Conflict of interest

There are no conflicts of interest to be disclosed.

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Association between tooth loss and dementia among older people: a meta-analysis

Introduction

Dementia is one of the most disabling health conditions worldwide, and it reduces the life quality of patients and increases their family caregivers' burden. Nearly 24 million people are afflicted with dementia today, and a Delphi consensus study predicted that the number of people suffering from dementia will be set to 81 million throughout the world by the year 2040 (Ferri *et al.*, 2005; World Health Organization, 2012). Epidemiological research has identified potentially modifiable vascular and life-style risk factors for dementia. Meanwhile, the association between loss of teeth and the risk of dementia was evaluated in as early as 20 years ago. Research suggested that tooth loss can cause the brain chronic to exposure to pathogenic oral bacteria; it may exacerbate/initiate inflammatory process in the central nervous system, such changes would activate glial cells and stimulate the secretion of inflammatory sub-products, leading to neurodegeneration, loss of cognitive function and dementia (Gatz *et al.*, 2006; Stein *et al.*, 2007). Based on the aforementioned associations, many epidemiology studies have explored the association between tooth loss and the risk of dementia. However, the associations are conflicting in observational studies. Accordingly, we performed a meta-analysis to derive an estimation of the relationship between tooth loss and dementia risk among old people.

Method

A literature search for available articles published in English or Chinese up to June 2015 was conducted from these databases: (1) PubMed; (2) Web of science;

Table 1 Characteristics of studies included in the meta-analysis of tooth loss and dementia

Author (year) Journal/ Volume/ Issue/Page	Country	Study design age	Sample size (case)	RR (95%CI) for highest vs. lowest category
Luo *et al.* (2015) PLoS One/ 10/ 3/ e0120986	China	cross-sectional ≥60	3063 (120)	1.56 (1.12–2.18)
Stewart *et al.* (2015) J Am Geriatr Soc/ 63/ 1/ 100–105	Sweden	cohort 70–92	580 (113)	1.62 (0.84–3.11)
Nilsson *et al.* (2014) Acta Odontol Scand/ 72/ 8/ 639–644	Sweden	cross-sectional 60–96	1041 (—)	1.90 (1.20–3.00)
Peres *et al.* (2014) Aging Ment Health/ 19/ 10/ 876–884	Brazil	cross-sectional ≥60	1705 (150)	3.30 (1.20–9.30)
Yamamoto *et al.* (2012) Psychosom Med/ 74/ 3/ 241–248	Japan	cohort ≥60	4425 (220)	1.41 (0.42–4.70)
Paganini-Hill *et al.* (2012) J Am Geriatr Soc/ 60/ 8/ 1556–1563	America	cohort 52–105	5468 (1145)	1.10 (0.89–1.36)
Arrive *et al.* (2011) Community Dent Oral Epidemiol/ 40/ 3/ 230–238	France	cohort 68–75	405 (72)	0.60 (0.17–2.08)
Stein *et al.* (2007) J Am Dent Assoc/ 138/ 10/ 1314–1322	America	cohort 75–98	101 (32)	2.20 (1.10–4.50)
Gatz *et al.* (2006) Alzheimers Dement/ 2/ 2/110–117	Sweden	case-control ≥60	3373 (310)	1.49 (1.14–1.95)
Shimazakil *et al.* (2001) J Dent Res/ 80/ 1/ 340–345	Japan	cohort 59–107	517 (156)	2.40 (0.90–6.50)
Kondo *et al.* (1994) Dementia/ 5/ 6/ 314–326	Japan	case-control 52–77	180 (60)	2.60 (1.30–4.90)

RR, relative risk; CI, confidence interval.

and (3) CNKI, using the following search terms: "tooth loss", "missing teeth", "oral health", "dementia", and "cognitive impairment". Studies were included if the highest versus lowest categories relative risk (RR; 95% confidence interval [CI]) of tooth loss number associated with dementia could be extracted. We extracted RRs adjusted with the most confounders. Pooled measure was calculated as the inverse variance weighted mean of the logarithm of RR with 95% CI to assess the strength of association between tooth loss and risk of dementia. The I^2 statistical measure was used to assess heterogeneity (Higgins *et al.*, 2003). All statistical analyses were performed with STATA version 12.0 (Stata Corporation, College Station, Texas, USA).

