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Impact of Omega 3 and Glutamine Supplementation on Fistula Formation in Patients Undergoing Hemiglossectomy

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Abstract

Background: Surgical intervention for head and neck cancer has the potential to induce uncontrolled inflammation and immune suppression, which may result in tissue injury and an elevated risk of infectious complications. The immune response can be modulated, and immunonutrients can influence the progression of diseases. The study investigated the effect of adding omega 3 and Dipeptiven to standard feeding in head and neck patients undergoing oral cavity or mandibular resection.

Methods: This pilot study was performed on 70 cancer patients aged from 20 to 60 years old, both sexes, undergoing hemiglossectomy with/without submental flap with body mass index between 18.5-24.9, serum albumin above 3 gm. Patients were divided into two equal groups receiving standard feeding with caloric distribution (45%-50% carbohydrates,20-35% from fats, and 10-35% from protein) in group A, plus perioperative supplementation with omega 3 and dipeptiven (immunonutrition mixture) in group B.

Results: Demographic data, duration of surgery, and cancer types were comparable between both groups. Fistula formation and healing duration were significantly decreased in group B than in group A (P value=0.01).

Conclusions: Immunonutrition considerably affects lowering fistula incidence in hemiglossectomy patients. Also, immonutrition lowered the healing time of this fistula.

Keywords: Omega 3 and glutamine supplementation, fistula formation, hemiglossectomy, fistula healing.

Introduction:

Both cancer and its many treatment methods are factors that lead to cachexia. Malnutrition often occurs in cancer patients and may have a detrimental impact on treatment outcomes. Conversely, the adverse effects of anticancer treatments might result in insufficient food consumption and eventual malnutrition [1, 2].

The European Society of Clinical Nutrition and Metabolism (ESPEN) recommendations identify 3 forms of malnutrition: disease-related malnutrition (DRM) with inflammation, DRM without inflammation, and malnutrition/undernutrition without illness [3]. Furthermore, DRM accompanied by inflammation might be linked to chronic conditions like cancer and chronic renal illnesses, as well as acute conditions such as sepsis or acute traumas. Chronic DRM with inflammation was seen as synonymous with cachexia [4].

Immunonutrition (IN) is the ability to influence the immune system's function via targeted food treatments. This notion may be used when a changed nutrition supply affects inflammatory or immunological responses. The administration of immunosuppression after major surgery raises the risk of infection-related morbidity and mortality. Infection-related complications may be mitigated by enhancing immune function during this time [5].

Immunonutrients are substances or nutrients that modulate the activities of immune activation when consumed more substantially than are typically found in the diet. W-3 polyunsaturated fatty acids, glutamine, arginine, nucleotides, taurine, probiotics, and numerous others are some immunonutrients. Hospitalized patients receiving these nutrients have a reduced stay and infection rate [6, 7].

The current research focused on omega 3 and glutamine supplementation's effect on fistula formation and healing in hemiglossectomy patients with/without submental flap.

The study investigated the effect of adding omega 3 and Dipeptiven to standard feeding in head and neck patients who undergo oral cavity tumor resection or mandibular tumor resection (IN mixture) on wound infection, fistula formation, and length of hospital stay, total dose of intraoperative and postoperative opioids, pain incidence, mortality, and other postoperative complications.

Patients and Methods:

This pilot study was performed on 70 cancer patients aged from 20 to 60 years old, both sexes, American Society of Anesthesiologists (ASA) physical status I or II undergoing hemiglossectomy with/without submental flap with body mass index (BMI) between 18.5-24.9, with serum albumin above 3 gm. The study was done from February 2023 to August 2023 after approval from the Ethical Committee Cairo University Hospitals. Informed written consent was obtained from the patient.

The exclusion criteria included patients classified as ASA III or IV, aged over 60 or under 18, with serum albumin levels below 3, pre-existing severe malnutrition, allergies to test substances, and patients using tranquilizers, hypnotics, sedatives, psychiatric medications, steroids, or NSAIDs.

Patients were divided into two equal groups. Group A (standard feeding): received only standard feeding with caloric distribution (45%-50% carbohydrates,20-35% fats, and 10-35% from protein). Group B (IN mixture): The patient received perioperative supplementation with omega-3, dipeptiven (IN mixture), and standard feeding. Participants and outcomes assessors were blind to group allocation.

Group B received supplements (L Alanyl L Glutamine at 1 gm/kg/day via intravenous infusion and omega 3 at a dose of 3 gm daily orally) five days before the operation. Group B received supplements and standard feeding, while Group A received only standard feeding. Patients had hemiglossectomy with or without a submental flap.

