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Side Effects of Radiation Therapy in Patients with Head and Neck Cancer According to the Late Effects of Normal Tissues-Subjective Objective Management and Analytic Questionnaire

Late Effects of Normal Tissues-Subjective Objective Management and Analytics Anketine Göre Baş Boyun Kanserli Hastalarda Radyasyon Tedavisinin Yan Etkileri

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Abstract

Objective: The present study explored the oral side effects of radiation in patients with head and neck malignancies.

Materials and Methods: The study sample consisted of 60 patients who were candidates for radiation therapy and had head and neck malignancies. After collecting each patient's demographic information, the late effects of normal tissue-subjective objective management and analytic questionnaire were used to verify the diagnostic and treatment data.

Results: Sore throat, otalgia, and pain in the jaw and mouth were the most common complaints among patients receiving therapy, whereas toothache was the least common. After one and three months of therapy, 60% and 80% of the patients, respectively, exhibited severe xerostomia. Before beginning therapy, 73.3% of patients did not have any difficulty chewing.

Conclusion: Following one month of therapy, these adverse effects reach their maximum rate, and from then until the end of the third month after treatment, they continue to improve until they are near to their pre-treatment levels.

Keywords: Radiotherapy, head, neck, cancers

Öz

Amaç: Bu çalışma, baş ve boyun maligniteleri olan hastalarda radyasyonun oral yan etkilerini araştırmaktadır.

Gereç ve Yöntemler: Çalışmanın örneklemini radyasyon tedavisine aday olan ve baş-boyun malignitesi olan 60 hasta oluşturmuştur. Her hastanın demografik bilgileri toplandıktan sonra, teşhis ve tedavi verilerini doğrulamak için normal doku-öznel objektif yönetimin ve analitik anketin geç etkileri kullanıldı.

Bulgular: Boğaz ağrısı, otalji, çene ve ağızda ağrı tedavi alan hastalarda en sık görülen şikayetler iken diş ağrısı en az görülen şikayetlerdi. Bir ve üç aylık tedaviden sonra hastaların sırasıyla %60 ve %80'inde ciddi ağız kuruluğu görüldü. Tedaviye başlamadan önce hastaların %73,3'ünde çiğneme güçlüğü yoktu.

Sonuç: Bir aylık tedaviden sonra bu yan etkiler maksimum oranlarına ulaşır ve tedaviden sonraki üçüncü ayın sonuna kadar tedavi öncesi seviyelerine yaklaşana kadar düzelmeye devam eder.

Anahtar Kelimeler: Radyoterapi, baş, boyun, kanserler

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Introduction

The global incidence of oral cavity, pharynx, and larynx cancer is around 500,000 cases yearly, with an average yearly mortality rate of 270,000. Head and neck cancer accounts for approximately 4% of these malignancies (1). Except for skin cancer, these instances represent 5% of all cancer-related mortality, with about three-quarters attributable to oral cavity and pharynx malignancies and the remaining 1.4% attributable to laryngeal cancer (2).

Radiotherapy is one of the primary treatments that is sometimes used alone and sometimes in conjunction with other treatments (3). In situations of irradiation of the oral cavity and salivary glands, problems such as the death of taste bud cells, the diminution of salivary gland secretory function, oral mucositis, and peripheral neuropathy are unavoidable. These patients frequently feel dry mouth, altered taste perception, difficulty in opening the mouth (trismus), and difficulty in swallowing (dysphagia) (4).

Another problem is radiation-induced somatic nerve damage, which produces discomfort. 30-80% of patients with cancer endured discomfort. Pain in the oropharynx, face, or neck, or as a headache, is the initial clinical finding in these individuals (5).

The limited studies have been conducted based on patients' complaints about the oral side effects of radiotherapy, and have only addressed a few oral side effects, and no study using this questionnaire has been conducted on the Iranian population. Therefore, the purpose of this study is to investigate the side effects of radiation therapy in patients with head and neck cancer according to the late effects of normal tissues - subjective objective management and analytic (LENT-SOMA) questionnaire.

