Proactive versus Reactive Nutrition Therapy in Head and Neck Cancer Patients Treated with Chemoradiotherapy: A Case Series

Dian Araminta Ramadhania*, Diyah Eka Andayani, Wina Sinaga
Department of Nutrition, Faculty of Medicine, Universitas Indonesia - dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

ARTICLE INFO
Received : 28 September 2022
Reviewed : 13 October 2022
Accepted : 16 November 2022

Keywords:
chemotherapy, head and neck cancer, nutrition therapy, radiotherapy

ABSTRACT
Introduction: Malnutrition is frequently found in head and neck cancer (HNC) patients subjected to chemoradiotherapy. Furthermore, the condition can hinder therapy and increase patient mortality. Nutrition therapy may be given proactively and reactively before and during chemoradiotherapy, as a response to nutritional status deterioration. Early or proactive nutrition therapy is considered superior in minimizing weight loss and interruption days during chemoradiotherapy. Therefore, this study aims to explore the clinical impact of proactive and reactive nutrition therapies.

Case Presentation: A total of 4 HNC patients were subjected to chemoradiotherapy and received nutrition therapy at different points. Approximately 2 patients received proactive nutrition therapy, while the other 2 underwent reactive nutrition after cancer treatment. Increased intake was achieved through administering oral nutrition supplements and supporting a nasogastric tube. Patients who received proactive nutrition therapy experienced less weight loss compared to reactive therapy. Delayed initiation of nutrition therapy resulted in a more pronounced weight loss. Therefore, it was crucial to maintain energy intake in line with established recommendations to effectively uphold the nutritional status of cancer patients.

Conclusions: Proactive nutrition therapy should be provided to HNC patients before the commencement of cancer therapy.

INTRODUCTION
Head and neck cancer (HNC) is the 7th most common cancer found in developing countries, specifically in Southeast Asia. HNC patients have a relatively higher prevalence of malnutrition due to the cancer location which may disrupt swallowing function and approximately 74.2% are malnourished. Malnutrition is caused by cancer and acute toxicity associated with multimodality treatment, such as nausea and vomiting, xerostomia, severe mucositis, dysgeusia, and dysphagia [1,2].

Malnutrition in HNC patients is a serious clinical concern capable of increasing chemoradiotherapy toxicity and interruption, diminishing the quality of life (QoL), and increasing mortality. Therefore, adequate nutrition therapy is crucial to maintain their nutritional status. The study by Kapala et al. [3] showed that nutrition therapy during chemoradiotherapy significantly minimized weight loss by 2–3 kg and enteral nutrition support was recommended for these patients. However, the optimal timing of tube feeding commencement remains an ongoing debate. Nutrition therapy can be given before the commencement (proactive or prophylactic) or during cancer treatment when deemed necessary (reactive). Paccagnella et al. [4] proved that patients who received proactive nutrition therapy before the start of chemoradiotherapy lost less weight compared to the early nutrition therapy program (-4.6±4.1% vs. -8.1±4.8% of pre-treatment weight). Fewer patients in the first group experienced radiotherapy breaks due to toxicity compared to the latter group (30.3% vs. 60.1%). Another study implied that QoL was decreased due to prolonged tube dependency and a sense of desolation [5]. Therefore, this case series will explore the clinical impact of nutrition therapy commencement timing during chemoradiotherapy in HNC patients.
CASE PRESENTATION

This case series study reported 4 HNC patients who were subjected to concurrent radiotherapy of total doses of 70 Gy and cisplatin-based chemotherapy at Instalasi Pelayanan Terpadu Onkologi Radiasi (IPTOR), dr. Cipto Mangunkusumo Hospital (RSCM). The initial examination was carried out when patients were first consulted and came to the nutrition outpatient clinic at IPTOR. Body composition was assessed using OMRON Karada ScanTM body composition monitor HBF-375 and the initial characteristics of the four patients are shown in Table 1.

Case 1

The 1st patient received nutrition therapy since pre-chemoradiation (reactive therapy) and was subjected to head and neck chemoradiotherapy for approximately 6 weeks. During the process, the patient mainly complained of xerostomia and odynophagia which caused a decrease in appetite. In the 4th week, the intake increased after consuming oral nutrition supplements (ONS) amounting to 40% of the total daily energy. Consumption of ONS was continued until 1 week post-chemoradiotherapy and total weight loss was 11.1 kg or 13.7% during chemoradiotherapy. The patient had suffered from COVID-19 since the therapy was delayed, experiencing a weight loss of 5 kg during the infection period. At the end of chemoradiotherapy, the muscle and fat mass increased to 28.4% and 28.9%, respectively. The average weekly intake and weight changes can be seen in Figure 1.