We monitored both groups for fistula occurrence and tracked the healing progress of the fistula throughout their hospital stay and for one-month post-surgery.
The primary outcome was the occurrence of fistula. The secondary outcomes was healing time for this fistula.

Sample size calculation:
G*Power 3.1.9.2 (Universitat Kiel, Germany) was utilized to compute the sample size. The incidence of fistula formation (the primary outcome) was 40% in group A and 10% in group B, according to the results of a pilot study (10 cases in each group). 80% study power, a 95% confidence interval, a group-to-case ratio of one to two, and the addition of two cases to each group to account for attrition all influenced the determination of the sample size. Consequently, 35 patients were recruited for each cohort.

Statistical analysis
SPSS v26 (IBM Inc., Chicago, IL, USA) was used for statistical analysis. The normality of the data distribution was assessed using histograms and the Shapiro-Wilks test. Using an unpaired Student's t-test, quantitative parametric variables were compared between the two groups in mean and standard deviation (SD). When applicable, the Chi-square or Fisher's exact test was utilized to analyze qualitative variables expressed as frequency and percentage (%). A two-tailed P value < 0.05 was considered statistically significant.

Results:
Eligibility was determined for eighty-nine patients in this investigation; A total of eight individuals declined to participate, while eleven did not meet the criteria. Two equal groups, each consisting of thirty-five patients, were established from the randomization of seventy patients. All patients were followed up and analyzed statistically. Figure 1
Demographic data and duration of surgery were comparable between both groups. Table 1
Cancer types were comparable between both groups. Table 2
Fistula formation and healing were significantly lower in group B than in group A (P value=0.01)**.** Table 3

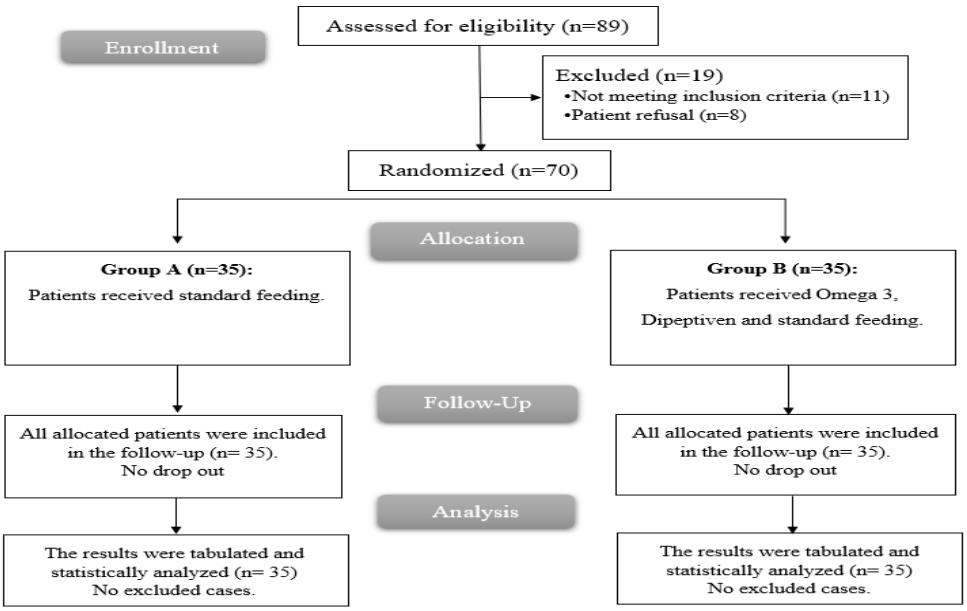

Figure 1: CONSORT flowchart of the enrolled patients

Table 1: Demographic data and duration of surgery of the studied groups

		Group A (n=35)	Group B (n=35)	P value
Age (years)		41.09 ± 10.32	39.17 ± 11.76	0.472
Gender	**Male**	16 (45.71%)	17 (50%)	0.811
	Female	19 (54.29%)	18 (51.43%)	
BMI (kg/m^2)		21.84 ± 2.03	22.38 ± 1.69	0.232
Duration of surgery (min)		144.29 ± 22.59	149.86 ± 20.67	0.286

Data are presented as mean ± SD or frequency (%). BMI" Body mass index.