Material and Methods

This work is descriptive-analytical research about 60 patients with head and neck malignancies referred to "Shafa Hospital" in Kerman before, during, and one to three months following radiation between 2018 and 2019.

The inclusion criteria of the present study was the presence of primary cancer in the head and neck region requiring radiation as primary or adjunctive therapy. The patient must be free of oral mucosa disorders and systemic conditions impacting saliva. Exclusion criteria include cancer recurrence in the investigated regions and individuals who have had a significant resection.

The LENT-SOMA questionnaire, which is regarded as a valid questionnaire in the field of oral diseases, has been utilized after recording the demographic information of each patient through interview and file review to verify diagnostic and treatment information (6,7).

The validity and reliability of the applied questionnaire has been established by Rabiei et al. (8). The final year student performed the Persian version of the LENT-SOMA questionnaire as a control for all patients prior to radiation treatment, during radiotherapy treatment (7 to 14 days from the start of radiotherapy) and one to three months after the conclusion of radiotherapy treatment. The goal of the study was first explained to each participant, and they were provided with the questionnaire if desired. In addition, all respondents were promised that the information they provided on the questionnaire would remain secret and would be studied solely from a statistical standpoint; the questionnaire was also anonymous (verbal consent). This project was approved by the Ethical Committee of Kerman University of Medical Sciences of the university with the code IR.KMU.REC.1399.488 (date: 17.08.2023).

Statistical Analysis

The data analysis was performed using chi-square, ANOVA, and SPSS 21 (IBM SPSS Statistics V21, SPSS Inc., Chicago, Ill., USA).

Results

This research investigated sixty patients. Thirty patients completed the questionnaire before and during therapy, and rest of them completed the questionnaire before, during, and one and three months following treatment. The age ranges of the patients was 81 to 25 years, with an average age of 59.49.3 years (Table 1).

The minimum and maximum radiation dosages were 700 and 6,900 cGy, respectively. The most prevalent site of involvement was the larynx in 14 individuals (23.3%), followed by the nasopharynx in 9 people (15%), the hypopharynx in 6 people (10%), the tonsil in 4 people (6.7%), the oropharynx in 6 people (10%), and the oropharynx in 7 people (11.7%) (Table 2).

Before beginning radiation therapy, all patients described their discomfort as bearable. Most locations had a more severe kinds of pain during and one month after treatment. One month following treatment, the most extreme pain or type of sciatica was reported in the majority of affected locations.

One month following therapy, mouth discomfort (16.6%), ear ache (63.3%), jaw pain (6.6%), and sore throat (6.6%) were regarded as excruciatingly painful. After three months of therapy, pain severity decreased in all locations (Table 2).

Table 1. The demographic characteristics of study participants

Variable		No	%
Gender	Male	25	41.6
	Female	35	58.4
Profession	Employed	41	68.3
	Non-working	19	31.7
Education	Diploma≥	31	51.6
	>Diploma	29	48.4

50% of ear discomfort, 53.3% of throat pain, 40% of jaw pain, and 16.6% of mouth pain were unbearably unpleasant throughout therapy. Three months following radiation, 98 % of patients reported frequent discomfort and four patients reported terrible pain in these locations (Table 3).

A month after radiation therapy, 89% of patients with a sore throat, 81.2% of patients with mouth pain, 82.5% of patients with ear discomfort, 79.2% with jaw pain, and 61.3% of patients with tooth pain utilized housing constantly.

By separating the analyzed periods within one month following treatment, the severity of discomfort, the frequency of pain complaints, and the frequency of taking medication to ease pain in the throat, ear, jaw, and mouth were considerably higher than at other times (p=0.001). Additionally, the degree of toothache was greater one month after therapy than on other occasions.

