Review

Association between environmental tobacco smoke and periodontal disease: A systematic review

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A B S T R A C T

The aim of the present study was to systematically review the association between environmental tobacco smoke (ETS) and periodontal disease. The addressed focused question was “Is there a relationship between ETS and periodontal disease?”

PubMed/MEDLINE and Google-Scholar databases were searched from 1987 up to March 2014 using different combinations of the following keywords: “Environmental tobacco smoke”, “passive”, “periodontal disease”, “secondhand” and “smoking”. Letters to the Editor, review articles, commentaries, case-reports and articles published in languages other than English were excluded.

Thirteen studies were included. Nine studies were clinical and 4 studies were performed in-vitro. Five studies reported the odds ratios for periodontal disease to be significantly higher among individuals exposed to ETS than controls (non-smoking individuals unexposed to ETS). In 2 studies, ETS exposure showed no association with periodontal disease. In 2 studies, salivary aspartate aminotransferase, lactoferrin and albumin levels were reported to be significantly higher in individuals exposed to ETS than controls. In one study, levels of salivary interleukin-1β were reported to be significantly higher in individuals exposed to ETS than controls. The in-vitro studies reported ETS exposure to enhance the production of proinflammatory proteins and phagocytic activity of salivary polymorphonuclear leukocytes thereby contributing to periodontal disease. The association between ETS and periodontal disease remains debatable and requires further investigations.

1. Introduction

It is well-known that periodontal inflammatory conditions are worse in tobacco-smokers compared to individuals not using tobacco in any form (Javed et al., 2007, 2013; Rheu et al., 2011). However, non-smoking individuals who are exposed to environmental tobacco smoke (ETS: synonymous with passive or secondhand smoking) are also prone to oral and systemic diseases (Nishida et al., 2008; Sanders et al., 2011; Chen et al., 2013).

Erdemir et al. (2010) assessed the clinical periodontal health status and cotinine levels in the gingival crevicular fluid (GCF) of 51 children exposed to ETS and compared them to 58 unexposed children. In this study, the children were aged between 6 and 12 years. The results showed significantly raised GCF cotinine levels and reduced clinical attachment levels (CAL) in children exposed to tobacco smoke compared to unexposed children (Erdemir et al., 2010). Similar results were reported by Yamamoto et al. (2005). Likewise, in a 2-year longitudinal study, association between ETS exposure and periodontal disease progression with emphasis on salivary inflammatory and microbiologic markers was investigated (Nishida et al., 2008). In this study (Nishida et al., 2008), multiple logistic regression results showed significantly higher periodontitis odds ratios (OR) among individuals exposed to ETS compared to unexposed non-smokers following adjustment for covariates. The results also showed increased salivary albumin, aspartate aminotransferase (AST) and lactoferrin levels compared to non-smokers unexposed to ETS (controls) (Nishida et al., 2008). Furthermore, exposure to ETS suppress the function of gingival fibroblasts and B-cells, impair epithelial cell growth and increase the production of interleukin (IL)-4, IL-5, IL-10 and IL-13 resulting in a chronic inflammatory reaction in the body tissues (Holt, 1987; Zhang and Petro, 1996; Frazer-Abel et al., 2004; Kum-Nji et al., 2006; Semlali et al., 2011a, 2011b). However, Tanaka et al. (2013) reported no association between ETS exposure and periodontal disease among young Japanese females. An analytic cross-sectional study assessed...
the relationship between periodontitis and exhaled carbon monoxide (CO) among 296 Thai active and passive smokers (Chatrchaiwiwatana and Ratanasiri, 2011). The results demonstrated no relationship between ETS exposure and periodontal disease (Chatrchaiwiwatana and Ratanasiri, 2011). It is hypothesized that passive smokers are more susceptible to periodontal disease as compared to non-smokers who are unexposed to tobacco smoke.

The aim of the present study was to systematically review the association between ETS and periodontal disease.

2. Materials and methods

2.1. Focused question

The addressed focused question was “Is there a relationship between ETS and periodontal disease?”

