XEROSTOMIA: 12-MONTH CHANGES IN SALIVA PRODUCTION AND ITS RELATIONSHIP TO PERCEPTION AND PERFORMANCE OF SWALLOW FUNCTION, ORAL INTAKE, AND DIET AFTER CHEMORADIATION

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Abstract: *Background.* Previous investigators have found permanent changes in saliva production after chemoradiation but have not examined these in relation to swallowing measures, diet changes, and patient comfort over time.

Methods. Thirty patients with advanced stage cancer of the oropharynx treated with chemoradiation were followed with videofluoroscopic swallow studies, a measure of stimulated total saliva production, a questionnaire of their perception of dry mouth, and a questionnaire on the nature of their oral intake at pretreatment until 12 months after treatment.

Results. Saliva declined significantly from pretreatment to 12 months. Swallowing-related complaints increased significantly over the 12 months, especially in patients with lower saliva weights. Diet choices increased over time after treatment, except crunchy foods. Swallow measures did not relate to saliva weight.

Conclusions. Reduced saliva weight does not correlate with slowed or inefficient swallow. Instead, reduced saliva weight seems to change patients' perceptions of their swallowing ability and, on that basis, their diet choices. © 2003 Wiley Periodicals, Inc. *Head Neck* **25:** 432–437, 2003

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In an earlier article, we examined the effects of xerostomia, measured as saliva weight in grams, on perception and performance of swallow func-

tion in 36 patients with advanced stage cancer of the oropharynx before treatment and 3 months after treatment using chemoradiation. Results of this article confirmed the results of earlier studies[2,3] that chemoradiation caused xerostomia and a significant increase in patient perception of swallowing difficulties. However, although the xerostomia did not affect physiologic aspects of bolus transport during swallow, it did significantly affect the patient's comfort in eating and diet choices. Other authors[4–6] have found permanent changes in saliva production but have not examined these in relation to swallowing measures and diet choices. The question remains as to whether the changes in diet choices and comfort in eating as well as the xerostomia continue beyond 3 months after treatment completion.

In this study, we examined 30 patients with advanced stage cancer of the oropharynx treated with chemoradiation followed from before treatment until 12 months after treatment. This study is needed to answer the question, "Do xerostomia, swallow function, and normalcy of diet improve over the first 12 months after treatment in patients treated with chemoradiation?"

METHODS

Subjects for the study were 30 individuals between the ages of 38 and 75 accrued sequentially from participating institutions, who received full-course radiotherapy and chemotherapy to the oral cavity or oropharyngeal areas and who were observed at all four time points. All patients received at least 6000 cGy with concurrent chemotherapy (Table 1). The area radiated was virtually identical for all patients (±2 mm).

Each patient received four test procedures before beginning their treatment and again at 3, 6, and 12 months after completion of their treatment: (1) a questionnaire containing 12 questions requesting information on the patient's perception of dry mouth, food sticking, and other items

Table 1. Age, gender, site of disease, disease stage, total radiation dose delivered, and chemotherapy used in the 30 head and neck cancer patients.

Subject no.	Age	Gender	Site of disease	Disease stage	Total RT delivered dose (cGy)	Drugs
1	50	Female	Nasopharynx	IV	7000	Taxol, 5-FU hydrea Procrit
2	50	Female	Nasopharynx	IV	7050	Carboplatin taxol hydrea 5-FU
3	66	Male	Oropharynx	II	7350	Taxol, 5-FU hydrea
4	65	Male	Oropharynx	III	7050	Taxol, 5-FU hydrea
5	60	Male	Oropharynx	III	7000	Cisplatin (RADPLAT)
6	75	Male	Oropharynx	IV	7150	Cisplatin 5-FU
7	49	Male	Oropharynx	IV	7350	Taxol, 5-FU hydrea
8	67	Male	Oropharynx	IV	7350	Taxol, 5-FU hydrea
9	66	Male	Oropharynx	IV	7650	Taxol, 5-FU hydrea
10	69	Male	Oropharynx	IV	7000	Cisplatin (RADPLAT)
11	69	Female	Oropharynx	IV	7000	Cisplatin taxol
12	54	Male	Oropharynx	IV	7000	5-FU hydrea
13	60	Male	Oropharynx	IV	7400	Taxol, 5-FU hydrea
14	65	Male	Oropharynx	IV	7500	Carboplatin taxol hydrea 5-FU
15	65	Male	Hypopharynx	III	7000	Cisplatin taxol
16	52	Male	Hypopharynx	IV	7050	Taxol, 5-FU hydrea
17	61	Male	Larynx	III	6900	5-FU hydrea
18	51	Female	Larynx	III	7050	5-FU hydrea
19	40	Female	Larynx	III	7100	Cisplatin (RADPLAT)
20	56	Female	Larynx	IV	7050	Taxol, 5-FU hydrea
21	50	Male	Larynx	IV	7200	Carboplatin taxol hydrea 5-FU
22	52	Female	Larynx	IV	7400	Taxol, 5-FU hydrea procrit
23	44	Male	Larynx	IV	7500	Carboplatin taxol hydrea 5-FU
24	53	Male	Larynx	IV	7350	Carboplatin taxol hydrea 5-FU
25	60	Male	Larynx	IV	7000	Carboplatin 5-FU
26	70	Male	Larynx	IV	7200	Cisplatin (RADPLAT)
27	41	Male	Unknown primary	IV	6000	Taxol, 5-FU hydrea
28	38	Male	Unknown primary	IV	6000	Taxol, 5-FU hydrea
29	55	Male	Unknown primary	IV	6000	Taxol, 5-FU hydrea
30	61	Male	Unknown primary	IV	7500	Taxol, 5-FU hydrea

