Review Article

Common oral conditions associated with post-radiotherapy patients in Africa

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ABSTRACT

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Radiotherapy involves the use of high-energy radiation to shrink and or kill cancer cells, thus preventing the cells from growing, dividing, and spreading. Oral conditions associated with radiotherapy can affect the quality of life of post- radiotherapy patients when symptoms are not managed or prevented. The effects of radiotherapy on oral tissues is dependent on the total radiotherapy dose, fractionation system used, radiotherapy volume, radiation techniques used, entire and daily doses of radiotherapy and location of the tumour. Age, poor oral hygiene status prior to radiotherapy, gender, alterations in salivary production, mucosal trauma and nutritional status of the patient are some factors associated with radiotherapy related oral manifestations .

After searching PubMed, ScienceDirect, African journal online and Google scholar by two independent investigators. The aim of this article was to review the available studies on the prevalence and common oral conditions/manifestations associated with post-radiotherapy patients in Africa. The oral conditions or manifestations reported from Africa based studies are oral mucositis , xerostomia ,dysphagia, radiation-related dental caries, dermatitis, altered taste sensation and osteoradionecrosis of the mandible. Treatment options for oral mucositis include basic oral care, sodium bicarbonate mouthwash, cryotherapy , chlorhexidine mouthwash, mixed medication mouthwash, anti-inflammatory agents, anti-microbial agents, local anesthetics, analgesics and natural agents such as honey. Xerostomia (dry mouth) can affect speech , taste ,chewing, swallowing and quality of life. There is need for more research towards understanding the preventive and treatment interventions to improve quality of life of post-radiotherapy patients.

KEY WORDS

Africa, Prevalence, manifestations, studies, radiotherapy.

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INTRODUCTION

Radiotherapy alone can be a primary treatment modality, 1 or radiotherapy in combination with chemotherapy before or after surgical resection2 can be an effective and standard treatment modality for head and neck cancers. Radiotherapy uses high-energy radiation 3to shrink and or kill cancer cells, thus preventing the cancerous cells from growing, dividing, and spreading. Oral conditions associated with radiotherapy can affect the quality of life3 of patients when symptoms are not managed or prevented. Effects of radiotherapy to oral tissue is dependent on the total radiotherapy dose2, fractionation system used, radiotherapy volume, radiation techniques used, entire and daily doses of radiotherapy and location of the tumour. Factors associated4-8 with radiotherapy related oral manifestation are age, poor oral hygiene status prior to radiotherapy, gender, alterations in salivary production, mucosal trauma and nutritional status of the patient. Radiation doses above 20 Gy can cause damage to the salivary glands2, and doses above 30 Gy (Gy) can cause damage to the lacrimal glands.

Electronic searching of PubMed, ScienceDirect, African journal online and Google Scholar by two independent investigators was done in November, 2024. The keywords used were oral conditions, radiotherapy , Africa countries, oral manifestation, post- radiotherapy ,sub-Saharan Africa and Africa. Search terms and keywords were combined by Boolean operators. The inclusion criteria were original (primary) research articles with information on prevalence and common oral manifestations associated with post-radiotherapy patients in Africa , published in English and with accessible full text. While review articles, systematic reviews, thesis, communications and dissertations related to prevalence and common oral conditions /manifestations associated with post-radiotherapy patients in Africa were excluded. The aim of this article was to review the available studies on the prevalence and common oral conditions/ manifestations associated with post-radiotherapy patients in Africa

COMMON ORAL CONDITIONS ASSOCIATED WITH POST-RADIOTHERAPY PATIENTS

The oral manifestations 5that develop during the course of radiotherapy can occur indirectly as a result of the production of reactive oxygen species (ROS) and pro-inflammatory cytokines responsible for the initiation of inflammatory processes8 that can affect cell proliferation.It can occur directly by inhibiting DNA duplication or damage of the DNA double helix resulting in cell damage or death. The oral conditions or manifestations that develop during the course of radiotherapy reported from Africa based studies9-10 are oral mucositis , xerostomia ,dysphagia, radiation-related dental caries, altered taste sensation and osteoradionecrosis of the jaw. Among these oral manifestations, the acute ones which may occur during the period of radiotherapy includes oral mucositis, xerostomia, radiation-induced dermatitis, dysphagia, altered taste sensation and candidal infection.11 In Tanzania, among head and neck patients who had external beam radiotherapy10 by a two dimensional (2D) machine that uses Cobalt-60 to emit gamma rays with 1.17 and 1.33 MeV at1.8 to 2 Gy per fraction for about 20 to 25 fractions. Findings from the study reported that 90% of the study participants had xerostomia, 80% had oropharyngeal mucositis, 76.2% developed taste disorders and 50% had dysphagia after radiotherapy. Patients with sinonasal cancers10 had the least occurrence of oral and oropharyngeal mucositis (50%) and xerostomia (64.3%) compared with patients with oropharyngeal cancer (100%), hypopharyngeal cancer (100%) and oral cancer (96.2%). Tumour location or proximity to orofacial tissue plays a role in the development of some oral manifestations. Another study from Egypt9, reported that 97.3% of the study participants presented with oral mucositis, 84.4% presented with xerostomia, 64.6% had dysphagia and 53.7% complained of altered taste sensation. This variation in study findings could be as a result of the location of the tumor, total radiotherapy dose, fractionation system used, age5,7-8, oral hygiene status prior to radiotherapy, gender, presence of mucosal trauma, entire and daily doses of radiotherapy, nutritional status of the patient and radiation techniques used.5,7

