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Utility of a perioperative nutritional intervention on postoperative outcomes in high-risk head & neck cancer patients

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SUMMARY

Objectives: Investigate both the utility and feasibility of perioperative nutritional supplementation with an arginine-enriched immunonutrition formula to high-risk head and neck cancer surgical patients and examine its effects on acute post-operative clinical outcomes.
Materials & Methods: This prospective, non-randomized, interventional cohort study compared high-risk head and neck cancer surgical patients who consumed a pre- and post-operative arginine-based nutritional supplement to those that did not. Outcome measures included post-operative complications, length of hospitalization, readmission rates and measurement of nutritional biomarkers.
Results: 195 high-risk head and neck cancer surgical patients were enrolled. 59% of the patients used the nutritional supplement, 41% did not. Of the 80 patients who did not receive the immunonutrition formula, 38 (47.5%) experienced post-operative complications of all types as compared to 29 of the 115 (25.2%) patients who did consume the product ($p = 0.0021$). Pharyngeal leaks or fistulas were the most common post-operative complications in both groups and more common in patients who did not receive supplementation ($p = 0.007$). Length of stay was on average 2.8 days longer in patients who did not have enhanced nutrition ($p = 0.02$), while readmission rates between the two groups were similar ($p = 0.91$). Measurements of nutritional biomarkers were not reported secondary to low collection rates.
Conclusion: Enhanced perioperative nutrition may result in significant reductions of post-operative fistula formations and decreased length of stay in a high-risk head and neck cancer population, even in the setting of poor compliance. The potential quality improvement in both patient care and healthcare cost is both real and significant.

Introduction

Significant malnutrition exists in up to 60% of all head and neck cancer patients [1]. The intimate relationship between the location of tumors of the head and neck and the aerodigestive tract clinically manifest as local pain, trismus, dysphagia and aspiration, all of which impose significant functional limitations on the ability to achieve appropriate nutrition by mouth. Moreover, regardless which type of therapy a patient pursues, there are substantial side effects of each. Surgery, irradiation and chemotherapy alike will further limit the ability to take nutrition by mouth in the immediate post-treatment period, as well as potentially chronically, depending on the type of therapy pursued and the extent of the patient's disease [2]. Furthermore, numerous authors have documented the immunosuppressive nature of both the tumor as well as the treatments for head and neck cancer, thereby increasing the risks of post-treatment complications [3–7].

Meanwhile, malnutrition is directly associated with increased morbidity, mortality, post-operative complications and decreased quality of life [2,8–11]. It has been well-reported that between 20% and 50% percent of high-risk surgical head and neck cancer patients will encounter various post-operative complications including major wound infections, fistulas, anastomotic leaks, or other medical issues that acutely lead to a prolonged length of stay (LoS) and ultimately a worse prognosis [2]. As a response, multiple investigations have attempted to address both malnutrition and immunosuppression in the head and neck cancer patient by examining the efficacy of perioperative immune-enhanced

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supplementation, specifically with the use of arginine-enriched enteral formulas [12].

Arginine, a conditionally essential amino acid, along with other amino acids and nutrients such as ω-3 fatty acids, nucleotides and vitamins have demonstrated a pharmacological effect on the immune system and thus have been labeled as immunonutrients [13]. In turn, delivery of these nutrients is known as immunonutrition. The study of immunonutrition in the field of head and neck cancer has largely focused on the reduction of post-operative complications such as fistulas, wound infections and prolonged LoS. Immunonutrition remains a relatively new area of investigation in head and neck surgery when compared to other surgical fields such as gastrointestinal surgery. Several smaller studies in the head and neck literature have demonstrated a significant reduction in post-operative fistula formation and hospital stay in patients who were administered arginine-enriched formulas postoperatively [12]. One of these studies even revealed an improved long-term overall and disease specific survival [14].

The purpose of this prospective, nonrandomized, interventional cohort study was to investigate both the utility and feasibility of the administration of perioperative nutritional supplementation with an arginine-enriched immunonutrition formula at a tertiary medical center. The main clinical outcome measures of this study focused on post-operative complications, length of stay and readmission rates. In addition, we examined the value of perioperative screening of biochemical markers of nutritional status to assess the effect of an immunonutrition formula.

Methods

This study received approval from the University of Pittsburgh Institutional Review Board. An initial quality improvement project undertaken over a 12 month period served to facilitate a perioperative immunonutrition initiative by coordinating distribution of arginine-enriched[1] formulas in the preoperative outpatient setting and ensuring delivery of a similar formula in the postoperative inpatient setting. This quality improvement initiative was also responsible for procurement of preoperative and operative day laboratory blood draws.