After one and three months of therapy, 60% and 80% of patients, respectively, exhibited significant xerostomia.

Before beginning therapy, 73.3% of patients had no difficulty chewing. The data analysis about patients conducted over the course of one month revealed that 36.6% had trouble chewing hard foods, and 16.6% had difficulty eating soft foods. 98% of patients could not swallow soft meals one month following therapy, while 93,4 % were unable to consume beverages at this time. However, three months following therapy, a more significant proportion of patients were able to chew soft meals with more ease (Table 4).

This study revealed that, after adjusting for age and gender, changes in the sensation of taste, dysphagia, the frequency of experiencing dry mouth, the severity of xerostomia, and its influence on chewing different types of food were substantially greater one month after therapy than at previous periods (p=0.001).

One month after radiotherapy, the consequences of irradiation were identified in some variables. The pain in the ear and jaw exhibited a statistically significant association with the radiation dosage (p=0.001). Also, the present findings showed an increase in the rate of discomfort with age and gender (p=0.001).

Discussion

This study investigated the oral side effects of radiation in patients before, during, and one month and three months following treatment according to the LENT-SOMA questionnaire.

Compared to the research work by Rabiei et al. (8), the present study reveals that 60% of patients comprehend their pain experience since initiating therapy. In other investigations, pain has been identified as the most common side effect of radiation, with incidence rates ranging from 30% to 80% (9). Oral mucositis pain is the most prevalent symptom affecting mouth and jaw function (10).

In the study conducted by Elting et al. (11), the severity of mucositis and associated discomfort lessened throughout the sixth month (12).

The majority of patients related their pain to the tumor and/or cancer treatment. Whereas 59% reported their pain to be less severe than they expected, 29% were not satisfied with their level of pain despite pain management during cancer therapy. The most common neuropathic pain descriptors chosen were aching (20%) and burning (27%); nociceptive words chosen were dull (22%), sore (32%), tender (35%), and throbbing (23%), and affective/evaluative descriptors were tiring (25%) and annoying (41%).

Rose-Ped et al. (13) showed that painful sore throat takes place the most frequently (20%), followed by mouth sores and pain (18%), and dry mouth (14%) (13%).

One and three months following therapy, 60% and 80% of patients, respectively, exhibited significant xerostomia, which is less than the finding by Rabiei et al. (8).

Dirix et al. (14) research showed that dry mouth improved three to four weeks following radiation.

Three months following therapy, the process of restoring the sense of taste is nearing completion. Consistent with the observations of Yamashita et al. (15), Rabiei et al. (8), and Chen et al. (16). In the research by Shenoy et al. (7), some improvement of the sensation of taste occurred between 20

Table 2. The Otalgia, toothache, jaw pain, mouth pain, sore throat in patients

Pain	No of patients: 30				*p-value	No of patients: 30								**p-value
	Before therapy		During therapy			Before therapy		During therapy		One month after therapy		Three months after therapy		
	n	%	n	%		n	%	n	%	n	%	n	%	
Otalgia	0	0	5	16.6	0.01£	0	0	6	20	7	23.3	2	6.6	0.001£
Toothache	0	0	0	0	0.21	0	0	0	0	2	6.6	1	3.3	0.05
Jaw pain	1	3.3	2	6.6	0.08	2	6.6	3	10	5	16.6	1	3.3	0.04£
Mouth pain	1	3.3	2	6.6	0.08	1	3.3	2	6.6	5	16.6	0	0	0.05
Sore throat	3	10	9	30	0.01£	1	3.3	12	40	10	33.3	2	6.6	0.001£

*Chi-square, **ANOVA, £ P<0.05

and 60 days following the conclusion of therapy, and it was totally restored four months later.

Trismus is common following radiation. In the research by Rabiei et al. (8), 9.8% of patients had trismus of the head and neck muscles, which persisted after three months of therapy. In McSweeney's (17) study, there was no significant change in the mouth opening rate during the first 1-9 months after radiation treatment.

