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Complications of Radiation Therapy for Head and Neck Cancers

The Patient's Perspective

KEY WORDS

Morbidity
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Stomatitis
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Oral
complications

Newer treatments for head and neck cancers, including altered fractionation and the use of concomitant radiotherapy and chemotherapy, may provide better local-regional tumor control rates; however, patients may experience more frequent and more severe acute toxicities that result in considerable suffering. Through this study, we sought a better understanding of patients' experiences when undergoing radiotherapy. Personal interviews were conducted with 33 individuals who had received radiotherapy for head and neck cancers. These individuals described their treatment experiences and identified the most troublesome and debilitating side effects of radiotherapy. Overall, lethargy and weakness, dry mouth, mouth sores and pain, taste changes, and sore throat were the most frequently reported troublesome or debilitating side effects. The single most debilitating side effect was oropharyngeal mucositis that was characterized by patients as sore throat, and mouth sores and pain; both negatively affected the patient's ability to eat and drink, causing many patients to experience significant weight loss. Trends toward more aggressive management of head and neck cancers underscore the need for new and effective therapies for oropharyngeal mucositis occurring in patients receiving radiotherapy.

■ Introduction

reatment for head and neck cancers primarily involves 3 modalities: surgery, radiation, and chemotherapy, administered alone or in combination.^{1,2} Radiation

therapy (RT) alone is the most common treatment for certain types of head and neck cancers, such as cancer of the nasopharynx, larynx, and oropharynx.³ Conventional RT in locally advanced head and neck cancers results in long-term local control of the tumor in few patients.⁴ To improve cure rates, pro-

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tocols that deliver more intense radiation, such as accelerated and hyperfractionated radiation, are being evaluated.⁵ The use of concurrent or sequential radiation and chemotherapy is also increasing because the combination is more likely to preserve structures in the head and neck when compared with surgical resection of the tumor.²

Virtually all patients with head and neck cancers who receive RT develop notable mucosal toxicities.⁶ One consequence of combining radiation and chemotherapy is a significant increase in the incidence, severity, and duration of oropharyngeal mucositis, especially when chemotherapy, or accelerated or hyperfractionated radiation, is used.^{2,5,7-13} The severity of oropharyngeal mucositis may limit or interrupt treatment with RT, thus compromising the chance for a cure. 11,14 The adverse effects of radiation result from epithelial, connective tissue, and vascular reactions within the radiation field^{8,15} and include mucositis, xerostomia (hyposalivation), taste changes, dysphagia, and dysphonia, as well as negative effect on dentition and quality of life.1,8,9,14,16-22 Severe acute effects on the mucosa can also result in consequential effects that can chronically impair organ function.¹⁰

Because morbidity from oropharyngeal mucositis can be severe, effective therapies for preventing and/or treating this complication are needed. 9,14,16,17,23,24 Good oral hygiene 9,14,16,21,24 and analgesics 14,21 are the approaches most commonly used to prevent and treat the symptoms associated with oropharyngeal mucositis.

To understand the impact of RT regimens on overall patient well-being, we undertook in-depth interviews with former patients with head and neck cancers. Our objective was to characterize, from the patient's perspective, the effects or consequences resulting from RT.

Patients and Methods

Patients were recruited by telephone to participate in face-to-face interviews conducted in market research facilities located in five major metropolitan areas (Table 1). Patients were identified through nurse and physician referrals, support groups for patients with cancer, and newspaper advertisements. Entry criteria included a willingness to participate, a history of head and neck cancers treated with RT with or without chemotherapy, and completion of RT between January 1997 and October 1998. To facilitate patient recruitment, the treatment win-

Table 1 • Location and Number of Participants by City					
Location	No. of Participants				
San Francisco, Calif	7				
Los Angeles, Calif	12				
Raleigh, NC	5				
Philadelphia, Pa	3				
Dallas, Tex	6				
Total	33				

dow was expanded to include a small number of patients who completed RT before January 1997; these patients met all other inclusion criteria. No attempt was made to specifically recruit patients who had experienced oropharyngeal complications

In January 1999, an experienced independent medical interviewer conducted in-depth personal interviews with 33 individuals who had previously undergone RT, with or without chemotherapy, for the treatment of head and neck cancers. An interview guide, consisting of both open- and closed-ended questions (Appendix 1), was used with each interview, which lasted approximately 45 minutes. Based on the patient's recall, his or her treatment experience was explored using questions pertaining to the cancer type, treatment received, duration of treatment, side effects experienced, and type of supportive care used during and after RT. In addition to a general discussion of side effects experienced, the patients were asked to identify the most debilitating or troublesome side effect. Other questions focused on the type of oral care received before RT, changes in taste experienced, and changes in the mouth and/or throat that occurred during or after treatment. Patients received a \$100 honorarium as compensation for their time.