Table 2: Cancer type of the studied groups

	Group A (n=35)	Group B (n=35)	P value
Hemiglossectomy with submental flap	22 (62.86%)	19 (54.29%)	0.627
Hemiglossectomy without submental flap	13 (37.14%)	16 (45.71%)	

Data are presented as mean ± SD or frequency (%).

Table 3: Fistula formation and healing duration of the studied groups

	Group A (n=35)	Group B (n=35)	P value
Fistula formation	11 (31.43%)	2 (5.71%)	**0.01***
Healing duration (weeks)	3.6 ± 0.55	2 ± 0	**0.01***

Data are presented as frequency (%). *Significantly different as P value ≤0.05.

Discussion

The incidence of malnutrition among head and neck cancer patients is high due to the tumors' impact on metabolism and swallowing function, leading to a higher risk of postoperative complications. Administering perioperative IN may decrease complications and length of stay following surgery [8]. An intact immune system is essential for postoperative recovery, particularly wound healing. However, tumor-associated immunosuppression may damage it. [9].

The present study exhibited that the rate of fistula formation in hemiglossectomy with/without submental flap decreased in the experimental group than in the control group.

In accordance with our findings, Muller et al. [10] investigated the influence of IN on post-head and neck cancer salvage surgeries complications. They showed that in the group that received IN, the overall complications incidence among patients was considerably reduced compared with the control group (35% vs. 58%, p = 0.027). The model's decrease remained statistically significant, including comorbidities, risk factors, tumor features, surgical type, flap reconstruction, and sociodemographic variables (p = 0.049). There was a reduction in all complication subcategories, specifically wound dehiscence, wound abscess, fistula, and hematoma/hemorrhage/seroma. Nevertheless, no statistically significant variations were observed in the severity of these complications. Comparing the two groups, there was no statistically significant difference in the overall local complication incidence (p = 0.57; control group: 22%; intervention group: 18%).

Similarly, a systematic review and meta-analysis of randomized controlled trials [11] Investigated the effect of perioperative IN on postoperative outcomes for patients undergoing cancer surgeries of the gastrointestinal tract or head and neck, IN decreased anastomotic leakage compared to conventional nutritional therapy.

Also, Howes et al. [12] exhibited that following head and neck cancer surgeries, IN may decrease the risk of fistula formation (the absolute risks were 11.3% in the standard care vs. 5.4% in IN groups).

Previous research [13] examined the effect of preoperative IN on short-term prognoses in patients who underwent head and neck squamous cell carcinoma surgeries. They illustrated that surgical complications incidence within 30 days was comparable across the two groups (29.9% vs 34.4%, P = .208). Patients with high compliance had considerably lower rates of local wound infections, wound abscesses, and fistulas compared to the control group. Both groups had comparable rates of local hematoma, hemorrhage, seroma, and flap necrosis incidences, with percentages of [12.0% vs. 9.6% (P = .291)] and [3.0% vs 3.8% (P = .274), respectively]. As determined by the Dindo classification, the highly compliant patients had significantly fewer local and systemic complications (21.0% vs 29.2%, P = .027). Regarding 30-day postoperative mortality, readmission rates, and surgical interventions due to complications, no statistically significant disparities were observed between the two groups.
This study found that healing time was faster in the experimental group than in the control group, around two weeks and 3.6 ± 0.55 weeks, respectively.
Similarly, a previous research [14] studied the nutritional, immunological, and wound healing results in patients who received IMN compared to a regular formula. Their statement indicated that wound healing results were comparable among the groups. Wounds in the therapy group seemed to exhibit serous leakage erythema for a shorter time, although most wounds healed well by the third week.
Also, Chow and Barbul [15] stated that IN's involvement in wound healing remains a subject of curiosity and debate. While it is established that shortages in some nutrients might hinder the healing process, particular immune-modulating nutrient supplementation lacks consistent evidence of enhanced wound healing. Supporting the immune system during wound healing by optimizing nutrition is crucial in medical and surgical professions due to the significant expenses associated with wound care and repair.
Also, Farreras et al. [16] found that administering a formulation containing omega-3 fatty acids, arginine, and ribonucleic acid shortly after surgery enhanced wound healing in patients who had gastrectomy for stomach cancer by increasing hydroxyproline production.
The study's limitations included the fact that the sample size was relatively small. The study was in a single center.

Conclusions:
Immunonutrition considerably affects lowering fistula incidence in hemiglossectomy patients. Also, immonutrition lowered the healing time of this fistula.
Financial support and sponsorship: Nil
Conflict of Interest: Nil

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