Evaluation of oral health impact profile-14 in head and neck cancer patients with oral manifestation

Evaluasi *oral health impact profile*-14 pada pasien kanker kepala dan leher dengan manifestasi oral

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ABSTRACT
Oral health impact profile-14 (OHIP-14) is a method used to measure *oral health quality of life* (OHRQoL) after radiotherapy. This case report aims to evaluate OHIP-14 before and after head and neck cancer treatment. In case-1, a 51-year-old man complained of an unpleasant sensation in the mouth, loss of taste, and dry lips after undergoing the 17th cycle of radiotherapy. Case-2, a 24-year-old man complained of dry mouth and unpleasant sensation inside the mouth especially when eating and drinking after undergoing 3rd cycle radiotherapy. Both were diagnosed with stage III tongue cancer. The patients were referred to the Department of Oral Medicine. The patients were diagnosed with oral mucositis, acute pseudomembranous candidiasis, exfoliative cheilitis and xerostomia. Patients were treated with mechanical cleaning using gauze soaked in 0.9% NaCl, gargling with 0.025% hyaluronic acid three times daily for oral mucositis, nystatin oral suspension for oral candidiasis, vaseline album and GC dry Mouth® topical commercial gel for dry lips and xerostomia. The OHIP-14 scores of both patients decreased. It was concluded that a decrease in OHIP-14 score indicates successful treatment of head and neck cancer patients with oral complications after radiotherapy.
Keywords: radiotherapy, cancer, OHIP, mucositis

ABSTRAK
Oral health impact profile-14 (OHIP-14) adalah sebuah metode yang digunakan untuk mengukur *oral health quality of life* (OHRQoL) setelah radioterapi. Laporan kasus ini bertujuan untuk mengevaluasi OHIP-14 sebelum dan setelah perawatan kanker kepala dan leher. Pada kasus-1, seorang laki-laki 51 tahun mengeluhkan sensasi tidak enak di dalam mulut, kehilangan rasa, dan bibir kering setelah menjalani radioterapi siklus ke-17. Kasus-2, seorang laki-laki 24 tahun mengeluhkan mulut kering dan sensasi tidak enak di dalam mulut terutama saat makan dan minum setelah menjalani radioterapi siklus ke-3. Keduanya didiagnosis menderita kanker lidah stadium III. Para pasien dirujuk ke Departemen Oral Medicine, didiagnosis dengan mukositis oral, kandidiasis pseudomembran akut, cheilitis eksfoliatif, dan serostomia. Pasien dirawat dengan pembersihan mekanis menggunakan kain kasa yang dibasahi NaCl 0,9%, berkumur dengan asam hialuronat 0,025% tiga kali sehari untuk mukositis oral, suspensi oral nistatin untuk kandidiasis oral, album vaselin dan gel komersial topikal GC dry Mouth® untuk bibir kering dan serostomia. Skor OHIP-14 dari kedua pasien mengalami penurunan. Disimpulkan bahwa penurunan skor OHIP-14 mengindikasikan keberhasilan pengobatan pasien kanker kepala dan leher dengan komplikasi oral setelah radioterapi.
Kata kunci: radioterapi, kanker, OHIP, mukositis
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INTRODUCTION

Today, there has been a shift in the trend of human diseases from communicable to noncommunicable diseases. Cancer is a noncommunicable disease that is currently becoming problem. Cancer is a disease caused by the accumulation of several DNA mutations, and generally initiated by cells that grow uncontrollably. Cancer occurrence is due to abnormalities in cellular process, including proliferation, differentiation, and growth. Cancer initiation and progression are initiated by carcinogenic agents, including physical, chemical or biological agents.[1]

Head and neck cancer (HNC) is one of the highest rates of occurrence worldwide. The HNC is the 7th most common cancer worldwide and accounts for more than 800,000 new cases annually. The death rate from cancer is approximately 300,000 deaths per year.[2,3] The characteristics of HNC often occur in patients aged 50-70 years.[4] Based to guidelines from the National Comprehensive Cancer Network, guidelines for the management of HNC are divided into several locations, namely the lips, oral cavity, pharynx, larynx, paranasal sinuses, salivary gland cancer, and mucosal melanoma.[5]