Table 2. Mean (± SEM) saliva weight, percentage of patients taking 50% or less of their nutrition orally, and percentage of patients who did not eat all food consistencies at before treatment and 3, 6, and 12 months after treatment.

	Saliva weight			<50% Oral intake		Did not eat all consistencies	
	n	Mean	(SEM)	*n*	No. (%) ≤50%	*n*	No. (%)
Before	30	5.21	0.45	30	1 (3%)	30	10 (30%)
3 months	30	0.84	0.17	30	6 (20%)	30	18 (60%)
6 months	30	0.93	0.14	30	3 (10%)	30	18 (60%)
12 months	30	1.07	0.18	30	2 (7%)	30	14 (47%)
p Value		<.0001			.01		.03
Pairwise comparisons*		1,2,3			1, 4		1, 2

**1:* p < *.05 before vs. 3 mos; 2:* p < *.05 before vs. 6 mos; 3:* p < *.05 before vs. 12 mos; 4:* p < *.05 3 mos. vs. 12 mos.*

listed in Table 3, completed during patient interview; (2) stimulated whole saliva production (from all salivary glands) evaluated by weighing a 4″ x 4″ gauze pad before and after the patient chewed the gauze for 2 minutes[7] and reported in grams; (3) a videofluorographic study of oropharyngeal swallow during which patients were given two swallows each of 1, 3, 5, and 10 mL of thin liquid and 3 mL of pudding consistency[8]; and (4) a questionnaire on the nature of their oral intake consisting of questions on percentage of oral intake of various food consistencies. All patients were disease free at time of follow-up and completed all evaluation points. The protocol was approved by the Institutional Review Board of Northwestern University and participating institutions, and all patients signed informed consent statements.

The videotape of the videofluorographic study of oropharyngeal swallow was analyzed in slow motion and frame by frame to make two temporal measures of the oropharyngeal swallow and two observations of residual food remaining in the oral cavity and pharynx after the swallow: (1) oral transit time (the time from initial posterior movement of the bolus in the oral cavity until the leading edge of the bolus reached the point at which the lower rim of the mandible crosses the tongue base); (2) pharyngeal delay time (the time when the bolus head or leading edge reached the point at which the mandible crosses the tongue base until laryngeal elevation is seen to begin, indicating the onset of the pharyngeal motor response); (3) approximate percentage of the bolus remaining in the oral cavity after the swallow (oral residue); and (4) the approximate percentage of the bolus remaining in the pharynx after the swallow (pharyngeal residue). These measures and observations were made for each of the liquid swallows and each of the pudding swallows. Average interobserver and intraobserver reliability on these measures and observations were .93 and .99, respectively.

Statistical Analysis. Repeated measures analysis of variance was used to test for differences in mean saliva weight over time. Cochran's Q was used to test for differences in oral intake (≤50%

Table 3. Frequency of eating and swallowing-related complaints (number and percent) in the 30 patients completing pretreatment, 3, 6, and 12 months.

