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.

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

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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/year1.

As a consequence of the radiotherapy treatment, the patients may present alteration of the buccal microbiota, favoring opportunistic infections onset, especially candidiasis2. It is associated with immunosuppressive status, decreased salivary flow induced by oncological treatment, mucositis, neutropenia, microbial imbalance and use of prosthesis2.

Candida spp. can spread to other organs through the bloodstream compromising the patient’s general condition and his or her prompt recovery4,5. 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 understood6-9.

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 capabilities10.
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, the other one is writing in Chinese and the last one is a book chapter with a different thematic from that proposed in this study. Thus, only eight articles were found in this search, showing the scarcity of studies in this research field.

Table 1 - Articles analyzed

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

Source: Research Data.

Of the remaining eight articles, one is a review 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 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 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. Gallé and collaborators 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 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.

In the study carried out by Almstahl and collaborators, *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' 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 radiotherapeutic treatment was associated with positivity 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 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