DOI: http://dx.doi.org/10.17921/2447-8938.2018v20n2p119-121

Candidíase Orofaríngea em Pacientes Submetidos a Radioterapia para Câncer de Cabeça e Pescoço: Revisão de Literatura

Oropharyngeal Candidiasis in Patients Undergoing Radiotherapy for Head and Neck Cancer: Literature Review

Thainah Bruna dos Santos[a]*; Solange de Paula Ramos[b]; Nora Gavilanes[c]; Ricardo Sergio Almeida[b]

[a]Universidad San Gregorio de Portoviejo, Carrera de Odontologia Ecuador.
[b]Universidade Estadual de Londrina, Programa de Pós-Graduação Stricto Sensu em Odontologia. PR, Brasil.
[c]Universidade Técnica de Manabí, Departamento de Ciências da Saúde Equador.
*E-mail: thainahbruna@gmail.com
Received: November 17, 2017
Approbed: March 2, 2018

Abstract

Candidiasis is closely related to patients undergoing head and neck radiotherapy due to the immunosuppressive state, induced xerostomia, mucositis and difficulties in establishing adequate oral hygiene. Therefore, the aim of this study was to discuss the relationship between candidal infections and the radiotherapy of the head and neck region, based on available scientific literature. In order to identify the studies included or considered in this study, a search strategy was carried out for the following databases: SCOPUS, Web of Science and PubMed. Inclusion criteria were publications that addressed key words: *Candida* spp. of the oral cavity and head and neck cancer. Therefore, this work exposes the necessity for studies relating candidal infections with radiotherapy treatment of the head and neck region. However, it is possible suggest that colonization and infection by Candida spp. can be increased by radiotherapy. Additionally, it can be suggested that patients irradiated at the head and neck region should be periodically investigated for the presence of pathogenic yeasts in the oral cavity, followed by greater care with oral hygiene and nutrition.

Keywords: *Candida* Spp. Xerostomia. Oral Health. Publications.

Resumo

A candidíase está intimamente relacionada com pacientes submetidos a radioterapia de cabeça e pescoço devido ao estado imunossupressor, xerostomia induzida, mucosite e dificuldades no estabelecimento de higiene bucal adequada. Portanto, o objetivo deste estudo foi discutir a relação entre infecções por Candida spp. e a radioterapia da região da cabeça e pescoço, com base na literatura científica disponível. Para identificar os estudos incluídos ou considerados neste estudo, foi realizada uma estratégia de busca para os seguintes bancos de dados: SCOPUS, Web of Science e PubMed. Os critérios de inclusão foram publicações que abordavam as palavras-chave: Candida spp. da cavidade oral e câncer de cabeça e pescoço. Desta forma, este trabalho expõe a necessidade de estudos relacionados às infecções por Candida spp. com tratamento de radioterapia da região da cabeça e pescoço. No entanto, podemos sugerir que a colonização e a infecção por Candida spp. pode ser aumentada por radioterapia. Além disso, pode-se sugerir que os pacientes irradiados na região da cabeça e pescoço devem ser investigados periodicamente quanto à presença de leveduras patogênicas na cavidade bucal, seguido de maiores cuidados com higiene bucal e nutrição.

Palavras-chave: *Candida Spp. Xerostomia. Saúde Bucal. Publicações.*

1 Introduction

Head and neck cancer represents the sixth most frequent neoplasia worldwide. About 650.000 new cases are diagnosed each year. Despite advances in treatment methods, there are high rates of morbidity and mortality, with approximately 350.000 deaths/year[1].

As a consequence of the radiotherapy treatment, the patients may present alteration of the buccal microbiota, favoring opportunistic infections onset, especially candidiasis[2]. It is associated with immunosuppressive status, decreased salivary flow induced by oncological treatment, mucositis, neutropenia, microbial imbalance and use of prosthesis[3].

Candida spp. can spread to other organs through the bloodstream compromising the patient's general condition and his or her prompt recovery[4,5]. Several studies deal with colonization by *Candida* spp. in patients irradiated in the head and neck. However, the incidence of oropharyngeal candidiasis related to oral lesions is still little understood[6-9].

The search and selection of relevant scientific articles is a skill that must be developed by the scientific community that needs constant updating. The health community, in general, uses Medline, an integral part of PubMed (http://www.ncbi.nlm.nih.gov/pubmed). There are other databases available as SciELO (http://www.scielo.org), which gathers journals of all Latin American and Caribbean territory, specialized in health sciences, among other areas of knowledge. Scopus (www.scopus.com), owned by Elsevier, has a vast collection, with approximately 12,850 journals and Web of Science (www.webofscience.com), which has about 8,700 journals and provides quotes analysis, offering good graphics capabilities[10].

Therefore, the aim of this study was to discuss the relationship between candidal infections and the radiotherapy of the head and neck region, based on available scientific literature.

2 Material and Methods

In order to identify the studies included or considered in this study, a search strategy was carried out for the following databases: Scopus, Web of Science and PubMed.