After assessing the feasibility of this initiative and subsequent continuation of this improvement project, a total of 195 high-risk head and neck cancer surgical patients were enrolled. Patients were labeled as high-risk if they met one of three criteria: AJCC Stage III or greater disease [15], prior definitive radiotherapy as a part of primary treatment, or use of a microvascular free flap for reconstruction. 5 days worth (3 cartons per day) of a commercially available arginine-based nutritional formula, IMPACT Advanced Recovery® (Vevey, Switzerland) was offered to all patients in the preoperative setting. At the time of distribution of the formula, pre-operative laboratory markers of nutritional status (prealbumin, thyroid stimulating hormone (TSH), and C-reactive protein (CRP)) were gathered. On the morning of the patient's operation, and again on post-operative day 5, the identical laboratory markers were assessed. A similar, commercially available formula, IMPACT Peptide 1.5® (Vevey, Switzerland) was administered as tube feedings based on a patient's body weight until at least post-operative day 5. The ingredients of each formula are listed in Table 1 [16,17].

Post-operative complications including wound infection, pharyngeal leak, pharyngocutaneous fistula formation, microvascular free flap failure or dehiscence, post-operative pneumonias or bleeding that required operative repair and other post-surgical complications were recorded. Additionally, the medical record was reviewed and readmissions within a 30 day period within the same hospital system were tabulated. Early in the initial quality improvement initiative, it was apparent there was poor patient compliance in obtaining the pre-operative formula and as such, patients who did not receive the formula were used as a comparison to those patients that did obtain and consume the immunonutrition formula. Statistical analysis was performed using $\chi 2$ or Student's t-test where appropriate.

Table 1
Ingredients of pre- and post-operative nutritional formulas.

	IMPACT Advanced Recovery (237 mL carton)	IMPACT Peptide 1.5 (250 mL carton)
kcal/mL	1.4	1.5
Calories	340 kcal	375 kcal
Total fat	9.2 g	15.9 g
n-3 fatty acid	1.1 g	1.2 g
Total carbohydrates	45 g	35 g
Dietary fiber	3.6 g	–
Total protein	18 g	23.5 g
L-Arginine	4.2 g	4.675 g
Dietary nucleotides	430 mg	450 mg
Prescribed intake	3 cartons/day	per patient's body weight

Results

Between January 2012 and May of 2014, 195 high-risk head and neck cancer surgical patients were enrolled into this non-randomized interventional cohort study. 115 (59%) of the patients received the formula while 80 (41%) patients did not. There were more men than women in both categories, but proportionately more women in the group that did not receive the formula ($p = 0.0042$). There were no differences in age or proportion of primary tumor locations ($p = 0.82$ and 0.26 respectively) (Table 2).

Of the 80 patients who did not receive the immunonutrition formula 38 (47.5%) experienced post-operative complications of all types as compared to 29 (25.2%) of the 115 patients who did consume the product (Fig. 1) ($p = 0.0021$). The first and second most common post-operative complications in both groups were pharyngeal leak or fistula formation followed by surgical site infections. Pharyngeal leaks and fistula formation were more common in patients who did not receive the nutritional supplement ($p = 0.007$). Meanwhile, pneumonias were more commonly identified in patients who did not receive the arginine-based formula, but this was not a statistically significant difference ($p = 0.11$) (Fig. 2).

The average length of stay in those who did not receive the formula was 12.48 days with a standard deviation of 10 days as compared to 9.68 days ± 6.9 days, for an average difference of 2.8 days ($p = 0.02$). Meanwhile, the readmission rates for the 2 groups were similar at 16.25% in those who did not take the formula and 15.65% in those who consumed the product ($p = 0.91$) (Table 3).

The measurement of nutritional biomarkers was sporadic and collection rates ranged from as high as 90% to as low as 5%. Furthermore, there was great variability on the dates of collection relative to the patient's surgery, and thus given this discordance, the majority of these results have been omitted from this study. The only reliably collected nutritional marker was pre-operative and pre-supplement prealbumin levels in patients who did not receive the nutritional supplement as compared to those who did respectively. Pre-operative prealbumin levels were measured in 68.8% of patients who did not receive the nutritional supplement as compared to 71.3% of those that received the supplement. Average prealbumin levels were found to be within the normal range

[1] LoS: length of stay.