Results

A total of 11 published articles involving 20,858 participants were included in the present meta-analysis. The detailed characteristics of included studies are shown in Table 1. The overall result indicated that tooth loss was significantly associated with increased risk of dementia 1.43 (95%CI, 1.26–1.63; $I^2 = 44.0\%$; FEM; $P_{heterogeneity} = 0.057$). In the subgroup analysis by study design, the pooled RRs for cross-sectional studies, cohort studies, and case-control studies were 1.75 (95%CI, 1.35–2.26; $I^2 = 2.7\%$; FEM; $P_{heterogeneity} = 0.358$), 1.22 (95%CI, 1.01–1.46; $I^2 = 32.6\%$; FEM; $P_{heterogeneity} = 0.192$), and 1.61 (95%CI, 1.26–2.07; $I^2 = 57.0\%$; FEM; $P_{heterogeneity} = 0.127$), respectively. With regard to the subgroup of continent, the pooled RRs for America, Europe, and Asia were 1.21 (95%CI, 0.99–1.48; $I^2 = 72.3\%$; FEM; $P_{heterogeneity} = 0.027$), 1.54 (95%CI, 1.25–1.91; $I^2 = 2.1\%$; FEM; $P_{heterogeneity} = 0.382$) and 1.76 (95%CI, 1.33–2.32; $I^2 = 0.0\%$; FEM; $P_{heterogeneity} = 0.505$). To explore the sources of heterogeneity, univariate meta-regression analysis was performed with the covariates as follows: year; continent; study design; and status of adjusting for BMI, income, education, and measurement. However, the result showed no covariate had a significant impact on between-study heterogeneity ($p > 0.05$). For the "leave-one-out" sensitivity analysis, study of Paganini-Hill was found to contribute toward between-study heterogeneity. After further excluding this study, no heterogeneity ($I^2 = 0.0\%$) was found, and the pooled RR was 1.68 (95% CI, 1.42–1.97, $P_{heterogeneity} = 0.502$). Influence analysis revealed that no individual study had excessive influence on the pooled estimate. The visual inspection of the funnel plot and Egger's test showed no evidence of small-study effect for all included studies ($P_{heterogeneity} = 0.083$).

Discussion

Findings from this meta-analysis identified that tooth loss is a risk factor for dementia. Furthermore, we

conducted subgroup analysis by study design; the association remained significant in cohort studies, cross-section studies, and case-control studies.

Our meta-analysis has several strengths. First, a significant association was evaluated from our prospective cohort studies (RR = 1.22, 95% CI 1.01–1.46, n = 6), strongly identifying the effect of tooth loss on dementia risk. Second, the large number of participants included in this meta-analysis reduced the sampling error to a great extent and allowed a much greater possibility of reaching a reasonable conclusion.

Other limitations should be considered. The time of the occurrence of tooth loss and the length of the edentulous period cannot be determined exactly; this may lead to the bias of incomparability of results to some extent.

In conclusion, our meta-analysis indicates that tooth loss might be positively associated with the increased risk of dementia among older people.

Conflicts of interest

None declared.

Key points

- Meta-analysis of our study found that tooth loss might be positively associated with increased risk of dementia among older people.

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Acetaminophen for self-reported sleep problems in an elderly population (ASLEEP): a randomized double-blind placebo-controlled trial

Sleep disorders are highly prevalent in older age and may have serious health implications. Benzodiazepines are frequently used although they have serious side effects. In geriatric clinical practice, we have observed that older community dwelling patients often use acetaminophen as self-prescription for chronic sleep problems without having specific underlying pain complaints (Sproule *et al.* 1999). Possibly, acetaminophen relieves unrecognized pain complaints during the night, or lowers body temperature, which is related to better sleep (Lack *et al.* 2008). Also, its purported effect could be mainly placebo.

We performed a randomized, double-blind, placebo-controlled trial to investigate whether acetaminophen is effective in treating self-reported sleep problems among people aged ≥ 65 years (van de Glind *et al.* 2014). These could be any of the following: difficulties with falling asleep, maintaining sleep and early