2.2. Inclusion and exclusion criteria

The following eligibility criteria were entailed: (a) Clinical studies; (b) laboratory-based investigations; (c) intervention: clinical periodontal parameters and biomarkers in saliva and GCF of individuals exposed to ETS and controls (non-smokers unexposed to ETS); (d) studies published only in English language. Letters to the Editor, historic reviews, commentaries and case-reports were excluded.

2.3. Search protocol

PubMed/Medline (National Library of Medicine, Washington, DC) and Google-Scholar databases were searched from 1987 up to and including March 2014 using different combinations of the following key words: “Environmental tobacco smoke”, “passive”, “periodontal disease”, “secondhand” and “smoking”. Titles and abstracts of studies identified using the above-described protocol were screened by the authors and checked for agreement. Full-texts of studies judged by title and abstract to be relevant were read and independently evaluated by the authors (FJ, HBA and GER) with reference to the inclusion and exclusion criteria. Reference lists of articles retrieved from the initial search were hand-searched to identify any studies that could have remained unidentified in the previous step. Any disagreement between the authors regarding study selection was resolved via discussion (Fig. 1).

Thirty-eight studies were initially identified. Twenty-five studies which did not fulfill the eligibility were excluded (see Appendix A). In total, 13 studies were included and processed for data extraction (Numabe et al., 1998; Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011; Semlali et al., 2011a, 2011b, 2012; Tanaka et al., 2013). The pattern of the present systematic review was customized to mainly summarize the relevant data.

3. Results

3.1. Characteristics of clinical studies

Nine studies (Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011; Tanaka et al., 2013) were clinical and 4 studies (Numabe et al., 1998; Semlali et al., 2011a, 2011b, 2012) had an in-vitro design. All clinical studies (Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011; Tanaka et al., 2013) were cross-sectional and the numbers of participants included ranged between 45 and 6611 individuals. Eight studies (Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011; Tanaka et al., 2013) reported the mean age of study individuals, which ranged between 9.9 and 62.4 years. Eight studies (Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011; Tanaka et al., 2013) reported the numbers of individuals exposed to ETS included, which ranged between 10 and 923 individuals. In 6 studies (Yamamoto et al., 2005; Nishida et al., 2006, 2008; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Tanaka et al., 2013) 10–343 active-smokers were included in the study populations. Two studies (Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011) reported the daily cigarette consumption by active-smokers, which was at least one cigarette per day. Duration of cigarette smoking habit among active-smokers was not reported in any study. Three clinical studies reported the duration and/or frequency of ETS exposure (Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011) reported the daily cigarette consumption by active-smokers, which was at least one cigarette per day. Duration of cigarette smoking habit among active-smokers was not reported in any study. Three clinical studies reported the duration and/or frequency of ETS exposure (Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011). These results are summarized in Table 1.

3.2. Characteristics of laboratory-based investigations

Three in-vitro studies (Semlali et al., 2011a, 2011b, 2012) were performed on periodontal tissues and in one in-vitro study (Numabe et al., 1998) effect of ETS exposure on salivary polymorphonuclear leukocytes was assessed (Table 1).
3.3. Outcomes of clinical studies

Five studies (Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2008; Erdemir et al., 2010; Sanders et al., 2011) reported the OR for periodontal disease to be significantly higher among individuals exposed to ETS than controls. In these studies (Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2008; Erdemir et al., 2010; Sanders et al., 2011), periodontal CAL were significantly compromised in individuals exposed to ETS than controls. Chatrchaiwiwatana and Ratanasiri (2011) and Tanaka et al. (2013) reported no significant association between ETS exposure and periodontal disease. In two studies (Nishida et al., 2006, 2008), salivary AST, lactoferrin and albumin levels were reported to be significantly higher in individuals exposed to ETS than controls. In one study, levels of salivary interleukin-1β were reported to be significantly higher in individuals exposed to ETS than controls. Numabe et al. (1998) reported that the phagocytic activity of salivary PMNL increases after ETS exposure (Table 2).

3.4. Outcomes of laboratory-based investigations

In-vitro results by Semlali et al. (2011a,b, 2012) showed that ETS exposure inhibits the growth of gingival epithelial cells, impairs the morphology and function of gingival fibroblasts and increases the expression of proinflammatory proteins in gingival tissues (Table 3).