Tongue cancer (TC) and nasopharyngeal carcinoma (NC) are two kinds of HNC of the oral cavity. The incidence of TC is around 95% of all cancer cases, with an incidence of approximately 40%.[6,7] Based on data from the Jakarta Dharmais Cancer Hospital, the incidence of TC in Indonesia is approximately 14% of the all cancers. The TC is a high progressiveness.[6] The NC in Indonesia is the most common malignancy in head and neck region and ranks 5th with 19,943 new cases (5%) and 13,399 deaths (5.7%) in 2020.[8]

Patients with HNC receive treatment based on their indications. The therapies are chemotherapy, radiotherapy, and surgery. There are side effects after the treatment, that are manifested in the oral cavity. The patient can feel pain at any site in the mouth due to ulceration of the oral mucosa. In addition, patients are at risk of fungal infections in the oral cavity, accompanied by dry lips. These side effects affect patients' quality of life. Oral mucositis has negative clinical and economic impacts on patients. This can reduce the patient's quality of life. The patients had difficulty in eating, chewing, speaking, and brushing their teeth. The patients experienced weight loss and dehydration.[9-14]

Quality of life of patients with HNC is one of the goals of oral treatment. There is a correlation between the quality of life and oral health. Oral health-related quality of life (OHRQoL) is a multidimensional concept that is used to measure dental and oral health disorders related to physical, psychological, and social functioning. The OHRQoL has been widely used to evaluate oral health needs, and its measurement is combined with clinical indicators to better identify the symptoms of oral disease and the patient's ability to perform daily activities. One of the most widely used OHRQoL in international epidemiological studies is the oral health impact profile (OHIP-14).[15,16]

A dentist is expected to provide comprehensive treatment for the oral side effects found in patients with HNC. This case report aimed to evaluate the quality of life using the OHIP-14 questionnaire before and after treatment in a patient with TC and NC accompanied by oral complication such as oral mucositis, oral candidiasis, exfoliative cheilitis, and xerostomia.

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CASE-1

A 51-years-old male patient with stage III TC was referred from the Radiation Oncology Department to the Oral Medicine Department of Hasan Sadikin Hospital, Bandung. The patient underwent hemiglosectomy before visiting the oral medicine department. The patient was currently undergoing radiotherapy (RT) and completed the 17th cycle of RT. The patient complained of discomfort-fort, loss of taste sensation on the tongue, and dry lips. There is no drug and food allergies. The patient had smoking habitual since young and stopped since he got TC.

The patient was comprehensively examined; extraorally showed that the patient was in good general condition, with non-anemic conjunctiva and non-icteric sclera. The upper and lower lips appeared dry and exfoliative. Intraoral examination (Fig.1) revealed a layer of white plaque that could be removed, leaving a painful reddish area on the upper and lower labial mucosa, palate, and dorsum of the tongue. In addition, ulceration was found to have an irregular shape with diffuse borders accompanied by pain in the lower labial mucosa, right and left buccal mucosa, and the palate.

Laboratory examination revealed that all results were within normal limits. The results of the examination included hemoglobin: 14.6 g/dL, hematocrit: 44.6%, leukocytes: 7.21x10^3 uL, erythrocytes: 4.83 million/uL, platelets: 250,000/uL, MCV: 92.3 fl, MCH: 30.2 pg, MCHC: 32.7%. The patient was diagnosed with grade III oral mucositis, acute pseudomembranous candidiasis, and exfoliative cheilitis. The patient was treated with non-pharmacological and pharmacological therapies. The patient was first educated on how to improve oral hygiene, and asked to brush the teeth, tongue, and all of the parts of the oral mucosa by using gauze soaked in 0.9% NaCl slowly. The patient was then instructed to rinse his mouth with 0.025% hyaluronic acid 3 times a day, then continued with 2 mL of nystatin ingested rinse 4 times a day. For extraoral care, the patient was asked to apply vase-line album to the upper and lower lips at least 3 times a day.

