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Symptom Cluster Management of Mucositis, Xerostomia, Dysgausia, and Dysphagia in Patients with Head and Neck Cancer Receiving Concurrent Chemoradiation Therapy

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Abstract

Evidence of symptom clusters and their effects on individual outcomes in head and neck cancer patients, especially when they received chemoradiation therapy is limited and few studies have been undertaken recently. Symptoms cluster of mucositis, xerostomia, dyagausia, and dysphagia in patients with head and neck cancer have been identified during their active treatments would be more beneficial for healthcare provider to manage the symptoms, be reminded of the most severity symptoms, and evaluate the symptom status outcome for effective management. Therefore, this symptom cluster should be identified by radiation oncology nurses and providing early effective intervention will improve patients' self-management and adherence with treatment without disrupted will promote outcome and experience.

Keywords:

Symptom cluster, Symptom management, Head and neck cancer, Chemoradiation therapy.

Introduction

Cancer patients are rarely presented with a single symptom. They encounter multiple symptoms and differences in each individual person to rate their sufferings from those symptoms [1-4]. Prevalence and severity of cancer symptoms depends on disease-

related or treatment-related symptoms and can change over the stage of disease and the duration of treatment trajectory. Dodd et al. introduced symptom cluster which is defined as three or more concurrent symptoms that are related to each other and may or may not share the same etiology [5]. Other researchers defined the term as at least two related symptoms which occur together and form a stable group and are relatively independent of other clusters [6].

Head and neck squamous cell carcinomas (HNSCC) accounts for 90% of all head and neck cancer cases and is the 6^{th} leading cancer type [7]. Global estimated number of newly diagnosed with head and neck cancer is more than 550,000 cases per year. Male is significantly affected more than female in the ratio ranging from 2:1 to 4:1. It is a cause of death for approximately 380,000 people each year [7,8]. In Thailand, head and neck cancer remains a public health concern with oral cavity, oropharyngeal, nasopharyngeal and hypopharyngeal cancers having the averaged incidence above 1 per 100,000 populations [9]. Risk factors for head and neck cancers encompass tobacco use, alcohol consumption and infection with oncogenic viruses. Human papilloma virus-associated oropharyngeal cancer rate is increasing in developed countries and could exceed that of cervical cancer by 2020 [10].

The suggested standard treatment for advanced stage Head and Neck cancer (HNC) is concurrent chemoradiotherapy which has been established for inoperable disease or in patients who will have unacceptable morbidity from surgery [11-13]. The current chemotherapeutic regimen is cisplatin, adding chemotherapy agent with radiation therapy can increase 5 year survival up to 6.5% compared with Radiation Therapy (RT) alone [14-16]. The widely used chemotherapy regimen is scheduled for every three week with 100 mg/m^2 and high-dose bolus; the patients normally need hospitalization for a few days [17]. Addition of chemotherapy with external beam radiation therapy often increases toxicity and treatment-relates side effects which discourage patient's compliance to complete the treatment course [14,15,18]. A cluster of symptoms with dry mouth, mouth/throat mucus problem, difficulty chewing/swallowing, mouth/throat sores, and problem tasting food in patients with head and neck cancer typically develops during the active treatment phase of radiation therapy and chemoradiotherapy [19-21]. This reviewed article will be described symptom cluster of mucositis, xerostomia, dyagausia, and dysphagia in patients with head and neck cancer during their active treatments.

Literature Review

A recently reported, cross-sectional study has found that the symptoms occurring in nasopharyngeal cancer patients receiving chemoradiotherapy appear in the same cluster which composes of problem with mucus, mouth/throat sore, difficulty swallowing/ chewing, problem with tasting food, respectively [19]. Similarly, results of a previous longitudinal study focused on patterns of symptom burden during radiotherapy showed that the local symptom cluster covered the symptoms of problem with dry mouth, mouth/throat mucus, difficulty chewing/swallowing, mouth/throat sores, and problem tasting food [20].

Mucositis or mouth/throat sores

Mucositis is an acute injury to mucosal lining of head and neck region associated with cancer treatment, characterized by erythema, edema, and ulcerations [22]. Mucositis is the most common toxicity reported in patients being treated with radiation therapy or with certain forms of chemotherapy for HNC [23]. The condition usually begins in the first week of treatment with symptoms of burning sensation and mucosal erythema [24]. Within 2 weeks, breaks in the mucosa are apparent as evidenced by appearance of irregular ulcers, generally on the movable mucosa of the lips, cheeks, lateral or ventral tongue, or soft palate [24]. More severe stages occur once the total accumulated dose exceeds 30 Gy, which is usually after the third week of treatment [25]. The proposed aetiopathogenic model develops mucositis over five phases: initiation, message generation, signal amplification, ulceration, and healing. The NF-κB pathway is among one of the most studied mechanisms related to mucositis and illustrates the robustness of the biology underlying oral mucositis [24,26]. Marked xerostomia and dysgeusia can also occur under the same period of treatment [27].

