Critical Review
Infection Control

Head and neck cancer therapy-related oral manifestation management in the COVID-19 pandemic: a critical review

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Abstract: With the onset of the new coronavirus disease (COVID-19) pandemic, the dental treatment of patients at risk of infection has become quite challenging. In view of this, patients with head and neck cancer may present with oral complications due to anticancer therapy, making dental assistance necessary. Thus, the objective of the study was to review the literature and critically discuss important concerns about the treatment of patients with head and neck cancer during the COVID-19 pandemic. Because dental professionals are in close contact with the main viral transmission routes, this study presents recommendations for management and protection during clinical dental care. The main characteristics and transmission routes of COVID-19 are also discussed. Dental professionals should control pain and the side effects of antineoplastic treatment and use preventive measures for infection control. During this pandemic, patients with head and neck cancer should not undergo elective procedures, even if they do not have symptoms or a history of COVID-19; therefore, in asymptomatic or painless cases, only preventive actions are recommended. In symptomatic or painful cases, precautions for safe interventional treatments must be implemented by following the hygiene measures recommended by health agencies and using personal protective equipment. During health crises, new protocols emerge for cancer treatment, and professionals must act with greater attention toward biosafety and updated knowledge. It is important to offer adequate individualized treatment based on the recommendations of preventative and interventional treatments so that patients can face this difficult period with optimized quality of life.

Keywords: Covid-19; Coronavirus Infections; Dental Care; Head and Neck Neoplasms; Practice Management, Dental.

Introduction

Coronavirus disease (COVID-19) is caused by a beta coronavirus, formally known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus emerged in the city of Wuhan, Hubei province, China, in December 2019 and then spread rapidly across the country and globally.[1] On March 12, 2020, the World Health Organization (WHO) declared it as a global pandemic.[2] Overall, 13,378,853 cases and

580,045 deaths due to COVID-19 were confirmed as of July 16, 2020.[2] In Brazil, which has the highest number of infected people in Latin America, 2,012,151 cases and 76,688 deaths have already been confirmed.[3]

The COVID-19 pandemic poses an unexpected public health challenge. Measures are being implemented worldwide by governments, non-governmental organizations, and individuals with an aim toward delaying the spread of the virus and, consequently, avoiding overburdening health systems.[4] The disease spreads primarily through human-to-human transmission of SARS-CoV-2 (through close contact or respiratory droplets produced when an infected person coughs or sneezes) and secondarily through contact with surfaces or objects contaminated by the virus.[5]

Hypertension and respiratory, cardiovascular, and metabolic diseases such as diabetes mellitus are important risk factors for COVID-19, particularly contributing to disease severity.[6] In addition to individuals with these comorbidities, current studies point to the elderly, obese, and those with chronic diseases as potential risk groups with repercussions on hemodynamics and immunology.[6] Patients in immunocompromised states, such as those with transplanted organs or active cancer, and using immunosuppressive agents are more susceptible and likely to progress to the most severe stage.[7,8]

Health care for patients with cancer is extremely challenging during this pandemic.[7] A recent study from China found that cancer patients with COVID-19, when compared to patients without cancer, have a higher risk of severe events, quantified by the need for admission to the intensive care unit requiring invasive ventilation or death.[9] Cancers those located in the head and neck region account for 5% of all types of cancers. The recent global cancer statistics reported an estimated 887,649 new cancer cases and 453,307 cancer-related deaths worldwide.[10] Approximately 90% of the cases are squamous cell carcinomas originating from the epithelium, with tobacco and alcohol being the most significant risk factors. Regarding the location, this type of cancer can be found on the lips, oral cavity, nasal cavity, pharynx, larynx, sinuses, and the salivary glands.[11] Head and neck cancer can be treated with a combination of modalities such as surgery, radiotherapy, chemotherapy, or immunotherapy.[8] These therapies, however, cause side effects during and after treatment, resulting in oral manifestations such as mucositis, candidiasis, xerostomia, dysphagia, dysgeusia, trismus, radiation-related caries, and osteoradionecrosis, which require intervention or close monitoring by a dental professional.[12] Thus, dentists are among the professionals with the greatest risk of contracting COVID-19 because they have close contact with patients, aerosols, saliva, and blood and use sharp contaminated instruments in clinical practice.[1,13]

Thus, the objective of the study was to review the literature and critically discuss important aspects in the treatment of patients with head and neck cancer during the COVID-19 pandemic. We also make recommendations for the management and protection of professionals during clinical dental care of such patients.