Perceived problem	Pretreatment	3 Months	6 Months	12 Months	*p* value
1. Swallowing problems	15 (52%)	21 (70%)	17 (57%)	21 (70%)	.24
2. Dry mouth	10 (34%)	30 (100%)	28 (93%)	27 (90%)	<.0001
3. Food sticks in mouth	6 (21%)	20 (67%)	20 (69%)	20 (67%)	<.0001
4. Food sticks in throat	5 (17%)	14 (47%)	20 (69%)	20 (67%)	<.0001
5. Food will not go down	6 (21%)	18 (60%)	16 (55%)	17 (57%)	<.0001
6. Need water assist	7 (24%)	25 (83%)	26 (90%)	26 (87%)	<.0001
7. Choking	7 (24%)	16 (53%)	10 (34%)	14 (47%)	.007
8. Coughing	11 (38%)	18 (60%)	18 (62%)	20 (67%)	.0002
9. Food/liquid comes up	4 (14%)	6 (20%)	2 (7%)	8 (27%)	.14
10. Heartburn	14 (48%)	11 (37%)	10 (34%)	7 (23%)	.02
11. Night cough/gag	14 (48%)	15 (50%)	11 (37%)	10 (33%)	.48
12. Changes in taste	3 (10%)	24 (80%)	24 (89%)	18 (60%)	<.0001

Table 4. Comparison of mean saliva weight (g) between patients with and without eating and swallowing complaints.

	Pretreatment			3 months		
	With complaint	Without complaint	*p* value	With complaint	Without complaint	*p* value
1. Swallowing problems	4.93	5.75	0.39	0.75	1.10	0.51
2. Dry mouth	4.89	5.55	0.50	0.84	*	*
3. Food sticks in mouth	5.20	5.36	0.89	0.71	1.14	0.37
4. Food sticks in throat	5.76	5.24	0.67	0.86	0.85	0.98
5. Food will not go down	4.43	5.56	0.32	0.73	1.04	0.50
6. Need water assist	4.73	5.51	0.47	0.73	1.65	0.46
7. Choking	5.49	5.27	0.76	0.68	1.05	0.30
8. Coughing	5.81	5.03	0.35	1.07	0.55	0.09
9. Food/liquid comes up	5.55	5.29	0.85	0.53	0.93	0.10
10. Heartburn	4.94	5.69	0.42	0.80	0.89	0.80
11. Night cough/gag	6.28	4.43	0.04†	1.02	0.70	0.38
12. Changes in taste	4.68	5.40	0.64	0.71	1.42	0.37

[less than or equal to 50% oral intake], >50% [greater than 50% oral intake]) and inability to eat all food consistencies (yes, no) over time. Because the tests for these three variables were all significant ($p < .05$), pairwise comparisons were each done at $p < .05$ using either the paired t test or McNemar's test. The frequency of complaints was compared over time using Cochran's Q test. Comparisons of mean saliva weight between persons and with and without swallowing complaints were done using the independent sample t test. Repeated measures analysis of covariance was used to relate temporal swallowing measures and observations to saliva weight. All statistical analyses were done using the SAS statistical software.[9]

RESULTS

These 30 patients exhibited a significant decline in saliva production from pretreatment to 3 months after treatment, and this significant decline remained when 6- and 12-month posttreatment saliva production was compared with pretreatment levels (Table 2). The percentage of the 30 patients taking 50% or less of their nutrition orally (Table 2) increased significantly from pretreatment to 3 months after treatment and decreased significantly at 12 months after treatment compared with 3 months after treatment. The percentage of patients who did not eat all food consistencies increased significantly from pretreatment to 3 and 6 months after treatment, but differences between pretreatment and 12 months after treatment were not significantly different. Ten patients had gastrostomy tubes in place at one or more points in the follow-up. Three patients had a gastrostomy pretreatment (2 while taking 100% oral nutrition), 11 at 1 month (1 while taking 100% oral nutrition), 10 at 3 months, 4 at 6 months (1 while taking 100% oral intake), and 2 at 12 months.

The frequency of eating and swallowing-related complaints increased significantly from pretreatment to 3, 6, and 12 months, as reflected in Table 3. Only the general complaint of swallowing problems and complaint of food/liquid coming up and night cough or gag (both possible signs of gastroesophageal reflux disease) did not increase after treatment. Comparisons of saliva weight in patients with and without swallow complaints are shown in Table 4. In general, patients with swallowing complaints had lower saliva weights than patients without swallowing complaints. Complaints in which saliva weights were significantly different for patients with and without those complaints did not occur at more than one point.

By use of analysis of covariance, regression coefficients between temporal measures and observations of oropharyngeal swallow and saliva weight pooled revealed no significant correlation coefficients. On this basis, saliva weight does not seem to relate to swallow transit times (bolus movement), pharyngeal delay, or oral or pharyngeal residue.