Ozdere et al. (18) showed that trismus is a commonly observed sequela in patients who have undergone radiation therapy to treat malignancies of the head and neck.

According to the present findings, the adverse effects of radiotherapy were a pain in the ear and jaw region and exhibited a statistically significant association with the radiation dosage one month after treatment, and discomfort in the mouth region increased with age and gender.

Patients who undergo RT for HNC can develop hearing especially when receiving 60 Gy. Complaints include ear heaviness, earache, decreased hearing, tinnitus, and dizziness (19).

Epstein et al. (12) showed that as radiation exposure rose, somatic nerve injury increased, followed by pain in the regions exposed to radiation. In the research by Rabiei et al. (8), increasing the dosage was associated with ear and tooth discomfort.

Around 1950, external beam radiotherapy was performed with a device that produced a voltage greater than 300 kvp. After that, with the development of cobalt devices in the 1950s and 1960s, kilovoltage devices were used less. It is worth mentioning that the gamma-ray therapy devices are divided into several categories based on energy and type of operation. Megavoltage therapy devices include accelerators and gamma-ray teletherapy devices such as cobalt (Co60). The Cobalt 60 is an old device and has its own disadvantages. It burns the skin in high doses because it does not protect the skin. Also, this device has penumbra due to not having a point source of radiation production. Besides, as a result of the interaction between gamma photons and the source itself, its casing, and collimators of the device, low-energy, and scattered gamma-rays are produced, and for this reason, the uniformity of the beam

Table 3. The report of pain in different head and neck regions among study populations

Questions		Initiation of therapy		During therapy		after therapy		Three months after therapy		*p-value
		No	%	No	%	No	%	No	%	
How severe was your otalgia?	Not severe	28	93.3	1	3.3	1	3.3	21	70	£0.001
	Tolerable	2	6.6	4	13.3	2	6.6	6	20	
	Severe	0	0	10	33.3	8	26.6	1	3.3	
	Excruciating	0	0	15	50	19	63.3	2	6.6	
How severe was your toothache?	Not severe	30	100	30	100	25	83.3	24	80	0.06
	Tolerable	0	0	0	0	1	3.3	1	3.3	
	Severe	0	0	0	0	2	6.6	0	0	
	Excruciating	0	0	0	0	2	6.6	5	16.6	
How severe was your mouth pain?	Not severe	20	66.6	13	43.3	10	23.3	14	46.6	£0.001
	Tolerable	4	13.3	5	16.6	7	23.3	12	40	
	Severe	5	16.6	7	23.3	8	26.6	4	13.3	
	Excruciating	1	3.3	5	16.6	5	16.6	0	0	
How severe was your jaw pain?	Not severe	20	66.6	12	40	19	63.3	20	66.6	£0.001
	Tolerable	3	10	4	13.4	7	23.3	5	16.6	
	Severe	5	16.6	2	6.6	2	6.6	4	13.3	
	Excruciating	2	6.6	12	40	2	6.6	1	3.3	
How severe was your sore throat?	Not severe	20	66.6	10	33.5	12	40	19	63.3	£0.01
	Tolerable	3	10	2	6.6	7	23.3	5	16.6	
	Severe	5	16.6	2	6.6	9	30	5	16.6	
	Excruciating	2	6.6	16	53.03	2	6.6	1	3.3	

*ANOVA, £ $p<0.05$

Table 4. The report of the effects of radiotherapy on xerostomia, mastication, trismus, and gustatory sensation in study population