Discussion

SARS-CoV-2: general aspects and oral specifics

According to results from genetic and epidemiologic studies, the COVID-19 outbreak appears to have started with a single animal-to-human transmission, followed by a sustained human-to-human spread.[14] This virus has a high rate of transmissibility, and based on data from the World Health Organization, each infected person could transmit the disease to 1.4 to 2.5 people.[15] In addition, scientific evidence shows that the median incubation period is approximately 5 days and that symptoms will develop after 14 days of active monitoring or quarantine.[16]

Due to close face-to-face contact with patients and the frequent use of devices, dental professionals are repeatedly exposed to respiratory tract secretions, blood, saliva, and other contaminated body fluids, which increases the risk for viral transmission and COVID-19.[17] Transmission during dental services occurs through four main routes: direct exposure to respiratory secretions containing droplets, blood, or saliva; indirect contact with contaminated surfaces and/or instruments; inhalation of airborne

viruses; and mucosal contact with infected droplets and aerosols.[17]

It is important to mention that COVID-19 greatly impacted the behavior of dental patients.[18] At the onset of the pandemic, there was a reduction in the demand for dental care. Consequently, the incidence of dental and oral infections raised from 51% to 71.9% during the COVID-19 pandemic. This change was associated with service restrictions and the overall preference for staying at home.[19] This scenario was also reflected in patients who were undergoing antineoplastic treatment.[20] Considering the need for dental monitoring to minimize the side effects of head and neck cancer, it is necessary to understand oral changes and establish dental guides to maintain oral health and quality of life for these patients during and after the pandemic.

Oral manifestation in patients with head and neck cancer

It is a consensus that patients undergoing treatment for head and neck cancer can undergo acute and chronic changes in soft and hard tissues and sensory disturbances.[21] The treatment of head and neck cancer usually involves radiotherapy, chemotherapy, immunotherapy, and/or surgery and can affect healthy oral tissues, influencing the manifestation and progression of oral diseases and significantly affecting patients' quality of life.[22] Oral side effects of head and neck cancer treatment include oral mucositis, dysphagia, dysgeusia, and candidiasis, while the late effects include the loss of salivary gland function, trismus, radiation-related caries, and osteoradionecrosis.[12]

One of the most significant acute reactions in head and neck cancer patients is oral mucositis.[23] Radiation and/or chemotherapy causes cellular damage, which results in epithelial cell death. It is also believed that the generation of reactive oxygen species (free radicals) by radiation or chemotherapy plays a role at the beginning of the mucosal injury.[24] In its initial stage, erythema occurs due to epithelial thinning, which progresses to mucosal edema and inflammation. Over time, the mucosa becomes ulcerated and bleeds easily. The symptoms of this condition include severe pain and dysphagia.[25] The scale recommended by the WHO is mostly used to record the extent and severity of oral mucositis, which classifies mucositis in four degrees: Grade 0 (none) – No signs and symptoms; Grade I (mild) – Oral soreness, erythema; Grade II (moderate) – Oral erythema, ulcers, solid diet tolerated; Grade III (severe) – Oral ulcers, liquid diet only; Grade IV (life-threatening) – Oral alimentation impossible.[26] While the patient can still eat orally, the sensitive and inflamed oral mucosa makes it difficult to maintain oral hygiene and leads the patient to adopt a pasty diet rich in carbohydrates. These factors together increase the occurrence of periodontal disease and dental caries.[27]

Patients with dysphagia have difficulty with swallowing. Patients with head and neck cancer who have dysphagia, abnormal swallowing to severe oropharyngeal dysphagia (with the impossibility of oral feeding), can experience this problem for up to 12 months after oncological treatment.[28] Symptoms such as excessive chewing and drooling and complaint of food sticking in the throat are indicative of dysphagia. In addition, symptoms that require greater attention are those that indicate potential aspiration, such as coughing or clearing the throat before, during, or after eating.[29] During tumor removal, muscle, bone, and cartilage structures should be in a compromised state, as well as neck dissection or skull base surgery, favoring the appearance of dysphagia. The association of radiotherapy and chemotherapy may also affect the structures related to swallowing, mainly due to high doses of radiation, bilateral neck irradiation, or chemical damage to neuronal axons. The evaluation of swallowing disorders in these patients is difficult and requires the collaboration of a multidisciplinary team involving dentists, speech therapists, radiation oncologists, doctors, radiologists, and nutritionists.[30]