4. Discussion

From the literature reviewed, it is tempting to speculate that periodontal disease is worse in individuals exposed to ETS compared to non-smokers unexposed to ETS (controls). However, upon a vigilant review of the studies included in the present systematic review (Numabe et al., 1998; Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011; Semlali et al., 2011a, 2011b, 2012; Tanaka et al., 2013), it was observed that nearly 78% of the clinical studies (Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011) did not report the daily oral hygiene maintenance protocols in their respective study populations. In studies by Tanaka et al. (2013) and Sanders et al. (2011), scores of daily oral hygiene maintenance regimes among the study groups were comparable. The likelihood that a poor oral hygiene status may have contributed in jeopardizing the periodontal status of individuals exposed to ETS cannot be disregarded. Therefore, it is arduous to solely arraign ETS as a critical factor associated with compromised periodontal health. We support the results by Tanaka et al. (2013) which reported higher OR for periodontal disease in active-smokers (but not in individuals exposed to ETS) than controls. An explanation for this is that expression of receptors of advanced glycation end products is higher in gingival tissues of smokers (Katz et al., 2005), which induces a proinflammatory effect by stimulating the secretion of cytokines and reactive oxygen species (ROS). This in turn causes destruction of the periodontal apparatus (Katz et al., 2005, 2007). Results by Tanaka et al. (2013) are in accordance with previous clinical studies (Javed et al., 2007, 2012, 2013).

It is known that severity of periodontal disease is directly associated with duration and intensity/frequency of smoking (Salem et al., 2008). This is an essential parameter that remained poorly addressed in the studies (Numabe et al., 1998; Arbes et al., 2001; Yamamoto et al., 2005; Nishida et al., 2006, 2008; Erdemir et al., 2010; Azar and Richard, 2011; Chatrchaiwiwatana and Ratanasiri, 2011; Sanders et al., 2011; Semlali et al., 2011a, 2011b, 2012; Tanaka et al., 2013) included in the present review. For example, in the study by Sanders et al. (2011) participants reported to have been exposed to ETS 4.5 h and 48 h per week; however, the duration (in years or months) of ETS exposure remained unclear (Sanders et al., 2011). Similarly, in studies by Chatrchaiwiwatana and Ratanasiri (2011) and Azar and Richard (2011) individuals in the test-group were exposed to ETS 5 times a day; however, the duration of each exposure and the total time...
duration since which these individuals had been exposed to ETS was not reported. Moreover, in the in-vitro studies (Semlali et al., 2011a, 2011b, 2012), periodontal tissues were exposed to smoke only once following which they expressed raised proinflammatory cytokines compared to tissues unexposed to smoke. On the basis of these studies, it is hypothesized that long-term exposure to ETS several times daily compromises periodontal health to a greater extent as compared to short-term and infrequent exposures to ETS. Further long-term longitudinal clinical trials are warranted to test this hypothesis.

In studies by Nishida et al. (2006), (2008), significantly higher levels of albumin (an antioxidant) and AST, a marker of cell destruction, were observed in individuals exposed to ETS than controls. It is possible that raised salivary albumin were expressed to thwart the detrimental action of free radical and ROS derived from ETS or inflammatory cells in order to protect oral tissues including those of the periodontium. Moreover, AST has been correlated with periodontal inflammatory conditions, such as periodontal pockets and gingival bleeding (Cesco Rde et al., 2003). These findings may partially have been associated with