Quality of life analysis was assessed using the OHIP-14 questionnaire before and after treatment. The results showed a decrease in the number of questionnaires from 32 to eight. This indicates that the patient's quality of life improved after oral treatment.

The patient was reexamined at the second visit, which was the first follow-up visit, four days after the first patient

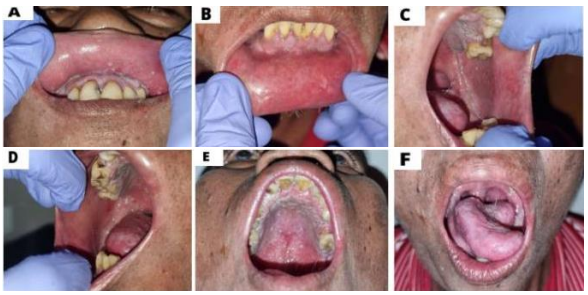

Figure 1 Clinical feature of oral mucosa at the first visit; yellowish white plaque that cannot be cleaned on the intraoral mu-cosa; **A** upper labial, **B** lower labial, **C** left buccal mucosa, **D** right buccal mucosa, **E** palatal, **F** dorsal of the tongue.

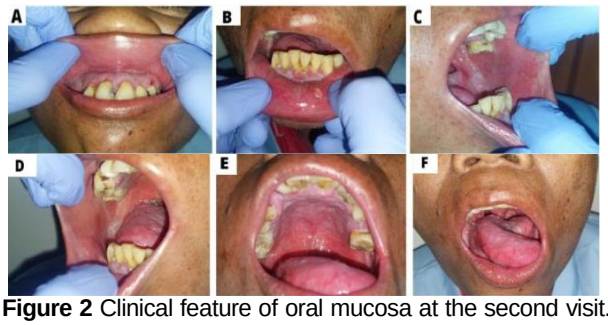

Figure 2 Clinical feature of oral mucosa at the second visit. There is improvement on the oral mucosa; **A** upper labial, **B** lower labial, **C** left buccal mucosa, **D** right buccal mucosa, **E** palatal, **F** dorsal of the tongue

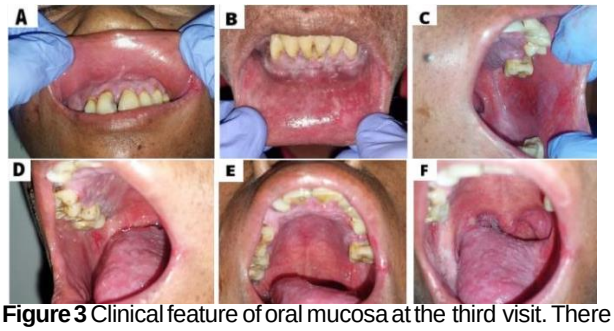

Figure 3 Clinical feature of oral mucosa at the third visit. There is improvement on the oral mucosa; **A** upper labial, **B** lower labial, **C** left buccal mucosa, **D** right buccal mucosa, **E** palatal, **F** dorsal of the tongue

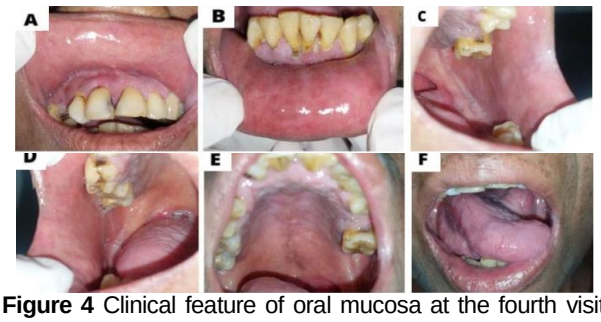

Figure 4 Clinical feature of oral mucosa at the fourth visit. There is improvement on the oral mucosa, **A** upper labial, **B** lower labial, **C** left buccal mucosa, **D** right buccal mucosa, **E** palatal, **F** dorsal of the tongue

visit (Fig.2). The patient's oral cavity condition improved. The patient can eat and drink more, and the pain decreases when eating and drinking, especially in the palate and tongue. intraoral examination revealed erythematous areas on the lower labial mucosa, right and left buccal mucosa, palate, and dorsum of the tongue. The patients were instructed to maintain oral hygiene and continue treatment. The intraoral examination revealed an improvement in the patient's condition.