Xerostomia or dry mouth or problem with mouth/throat mucus

Xerostomia is the subjective sensation of dry mouth deriving from lack of saliva and represents a common complaint in patients who undergo treatment of HNC [28]. Xerostomia may be secondary to true salivary gland hypofunction or qualitative changes of saliva. Radiotherapy may lead to hyposalivation (within a week), decreased saliva pH, and altered saliva consistency [29]. Moreover, radiation causes destruction of progenitor cells and stem cells. The severity and incidence of xerostomia in patients receiving intensity-modulated radiation therapy is lower compared to the patients with HNC receiving conventional radiotherapy [28]. As a of decrease salivary output result leading to oral discomfort, sore throat, altered taste and difficulty in speaking, chewing, and swallowing can occur during the acute or late period following RT [30].

Dysgausia or problem with tasting food or taste disturbance

Taste disturbance is a commonly reported symptom from radiation therapy treatment especially to the HNC region and 90% were affected at some degree [31]. Patients with HNC may experience taste alteration (dysgeusia), loss of taste (ageusia), heightened sensitivity (hypergeusia), or reduced taste sensitivity (hypogeusia) [32]. In particular, studies have shown that patients treated with cisplatin may develop taste changes, including ageusia or hypogeusia. Chemotherapeutic agents target rapidly dividing cells and may damage taste buds or their receptors [33]. Patients may complain of a metallic or chemical taste during the delivery of chemotherapy [32]. Dysgeusia is also an early complication of radiation treatment and may precede mucositis [31]. Xerostomia secondary to radiotherapy may also lead to taste changes, as saliva dissolves food particles allowing presentation of tastants to the receptors.

Dysphagia or difficulty chewing/swallowing

Dysphagia is defined as difficulty in swallowing because of structural or movement abnormalities involving the oral cavity, oropharynx, velopharynx, hypopharynx, larynx, and upper esophageal sphincter [34]. Patients with cancer of head and neck have signs and symptoms of swallowing problems because the primary neoplasm affects the organs of swallowing and/or because the treatment itself affects swallowing [35]. Resulting pain, copious mucous production, xerostomia, and tissue swelling contribute to acute dysphagia [36]. Acutely, radiation therapy results in damage to the mucosa and soft tissue within the

radiation treatment volume [36,37]. Pain, thickened and more viscous mucous production, xerostomia, and tissue swelling can all contribute to acute dysphagia. Acute mucositis can worsen dysphagia [34].

These acute side effects of the treatment are the adversities from cumulative doses of radiation therapy to mucosa in oral cavity and the organ affected is salivary gland which disrupts eating habit, choices of food intake and difficulty swallowing. These symptoms might cause malnutrition status in the patients [13,38,39]. The incidence of severe toxicities (grade 3 or 4) can cause 40% of the patients required at least one hospital admission for managing their acute toxicities as reported in a clinical trial [14]. Factors contributing to increase risk for symptom severity include of disease itself in staging and location. Treatment-related factor are robustly evidenced in combination of chemotherapy with radiation therapy. Consuming tobacco, alcohol, poor oral hygiene, and co-morbidities are patients-related factors [23,29,30,40,41].

Assessment of mucositis, xerostomia, dysgausia, and dysphagia in patients with head and neck cancer

The major challenge in assessing the prevalence, severity, distress of treatment related toxicities is lack of uniformity in the design and in the use of scoring scale [40]. Each tool the clinician or researcher developed for clinical trial aims to monitor the patient's tolerance and experience during treatment. Symptom status would be the independent variable or outcome depending on research objective [42]. Symptoms related to treatment toxicities in HNC patients have been reported in Table 1.

Symptom/outcome	**Assessment tools**
Mucositis	The World Health Organisation (WHO) scale
	Oral Assessment Guide (OAG)
	Oral Mucosa Rating Scale (OMRS)
	Oral Mucositis Index (OMI)
	Oral Mucositis Assessment Scale (OMAS)
	The MacDibbs Mouth Assessment Tool
	National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE V4)
	Daily Mucositis Score (DMS)
	Oral Mucositis Weekly Questionnaire-Head and Neck Cancer
	Patient-Reported Oral Mucositis Symptom (PROMS) Scale.
	Patient diaries
	Oral Mucositis Weekly Questionnaire-Head and Neck Cancer (OMWQ-HN)
Xerostomia	RTOG/EORTC grading system.
	Late Effects Normal Tissue (LENT)-Subjective, Objective, Management, Analytic (SOMA) scoring
	National Cancer Institute Common Toxicity Criteria (version 3.0)
	Sialometry
	Xerostomia Questionnaire (XQ)
Dysgausia	Chemosensory questionnaire
	Taste change survey
	The Scale of Subjective Total Taste Acuity (STTA)
Dysphagia	Modified barium swallow (MBS)
	Swallowing-Quality of Life Questionnaire(SWAL-QOL)
	MD Anderson Dysphagia Inventory (MDADI)
	Performance Status Scale for Head and Neck Cancer (PSS-HN)
Acute toxicity	CTCAE v 4
Symptom burden	MD Anderson Symptom Inventory–Head and Neck Cancer module; (MDASI-HN)
	Vanderbilt Head and Neck Symptom Assessment Scale; (VSSN)