■ Results

The mean age of patients was 56.4 years (range 35 to 77). Fifteen percent were younger than 40 years of age, 18% were 41 to 50 years, 21% were 51 to 60 years, 34% were 61 to 70 years, and 12% were 71 years or older. Nearly two thirds (61%) were men, and 39% were women. Most patients were either retired or unemployed. Patients reported the following types of head and neck cancers: tongue, mouth, tonsil, oropharynx, nasopharynx, hypopharynx, larynx, thyroid, and salivary gland.

Treatment Experience

All study participants received RT for the treatment of head and/or neck cancers. Most patients (52%) received their RT in 1998, whereas one third (33%) received RT in either 1997 or 1996. The remainder (15%) reported receiving treatment during or before 1995. In addition to undergoing RT, 42% of the patients had their tumor surgically removed. About half (45%) received chemotherapy in addition to surgery and/or RT.

The treatment modality varied by type of cancer (Table 2) and geographic area (Table 3). Seventy-five percent of the patients received one radiation treatment per day, for 5 days each week, lasting an average of 6.4 weeks (range 3 to 16 weeks). Nearly half received induction chemotherapy before the start of their radiation treatments, with 40% receiving concurrent radiation and chemotherapy. Only 13% had radiation treatments before the start of chemotherapy.

Most (73%) patients were not hospitalized during the course of their radiation and/or chemotherapy treatments. However, 27% were hospitalized due to treatment complications, such as dehydration, inability to eat or drink, mouth

Table 2 • Treatment by Cancer Type (Site)						
Treatment Administered						
Cancer Type*	Surgery, %	Chemotherapy, %	Radiation Therapy, %			
Pharynx/throat	36	71	100			
Larynx	54	0	100			
Tongue	29	29	100			
Neck	75	25	100			

^{*}Some patients reported cancer in more than one site.

pain, extreme weakness, and fatigue. The average duration of hospitalization was 5.7 days (range 1 to 14 days).

Almost two thirds (61%) of study participants received an oral examination by a dentist or an oral surgeon before undergoing RT. Sixty-five percent of those who received prophylactic oral care reported that their physicians or dentists recommended or prescribed some type of oral product. A mouthwash or rinse was most frequently mentioned.

Most Troublesome or Debilitating Side Effects

Lethargy and weakness, dry mouth, mouth sores and pain, taste changes, and sore throat were the side effects mentioned most frequently that were troublesome or debilitating from the patients' perspectives. In addition to identifying all the troublesome or debilitating side effects they experienced, patients were asked to identify the one side effect that was most debilitating. Painful sore throat was mentioned most frequently (20%), followed by mouth sores and pain (18%), and dry mouth (14%) (Figure 1). Reasons for mentioning sore throat and mouth sores included the accompanying pain and burning that not only caused significant discomfort but also led to an inability to eat, drink, or swallow. The actual expe-

Table 3 • Use of Surgery by Geographic Location					
	Sample	Patient Treated Surgically			
Location	Size	No, %	Yes, %		
East Coast or Midwest	14	29	71		
West Coast	19	79	21		

rience was best illustrated by a patient's own words, "The sore throat, the raw throat, that was the worst. My throat was so raw that I couldn't eat anything. This is the reason I lost weight. I couldn't eat."

Oropharyngeal Changes

Nearly all patients (90%) reported experiencing changes in their taste sensation. Taste alterations included a complete loss of taste (54%), distorted taste (33%), or reduced taste (13%).

About three quarters of patients also reported experiencing changes in the condition of their mouths. Most frequently mentioned were mouth sores, loss of saliva or dry mouth, mouth pain and irritation, and sores or blisters on the tongue. Eighty-eight percent also reported changes in the throat or esophagus.

The percentage of patients reporting changes in the mouth varied by the site of the cancer. For instance, all of those with tongue cancer and 86% of those with pharyngeal cancer reported experiencing oral changes, whereas only 25% with neck cancer reported changes in the oral cavity.

Patients reported that oropharyngeal mucositis developed within approximately 2.5 weeks (range 1 to 8 weeks) after the start of RT. Healing time varied widely, ranging from 2 to 24 weeks (mean 8.7 weeks) after completion of RT. Nearly all (92%) patients received supportive care in response to the

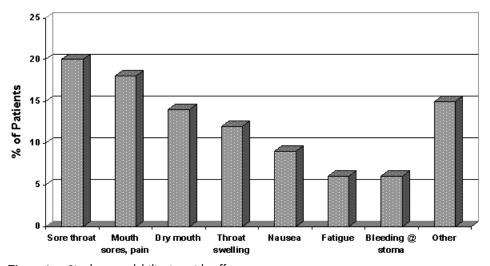


Figure 1 ■ Single most debilitating side effect.

onset of mucositis. The therapies mentioned most frequently include opioid analgesics, mouthwashes or rinses, and nutritional supplements.