Questions		Initiation of therapy		During therapy		One month after therapy		Three months after therapy		*p-value
		No	%	No	%	No	%	No	%	
How often do you feel your mouth is dry?	Never	22	73.3	15	50	2	6.6	2	6.6	£0.002
	Rarely	5	16.6	5	16.6	5	16.6	2	6.6	
	Sometimes	2	6.6	7	23.3	5	16.6	3	10	
	Mostly	1	3.3	3	10	18	60	23	80	
Do you have problem chewing?	Never	22	73.3	14	46.6	12	40	24	80	£0.01
	With hard food	6	20	11	36.6	11	36.6	3	10	
	With soft food	2	6.6	5	16.6	7	23.3	3	10	
Do you have problem swallowing?	Never	20	66.6	13	43.3	15	50	20	66.6	0.05
	With hard food	5	16.6	5	16.6	7	23.3	5	16.6	
	With soft food	2	6.6	2	6.6	4	13.3	2	6.6	
	I only can swallow liquid	2	6.6	5	16.6	2	6.6	2	6.6	
	I cannot swallow anything	1	3.3	5	16.6	2	6.6	1	3.3	
Do you have problem opening mouth?	No	20	66.6	14	46.6	12	40	19	62.7	£0.001
	To some extent	3	10	5	16.6	7	23.3	5	16.6	
	I usually have problem eating	4	13.3	5	16.6	8	26.6	5	16.6	
	I hardly can eat	2	6.6	4	13.3	2	6.6	1	3.3	
	I cannot eat	1	3.3	2	6.6	1	3.3	0	0	
Has your sense of taste changed?	Never	20	66.6	13	43.3	15	50	20	66.6	£0.01
	Mildly	5	16.6	5	16.6	7	23.3	5	16.6	
	Moderately	2	6.6	2	6.6	4	13.3	2	6.6	
	Severely	2	6.6	5	16.6	2	6.6	2	6.6	
Has your voice become harsh?	Never	25	83.3	20	66.6	21	70	26	89.9	0.05
	To some extent	2	6.6	0	0	2	6.6	2	6.6	
	Sometimes	2	6.6	5	16.6	3	10	3	10	
	All the time	1	3.3	5	16.6	1	3.3	0	0	
Have you recently had loss of hearing?	Yes	5	16.6	10	33.3	8	26.6	3	10	0.07
	No	25	83.3	20	66.6	22	73.3	27	90	

*ANOVA, £ $p<0.05$

is slightly reduced. Therefore, it seems that the side effects caused by radiotherapy can be minimized by using new devices (20,21).

Conclusion

Following one month of therapy, these adverse effects reach their maximum rate, and from then until the end of the third month after treatment, they continue to improve until they approach near to their pre-treatment levels.

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Ethics

Ethics Committee Approval: This project was approved by the Ethical Committee of Kerman University of Medical Sciences of the university with the code IR.KMU.REC.1399.488 (date: 17.08.2023).

Informed Consent: Informed consent was obtained.

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Authorship Contributions

Concept: M.A.H., Design: M.A.H., Data Collection or Processing: A.E., A.R.G.N., Analysis or Interpretation: A.R., Literature Search: A.R., Writing: A.R.G.N.