The patients were re-examined at the third visit or second control. The second control group was treated on day 19 of the first visit; the patient's oral cavity condition improved. Patients can consume more food and drink than before, and pain decreases when eating and drinking, especially in the area of the palate and tongue. The patient complained of pain in the corner of the lower lip. Examination revealed a reddish-eroded lesion with irregular edges in the corner of the lower left lip (Fig.3). The patient regularly cleaned his mouth and continued the

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RT. The patient was instructed to maintain oral hygiene and continued to rinse his mouth with 0.025% hyaluronic acid, followed by applying 2% miconazole cream to the corner of his left lip, each done three times a day.

The patients were re-examined at the 42 day after the first visit. In the control group, the patient's condition in the oral cavity improved. Intraoral examination revealed improvements in all areas of oral mucosa. The clinical features did not show areas of ulceration, white plaques, or erythema (Fig.4). The patients could eat and drink more comfortably than before. Patients were educated to maintain OH by brushing their teeth and tongue at least 2 times a day, in the morning and at night, before going to bed and adopting a healthy lifestyle.

CASE-2

A 25-years-old male patient with NC cancer was referred from the Radiation Oncology Department to the Oral Medicine Department. The patient complained dry mouth and unpleasant sensation inside the mouth especially when eating and drinking after getting the 3rd cycle of RT. The patient was examined extraorally and intraorally. Extraoral examination showed that patient was in good condition but there is exfoliative cheilitis on the upper and lower labial. Intraoral examination showed erythema with irregular form and diffuse border on the left buccal mucosa (Fig.5). The patient did not feel pain at this site. We also find the frothy saliva inside the mouth. Besides that, the dorsal and buccal mucosa were sticky. The mouth mirror adheres to the tongue and buccal mucosa. The salivary flow rate of the patient was measured, it was 0.14 mL/minutes.

The patient was diagnosed with *mild xerostomia and oral mucositis grade* I. The patient was educated how to improve OH. The patient was asked to brush the teeth, tongue, and all parts of the oral mucosa regularly. The patient was instructed to rinse his mouth with 0.025% hyaluronic acid 3-times a day, then continued with topical commercial gel GC dry Mouth® three times a day on the tongue and buccal mucosa. For extraoral care, the patient was asked to apply vaseline album to the upper and lower lips at least 3 times a day. Patients' quality of life was also assessed using the OHIP-14 questionnaire before and after treatment. The results showed a decrease in the number of questionnaires from 25 to one

Figure 5 Clinical feature of oral mucosa at the first visit. Intraoral examination showed erythema with irregular form and diffuse border on the left buccal mucosa, **A** upper labial, **B** lower labial, **C** left buccal mucosa, **D** right buccal mucosa, **E**, palatal, **F** dorsal of the tongue

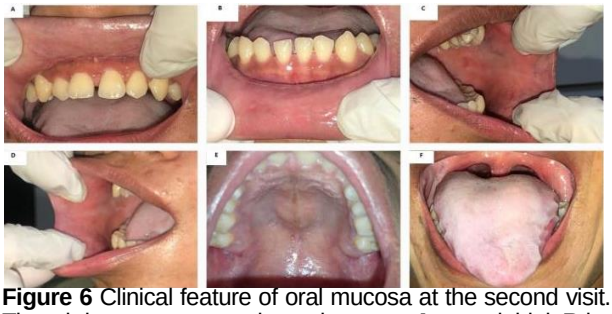

Figure 6 Clinical feature of oral mucosa at the second visit. There is improvement on the oral mucosa **A** upper labial, **B** lower labial, **C** left buccal mucosa, **D** right buccal mucosa, **E** palatal, **F** dorsal of the tongue

The patient's quality of life got improved after oral treatment.