The overall effect of oropharyngeal mucositis was explored with study participants. A large number (88%) could not eat or drink, or did so with extreme difficulty. Eighty-three percent reported significant weight loss, ranging from 12 to 79 pounds (mean 29 pounds). Weight loss led to gastric tube implantation for 29% of patients, many of whom expressed reluctance to use a feeding tube as a substitute for oral intake. Patients reported experiencing other side effects that they also attributed to the changes in their oral cavity, including depression (38%), difficulty talking (29%), sleep disturbance (25%), and hospitalization (13%) (Figure 2). One patient described his condition this way, "When you have a sore mouth you are thinking about it all the time . . . Since it is your mouth, you speak with it, you drink water with it, you have to eat with it, but it gets difficult . . . I stopped drinking anything but water."

Recovery time, as defined by resumption of normal activities, occurred within a mean of 5 months (range 1 to 15 months). At the time of the interview, 74% of patients reported that they had completely recovered from their treatment.

■ Discussion

Although oropharyngeal mucositis from RT for head and neck cancers has been proved to occur in almost all patients,⁶ the overall effect and specific effects of mucosal changes have not been well characterized from the patients' perspectives. In this study, patients reported, in detail, multiple specific effects

related to mucosal injury. They reported consequences that were painful and affected normal daily activities, such as eating and swallowing. This contrasts with randomized controlled clinical trials of various RT regimens, which typically report only the frequency, location, or grade of acute effects like oropharyngeal mucositis. 4,12,25-28 Grading systems used to assess oropharyngeal mucositis focus on objective anatomic changes or sequelae as observed by the clinician. These objective changes may include erythema, pseudomembrane formation, ulceration, bleeding, and the ability to eat. 17,29 No specific patient-reported effects related to the oral mucosa are included to assess mucosal damage.

More patient-specific experience is reported in quality of life (QOL) and functional status studies characterizing patients' symptoms, functional outcomes, and overall well-being after RT^{12,22,30-34}; however, these QOL studies use instruments to measure global changes in the patients' conditions and have not been designed to measure the acute effects related specifically to mucositis. A clear understanding of the patient's experience during the course of oropharyngeal mucositis is not available from QOL data.

Oral pain is reported to increase in severity through the course of RT and persists after treatment is complete.³⁵ Painful sequelae are memorable. Therefore, it is not surprising that painful sequelae were the consequence that patients recall as the worst part of their treatment experiences. That 4 of the 5 most frequently reported toxicities occurred in the head and neck area also underscores the importance of local toxicity associated with RT. Other sequelae reported, such as weakness and lethargy, may also be linked to oropharyngeal toxicities because the patient's ability to eat and drink is compromised, which may result in poor nutritional status and weight loss.

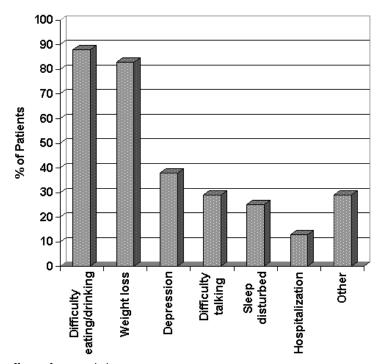


Figure 2 ■ Effects of mucosal changes.

Although optimal management strategies for RT-induced mucositis and its associated complications have not been identified, standard oral care protocols are used to prevent or minimize mucositis,36 even without substantive evidence of their clinical efficacy. Management of oral complications during and after RT is a multidisciplinary effort involving physicians, nurses, pharmacists, and oral medicine specialists. Nurses are, and should continue to be, involved in both research and clinical care in this area. Nurses involved in assessing, managing, and educating patients about self-care should be attentive to the patients' perspectives regarding the acute and long-term effect of mucositis. Oncology nurses can perform an essential role by promoting frequent and consistent oral care during and after cancer treatment to help reduce the debilitation associated with treatment-related mucosal injury.³⁷ Despite continued challenges associated with the lack of standard assessment tools and optimal prophylactic or therapeutic agents, emphasis on frequent and meticulous oral care continues to be an important approach for reducing the severity of oral complications.

■ Conclusion

Trends in the treatment of head and neck cancers have led to an increasing use of chemotherapy with RT and the development of more intense RT regimens. The consequence has been an increase in both the incidence and the severity of oropharyngeal mucositis. Findings from this study illustrate the debilitating nature of mucosal injury on patients with head and neck cancers, the need for new and effective therapies for oropharyngeal mucositis, and the importance of understanding the patients' perspectives of their treatment experience.