In turn, dysgeusia is the change or loss of taste. It can be a direct consequence of radiotherapy or chemotherapy and can also be associated with mucositis.[31] This may occur because the taste buds exposed to radiation undergo atrophy, leading to difficulty in perceiving the taste and temperature of food. The increase in the viscosity of saliva also forms a mechanical barrier, making physical contact with food difficult. Chemotherapy, however, promotes

direct cytotoxicity of the papillae. Antineoplastic drugs such as cisplatin may cause taste dysfunction because they can enter the oral cavity by diffusion through the capillaries. Many patients undergoing radiotherapy together with chemotherapy report metallic or very salty taste in the absence or presence of food.[32] The restoration of taste is quite variable among patients. Perception might either gradually return to normal or be permanent in cases of severe xerostomia.[22]

Radiation-induced hyposalivation results in decreased salivary flow and is often accompanied by xerostomia, the subjective perception of oral dryness. This affects the overall homeostasis of the oral cavity due to the decrease in salivary pH, increase in salivary viscosity, and changes in salivary chemical composition.[33] Chemotherapy-induced xerostomia can start from the second day of treatment, where the drugs begin to affect cells of the salivary glands, thereby causing atrophy of the acini, necrosis, degeneration, and fibrosis. In addition to decreasing salivary flow, chemotherapy also decreases the amount of salivary amylase and IgA immunoglobulins.[34] However, use of other medications such as hypertensive drugs, antidepressants, tranquilizers, antihistamines, and diuretics might also lead to this condition.[35] These changes trigger several other complications including dry lips, dysphagia, decreased resistance to oral infections such as candidiasis and halitosis.[12] The buffering and tooth remineralization capacity is reduced, leading to the loss of the demineralization/remineralization balance and facilitating a greater propensity for dental caries.[36] In addition, xerostomia causes discomfort, pain, and irritation related to oral dryness, altering the psychological dimension of patient.[33]

One of the late side effects is radiation-related caries, a multifactorial condition with a high potential for tooth destruction. It results from radiogenic damage to the dental structure, hyposalivation, alteration of the salivary composition, and decreased pH and buffering capacity in addition to the high-carbohydrate diet that is adopted due to oral mucositis, dysphagia, and dysgeusia.[37] Its clinical pattern differs from conventional caries in that conventional caries occurs mainly in pits, fissures, and the proximal region of teeth, while radiation-related caries develops in incisal/cuspal teeth and the entire cervical region, leading to enamel delamination, destruction of the underlying dentin, and amputation of the dental crown.[38]

Trismus in head and neck cancer patients may be caused by fibrosis in the masticatory muscles after surgery or radiotherapy, and contracture in the mastication structures, including the masseter and pterygoid muscles.[12,39] The prevalence of trismus primarily depends on the location and size of the tumor, being higher in patients with tumors close to the masticatory system, such as parotid and nasopharyngeal lesions or those located in the lateral oropharyngeal cavities or the posterior oral cavity.[40] The restricted opening of the mouth negatively affects the patient because improper mastication requires changes in food consistency and poses difficulties in maintaining oral hygiene, increasing the risk for oral infections and dental problems.[41]

Osteoradionecrosis is the most serious chronic complication of radiotherapy for the treatment of head and neck cancer.[12] It usually develops in the presence of odontogenic infection or traumatic bone intervention after radiotherapy.[40] Meanwhile, medication-related osteonecrosis corresponds to bone necrosis resulting from the use of antiresorptive and antiangiogenic agents. The drugs most often associated with this condition are bisphosphonates, which are used in the treatment of several diseases, including the control of metastases and bone tumors.[42] The clinical signs and symptoms of both pathologies are quite similar and include bone necrosis, pain, dysgeusia, oroantral fistula, fetid odor, trismus, difficulty in chewing, swallowing and phonation, extraoral fistula, pathological fracture, and sepsis.[12,42] Bone exposure to the oral environment has a poor prognosis and is difficult to treat, compromising the patient's general health and quality of life.[43]

Management of patients with head and neck cancer during the COVID-19 pandemic

Patients with head and neck cancer require special attention during the COVID-19 pandemic. As mentioned earlier, current research shows that

patients older than 60 years and/or presenting with systemic conditions or diseases, such as a history of head and neck irradiation, cardiovascular disease, organ transplantation, immunosuppression, diabetes mellitus, hematological diseases, and autoimmune diseases have a worse prognosis with COVID-19.[44] A multidisciplinary treatment strategy should be designed considering antineoplastic therapy and epidemic prevention.[45] Radiotherapy and chemotherapy should be continued[46] but with schemes that reduce the number of hospital visits.[45] Thus, radiation-related side effects will continue to affect the oral health-related quality of life of cancer survivors.[12]