QOL	European Organization for Research and Treatment
	Cancer Quality of Life Questionnaire-Core 30/Head and Neck 35-questionnaire; (EORTC QLQ-C30/H&N35)
	Functional Assessment of Cancer Therapy-Head and Neck;(FACT-H&N)
	University of Washington Quality of Life (UW-QOL)
Nutritional status	Anthropometrics
	Malnutrition Universal Screening Tool (MUST)
	Short Nutritional Assessment Questionnaire (SNAQ)
	Nutritional Risk Index (NRI)
	Eating Assessment Tool (EAT-10)

Table 1. Head and neck cancer-related concerns and recommended instruments for their measurement in clinical trials [23,26,29,30,33,42,43].

Management of mucositis, xerostomia, dysgausia, and dysphagia in HNC during CCRT

A number of interventions has been proposed and verified to be effective in dealing with the symptoms in patients with HNC. Management of each symptom both pharmacological and non-pharmacological is described in Table 2.

From various management strategies focusing on pharmacological and non-pharmacological approaches in HNC patients during the active treatment, more evidence is needed to support the statistical significant difference in those studies.

Limited studies were interested to solve symptoms in cluster or multiple symptoms together, which the majority are acute treatment-related toxicities [44]. Patient-education on intensive oral care protocol, avoiding smoking and dietary-counseling is likely to be effective, based on many research findings across the symptoms in patients with head and neck cancer during the active treatment. These non-pharmacological management strategies were shown to prevent the unexpected complication, delay onset of oral toxicities, and minimize the severity of symptoms in this cluster [25]. Patient education is an integral part of nurse's roles in supporting the patients to help them alleviate the symptom severity through the treatment trajectory. The education should discuss the prospect of oral complications, adequate nutrition, and list of signs and symptoms of infection [26].

Symptom	**Management**			
	Non-drug treatment	**Result**	**Traditional and drug treatments**	**Result**
Mucositis	-Patient education, hydration, nutritional support, infection control, supportive care	Recommended	-Honey, Manuka, Kanuka oil	E.S.
	-Oral preventive cares (improve oral hygiene, clean oral cavity every 4 hours, soft tooth brush, dental floss, alcohol'-free mouthwash)	Recommended	-Sucralfate	E.S
	-Artificial saliva and water'-soluble jellies	Recommended	-Zinc sulphate/ Zinc supplement	E.S
	-Saline or baking soda mouthwashes	E.S	-Allopurinol	E.S
	-Drinking sufficient liquids	Recommended	-Human placental extract	E.S.
	-Nutritional care	Recommended	-Essential oils	E.S.
	-Avoid smoking, alcohol, irritating foods	Recommended	-RhEGF	E.S.
	-Sucking ice cubes	Recommended	-Benzydamine HCL	E.S.
	-Laser therapy	E.S	-Indigowood root	E.S.
			-Cryotherapy	E.S.
			-Chlorhexidine	No E.S.
			-Aloe vera	No E.S.
			-Prostaglandins E1	No E.S.
			-Glutamine	No E.S.

			-Amifostine	No E.S.
			-Vitamin E	No E.S.
			-Povidine iodine	No E.S.
			-Pilocarpine	No E.S.
Symptom	**Management**			
	Non-drug treatment	**Result**	**Traditional and drug treatments**	**Result**
Xerostomia	-Stringent oral hygiene with fluoride agents and antimicrobials to prevent dental caries and oral Infection	Recommended	-Antimicrobial mouthwashes, such as chlorhexidine and hexitidine, play a central role in reducing the bacterial load and inhibiting cariogenesis.	E.S.
	-Regular dental care and appropriate oral hygiene.	Recommended	-Pilocarpine/saliva substitutes	E.S.
	-Drinking water/taking sips of fluid, gargling with bicarbonate mouthwash	Recommended	-Cevimeline	E.S.
	-Using an artificial saliva spray	Recommended	-Antifungal drugs, benzydamine, and natural agents	E.S.
			-Sialogogic agents to stimulate saliva production from remaining intact gland tissue.	E.S.
Dysgausia	-Provision of food choice and eating suggestions	Recommended	-Amifostine	E.S
	-Dietary counselling and modification by the addition of seasoning	E.S	-IMRT technique	E.S
	-Avoidance of unpleasant foods and extending dietary choice (e.g. pleasing color, form and smell)	Recommended	-Zinc sulphate	E.S
			-Clonazepam	No E.S.
			-Saliva substituted	No E.S.
Dysphagia	-Enteral nutrition	E.S	-PEG (Percutaneous endoscopic gastroatomy)	E.S
	-Swallowing training	E.S	-Parenteral feeding/Naso'-Gastric'-tube	E.S
	-Dietary teaching/modifications	E.S		
Note: E.S: Statistically Significant Results.				

Table 2. Head and neck cancer-related management strategies and interventions.

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