A study from Sudan12 reported a statistically significant relationship between the presence of xerostomia and pharyngeal cancer. The use of Intensity modulated radiotherapy (IMRT) for oral cavity tumours reduces the risks of xerostomia and osteoradionecrosis of the mandible through parotid and mandibular gland sparing in a study from Morrocco13. Hypofractionated radiotherapy14 is the radiation treatment regimen that involves division of the total dose of radiation into large doses and treatments are given once a day or less often. A study from Ethiopia reported that the use of hypofractionated radiotherapy improves symptoms control and quality of life of post-radiotherapy patients14 .

Oral mucositis (OM) are erythematous and painful ulcerative lesions7 of the oral mucosa due to destruction of the oral mucosal epithelial cells, observed in patients who are treated with chemotherapy, and/or with radiation therapy for oral cancers. Oral mucositis can manifest as atrophy, swelling, erythema7 and ulceration.15 It can appears initially by thinning of oral tissues which leads to erythema.7 As these tissues become thinner, ulceration eventually occurs7. The condition may be exacerbated by local factors,5.7-8 such as trauma from teeth or foreign appliance, poor oral hygiene, the presence of dental appliances, malnutrition, concomitant chemotherapy medications with radiotherapy,

medical conditions like uncontrolled diabetes, tobacco use and microbial colonization from oral bacteria . It is a painful post -radiotherapy manifestation that can cause dysphagia, alterations in taste, weight loss, and secondary infections which 15can significantly complicate treatment, extend hospitalization, and decrease the patient's quality of life .15

The pathogenesis of oral mucositis[5] are

Phase I—Initiation. Chemotherapy or radiation-induced reactive oxygen species (ROS) and lipid peroxidation results in DNA damage, release of pathogen-associated molecular pattern (PAMP) and damage-associated molecular pattern molecules (DAMPs) and cellular apoptosis

Phase II—Signaling. Reactive oxygen species stimulate the NF-kB pathway, which induces production of proinflammatory cytokines (TNF-α, IL-1β, IL-6)

Phase III – Amplification. Proinflammatory cytokines trigger tissue injury, apoptosis, vascular permeability, and activation of cyclooxygenase-2

Phase IV—Ulceration. Ulceration occurs, which serves as a portal of entry for microorganisms.

The presence of bacteria activate macrophages and neutrophils to further produce pro-inflammatory cytokines

Phase V—Healing. Signalling from the submucosa promotes epithelial migration, proliferation and differentiation

The assessment of oral mucositis according to World Health Organization (WHO) Oral Mucositis Scale5 are

Grade 1 (mild) -Oral soreness, erythema

Grade 2 (moderate) -Erythema, ulcers, but oral intake not prevented

Grade 3 (severe) -Oral ulcers interfering with oral intake and requiring liquids only

Grade 4 (life-threatening)- Oral ulcers to the extent that oral alimentation is impossible

Another subjective and objective scales for oral mucositis according to The National Cancer Institute (NCI) published Common Terminology Criteria for Adverse Events (CTCAE) include15

Grade 1—Erythema of the mucosa;

Grade 2—Patchy ulcerations or pseudomembranes;

Grade 3—Confluent ulcerations or pseudomembranes; bleeding with minor trauma,

Grade 4—Tissue necrosis; significant spontaneous bleeding; life-threatening consequences,

Grade 5—Death.

Treatment options for oral mucositis include basic oral care, sodium bicarbonate mouthwash, cryotherapy , chlorhexidine (CHX) mouthwash, mixed medication mouthwash, anti-inflammatory agents, anti-microbial agents, local anesthetics, analgesics, natural agents such as honey16 etc .Some of these treatment options can be done in resource limited setting in Africa.

Radiation-induced xerostomia (dry mouth) occur due to damage of the membranes of secreting granules in acinar cells17 by radiation-induced lipid peroxidation, and lysis of the cells by proteolytic enzymes in salivary flow rate. This level of damage is dependent on the total radiation dose received and the volume of salivary glands irradiated.18 Xerostomia can cause alterations in speech and taste as well as difficulty with mastication and deglutition, leading to secondary nutritional deficiencies and a decrease in quality of life.18 Radiation-induced damage to the parotid and submandibular glands can alters the volume, 17consistency, composition and pH of secreted saliva. Preventive strategies in some hospital settings include submandibular gland transfer before radiation therapy, and parotid gland sparing techniques with 3-dimensional conformal or intensity modulated radiation therapy.19-20 The studies identified might not reflects the level of research on prevalence and common oral conditions /manifestations associated with post-radiotherapy patients in Africa More studies from Africa countries will fill the gaps in knowledge and add to the existing literature.