The patient was followed up at the second visit which was the first control. The first control was performed on seven days after the first visit (Fig.6). The patient's oral cavity condition improved. The dry mouth sensation was decreased. The upper and lower labial was not exfoliative again. Intraoral examination revealed erythematous areas on left buccal mucosa, but the oral mirror was not adhering on the tongue and buccal mucosa. The frothy saliva was still found inside the mouth. The unstimulated salivary flow rate was increased, tobe 0.22 mL/minute. The patients were instructed to maintain OH and continue treatment.

DISCUSSION

Both of the patients had head and neck oral cancer.

Table 1 The result of OHIP-14 evaluation

No	OHIP-14 domains	OHIP-14 item	Case 1		Case 2	
			1st Visit	Control	1st Visit	Control
1	Functional limitation	Trouble pronouncing words	3	1	4	0
		Worsened taste	4	3	3	1
2	Physical pain	Aching in mouth	3	2	4	0
		Discomfort eating food	3	1	4	0
3	Psychological discomfort	Feeling self-conscious	2	1	3	0
		Feeling tense	2	1	0	0
4	Physical disability	Poor diet	3	1	3	0
		Interrupted meals	1	1	1	0
5	Psycological disability	Difficulty relaxing	3	1	3	0
		Embarrassment	2	0	0	0
6	Social disability	Irritability with other people	0	0	0	0
		Difficulties doing usual jobs	2	1	0	0
7	Handicap	Life less satisfying	2	0	0	0
		Inability to function	2	0	0	0
Total Score			32	13	25	1

zero=never, 1=hardly ever, 2= sometimes, 3= fairly often, 4= very often

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The first patient had stage-3 TC, and hemiglosectomy was performed. After the surgery, the patient underwent RT according to a protocol from the Radiation Oncology Department. The second patient had NC cancer. This patient was also undergoing RT for the cancer treatment. All the patients had oral mucositis after RT. The patient who underwent RT experienced complaints in the oral cavity after two weeks of exposure to radiation. The clinical features included redness or erythema of the patient's intraoral mucosa.[17] Oral mucositis is a side effect of RT in patients with HNC. The clinical features included erythema, ulceration, and pain in the patient's mouth.[9,18] This condition was the same as that experienced by the patients. The first patient got grade 3 oral mucositis during the first visit. Oral mucositis was found on the left and right buccal mucosal surfaces and in the lower labial and palate. The second patient got grade 1 oral mucositis at the first visit. There is erythema with irregular form and diffuse border on the left buccal mucosa

Radiation exposure can cause mucositis; oral mucositis is caused by damage to the basal epithelial cells. Radiation causes DNA damage, resulting in the breaking of DNA chains and death of basal epithelial cells. The pathogenesis of oral mucositis is complex. The main subject for this pathway is reactive oxygen species (ROS). This molecule was unstable and contained oxygen. ROS molecules can easily react with other molecules in cells; accumulate in cells, causing damage to DNA, RNA, and proteins, leading to cell death.[9,18–22]

Inflammation causes mucositis that leads to the activation of transcription factors such as nuclear factor κB and inflammatory pathways such as the cyclo-oxygenase pathway as well as the upregulation of pro-inflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-1β. Activation of these cytokines leads to thinning of the epithelium and damage to the oral mucosa caused by tissue injury and cell death.[23–26]

The first patient had fungal infection. At the first visit, the patient was diagnosed with oral candidiasis. Radiation exposure alters the structure of oral mucosa. The effects of ionizing radiation destroy the structure of the oral mucosal barrier, leading to the risk of locally and systemically.[27-30] Radiation exposure also destroys the salivary glands of patients. This causes the oral microbiome to become unbalanced. After this process, *Candida albicans* increased. The patient got opportunistic infection.[31] The previous research told that *C.albicans* is the most the significant pathogen that occurs in cases of RT and chemoradiotherapy.[30] There is 50% increasing of *C.albicans* in the patient undergoing RT.[32]