Oral health care professionals are now considered to be at the highest risk of infection; therefore, face-to-face appointments should be reduced.[6,47] Teledentistry (text messages, phone calls, or video calls) has provided a way of communication between the professional and the patient, which has helped decrease the risk of COVID-19.[6] This approach helps the dentist to evaluate the patient's needs, offer advice, monitor the ones undergoing treatment, and carry out follow-ups.[48] It also became a way to reduce anxiety and help patients to adapt to the new reality.[49]

During the pandemic, dental treatments are being divided into elective (non-urgent) and emergent cases.[50] The American Dental Association (ADA) recommends that elective dental procedures be avoided.[50] Thus, management is limited to the treatment of acute dental problems and the relief of symptoms of oral mucositis, xerostomia, trismus, and opportunistic infections.[51] Due to this unprecedented circumstance, the role of dentists for patients with head and neck cancer can be divided into two fronts: prevention for patients without pain and intervention for patients with pain.

Preventative treatment: patients without pain

Even when no oral symptoms are reported, it is imperative to follow-up patients through teledentistry to prevent or minimize some oral side effects of chemoradiotherapy, regardless of the treatment stage (before, during, or after). Dental professionals should strongly recommend and encourage patients to maintain good oral hygiene. Removal of dental plaque and reduction in the population of bacteria in the oral cavity require a combination of actions. Patients should be advised to brush three times a day with a soft or ultra-soft toothbrush.[52] The use of fluoride toothpaste is essential for the remineralization of enamel and dentin.[53] Toothpastes with mint flavoring and containing sodium dodecyl sulfate (surfactant) can irritate the mucosa and should be avoided.[52] If there is an increased risk of dental caries, toothpastes with high concentrations of fluoride are available and can be prescribed.[43, 52] Flossing or interdental cleaning aids are recommended to remove dental plaque or solid debris between teeth, crowns/bridges, or dental implants. Remineralizing solutions such as sodium fluoride alcohol-free solution[20, 43] or 1% sodium fluoride gel[37] should be used daily in patients with hyposalivation to prevent and remineralize carious lesions.[43]

For plaque accumulation and reduction in *Streptococcus mutans* counts, rinsing with non-alcoholic and non-flavored chlorhexidine digluconate 0.12–0.2% solution once or twice daily is also recommended,[52,54] maintaining sustained periodontal health. Care must be taken to ensure that the chlorhexidine solution does not interfere with the fluoride solution. If there is an interaction, rising of the mouth at different times of the day should be recommended.

Salivary hypofunction and xerostomia are frequent oral adverse effects. Salivary substitutes and/or stimulants (candies, gums, and sialagogic agents such as pilocarpine) may be recommended for relief when the residual function of the salivary gland is documented.[55] It is advisable to use lip care products, humidifiers, and nasal breathing[20] and avoid harmful habits that cause mucosal irritation, such as smoking and alcohol consumption.[45] The patients should be advised about decreasing consumption of acidic and spicy food because these foods aggravate the symptoms of xerostomia and pain from mucositis.[12]

Currently, prevention of trismus and osteoradionecrosis is needed. Immediately after commencing radiotherapy, patients should perform home exercises to maintain muscular mobilization. Specific exercises, using tongue spatulas or the TheraBite device, can help maintain

a maximal oral opening and jaw mobility.[56] To prevent osteoradionecrosis, oral hygiene, absence of trauma due to removable prostheses, and dental care are key.[45] Removable dental prostheses must be mechanically cleaned with or without chemical methods. At night, when not in use, the dentures should be placed in water.[52] This will prevent candidal and mucositis lesions.