Inclusion criteria were publications that addressed key words: *Candida* spp. of the oral cavity and head and neck cancer. Thus, only articles in English were selected. It should be noted that a search in Portuguese was performed in the Scielo database, but no article was found with the key words used here. Data were analyzed through the abstracts reading for subject selection. For further discussion, the related articles were read .

3 Results and Discussion

As shown in Table 1, the search showed that the surveys began since 1998 and that until February 28th, 2017, a total of 2 documents were obtained on the platform SCOPUS; Web of Science presented 2 articles and Pubmed presented 7 publications. Three of them were excluded, because one was duplicate among databases[11], the other one is writing in Chinese[12] and the last one is a book chapter with a different thematic from that proposed in this study[13]. Thus, only eight articles were found in this search, showing the scarcity of studies in this research field.

Table 1 - Articles analyzed

Title	First Author	Year	Type	Language	Database
Oral *Candida* species in head and neck cancer patients treated by radiotherapy	Freitas EM	2013	Research article	English	SCOPUS
Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements	De Sanctis V	2016	Review	English	SCOPUS
Candida oral colonization and infection in Brazilian patients undergoing head and neck radiotherapy: a pilot study	Jham BC	2007	Research article	English	Web of Science
Candida spp. in oral cancer and oral precancerous lesions	Gallè F	2013	Research article	English	Web of Science
The microflora associated with human oral carcinomas	Nagy KN	1998	Research article	English	Pubmed
Betel quid-associated oral lesions and oral *Candida* species in a female Cambodian cohort	Reichart PA	2002	Research article	English	Pubmed
Antifungal susceptibility testing of commensal and pathogenic clinical isolates of oral *Candida*	Zhao M	2006	Research article	Chinese	Pubmed
Microflora in oral ecosystems in subjects with radiation-induced hyposalivation	Almståhl A	2008	Research article	English	Pubmed
Candida spp. in oral cancer and oral precancerous lesions	Gallè, F	2013	Research article	English	Pubmed
Infectious agents associated with head and neck carcinomas	Hettmann, A	2016	Book chapter	English	Pubmed
Isolation and identification of *Candida* species in patients with orogastric cancer: susceptibility to antifungal drugs, attributes of virulence *in vitro* and immune response phenotype	De Sousa LVNF	2016	Research article	English	Pubmed

Sourde: Research Data.

Of the remaining eight articles, one is a review[14] focused on mucositis and the prophylactic treatment with fluconazole. The authors concluded that such treatment is not useful to prevent oral mucositis in the head and neck cancer patients undergoing radiotherapy.

Nagy and collaborators[15] evaluated the microbial biofilms content on the surfaces of oral squamous cell carcinomas and found *Candida albicans* at eight of the 21 tumor sites. Reichart and collaborators[16] isolated *Candida* species from the mouth of 48 Cambodian women with betel quid chewing (BQC) habit and found no relation between BQC and oral colonization by *Candida* species. Gallè and collaborators[11] evaluated patients with oral lesions (precancerous and cancerous) without treatment, isolating *Candida* spp. from 30% of the patients with cancerous lesions and 32% with precancerous lesions. De Sousa and collaborators[17] [(17)] assessed the yeasts virulence isolated from 59 patients with orogastric cancer (OGC), before the treatment started, demonstrating an increased virulence for these isolates. Although interesting, these data are not related to the theme of this study, once it seeks for the relation among candidal infections to the radiotherapy treatment of the head and neck region. Thus, only 3 articles remained which are directly related to the present topic.

Salivary glands can suffer atrophy and degeneration of the secretory portion after exposition to radiation. This side effect leads to a reduction in salivary flow (more significant after 1800

cGy) and, consequently, to a xerostomic state, which is the main complaint of irradiated patients[6].

In the study carried out by Almstahl and collaborators[18], *Candida albicans* was found in one or more sites in 54% of the radiotherapy subjects and in 15% of the controls. However, no case of oral candidiasis was reported, probably because this evaluation was made in only 13 dentate subjects, and after the radiotherapy completion (6–8 months).

Freitas and collaborators[6] isolated *Candida* species from saliva samples from 29 head and neck irradiated patients, 34 noninstitutionalized elderly patients and 29 institutionalized elders, and were able to show that radiotherapic treatment was associated with positiveness to *Candida*. Furthermore, irradiated patients presented a major prevalence of non-albicans species compared to elderly patients (institutionalized or not).

Studying 21 patients before, during, and immediately after radiotherapy, Jham and collaborators[19] showed that candidiasis occurred in 52% of the patients at some point of therapy. Interestingly, colonization rates were higher in patients that developed candidiasis, comparing with non-infected patients (54% and 30%, respectively). Thus, it can be suggested that such patients need greater care with oral hygiene and nutritional support.