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Appen	dix
Interview Guide Participant's Name: Date of Interview: Interview #: Introduction The purpose of this interview is to develop a better under-	 i. Did you receive both radiation therapy and chemotherapy or not? [] Yes —> Go to next question
standing of your experiences while undergoing treatment for cancer of the head and/or neck. The interview should last about 45 minutes. Do you have any questions before we begin?	 [] No — > Skip to question #2 j. For how many weeks did you receive both radiation therapy and chemotherapy as the treatment regimen for the head and/or neck cancer?
 a. With which type of cancer of the head and neck were you diagnosed? b. What type of treatment(s) (eg, surgery, radiation therapy, chemotherapy, and radiation + chemotherapy) did you receive for the head and/or neck cancer? Surgery Radiation therapy Chemotherapy Radiation plus chemotherapy (Ask questions #1c-e if radiation therapy mentioned in question #1b. If radiation is not mentioned, go to question #1f.) Please describe the type of radiation that you received 	 a. What side effects, if any, did you experience during treatment that were debilitating or troublesome from your perspective? b. Of these, which side effect was most debilitating or troublesome to you? c. Were you hospitalized at any point during the time when you were receiving therapy (radiotherapy and/or chemotherapy) for treatment of head and/or neck cancer? (Probe: Why were you hospitalized, and for how many days did you remain in the hospital?) 3. What type(s) of care or support did you receive in conjunction with your cancer treatment? (Probe for nutritional support, home care, counseling, etc)
 (eg, location)? d. How many times per day and for how long did you receive radiation therapy? e. Where did you receive your radiation therapy? (Probe: Radiation department in the hospital, community radi- 	MOUTH CARE a. Before starting radiotherapy and/or chemotherapy, did you receive an examination of your mouth by a physician specializing in oral care, such as a dentist or an oral surgeon or not?
ation oncology practice, clinic, etc) f. Did you receive chemotherapy for treatment of the head and/or neck cancer or not? [] Yes — > Go to next question [] No — > Skip to question #1h g. Which chemotherapeutic agent(s) did you receive?	[] Yes —> Go to next question [] No —> Skip to question #5 b. Did this physician recommend and/or prescribe any oral products, such as mouth rinses (including saline rinses)? [] Yes —> (Probe: Which products were recom-

h. How many times per day (week) and for how long

(days or weeks) did you receive chemotherapy?

mended/prescribed? How were you instructed to

use them [eg, gargle, rinse, spit out, or swallow]?

How many times per day did you use these rinses? For how long (relative to start and end of radiation/chemotherapy treatment?) [] No ——> Skip to question #5 c. Did you have any difficulty in using these products? If	7. What medical care, if any, did you receive we conditions developed? (Probe for PEG to other nutritional support; oral antibiotics, otics; narcotic or other analgesics—oral, par swishes; topical anesthetics [eg, lidocaine].)
yes, how so?	8. What effect(s), if any, did these oral cond your overall mental and physical health and
CHANGES IN TASTE	ment experience? (Probe for inability to eal low, sleep, talk; weight loss; need for h
 5. a. During treatment (radiotherapy and/or chemotherapy) was your sensation of taste altered in any way or not? [] Yes —> Go to next question [] No —> Skip to question #6 b. How was it changed? (Probe for loss of taste, distortion 	interruption or delay in treatment; impact resume normal activities; feelings of de effects of narcotic analgesics [if applicable] 9. Did you experience any of the conditional conditions identified in
in taste (how), cravings for certain foods/flavors, etc.)	throat and/or esophagus or not? [] Yes ——> Which conditions?
CHANGES IN ORAL CONDITION	[] No 10. How much time elapsed after complet
6. a. Please describe changes in the condition of your mouth,	(radiotherapy and/or chemotherapy), bef

6. a if any, that you experienced during or following treatment. (Probe for: thick, ropy secretions, redness, tingling, swelling, burning, pain, tenderness, dryness,

mouth sores, etc.)

(Ask	questions	#6b i	and	#6c j	or	each	condition	mentioned	in ques-
tion	#6a.)								

b. When during treatment did _____ (condition(s) *identified in #6a)* develop?

c. How long did _____ (condition(s) identified in #6a) last?

- when these oral ube, TPN, or topical antibirenteral, patch;
- itions have on l/or your treatıt, drink, swalnospitalization; t on ability to epression; side etc.)

tions such as #6a) in your

- ing treatment fore you were able to resume your normal activities, such as working outside the home, eating out in restaurants, pursuing a hobby, going on vacation, exercising, etc.?
- 11. What type of medical insurance, if any, did you have during the time when you were being treated for head and/or neck cancer?
- 12. That was my last question. Do you any additional comments or suggestions for the company that is developing this new product?

Thank you!