Patients should be well informed about the importance of maintaining a normal and balanced diet to ensure adequate nutrition.[43] Pre-treatment evaluation of swallowing function and nutritional status is of paramount importance. Moreover, post-treatment swallowing function can benefit from pre-treatment swallowing exercises.[30] Changing the consistency of food may be inevitable due to pain and discomfort. Dietary management can be performed by a nutritionist to prevent or mitigate weight loss and reduce in overall quality of life.[57]

Interventional treatment: patients with pain

The second front of action is intervention when patients present with oral symptoms. Precautions must be taken, and every patient should be considered a potential asymptomatic carrier of COVID-19.[58] Pre-appointment screening including medical history, must be performed before the patient visits the dental office. The entire building must be properly prepared according to ADA recommendations.[50] In the waiting room, patients should wear masks, maintain a distance of 1 meter, and have their temperature checked.[19] Adequate ventilation should be provided, and long stay in this room should be avoided. Dentists must adhere to the infection control protocol. Hand hygiene using water and soap and then using 70% hydroalcoholic solution should be followed. Additionally the standard procedure for using personal protective equipment should be followed, including their donning and doffing. Disinfection of the clinical environment before and after dental care using disinfecting products such as 62–71% ethanol, 0.5% hydrogen peroxide, and 0.1% (1 g/L) sodium hypochlorite should be carried out. Disposable physical barriers on equipment should be used. Four-handed dentistry technique should be used, and the appropriate technique for garbage disposal must be followed.[13,14,46,50]

After identifying the urgent need for dental treatment, it is important to verify the risks and benefits associated with each treatment. Management with minimally invasive procedures is essential. Before every treatment, the patient should use a mouth rinse containing 1% or 1.5% hydrogen peroxide or 0.2% povidone.[19] Dentists should use a high-volume saliva ejector and a rubber dam and decrease the use of ultrasonic instruments, high-speed handpieces, and 3-way syringes to minimize the generation of aerosols.[13,14,59] Extra-oral images such as panoramic images should be preferred over intraoral radiographs to avoid the gag or cough reflexes.[60]

Irradiated head and neck cancer patients are at risk of developing candida and herpes. During the COVID-19 pandemic, reports of any symptoms should result in a quick appointment in the dental office for proper diagnosis and prescription of medications and instructions. Infections must be treated with antifungal and antiviral drugs.[61] Dentures should be appropriately cleaned and decontaminated with the same antimicrobial agent to avoid recontamination of the oral cavity by the microbial flora of dentures.[52]

Another oral side effect of cancer treatment that can bother patients is oral mucositis. Some guidelines suggested the implementation of multiagent combination oral care protocols, benzydamine mouthwash, combined topical application and systemic administration of honey, low-level laser therapy, and photobiomodulation for the prevention of oral mucositis.[62-66] Oral cryotherapy has been indicated for the prevention of this adverse effect for patients undergoing chemotherapy and receiving bolus 5-fluorouracil.[67] As treatment for oral mucositis-associated pain, topical morphine 0.2% is indicated for head and neck cancer patients undergoing radiotherapy and chemotherapy.[68]

A multidisciplinary management approach for dysphagia presented by some patients is essential. Pain management, as well as immediate treatment of the condition, will prevent critical weight loss. In patients with a high risk of weight loss, a short period of parenteral nutrition may be indicated.[30]

Radiation-related caries has a highly destructive potential and rapid evolution and can progress

to amputation of the dental crown.[69] In addition, injuries to the pulp can also occur. Thus, the strategies currently adopted to reduce the spread of microorganisms are the use of rubber dams, avoidance of rotatory instruments during cavity preparation, chemo-mechanical caries removal, and atraumatic restorative techniques.[1,54,59]

For acute periodontal disease, manual scaling is recommended, ultrasonic scalers should be avoided. If tooth extraction is necessary, atraumatic extractions should be performed, avoiding bone drilling and using resorbable sutures to minimize visits to the dental office.[20] Other measurements to reduce oral trauma should be performed to avoid osteoradionecrosis.[43] Once installed, hyperbaric oxygen has shown great improvement in its management since the 1960s;[43] however, during the pandemic, the indication for hyperbaric oxygen must be critically evaluated.

The suggestions for the management of patients with head and neck cancer undergoing antineoplastic treatment in this paper are general guidelines; therefore, the final decision will always depend on the professional's judgment, taking into account the patient's individual health situation.

Conclusion

This critical review aimed to discuss the impact of COVID-19 on the oral health of patients with head and neck cancer undergoing antineoplastic treatment and to present suggestions to minimize the signs and symptoms of the side effects. During health crises, new protocols are emerging for cancer treatment, and professionals must act with greater attention to biosafety and updated knowledge. It is important to offer adequate individualized treatment based on the recommendations of preventative and interventional treatments. We hope to help dental professionals and patients with head and neck cancer more easily face this difficult period.

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