Figure 1 presents the percentage of the 30 patients who could not eat thin liquids, thick liquids, pudding, soft masticated, and crunchy foods at each evaluation point. In general, the numbers of patients who could not eat each food consistency increased at 3 months after treatment but decreased over time. The most difficult diet type

Table 4. *(continued)*

	6 months			12 months		
	With complaint	Without complaint	*p* value	With complaint	Without complaint	*p* value
1. Swallowing problems	0.92	0.94	0.95	0.87	1.53	.25
2. Dry mouth	0.97	0.34	0.26	0.90	2.60	.30
3. Food sticks in mouth	0.74	1.41	0.09	0.95	1.31	.46
4. Food sticks in throat	0.92	1.01	0.76	0.85	1.49	.23
5. Food will not go down	0.90	1.01	0.69	0.82	1.39	.18
6. Need water assist	0.87	1.66	0.46	0.95	1.82	.48
7. Choking	0.70	1.08	0.21	0.85	1.26	.25
8. Coughing	1.08	0.74	0.20	1.15	0.91	.55
9. Food/liquid comes up	1.13	0.93	0.73	1.12	1.05	.87
10. Heartburn	0.73	1.06	0.28	1.71	0.87	.25
11. Night cough/gag	0.97	0.90	0.82	1.39	0.90	.32
12. Changes in taste	0.86	2.05	0.01†	1.02	1.13	.80

**100% of patients had this complaint.*
†p ≤ .05

was crunchy foods which 43% of the patients did not eat even at 12 months after completion of chemoradiation.

DISCUSSION

The reduction in saliva production seen in these 30 patients at 3 months after treatment continued for the rest of the year after treatment, supporting prior research[2,3] and discrediting the notion that xerostomia decreases over time after chemoradiation. These data do not address xerostomia caused by other etiologies, which may exhibit different patterns of changes over time. The percentage of patients who returned to 50% or greater oral intake increased significantly over the 12 months of follow-up despite the fact that xerostomia did not improve, indicating that changes in xerostomia may not be the major factor in the patients' return to increased oral intake. Swallowing and eating-related complaints also did not decrease in frequency over the 12 months, and saliva weight was lower but not significantly so in patients with complaints. Physiologic swallow measures of transit times, pharyngeal delay, and oral and pharyngeal residue were not related to saliva weight, indicating that the reduced saliva weight does not seem to result in actual slowed or inefficient swallow. Rather, the reduction in saliva weight seems to change the patient's perception of their swallowing ability and affects their diet choices.

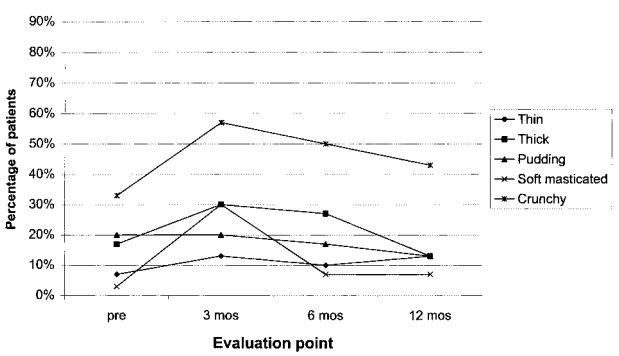

FIGURE 1. Percentage of the 30 patients who could not eat each type of food over the 12 months of follow-up.

Diet is a reflection of voluntary preferences and patient perception of their ability to eat various foods. Data on the diet choices of these 30 patients support patient perceptions of their difficulties in eating. Many patients chose to avoid crunchy foods, which they may have felt more uncomfortable chewing and swallowing.

Chemoradiation may affect the sensory nerve endings in the oral cavity, thus affecting the patient's perception. Other investigators have found perceptual changes in the presence of xerostomia.[10–12] Sensory changes in the oral cavity require further investigation in patients treated with chemoradiation. Increasing our knowledge of any sensory changes should help us in moving the patient back to a more normal diet.

These data present a challenge to the clinician managing the patient with xerostomia resulting from chemoradiation. There is no validated direct behavioral or other therapy for sensory damage. The patient may benefit from intensive counseling regarding their actual swallowing ability compared with their perception of it. Encouraging pa-

tients to continue to increase fluid intake and to alternate food and liquid may also be helpful. Further studies of these patients over time, investigations of medication effects, and effects of xerostomia resulting from other etiologies are needed.

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