Case 2

The 2nd patient was referred to Clinical Nutrition Department on the 4th week of chemoradiotherapy, and received nutrition therapy (proactive therapy), experiencing a weight loss of 5.8 kg or 8.7%. Analysis of intake during the first 3 weeks of chemoradiotherapy was not available. The patient mainly complained of xerostomia and stomatitis, making it difficult to eat, and only blended food and ONS were consumed during the 3rd week. Nasogastric tube (NGT) insertion was also advised but kept refusing until chemoradiotherapy was completed. A break in radiotherapy for 3 days was reported because the radiotherapy mask became loose due to weight loss. Furthermore, the total weight loss was 11.2 kg or 17% with muscle and fat mass decreasing and increasing to 32% and 20.4%, respectively. A few days after the last chemoradiotherapy fraction, the patient felt weak and subsequently agreed to use NGT for feeding to increase intake drastically. The average weekly intake and weight changes can be seen in Figure 2.

Table 1. Initial characteristics of the four subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54</td>
<td>41</td>
<td>47</td>
<td>55</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>NPC</td>
<td>NPC</td>
<td>NPC</td>
<td>SCC of the tongue (oropharynx)</td>
</tr>
<tr>
<td>Clinical staging</td>
<td>T,N,M&lt;sub&gt;i&lt;/sub&gt;</td>
<td>T,N,M&lt;sub&gt;i&lt;/sub&gt;</td>
<td>T,N,M&lt;sub&gt;i&lt;/sub&gt;</td>
<td>T,N,M&lt;sub&gt;i&lt;/sub&gt;</td>
</tr>
<tr>
<td>Radiation fraction</td>
<td>Pre-radiation</td>
<td>21 of 33</td>
<td>12 of 33</td>
<td>Pre-radiation</td>
</tr>
<tr>
<td>Chemotherapy cycle</td>
<td>Pre-chemo</td>
<td>3 of 5</td>
<td>2 of 6</td>
<td>Pre-chemo</td>
</tr>
<tr>
<td>MST score</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Weight changes in the last 6 months*</td>
<td>↑2.3 kg</td>
<td>↓6.8 kg (10%)</td>
<td>↓20.7 kg (25%)</td>
<td>↓9.6 kg (16.6%)</td>
</tr>
<tr>
<td>Decreased intake</td>
<td>No</td>
<td>52% TEE within the last 1 month</td>
<td>74% TEE within the last 6 months</td>
<td>49% TEE within the last 8 months</td>
</tr>
<tr>
<td>Nutritional status</td>
<td>BMI (kg/m2)</td>
<td>30.2 (obese 2)</td>
<td>22.5 (normoweight)</td>
<td>26.4 (obese 1)</td>
</tr>
<tr>
<td>Based on ASPEN criteria</td>
<td>No malnutrition</td>
<td>Moderate malnutrition</td>
<td>Moderate malnutrition</td>
<td>No malnutrition</td>
</tr>
<tr>
<td>Body composition</td>
<td>Fat mass (%)</td>
<td>31.6 (very high)</td>
<td>17.7 (normal)</td>
<td>36.9 (very high)</td>
</tr>
<tr>
<td></td>
<td>Muscle mass (%)</td>
<td>27.5 (low)</td>
<td>32.9 (low)</td>
<td>27.6 (normal)</td>
</tr>
<tr>
<td></td>
<td>FFMI (kg/m2)</td>
<td>20.7 (normal)</td>
<td>18.4 (normal)</td>
<td>16.6 (normal)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>DM type 2</td>
<td>AKI</td>
<td>Hypertension</td>
<td>AKI</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute on CKD</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: ↑ = increase; ↓ = decrease; AKI = acute kidney injury; ASPEN = American Society for Parenteral and Enteral Nutrition; BMI = body mass index; CKD = chronic kidney disease; DM = diabetes mellitus; FFMI = fat-free mass index; MST = Malnutrition Screening Tool; NPC = nasopharyngeal cancer; SCC = squamous cell carcinoma; TEE = total energy expenditure; TNM = tumor, nodes, metastases.
Case 3
The 3rd patient started receiving nutrition therapy in the 2nd week of chemoradiotherapy (reactive therapy), hence, the analysis of intake during the 1st week was unavailable. The reported complaints were nausea, xerostomia, and odynophagia, specifically since the 3rd week of chemoradiotherapy which caused a decrease in intake. The patient started consuming ONS approximately amounting to 20% of total energy intake, but only slightly increased the energy intake. The patient was advised to further increase the amount of ONS consumed and use NGT to aid the feeding process. During the 4th week, ONS consumption was increased to 50% of the total energy intake but only agreed to use NGT in the last week of chemoradiotherapy due to the inability to swallow food. Total weight loss was 7 kg or 10.7% and the muscle and fat mass decreased and increased to 22.9% and 35.6%, respectively. Meanwhile, the use of NGT was maintained until 2 weeks post-chemoradiotherapy. The average weekly intake and weight changes can be seen in Figure 3.