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References

1. Kawashita Y, Soutome S, Umeda M, Saito T. Oral management strategies for radiotherapy of head and neck cancer. Jpn Dent Sci Rev 2020; 56: 62-7.
2. Buglione M, Cavagnini R, Di Rosario F, Maddalo M, Vassalli L, Grisanti S, et al. Oral toxicity management in head and neck cancer patients treated with chemotherapy and radiation: Xerostomia and trismus (Part 2). Literature review and consensus statement. Crit Rev Oncol Hematol 2016; 102: 47-54.
3. Epstein J, Vabdr Waal I. Oral cancer. In: Greenberg MS, Glivk M, Ship JA. Burket's oral medicine. 11st eds. New Delhi: Decker Publishing. 2008: 153-89.
4. Ogama N, Suzuki S, Umeshita K, Kobayashi T, Kaneko S, Kato S, et al. Appetite and adverse effects associated with radiation therapy in patients with head and neck cancer. Eur J Oncol Nurs 2010; 14: 3-10.
5. Whale Z, Lyne PA, Papanikolaou P. Pain experience following radical treatment for head and neck cancer. Eur J Oncol Nurs 2001; 5: 112-20.
6. Vissink A, Jansma J, Spijkervet FK, Burlage FR, Coppes RP. Oral sequelae of head and neck radiotherapy. Crit Rev Oral Biol Med 2003; 14: 199-212.
7. Shenoy VK, Shenoy KK, Rodrigues S, Shetty P. Management of oral health in patients irradiatedfor head and neck cancer: a review. Kathmandu Univ Med J (KUMJ) 2007; 5: 117-20.
8. Rabiei M, Rahimi A, Kazemnezhad Leyli E, Jalalian B, Massoudi Rad S. Complication of post radiation in patients with head and neck cancer. J Gorgan Uni Med Sci 2014; 16: 114-20.
9. Park KU. Assessment of change of quality of life in terminally ill patients under cancer pain management using the EORTC Core Quality of Life Questionnaire (QLQ-C30) in a Korean sample. Oncology. 2008;74:7-12.
10. Ho KF, Farnell DJ, Routledge JA, Burns MP, Sykes AJ, Slevin NJ, et al. Developing a CTCAEs patient questionnaire for late toxicity after head and neck radiotherapy. Eur J Cancer 2009; 45: 1992-8.
11. Elting LS, Keefe DM, Sonis ST, Garden AS, Spijkervet FK, Barasch A, et al. Patient-reported measurements of oral mucositis in head and neck cancer patients treated with radiotherapy with or without chemotherapy: demonstration of increased frequency, severity, resistance to palliation, and impact on qualityof life. Cancer 2008; 113: 2704-13.
12. Epstein JB, Wilkie DJ, Fischer DJ, Kim YO, Villines D. Neuropathic and nociceptive pain in head and neck cancer patients receiving radiation therapy. Head Neck Oncol 2009; 1: 26.
13. Rose-Ped AM, Bellm LA, Epstein JB, Trotti A, Gwede C, Fuchs HJ. Complications of radiation therapy for head and neck cancers. The patient's perspective. Cancer Nurs 2002; 25: 461-7; quiz 468-9.
14. Dirix P, Nuyts S, Vander Poorten V, Delaere P, Van den Bogaert W. The influence of xerostomia after radiotherapy on quality of life: results of a questionnaire in head and neck cancer. Support Care Cancer 2008; 16: 171-9.
15. Yamashita H, Nakagawa K, Tago M, Nakamura N, Shiraishi K, Eda M, et al. Taste dysfunction in patients receiving radiotherapy. Head Neck 2006; 28: 508-16.
16. Chen LC, Lin HY, Hung SK, Chiou WY, Lee MS. Role of modern radiotherapy in managing patients with hepatocellular carcinoma. World J Gastroenterol 2021; 27: 2434-57.
17. McSweeney E. Critical review: effectiveness of trismus treatment in irradiated patients with head and neck cancer. Available from: https://www.uwo.ca/fhs/lwm/teaching/EBP/2007_08/McSweeney,E.pdf
18. Ozdere E, Ozel GS, Aykent F. Management of restricted mouth opening caused by radiation: A clinical report. J Prosthet Dent 2016; 115: 263-6.
19. Nader ME, Gidley PW. Challenges of Hearing Rehabilitation after Radiation and Chemotherapy. J Neurol Surg B Skull Base 2019; 80: 214-24.
20. Palazzi M, Tomatis S, Orlandi E, Guzzo M, Sangalli C, Potepan P, et al. Effects of treatment intensification on acute local toxicity during radiotherapy for head and neck cancer: prospective observational study validating CTCAE, version 3.0, scoring system. Int J Radiat Oncol Biol Phys 2008; 70: 330-7.
21. CK Bomford, IH Kunkler. Walter and Miller's Textbook of Radiotherapy (6th ed), 2002: 311-2.