<table>
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<tr>
<th>Authors et al.</th>
<th>Clinical periodontal outcomes</th>
<th>Laboratory-based outcomes</th>
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<tbody>
<tr>
<td>Sanders et al. (2011)</td>
<td>OR for CAL ≥ 3 mm were significantly higher for individuals exposed to ETS for 26 h/week than those exposed to ETS for &lt; 26 h/week</td>
<td>-</td>
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<tr>
<td>Nishida et al. (2008)</td>
<td>OR for periodontal disease progression were higher in active-smokers and ETS-exposed individuals than controls</td>
<td>-</td>
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<tr>
<td>Erdemir et al. (2010)</td>
<td>Mean CAL was significantly less in ETS-exposed children than controls</td>
<td>-</td>
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<tr>
<td>Arbes et al. (2001)</td>
<td>OR for periodontal disease were 1.6 higher for individuals exposed to ETS than controls</td>
<td>-</td>
</tr>
<tr>
<td>Yamamoto et al. (2005)</td>
<td>CAL ≥ 3.5 mm was significantly higher in active-smokers and ETS-exposed individuals than controls</td>
<td>-</td>
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<tr>
<td>Tanaka et al. (2013)</td>
<td>No significant association between ETS exposure and periodontal disease</td>
<td>-</td>
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<tr>
<td>Chatrchaiwiwatana and Ratanasiri (2011)</td>
<td>No significant association between ETS exposure and periodontal disease</td>
<td>-</td>
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<tr>
<td>Azar and Richard (2011)</td>
<td>-</td>
<td>Significantly higher in active- and ETS-exposed individuals than controls with no difference active-smokers and ETS exposed individuals</td>
</tr>
<tr>
<td>Nishida et al. (2006)</td>
<td>-</td>
<td>Significantly higher in ETS-exposed individuals than controls</td>
</tr>
<tr>
<td>Numabe et al. (1998)</td>
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AST: aspartate aminotransferase, CAL clinical attachment level, Controls: non-smoking individuals unexposed to ETS, ETS: environmental tobacco smoke, IL: interleukin, NA: not available, OR: odds ratios.

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<th>Authors et al.</th>
<th>Effect of environmental tobacco smoke on periodontal tissues</th>
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<tr>
<td>Semlali et al. (2011a)</td>
<td>Inhibition of gingival epithelial cell growth by apoptosis</td>
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<tr>
<td>Semlali et al. (2011b)</td>
<td>Reduction in growth and adhesion in gingival fibroblasts</td>
</tr>
<tr>
<td>Semlali et al. (2012)</td>
<td>Increased expression of human β-defensins and IL-1β, and IL-6 expression</td>
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IL: interleukin.
the raised levels of IL-1β in individuals exposed to ETS than controls as observed in studies by Nishida et al. (2006), (2008). The increased phagocytic function of salivary PMNL as reported by Numabe et al. (1998) may be associated with periodontal destruction by releasing excessive enzymes around periodontal tissue (Weiss, 1989; Miyasaki, 1991). However, further studies are required to assess the role of salivary PMNL in jeopardizing periodontal tissues in passive-smokers.

A limitation of the present study is that articles primarily addressing the association between ETS exposure and periodontal disease were sought; however, it is known that detrimental effects of ETS exposure are not merely restricted to the oral cavity. ETS exposure has also been associated with systemic disorders such as asthma, lung cancer and cardiovascular disorders (Kim et al., 2014; Silvestri et al., 2014; Hagstad et al., 2013).

Regardless of whether or not additional studies affirm an association between ETS exposure and periodontal disease, results from the present systematic review emphasize that it is imperative for healthcare providers to educate their patients about the hazards of smoking and ETS on health.

5. Conclusion

The association between ETS and periodontal disease remains debatable and requires further investigations.

Conflict of interest and financial disclosure

The authors report no conflict of interest related to the present authors. There was no external source of funding for the present study.

Acknowledgment

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Appendix A. List of excluded studies. Reason for exclusion is shown in parenthesis

(b) Sadaoka, S., Yagami, K., Maki, S., 2013. Nicotine in cigarettes promotes chromogranin A production by human periodontal ligament fibroblasts. Arch. Oral. Biol. 58, 1029-1033. (Focused question was not answered)
(f) Brook, L., 2011. The impact of smoking on oral and nasopharyngeal bacterial flora. J. Dent. Res. 90, 704-710. (Focused question was not answered)
(g) Baskaradoss, J.K., Geeverghese, A., Kutty, V.R., 2011. Maternal periodontal status and preterm delivery: a hospital based case-control study. J. Periodontal. Res. 46, 542-549. (Focused question was not answered)
(s) Wimmer, G., Köhldorfer, G., Mischak, I., Lorenzoni, M., Kallus, K., W., 2005. Coping with stress: its influence on periodontal therapy. J. Periodontol. 76, 90-98. (Focused question was not answered)
(t) Billings, R.J., Berkowitz, R.J., Watson, G., 2004. Teeth. Pedia- trics. 113 (4 Suppl.), 1120-1127. (Review article; Focused question was not answered)

References