritional regimen received and risk degree of post operative complications according to the value of nutritional risk index (NRI). Where the risk degree of post operative complication decreased among the patients received Immune enhancing formula compared to group I and II. Also it was found from the findings of ***present study*** that the relative risk of postoperative complication increased significantly post nutritional regimen among the patients of group I and this suggest ***firstly*** that the hospital formula not sufficient to meet the patient nutritional needs, 40% of patient in group (I) had severe depletion of serum albumin post nutritional regimen and this indicate severe malnutrition. Also, the patient weigh post nutritional regimen for group I decreased to 70. 8 kg.

Further, these two parameters (serum albumin and patient weight) are essential in determining nutritional risk index (NRI) and consequently the risk degree of post operative complication. ***Schiesser et. al, (2009)*** [97] who study the correlation of NRI with postoperative

complications in patients undergoing gastrointestinal surgery. He study many nutritional risk scores to predict nutrition related complication in gastrointestinal surgery, among them, the nutritional risk index (NRI) has been shown to identify patients at risk for postoperative complications, including wound complications.

Also ***Schiesser et. al, (2009)*** [97] recognized that, A successful outcome after surgery of GIT patient is highly dependent on the incidence and severity of postoperative complications, and malnutrition has been reported to be as an important risk factor for Perioperative morbidity and mortality. In the same context many authors [98, 99, 100] found that low serum albumin was one of the factors correlated with postoperative complications.

Conclusion:

A relationship exists between types of nutritional regimen used preoperatively and post operative out come of the upper gastrointestinal cancer patient. Standard enteral formula had a better or positive effect on the nutritional health state and postoperative outcome than the hospital formula. Both immune-enhancing and standard enteral formulas had a positive effect on the nutritional health state and postoperative outcomes but the immune-enhancing formula more effective than the other two formulas, standard enteral formula and hospital formula. So prior to surgery Immune nutrition should be utilized in malnourished upper GI surgical patient support 7 – 10 days.

Recommendation

1. Patients who do not meet their requirement from normal diet should be encouraged to take oral supplements or enteral nutrition prior to surgery. Immune nutrition support should be utilized in malnourished upper GI cancer patient undergoing surgery 7 – 10 days prior to surgery.

2. Both SGA and NRI nutrition tests are predictive for malnutrition and post operative complications in patient undergoing upper GIT surgery so it should be used as routine preoperative assessment for those patient.

3. Nutritional health team involving, dietitians, oncology nurse specialist, physician, lab technician) should work together to provide an interdisciplinary nutritional care to provide accurate and adequate caloric needs for upper GIT cancer patient's needs and the appropriate type of feeding and formulas.

4. The daily flow sheets or nursing records must include a section on nutrition include weight measures and tolerance to nutritional therapy. Also application of the appropriate technique in measuring the dietary intake as24-Hour recall, food record, or diary and food frequency questionnaires which are a valuable indirect indicator of nutritional status.

Further studies

A. Effect of Perioperative immune nutrition on post operative clinical outcome for upper GIT cancer patient.

B. Impact of preoperative immune nutrition in malnourished patient with upper and lower GIT cancer.

C. Factors determining immune nutrition in the preoperative gastrointestinal cancer patient.

D. Comparing the effect of immune nutrition on the incidence of infections complication in well and malnourished gastrointestinal cancer patient.

E. Assessing the obstacles facing the critical care oncology nurse regarding the usage of immune nutrition and their effect on nurses' performance and patient outcome.

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