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Is there a relationship between periodontal disease and oral cancer? A systematic review of currently available evidence

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ABSTRACT

Oral cancer (OC) is known to have a multi-factorial etiology; tobacco, alcohol and betel quid being the major risk factors. Tooth loss and periodontal disease (PD) have been implicated to increase the risk of developing various cancers. The aim of this systematic review was to assess any possible association between PD and OC. Indexed databases were searched using different combinations of the following key words: "oral cancer", "periodontal disease", "tooth loss", "squamous cell carcinoma", "missing teeth" "alveolar bone loss", "clinical attachment loss" and "periodontitis". PRISMA criteria were followed to accrue data and databases were searched from 1984 up to and including June 2015. In total, 12 case–control studies were selected from the published literature.

Results: Nine studies reported a 2–5 fold increase in the risk of OC among patients with PD as compared to those without PD. Three studies reported no association between PD and OC. In one study, an increased risk of tongue cancer was associated with each millimeter of alveolar bone loss and in two studies clinical attachment loss of more than 1.5 mm was associated with an increased risk of OC. In studies reporting significant findings these associations persisted after adjusting for major risk factors. PD is associated with a small but significant increase in risk for OC. In several reported studies this association was attenuated following adjustment for tobacco and alcohol use.

1. Introduction

Periodontal disease (PD) is an inflammatory disease that affects the supporting structures of teeth including the gingiva, periodontal ligament and alveolar bone (Ozden et al., 2015). PD is characterized by inflammation of the supporting structures of teeth

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(cementum, gingivae, periodontal ligaments and alveolar bone) (Pihlstrom et al., 2005). If left untreated, PD may cause annihilation of these supporting structures and ultimately tooth loss. In the year 2010, the global age-standardized prevalence of severe periodontitis was estimated at 10.5–12.0% (Kassebaum et al., 2014). The most common risk factors associated with PD and tooth loss include poor oral hygiene maintenance (Javed et al., 2007), ageing (Fah and Schatzle, 2014; Schatzle et al., 2010) systemic disorders such as prediabetes and poorly-controlled diabetes mellitus (Javed et al., 2007; Taylor et al., 2013; Chapple and Genco, 2013), lifestyles such as smoking (Fah and Schatzle, 2014; Bergstrom, 2004) and chewing smokeless tobacco (Javed et al., 2013). Moreover, an underprivileged socioeconomic status (Jin et al., 2011) may influence the risk most likely through the confounding effects of poor oral hygiene or tobacco use. It is noteworthy that some of the risk factors of PD, particularly tobacco and betel quid use, have also been linked with the etiology of oral cancer (OC) (Warnakulasuriya, 2009a; Johnson et al., 2011).

Cancer is among the leading causes of global mortality and oral and pharyngeal cancers are its most common forms (Warnakulasuriya, 2009b). The annual global incidence of OC has been reported to be approximately 500,000 and over 60% of these cases occur in Asian and Pacific countries including India, Pakistan, Sri Lanka, Taiwan and Papua New Guinea (Siegel et al., 2013). About a quarter of the patients undergoing cancer treatment in any of the aforementioned high-risk countries are diagnosed with OC (Warnakulasuriya, 2009b). Several narrative reviews have reported an association between tooth loss, PD and cancer (Seymour, 2010; Meyer et al., 2008; Fitzpatrick and Katz, 2010). It has been suggested that patients with PD are at a greater risk of having various forms of cancer (including pancreatic, skin, colon, breast, kidney, hematological cancers) as compared to those without PD (Michaud et al., 2008). It is probable that dental biofilms (Seneviratne et al., 2011) and the resulting dysbiosis can lead to a variety of oral diseases, including cancer (Ahn et al., 2012).

The aim of the present study was to assess any possible association between PD and OC through a systematic review of published literature and to discuss the role of chronic inflammation of the periodontium as a link in the causation of cancer.

2. Materials and methods

2.1. Literature search and eligibility criteria

We conducted a literature search using PubMed (National Library of Medicine, Washington, DC), Google-Scholar, EMBASE, MEDLINE (OVID) and Web of Knowledge databases addressing the focused question—"Is there a relationship between PD and OC?" Databases were searched from 1984 up to and including June 2015 using different combinations of the following key words: "oral cancer", "periodontal disease", "tooth loss", "squamous cell carcinoma", "missing teeth" "alveolar bone loss", "clinical attachment loss" and "periodontitis".

The following eligibility criteria were pre-selected: (a) clinical human studies; (b) prospective and retrospective studies; (c) inclusion of a control group; and (d) articles published only in English language. Letters to the Editor, case-reports, historic reviews and experimental studies were excluded (Table 3).

Full-texts of studies obtained using the eligibility criteria were screened by the authors (FJ and SW) and checked for agreement. In the next phase, searching of the reference lists of potentially relevant original and review studies was performed and any disagreement among the authors regarding study selection was resolved via discussion.

Search strategy is available from the corresponding author on request. The flow diagram of article selection is shown in Fig. 1.

3. Results

All studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001; Zheng et al., 1990; Talamini et al., 2000; Divaris et al., 2010; Ansai et al., 2013) were performed on humans and under healthcare or university settings. All studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001; Zheng et al., 1990; Talamini et al., 2000; Divaris et al., 2010; Ansai et al., 2013) had a case–control study design. In 5 studies (Rosenquist et al., 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001), interviews or questionnaire-based surveys were performed; and in 2 studies (Rosenquist, 2005; Garrote et al., 2001), participants were interviewed and also underwent a clinical oral examination. In studies by Guha et al. (2007) and Tezal et al. (2007) medical and dental records of the participants were evaluated, respectively. Methodology of 3 studies (Tezal et al., 2005; Zheng et al., 1990; Ansai et al., 2013) was based on clinical dental/oral examinations (Table 1).

These primary studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001; Zheng et al., 1990; Talamini et al., 2000; Divaris et al., 2010; Ansai et al., 2013) were conducted in the following countries: Argentina, Australia, Brazil, China, Cuba, Denmark, India, Japan, Poland, Romania, Russia, Sudan, Sweden and United States of America. The number of study participants ranged between 200 and 13,798 individuals with age ranging between 18 years and 91 years. In all studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001; Zheng et al., 1990; Talamini et al., 2000; Divaris et al., 2010; Ansai et al., 2013), most of the participants were males. In 9 studies (Rosenquist, 2005; Rosenquist et al., 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001; Zheng et al., 1990; Talamini et al., 2000; Divaris et al., 2010), data was adjusted for age, gender and alcohol/tobacco consumption (Table 1).

3.1. Outcomes of studies included

3.1.1. Periodontal disease

In all primary studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001; Zheng et al., 1990; Talamini et al., 2000; Divaris et al., 2010; Ansai et al., 2013), the assessment of PD was made by determining the numbers of missing teeth (MT). Guha et al. (2007) assessed oral hygiene status by use of standard criteria designed to elicit the presence of tartar, gingival bleeding, mucosal irritation and decayed teeth. In the study by Garrote et al. (2001), indicators of oral hygiene were self-reported by means of specific questions.

Out of the 12 studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Guha et al., 2007; Garrote et al., 2001; Zheng et al., 1990; Talamini et al., 2000; Divaris et al., 2010; Ansai et al., 2013) that fulfilled our eligibility criteria, 9 studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Garrote et al., 2001; Zheng et al., 1990; Ansai et al., 2013) reported a positive association between PD and OC. These studies (Rosenquist, 2005; Rosenquist et al., 2005; Tezal et al., 2007, 2005; Bundgaard et al., 1995; Marshall et al., 1992; Garrote et al.,