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ORAL COMPLICATIONS OF HEAD AND NECK IRRADIATION

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Summary

Almost all patients (90-100%) who have undergone radiation treatment (RT) of head and neck region develop at least one oral complication. Oral complications of head and neck RT can be acute and chronic. Acute complications occur during RT and include oral mucositis, dry mouth and taste sensation disorder. Chronic complications occur several weeks, months or years after RT cessation, and include radiation caries, osteoradionecrosis and trismus.

KEY WORDS: *oral cavity, head and neck irradiation, acute complications, chronic compllications.*

ORALNE KOMPLIKACIJE ZRAČENJA GLAVE I VRATA

Sažetak

Gotovo svi pacijenti (90-100%) koji su podvrgnuti terapijskom zračenju u području glave i vrata razviju neku od komplikacija u usnoj šupljini. Oralne komplikacije terapijskog zračenja glave i vrata mogu biti akutne i kronične. Akutne komplikacije nastaju tijekom zračenja i u njih ubrajamo oralni mukozitis, suhoću usta i poremećaj okusne osjetljivosti. Kronične komplikacije nastaju nekoliko tjedana, mjeseci ili godina po završetku zračenja, i podrazumijevaju radijacijski karijes, osteoradionekrozu i trizmus.

KLJUČNE RIJEČI: *usna šupljina, radioterapija glave i vrata, akutne komplikacije, kronične komplikacije.*

INTRODUCTION

Oral complications of head and neck irrradiation can be acute and chronic. Acute complications occur during the radiation treatment (RT) and last 3-4 weeks after completion of therapy. These complications are result of toxic products that arise in irradiated tissue. Acute complications are oral mucositis, taste loss and dry mouth. Chronic complications develop gradually; weeks, months or years after the end of RT, as a result of decreased blood supply to the tissue, the formation of connective tissue and muscle fibrosis, and changes in cell number (1). Chronic complications are radiation caries, trismus and osteoradionecrosis (2).

ACUTE COMPLICATIONS OF HEAD AND NECK IRRADIATION

Oral mucositis

The first acute and the most common oral complication of head and neck RT is oral mucositis

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(OM). This mucosal damage develops in 80-90% of the patients during the early phase of RT and continues for 2–3 weeks post treatment period (3). Oral mucositis is defined as an inflammation of the oral mucosa due to damage of DNA and subsequent death of basal keratinocytes. Clinically, OM manifests as ulcerative inflammation (Figure 1) of the mouth associated with pain, dysphagia, odynophagia and difficulty speaking which can lead to discontinuation of RT. Pathogenesis of OM involves five stages: initiation, activation, signal amplification, ulceration and healing. During the ulceration stage, patients develop ulcerations colonized by microorganisms that further promote epithelial damage. The healing stage starts when DNA is no longer exposed to irradiation (4).

The first clinical sign of OM, which develops during the first week of RT, is whitish of oral mucosa. During the third week of RT, patients develop ulcerations covered with fibrinous pseudomembranes that are prone to secondary infection. The intensity of OM depends on several factors related to RT, and they include total dose, fraction size, field size, number and frequency of fraction, and type of ionizing irradiation (3,4). Numerous scoring scales are available for the classification of OM (5-7), but the most used one is the one established by the World Health Organization (WHO) (8).

The WHO scoring scale for OM according to WHO based on clinical appearance and functional status:

- grade 0 (none) = no pain,
- grade 1 (mild) = oral soreness and erythema,
- grade 2 (moderate) = erythema and ulcerations, solid diet tolerated,
- grade 3 (severe) = oral ulcers, liquid diet only,
- grade 4 (life-threatening) = oral alimentation impossible.

Up till now, there is still no effective therapy for the prevention of OM in head and neck irradiated patients. The treatment of OM is symptomatic, and involves pain management, infection prevention and maintaining normal functioning of oral cavity (9).

Xerostomia

Xerostomia is one of the most common and difficult oral complication of RT. It develops in the early phase of RT and becomes chronic oral complication due to irreversible irradiation damage of salivary glands (Figure 2). Lack of saliva predisposes other oral complications such as dental caries, oral infections, dysgeusia, dysphagia, oral pain and discomfort (10). Consequently, amount of saliva decreases, together with salivary composition changes. Concentration of different saliva ions and proteins increases, while the concentration of the bicarbonate ion decreases, causing low pH and low buffer capacity (11,12). Parotid glands mostly produce stimulated, watery saliva and it's serous acinar cells are more radiosensitive than mucous cells of submandibular and sublingual glands (13). The main etiologic factor for the development of xerostomia is irradiation of parotid glands, as well as total dose of irradiation (14). Xerostomia becomes chronic oral complication if radiation dose exceeds 40 Gy, which is usually the case in the treatment of head and neck tumors, when total dose is greater than 60 Gy. In that case, salivary production decrease up to 80% (1). It has been shown that use of intensity-modulated radiation therapy (IMRT) can reduce the radiation dose to salivary glands and decrease symptoms of xerostomia (15,16). Changes in saliva seriously affect the quality of life, and salivary glands preservation during RT may reduce long-term salivary gland hypofunction. Treatment options implies the use of saliva substitutes which are mainly based on carboxymethylcellulose (10).