4 Conclusion

Therefore, this work exposes the necessity for studies regarding candidal infections with radiotherapy treatment of the head and neck region. However, it is possible to suggest that colonization and infection by *Candida* spp. can be increased by radiotherapy. Additionally, it can be suggested that patients irradiated at the head and neck region should be periodically investigated for the presence of pathogenic yeasts in the oral cavity, followed by greater care with oral hygiene and nutrition.

References

1. Cognetti DM, Weber RS, Lai SY. Head and neck cancer. Cancer 2008;113(S7):1911-32.
2. Jensen DH, Oliveri RS, Kølle S-FT, Fischer-Nielsen A, Specht L, Bardow A, *et al*. Mesenchymal stem cell therapy for salivary gland dysfunction and xerostomia: a systematic review of preclinical studies. Oral Surg Oral Med Oral Pathol Oral Rad 2014;117(3):335-42
3. Leung WK, Dassanayake RS, Yau JY, Jin LJ, Yam WC, Samaranayake LP. Oral colonization, phenotypic, and genotypic profiles of Candida species in irradiated, dentate, xerostomic nasopharyngeal carcinoma survivors. J Clin Microbiol 2000;38(6):2219-26.
4. Akpan A, Morgan R. Oral candidiasis. Postgrad Med J 2002;78(922):455-9.
5. McNeill HE. Bitting back oral hygiene. Int Crit Care Nur 2000;16(6):367-72.
6. Freitas EM, Nobre SA, de Oliveira Pires MB, Faria RVJ, Batista AUD, Bonan PRF. Oral Candida species in head and neck cancer patients treated by radiotherapy. Auris Nasus Larynx 2013;40(4):400-4.
7. Bonan PRF, Pires FR, Lopes MA, Di Hipólito Júnior O. Colonização e espécies de Candida em pacientes submetidos à radioterapia cervicofacial. J Bras Patol Med Laboratorial 2007;43(6):407-12. doi: http://dx.doi.org/10.1590/S1676-24442007000600004.
8. Singh GK, Capoor MR, Nair D, Bhowmik K. Spectrum of fungal infection in head and neck cancer patients on chemoradiotherapy. J. Egyptian National Cancer Institute. J Egypt Natl Canc Inst 2017;29(1):33-7. doi: 10.1016/j.jnci.2017.01.006.
9. Jardim Junior EG, Sales Cunha-Correia A, Okamoto AC, Gaetti-Jardim EC. Oral microbiota and mucositis in patients with head and neck cancer undergoing radiotherapy: literature review. Arch Health Invest 2017;6(2):89-94. doi: http://dx.doi.org/10.21270/archi.v6i2.1797.
10. Bernardo WM, Nobre MRC, Jatene FB. A prática clínica baseada em evidências: parte II-buscando as evidências em fontes de informação. Rev Assoc Med Bras 2004;50(1):104-8
11. Gall F, Colella G, Di Onofrio V, Rossiello R, Angelillo IF, Liguori G. Candida spp. in oral cancer and oral precancerous lesions. New Microbiol 2013;36(3):283-8.
12. Zhao M, Zhou ZT. Antifungal susceptibility testing of commensal and pathogenic clinical isolates of oral Candida. Shanghai kou qiang yi xue. Shanghai J Stomatol 2006;15(2):218-20.
13. Hettmann A, Demcsák A, Decsi G, Bach Á, Pálinkó D, Rovó L. et al. Infectious agents associated with head and neck carcinomas. Adv Exp Med Biol 2016;897:63-80. doi: 10.1007/5584_2015_5005.
14. De Sanctis V, Bossi P, Sanguineti G, Trippa F, Ferrari D, Bacigalupo A. et al. Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements. Crit Rev Oncol Hematol 2016;100:147-66. doi: 10.1016/j.critrevonc.2016.01.010.
15. Nagy KN, Sonkodi I, Szöke I, Nagy E, Newman HN. The microflora associated with human oral carcinomas. Oral Oncol 1998;34(4):304-8.
16. Reichart PA, Schmidtberg W, Samaranayake LP, Scheifele C. Betel quid□associated oral lesions and oral Candida species in a female Cambodian cohort. J Oral Pathol Med 2002;31(8):468-72.
17. De Sousa LVNF, Santos VL, Souza Monteiro A, Dias-Souza MV, Marques SG, Faria ES, et al. Isolation and identification of Candida species in patients with orogastric cancer: susceptibility to antifungal drugs, attributes of virulence in vitro and immune response phenotype. BMC Infect Dis 2016;16:86. doi: 10.1186/s12879-016-1431-4
18. Almståhl A, Wikström M, Fagerberg□Mohlin B. Microflora in oral ecosystems in subjects with radiation□induced hyposalivation. Oral Dis 2008;14(6):541-9.
19. Jham BC, Françca EC, Reis RR, Santos VR, Kowalski LP, Freire ARS. Candida oral colonization and infection in Brazilian patients undergoing radiotherapy in the head and neck: a pilot study. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 2007;103(3):355-8. doi: 10.1016/j.tripleo.2006.02.005