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Meta-analysis on the association between toothbrushing and head and neck cancer

Xian-Tao Zeng [a,b,c,*,1], Wei-Dong Leng [b,1], Chao Zhang [c], Jing Liu [d], Shi-Yi Cao [e], Wei Huang [b]

[a] Center for Evidence-Based and Translational Medicine, Zhongnan Hospital, Wuhan University, Wuhan, China
[b] Department of Stomatology, Taihe Hospital, Hubei University of Medicine, Shiyan, China
[c] Center for Evidence-Based Medicine and Clinical Research, Taihe Hospital, Hubei University of Medicine, Shiyan, China
[d] Department of Otolaryngology, The 161 Hospital of PLA, Wuhan 430012, China
[e] School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

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SUMMARY

Background: Epidemiological studies have focused on the association between toothbrushing and head and neck cancer (HNC). However, the question of whether toothbrushing is associated with decreased risk of HNC remains unanswered. Since there is currently no systematic review or meta-analysis available to provide quantitative findings on this important clinical question; we consequently performed this meta-analysis to investigate the association between toothbrushing and HNC risk.
Methods: We searched PubMed and Embase up to January 13 (updated on October 20), 2014 to identify observational studies that investigated the association between toothbrushing and HNC. After study section and data extraction, the meta-analysis was conducted using RevMan 5.2 software.
Results: A total of 18 case-control studies involving 7068 cases and 9990 controls were included. The meta-analysis showed that compared with highest toothbrushing frequency, lowest level was significantly increased risk of HNC 2.08 times (odds ratio = 2.08, 95% confidence interval = 1.65–2.62). This significant association remained consistent after adjusting for smoking status and alcohol consumption. No publication bias was detected.
Conclusions: This meta-analysis found frequency of toothbrushing was significantly associated with HNC risk. Effective toothbrushing may be potentially important for the prevention of HNC and we suggest that the frequency be twice per day (morning and night).

Background

Head and neck cancer (HNC) consists of cancer developing from the mouth, throat, sinuses, nasal cavity, larynx, base of the skull, and head and it is the sixth most prevalent cancers worldwide [1] and represents a therapeutically-challenging, behaviorally-heterogenous category of disease. Identification of any possible risk factors of HNC is thus an important task. Tobacco and alcohol consumption have been well established as the predominant etiologic factors for HNC [2]. Other risk factors including genetic factors [3,4], human papillomavirus (HPV) infections [5], periodontal disease [6], tooth loss [7], poor oral hygiene [8], and poor dental status [9] have also been identified in the development of HNC.

Dental plaque is implicated in the etiology of dental caries, gingivitis, periodontal disease, tooth loss, and poor oral hygiene. Therefore, removal of dental plaque is thought to play a key role in the prevention of these diseases and consequently in the improve of oral hygiene [10–13]. Available evidence showed that toothbrushing is an effective method for removing dental plaque and preventing dental diseases and effective toothbrushing might reduce the risk of HNC [14–17]. In 1986, Young et al. [18] performed the first case-control study to investigate the association between toothbrushing and oral, oropharyngeal, and hypopharyngeal cancer risk. This statewide network study involving 317 cancer cases and 306 controls indicated that toothbrushing frequency was not associated with HNC. Despites this somewhat

Abbreviations: CI, confidence interval; CRD, Centre for Reviews and Dissemination; HNC, head and neck cancer; HPV, human papillomavirus; OR, odds ratio; OSCC, oral squamous cell carcinoma; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, international prospective register of systematic reviews; RR, relative risk; SE, standard error.

* Corresponding author at: Center for Evidence-Based and Translational Medicine, Zhongnan Hospital, Wuhan University, 169 Donghu Road, Wuchang District, Wuhan 430071, Hubei Province, China. Tel./fax: +86 027 67812817.
E-mail address: zengxiantao1128@163.com (X.-T. Zeng).
[1] Xian-Tao Zeng and Wei-Dong Leng are co-first authors.

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negative finding, interest in the relationship between toothbrushing and HNC risk reduction has been increasing since then. However, these studies have a modest sample size and evidence was found to be inconclusive. Meta-analysis is a statistical tool that integrates the results of several independent studies considered to be "combinable" and provides a more precise estimation [19,20]. To our knowledge, toothbrushing and HNC risk has not yet been evaluated using a meta-analytic methods and therefore, we conducted this meta-analysis to evaluate their association.

Methods

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [21]. Ethical approval was not required for this study.