The second patient complained dry sensation inside the mouth after receiving 3rd cycle of RT. The RT can destroy the salivary gland by specific mechanism. Previous studies using ionizing radiation-induced demonstrated acute salivary gland damage and detectable hyposalivation immediately after ionizing radiation. Loss of salivary gland function occurs within the first 3 days after ionizing radiation.[33] The ionizing radiation can destroy DNA of the cells directly by using *secondary electron* and or indirectly by ROS. This pathway can cause *double stranded breaks* (DSBs) in the cell.[34] Damage to the salivary glands as a result of RT results in a reduction in the volume of saliva produced, causing patients to experience xerostomia.[35] The salivary flow from the patient was measured. At the first visit, the salivary flow from patient was 0.14 mL/min. It means that the salivary flow was not normal. At the second visit, the salivary flow was increased. After first treatment, the salivary flow was 0,22 mL/min that means was in normal range.

Xerostomia is one of the side effects of RT. Human salivary gland, including major and minor salivary glands are vulnerable to the effects of radiation. Dysfunction of salivary gland induced RT can reduce amount of Saliva produced. The patient will feel dry sensation inside the mouth. It is estimated that >80% of HNC patients show xerostomia and salivary gland hypofunction after RT.[33] The RT can effect salivary gland macroscopically and microscopically. The previous research show that RT with doses 2.5-15 Gy will reduce the weight of the parotid and submandibular gland. This decrease is proportional to the radiation dose, where the weight of the parotid and submandibular glands decreases respectively to 60% and 40% of the initial value.[36] Several studies have investigated the effects of RT on salivary gland morphology. Among the microscopic changes observed in glandular tissue, mainly changes indicating cell death, cytoplasmic vacuolation, hypovascularization, formation of fibrous tissue and edema were found. The previous research shows the histologial analysis of parotid gland after cobalt-60 irradiation with the total doses 24 Gy. The result showed that there are hyperchromatic nuclei of acinar cells, gland atrophy, interstitial fibrosis, and duct changes with microlithiasia to the parotid gland. Another study showed that some of the parotid and submandibular glands that received a dose of 70 Gy had significant fibrosis, acinar atrophy and parenchymal loss.[37,38] The second patient in this case report feel the dry sensation after 3rd cycle which means that the total dose of radiation is about 6 Gy. It is found that the found the early sign of the xerostomia at this patient. The patient sufferfered mild xerostomia at the first visit dan we try to treat the patient soon.

All the patient was treated by pharmacological and non-pharmacological therapies. The pharmacological therapies are 0.025% hyaluronic acid mouthwash, nystatin oral suspension, topical commercial gel GC dry Mouth ® and vaseline album. Hyaluronic acid is a natural polymer found in skin. Hyaluronic acid is found in various tissues and body fluids of mammals, with the highest concentrations found in connective tissue and skin. Hyaluronic acid has been used in ophthalmology, rheumatology, and dermatology owing to its anti-inflammatory and anti-edema effects. Hyaluronic acid also plays a role in biological processes such as cell signaling, morphogenesis, matrix organization, regulation of gene expression, and cell proliferation.[39–42] All the patients showed good improvement after rinsing with 0.025% hyaluronic acid. The first patient was diagnosed with oral pseudo-

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membran candidiasis. Fungal infections are treated with nystatin oral suspension. This drug interacts with ergosterol, which is present on the fungal cell membrane. Fungi exhibited porosity and lysis.[43] Both of the patient got exfoliative cheiltis. The exfoliative cheilitis was observed on the patient's lips. The patient was given vaseline album was administered to treat this condition as covering agent that protects outer skin from climatic effects and sun exposure. Vaseline album also protects the inner skin by inhibiting water loss from the skin so that the skin is always moist.[44]

The second patient got xerostomia. The patient was treated with topical commercial gel GC dry Mouth®. The previous research told that GC dry mouth has good impact to xerostomia patient. Generally, GC dry mouth consist of carboxy methyl cellulose (CMC). This material has different profile among another polysaccharides. It has hydrophilic character because of its carboxylate groups. These carboxylate groups give more beneficial for this material. They are responsible for properties such as in situ gellation, bioadhesion, sensitivity to environmental stimuli and controlled drug release.[45] This material has good biocompatibility with intra oral human tissue. It can lubricant oral mucosa and generate the saliva production. Specifically, CMC has been commonly used as human saliva substitute. It has been proved as a decent clinical choice, especially for improving formulation's viscoelastic properties. The wetting properties of this material were comparable with natural saliva human oral mucosa.[46] The CMC has excellent capability of maintaining the moist environment. It can accelerate the cell growth, facilitates the functioning enzymes and hormones, and overall, enhances the cell growth factors significant. Besides that, this material can promote the proliferation and migration of keratinocytes and fibroblast.[47]