Taste disorder

During RT most of patients develop complete or partial taste loss. The preavlence of taste disorder in patients receiving RT alone is 66.5%, but when it is combined with chemotherapy it goes up to 76% (17). Taste disorder occurs as a result of direct radiation effect on taste buds which are radiosensitive and damaged at doses of 10 Gy (3). Except of taste buds damage, taste disorder also occurs due to changes in salivary flow and composition. However, most of patients state their taste disorder as moderate. Mostly, taste sensation return to normal within 2-6 months after RT cessation, and for that reason treatment is not necessary. However, in about 15% of patients, taste disorder can last longer, in some cases even after 5-7 years. To date, there are no recommended preventive and curative actions in this respect (17). Amifostine, zinc gluconate and dietary counseling

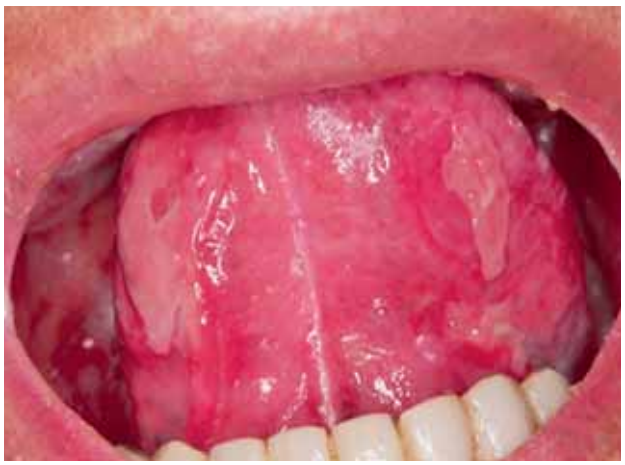

Figure 1. Oral mucositis

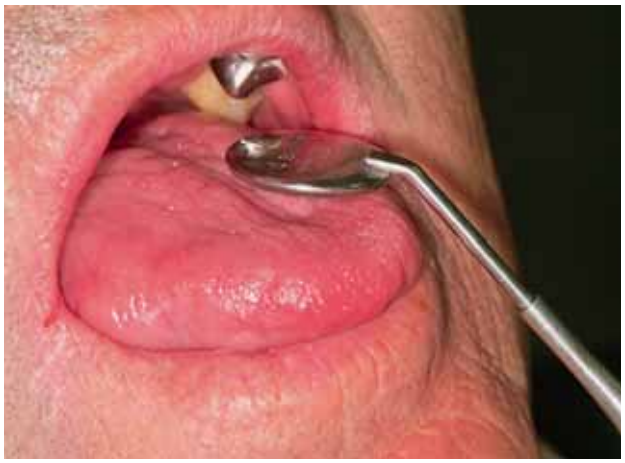

Figure 2. Xerostomia

have been tested for prevention or treatment of RT related taste disorder, but with varying success (18,19).

CHRONIC COMPLICATIONS OF HEAD AND NECK IRRADIATION

Radiation caries

Radiation caries is primarily result of salivary hypofunction, saliva composition changes and increase in acidogenic bacteria number. Therefore, secreted saliva is thick, sticky and viscous followed by decrease in pH values and increase in the number of acidogenic bacteria - *S. mutans, Lactobacillus sp. and Candida sp*. (10) These saliva changes increase the risk for dental caries and oral infections development. Irradiation also has a direct harmful effect on dental hard tissue, which depends on radiation dose, in case the teeth are located in the radiation field. Doses lower than 30 Gy cause minimal harmful effect on hard dental tissue, while doses greater than 60 Gy increase risk of tooth breakdown 10 times. Usually, radiation caries lesions are located in the cervical region, and most affected teeth are mandibular incisors (Figure 3). These caries lesions are very progressive and may lead to tooth breakdown in only few months (3,12). Despite their progressed clinical presentation, this lesions are painless (20).