CONCLUSION

Oral conditions associated with radiotherapy can affect the quality of life of patients when symptoms are not managed or prevented. There are predisposing or oral health related risk factors that can be managed before, during and after commencement of radiotherapy. Studies identified from Africa were few, which call for more research towards understanding the common oral manifestation after radiotherapy, preventive and treatment interventions to improve quality of life of post-radiotherapy patients

REFERENCE

1. Goel G, Alice KP, Negi P, Aggarwal N. Factors influencing radiation induced oral mucositis in head and neck cancer. J Can Res Ther 2024;20:1564-9.
2. Westgaard KL, Hynne H, Amdal CD, Young A, Singh PB, Chen X, et al. Oral and ocular late effects in head and neck cancer patients treated with radiotherapy. Scientific reports.2021 ;11(1):4026.
3. Lee HJ, Han DH, Kim JH, Wu HG. The effect of comprehensive oral care program on oral health and quality of life in patients undergoing radiotherapy for head and neck cancer: a quasi-experimental case-control study. Medicine 2021;100:16(e25540).
4. Raber-Durlacher JE, Elad S, Barasch A. Oral mucositis. Oral oncology. 2010 ;46(6):452-6.
5. Oronsky B, Goyal S, Kim MM, Cabrales P, Lybeck M, Caroen S, et al. A review of clinical radioprotection and chemoprotection for oral mucositis. Translational oncology. 2018;11(3):771-8.
6. Ferreira AS, Macedo C, Silva AM, Delerue-Matos C, Costa P, Rodrigues F. Natural products for the prevention and treatment of oral mucositis—a review. International Journal of Molecular Sciences. 2022 Apr 15;23(8):4385.
7. Gholizadeh N, Sheykhbahaei N, Sadrzadeh-Afshar MS. New Treatment Approaches of Oral Mucositis: A Review of Literature. Adv Hum Biol 2016;6:66-72.
8. Maria OM, Eliopoulos N. Muanza T . Radiation- Induced Oral Mucositis. Front. Oncol. 2017;7:89. doi: 10.3389/fonc.2017.00089
9. Abo el Fadel DM, Kamal Y, Hassouna AH, Ali A. Prevalence of oral side effects associated with chemo and radiotherapy in head and neck cancer treatment: A cross-sectional study in Egypt. Oral Oncology Reports. 2024 ;10:100177.
10. Abraham ZS, Ngunyale B, Massawe ER, Ntunaguzi D, Mpondo B. Oral and Otolaryngological Complications of Radiotherapy for Head and Neck Cancers among Patients attending Ocean Road Cancer Institute, Tanzania. Medical Journal of Zambia. 2018;45(1):32-43.
11. Haribhakti VV, Haribhakti VV. Morbidities Related to Adjuvant Radiotherapy and Chemotherapy. Restoration, Reconstruction and Rehabilitation in Head and Neck Cancer. 2019:275-306
12. Awooda EM, ElObied SE, Elbeshir EI .Oral Health and Experiences of Oral Care in Radiotherapy Patients with Head and Neck Cancer in Sudan Sudan JMS 2014(9);3:169-175
13. Zahrae TF, Fadwa A, Abdelrahmane EM, Touria B, Khalid H. Intensity-modulated radiation therapy reduces late salivary toxicity and mandibular osteoradionecrosis in the treatment of oral cavity cancer: retrospective study. J Surg Med. 2018;2(2):111-113.
14. Zingeta GT, Worku YT ,et al.Outcome of Hypofractionated Palliative Radiotherapy Regimens for Patients With Advanced Head and Neck Cancer in Tikur Anbessa Hospital, Ethiopia: A Prospective Cohort Study. JCO Global Oncol 10:e2300253 https://doi.org/10.1200/GO.23.00253
15. Daugėlaitė G, Užkuraitytė K, Jagelavičienė E, Filipauskas A. Prevention and treatment of chemotherapy and radiotherapy induced oral mucositis. Medicina. 2019 Jan 22;55(2):25.
16. Münstedt K, Momm F, Hübner J. Honey in the management of side effects of radiotherapy-or radio/chemotherapy-induced oral mucositis. A systematic review. Complementary therapies in clinical practice. 2019 ;34:145-52.
17. Dirix P, Nuyts S, Van den Bogaert W. Radiation-induced xerostomia in patients with head and neck cancer: a literature review. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2006 ;107(11):2525-34..
18. Lee MG, Freeman AR, Roos DE, Milner AD, Borg MF. Randomized double-blind trial of amifostine versus placebo for radiation-induced xerostomia in patients with head and neck cancer. Journal of medical imaging and radiation oncology. 2019 63(1):142-50.
19. Yang WF, Liao GQ, Hakim SG, Ouyang DQ, Ringash J, Su YX. Is pilocarpine effective in preventing radiation-induced xerostomia? A systematic review and meta-analysis. International Journal of Radiation Oncology* Biology* Physics. 2016;94(3):503-11.
20. Sood AJ, Fox NF, O'Connell BP, et al. Salivary gland transfer to prevent radiation-induced xerostomia: A systematic review and metaanalysis. Oral Oncol 2014;50:77-83.