The topical commercial gel GC dry Mouth has been widely used in dentistry. The previous study of Lam-ubol showed that GC dry mouth can decrease the number of *C.albican* and improve saliva properties in postradiation xerostomic patients. This material has neutral pH so it can stimulate the salivary flow of the patient.[48] Another research showed that continuous uses of saliva GC dry mouth at least a month can improve signs and symptoms of dry mouth and enhance swallowing ability. This pathway can improve clinical nutritional status of post-RT head and neck cancer patients.

Oral hygiene is a key factor in the treatment of oral condition after RT. The patient was instructed to maintain oral hygiene wisely. The patient was educated how to clean the mouth by gently wiping all surfaces of the intraoral mucosa with gauze soaked in 0.9% NaCl softly. The patient followed instructions; so accelerates healing process of oral mucositis in patients. Previous studies have reported a correlation between oral hygiene and the severity of oral mucositis.[49] The oral care procedures, brushing teeth, using dental floss and mouthwash, can decrease the duration and severity of oral mucositis.[50] The soft bristle that is used twice daily is also recommended for non-pharmacological treatment of oral mucositis patients.[51]

The patients' quality of life was evaluated through interviews using the OHIP-14 questionnaire, which consists of seven dimensions including functional limitations, physical pain, psychological discomfort, physical and psychological disability, social limitations, and constraints, assessed using a Likert scale: 0 = never, 1 = hardly ever, 2 = sometimes, 3 = fairly often, and 4 = very often. Data were collected and counted manually; a high score reflects a poor quality of life, a low score reflects good quality of life.[52] The OHIP-14 questionnaire has been shown to be valid, reliable, accurate, concise, practical, and consistent with differences between cultures.[53] The OHIP-14 questionnaire has been widely used in various quality of life studies related to dental and oral health.[15,53]

The quality of life and oral health of the patients were comprehensively evaluated both of the patients. At the first examination, the score of OHIP-14 for the first patient was 32 and for the second patient was 25. Both of the patient was in moderate score. The first patient experienced pain in the tongue and mouth of the oral mucosa for two weeks. The chief complaint has been decreasing, especially when eating and drinking. The clinical features at the first visit showed that the patient had oral mucositis grade 3. The second patient complained dry mouth and unpleasant sensation inside the mouth especially when eating and drinking after getting the 3rd cycle of RT. This patient had oral mucositis grade 1 and xerostomia. Oral mucositis has implications for quality of life. Oral mucositis can reduce the patient's quality of life because of the pain experienced by the patient.[25] Xerostomia can reduce the quality of life. The main cause of xerostomia is the low salivary flow rate that can impact the ability of patient to eat, drink, talk and another activity using the mouth. It can also impact the balance of the oral immune system and generate oral infection. Both of the patients were treated comprehensively. The patients were re-evaluated using the OHIP-14 questionnaire. The results showed that the patient's quality of life had improved. The OHIP-14 after treatment for the first and second patient were 8 and 1. The patient's quality of life improved with oral treatment. The quality of life of patients with oral mucositis was lower than that of those without oral mucositis.[54,55]

Dentist play an important role in managing side effect of RT in the oral cavity. The main goal of dental treatment for patients with TC receiving RT is to maintain good oral health. Oral health affects the quality of life of healthy oral conditions can support patients' activities of carrying out their daily tasks and functions properly.

It is concluded that the decreasing OHIP-14 score indicates successful treatment of TC patients with oral mucositis, acute pseudomembranous candidiasis, xerostomia and exfoliative cheilitis. The quality of life of patients improves with decreasing OHIP-14 scores after receiving treatment for the side effects of radiation in the oral cavity.

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