The risk of development of radiation caries in head and neck irradiated patients is lifelong, therefore proper oral hygiene, fluoride products usage and regular dental check-ups (every one to

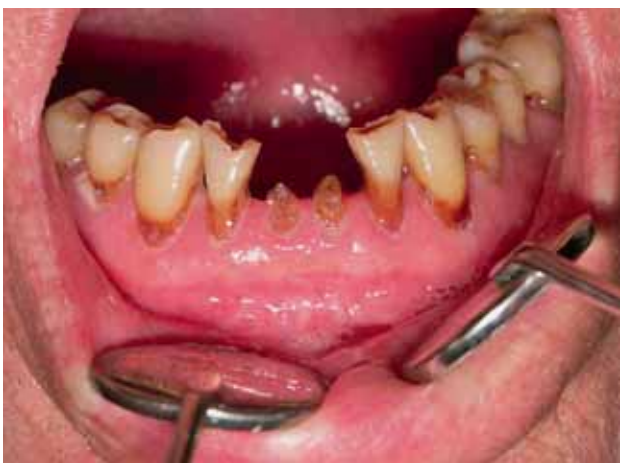

Figure 3. Radiation caries

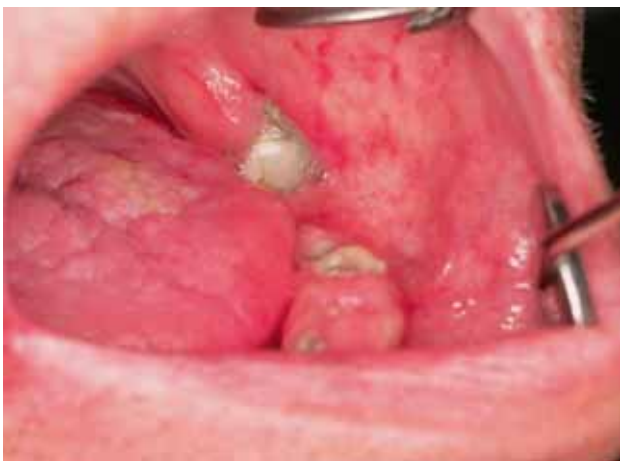

Figure 4. Mandibular osteoradionecrosis

three months) to avoid the most serious complication, which is osteoradionecrosis, are extremely important.

Osteoradionecrosis

The most serious chronic and irreversible radiation complication is osteoradionecrosis (ORN), a consequence of the harmful radiation effect on the bone. The definition of ORN is considered to be „exposed bone area without signs of healing for at least 3 months and without relapse of the underlying disease" (1). However, there is no universally accepted ORN definition in the literature, therefore, prevalence and incidence data of jaw ORN are not known. In the literature, relative frequency data ranges from 0-7.1%, but for the patients with oral cancer it is significantly higher and goes up to 13.6% (21). Two-thirds of ORN cases localized in the orofacial region are associated with some traumatic events such as tooth extraction, traumas with unadapted prosthesis, biopsy and periodontal surgery. For that reason, dental extractions must be avoided after RT cessation. In case dental extractions are necessary, it is recommended to perform them during the first 5-6 months after RT. Inflammation and obliteration of the blood vessels that appear after RT, and cause hypovascularization with decreased healing ability, is not process which occurs during one night. It takes 5-6 months to develop this degenerative processes. These changes are irreversible and progressive, and risk for ORN development remains viable. In one-third of cases ORN can occur spontaneously (22,23).

Risk of ORN increases with total radiation dose (> 65 Gy), volume of irradiated bone, irradiation mode and additional chemotherapy. Other risk factors reported in the literature are poor oral hygiene, malnutrition, trauma, smoking, uncontrolled diabetes and alcoholism (21,22). The most commonly affected bone in the orofacial region is the mandible (Figure 4). Subjective symptoms of ORN are pain, although in the initial stage it can be completely painless, taste changes, halitosis, dysesthesia and food accumulation in necrotized areas of exposed bone. Untreated ORN can lead to the fistula formation and pathological fractures of the affected bone (24). Management of ORN includes conservative treatment, surgical debridement with the use of adjunctives therapies of antibiotics and/or hyperbaric oxygen (HBO) treatment (25).

Trismus

Trismus or reduced mouth opening is a result of harmful radiation effects on the masticatory muscles and/or temporomandibular joint. It develops 3-6 months after RT cessation and very often is irreversible. RT causes spasm and fibrosis of masticatory muscles leading to reduced mouth opening with interincisal space less than 35 mm. Not every patient who receives RT of head and neck will develop trismus, and the prevalence of this condition, reported in the literature, is between 5-40% (26,27). The severity of trismus varies depending on the mode of irradiation, total dose of radiation, treatment modality, tumor location and physical condition (28,29). In the literature, reported data show that a total dose of radiation greater than 60 Gy increases the incidence of trismus up to 47% (28). Furthermore, use of IMRT decreases the incidence of trismus. Development of trismus negatively affects quality of life, resulting in difficulties with food intake, speech and maintaining oral hygiene (30). It is very important to identify early signs of trismus considering the fact that early treatment can significantly affect its prevention. For the prevention as well as for the treatment of reduced mouth opening passive and active physiotherapy can be performed (31).

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