Case 4
Similar to the first patient, the 4th patient received nutrition therapy since pre-chemoradiation (proactive therapy) and was subjected to chemoradiotherapy for 6 weeks. The reported complaints were nausea, xerostomia, and stomatitis which became more severe since the 2nd week of chemoradiotherapy, then started consuming ONS amounting to 15% of the total energy intake, and eating soft foods. The consumption of ONS was increased to 70% of the total energy intake during the 4th and 5th weeks, where the muscle and fat mass were decreased and increased to 23.9% and 30.1%, respectively. After the last fraction, the nausea worsened, which further decreased intake due to the usage of NGT for feeding support. The use of NGT was maintained until 2 weeks post-chemoradiotherapy and the total weight loss during chemoradiotherapy was 6.1 kg or 12.7%. The average weekly intake and weight changes can be seen in Figure 4.
Balancing the right timing, quantity, and quality of food intake is the mainstay of nutrition therapy during cancer treatment. Adequate nutrition is also required for the regeneration of healthy tissues that are influenced by chemoradiation [9]. The consumption of 25–30 kcal/day was recommended to maintain body weight in cancer patients [10]. However, consumption of daily energy of more than 30 kcal may be needed as shown in these four patients. Studies by Faria et al. [11] and Della Valle et al. [12] suggested that consumption of a minimum of 35 kcal/day was needed to maintain body weight in HNC patients undergoing chemoradiotherapy. Considering that the 1st patient suffered from major weight loss because of COVID-19 infection, approximately 6.1 kg was lost due to chemoradiotherapy. The 4th patient also lost 6.1 kg during chemoradiotherapy, while the 2nd and 3rd lost more weight, namely 11.2 kg and 7 kg, respectively.

DISCUSSION

This case series was conducted to examine the benefit of early nutrition therapy on nutritional status in HNC patients subjected to chemoradiotherapy. All patients experienced a decrease in intake, mainly due to the severity of radiation toxicity, specifically after week 2 of chemoradiotherapy. The most disturbing symptom is xerostomia or thickened saliva and stomatitis, making it difficult for the patient to swallow [6]. Patients in cases 1 and 4 received early medical nutrition therapy at the beginning of the process (reactive therapy), while the other 2 started receiving medical nutrition therapy in the middle (proactive therapy). The intake of all patients increased with the administration of ONS and experienced a drastic increase in intake after using an NGT [7]. However, patients were reluctant to use NGT for feeding support mainly because of social beliefs such as tube feeding reserved for terminally ill patients [8].
This showed that the 1st and 4th patients experienced less weight loss compared to the other two receiving reactive nutrition therapy. Furthermore, patients who started receiving nutrition therapy lost the most weight.

All patients experienced weight loss of >10% during chemoradiotherapy due to a decrease and increase in muscle and fat mass percentage [13,14]. Muscle mass percentage loss comparison with the same gender showed that patients receiving proactive nutrition therapy were more successful in maintaining muscle mass. This pattern was observed in the male group, which comprised the 1st and 2nd patients experiencing a gain of 0.9% in muscle and fat mass. Similarly, in the female group comprising the 3rd and 4th patients, there was a decrease of 4.7% and 2.3% in muscle mass. Systemic inflammation is the main cause of muscle wasting in cancer patients. Men suffered from greater muscle loss during inflammation, while women were more susceptible to disuse-induced muscle wasting. This was caused by different responses to inflammation due to differences in mitochondrial metabolism and hormone interactions [15]. However, this case series showed the opposite results where women experienced greater muscle loss during cancer treatment. This was explained by the variance in inflammatory and physical activity levels which was not considered in this study.

Other analyses showed that patients receiving early nutrition therapy within the first week of chemoradiotherapy or before significantly lost less weight. However, referral to the Clinical Nutrition Department for nutrition therapy usually occurs after the manifestation of symptoms and weight loss. Individualized and routine dietary counseling combined with oral supplementation and prompt tube feeding showed a reduction in weight loss, as well as a significant improvement in chemoradiotherapy tolerance and QoL. A total of 60.6% of HNC patients needed tube feeding during the chemoradiotherapy period. There were no standardized criteria for patient selection regarding prophylactic tube feeding placement, even though those with a greater risk associated with significant weight loss benefited from the procedure [4,16,17]. Patients had oral or oropharyngeal, and nasopharyngeal or hypopharyngeal cancers, and received chemoradiotherapy [17].

CONCLUSIONS

The administration of ONS and enteral nutrition was conducted through the NGT to achieve the nutrient intake target. Meanwhile, proactive nutrition support, provided before patients suffered from major weight loss helped to maintain nutritional status during cancer treatment.

DECLARATIONS

Competing of Interest
The authors declare no competing interest in this study.

Acknowledgment
Not applicable

REFERENCES