Protocol and registration

This meta-analysis is registered in PROSPERO (registration number is CRD42014007247), an international database of prospectively registered systematic reviews in social and health care) [22]. The review protocol is available on the Centre for Reviews and Dissemination website (http://www.crd.york.ac.uk/prospero/display_record.asp?ID=CRD42014007247).

Eligibility criteria

Cohort studies, case-control studies, and cross-sectional studies evaluating the risk of HNC in relation to toothbrushing were considered eligible for inclusion if the following criteria were met at the same time: (1) the exposure of interest was toothbrushing, the endpoint of interest was incidence of HNC; (2) adjusted and/or unadjusted odds ratios (ORs) or relative risks (RRs) and associated 95% confidence intervals (CIs), or the numbers of events that could calculate these were reported; (3) diagnosis of HNC was confirmed using microscopic examination; and (4) full-text articles were available. If more than one study covered the same population, only the report containing the most comprehensive information on that population was included.

Literature search

A comprehensive literature search of MEDLINE (via PubMed) and Embase was conducted up to January 13 (updated on October 20), 2014 using the search strategies as illustrated in Tables S1 and S2. We also screened the reference lists of included studies and recent review articles for potential additional studies.

Data extraction

Two authors independently extracted and tabulated the following study characteristics: first author's surname, publication year, country of origin, sample size, age range, tumor site and pathologic type of HNC, crude or adjusted ORs/RRs and 95% CIs, and the covariates features including the in the multivariable model. Discrepancies were resolved by discussion with a third author.

Statistical analysis

We used the ORs with 95% CIs as the common effect estimate across studies. We used the highest vs. lowest levels to assess the association of toothbrushing and HNC risk [23]. If the toothbrushing frequency was divided into 3 or more categories, we conducted dose-response estimates. In any included study, when ORs were reported separately for subgroups by the different cancer sites or age, we combined the results of the subgroups and calculated a common OR for the main analysis using a fixed-effects model if necessary [24]. If the study reported RR, we transformed it into OR with the method by Zhang et al. [25]. The various estimates of ORs and its 95% CIs were transformed into log ORs and the corresponding standard errors (SEs) and switched them into the same direction using the methods proposed by Greenland [26] and Cochrane Handbook for Systematic Reviews of Interventions [27].

Heterogeneity was tested using I^2 statistic and Cochran Q test [27]. The value of I^2 was no more than 50% and $p > 0.10$ indicated that heterogeneity was negligible and the fixed effect model was used; otherwise, we used random effect model. Forest plots and funnel plots were used to examine the overall effect and assess the publication bias, respectively. We also conducted subgroup analysis stratified by adjusted and unadjusted variables, where both smoking status and alcohol consumption were adjusted in models.

All analyses were performed using Review Manager (Version 5.2, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2013) [6], and all tests were two sided with a significance level of $p < 0.05$.

Results

Study selection

Our systematic literature search yielded 182 publications. After the exclusion of clearly irrelevant records, full-text articles of 18 titles/abstracts were retrieved for further assessment [18,28–44]. Of theses, two articles were excluded because they did not report relevant data of interest [18,31], one [41] was excluded due to the population was covered in the latter study [44]. Two studies [30,36] separated reported men and women, one [43] contained the Central Europe population and Latin America population and separated to report the results, hence we treated them as 6 independently case-control studies. We eventually included 15 publications of 18 case-control studies in this meta-analysis [28–30,32–40,42–44]. Our study selection process is illustrated in Fig. 1.

Study characteristics

Table 1 shows the baseline characteristics of the 15 included publications (18 case-control studies) involving 7068 cases and

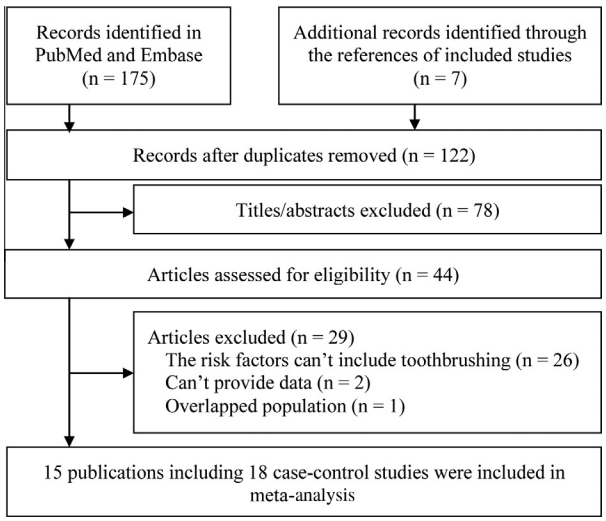

Fig. 1. Flowchart of study selection.