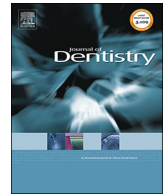




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Association between bruxism and symptomatic gastroesophageal reflux disease: A case-control study

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ABSTRACT

Objectives: To examine the relation between bruxism and gastroesophageal reflux disease (GERD) and the contribution of depression, anxiety and impaired sleep quality to that association.

Methods: A three-centre case-control study was conducted consisting of 887 consecutive clinically-diagnosed bruxism patients aged 18–75 years and 887 matched controls. Diagnosis of GERD was based on the Montreal definition: moderate/severe symptoms $\geq$ one day/week or mild symptoms $\geq$ two days/week. Logistic regression was used to evaluate the association between bruxism and GERD. Mediation analyses were used to test whether the association between bruxism and GERD was mediated by depression, anxiety or impaired sleep quality.

Results: Binary logistic regression identified that GERD was associated with bruxism (odds ratio, 6.87; 95% confidence interval (CI), 4.34–10.88). This association was stronger in females (odds ratio, 12.27; 95% CI, 5.81–25.91) than in males (odds ratio, 3.99; 95% CI, 2.17–7.32). Multinomial logistic regression identified that GERD was associated with all types of bruxism (sleep bruxism alone, odds ratio, 6.71, 95% CI, 4.22–10.68; awake bruxism alone, odds ratio, 13.06, 95% CI, 5.32–32.05; overlap of sleep bruxism and awake bruxism, odds ratio, 6.48, 95% CI, 3.05–13.77). Ordinal logistic regression identified that longer GERD duration (> 2 years vs ≤ 2 years) was associated with bruxism frequency (odds ratio, 1.50; 95% CI, 1.10–2.05). Mediation analyses found that the association between bruxism and GERD was partially-mediated through depression, anxiety and impaired sleep quality.

Conclusions: Clinically-diagnosed bruxism is associated with symptomatic GERD and is partially-mediated through depression, anxiety and impaired sleep quality.

Clinical Significance: Because bruxism is strongly associated with symptomatic GERD and patients with frequent bruxism symptoms tend to suffer from GERD for extensive time-periods, dentists should consider evaluation of GERD status as an elemental part of the medical examination of bruxism, especially severe bruxism.

1. Introduction

Bruxism is a movement disorder that is classified as sleep bruxism and awake bruxism. A positive association between sleep bruxism and gastroesophageal reflux disease (GERD) has been identified in two small observational studies, conducted in Brazil and Japan, respectively [1,2]. A recent randomised cross-over trial of 12 patients with sleep bruxism in Japan reported that proton pump inhibitors, the first line of

treatment for GERD, moderately reduced sleep bruxism episodes [3]. Experiments on healthy adults identify that oesophageal acidification increases sleep bruxism episodes, along with swallowing and arousals during sleep [4]. In addition, experimental oesophageal acidification during waking hours increases masseter muscle activities, especially involuntary muscle activity [5]. This finding indicates a possible association may also exist between awake bruxism and GERD.

There is ample epidemiological evidence supporting the connection

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between mental disorders and gastrointestinal diseases. Mental disorders that have been associated with GERD include depression and anxiety [6–8]. Bruxism patients are more likely to suffer from depression, anxiety and other mental disorders than healthy individuals [9]. Depression and anxiety are either potential mediators linking GERD and bruxism or underlying factors common to the pathophysiological processes. Impaired sleep quality is closely related to GERD [7,10,11] and bruxism [12]. To date, it is not known whether impaired sleep quality is an intermediate condition connecting GERD and bruxism. Previous epidemiological studies on the association between GERD and bruxism focused on sleep bruxism only and were limited by their small sample size. In addition, it is not known whether the severity of bruxism is associated with the duration of GERD.

Accordingly, the objectives of the present three-centre case-control study were to confirm the relationship between GERD and the different types of bruxism in a larger patient consort, to establish the association between the severity of bruxism and the duration of GERD, and to examine whether the association between bruxism and GERD was mediated by depression, anxiety or impaired sleep quality. The null hypotheses tested were: 1) there is no association between GERD and the different types of bruxism; 2) there is no association between the severity of bruxism and the duration of GERD; and 3) the association between bruxism and GERD is not mediated by depression, anxiety or impaired sleep quality.

2. Methods

The present study adhered to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines for case-control studies [13].

2.1. Study population

A case-control study was performed with consecutive adult patients diagnosed with bruxism from three sources in China from April 2017 to March 2018. The study was approved by the institutional review boards of all the respective institutions (Protocol ID: IRB-REV-2017028, xjqql-2017-No.031 and IRB1882017005). Informed consent was obtained from each participant.

Patients aged 18 to 75 years who visited the three hospitals and were diagnosed with bruxism based on defined diagnostic criteria were recruited. Bruxism was diagnosed by three trained and calibrated dentists (one from each centre). Diagnostic criteria for bruxism, sleep bruxism and/or awake bruxism were modified from the diagnostic criteria of sleep bruxism recommended by the American Academy of Sleep Medicine (AASM) [14]. Briefly, the diagnostic criteria included a self-report or partner-report of teeth clenching/grinding during sleep or waking hours in the past six months and one or more of the following symptoms: 1) abnormal tooth wear or wear on restorations; 2) discomfort of jaw muscle on awakening; and/or jaw locking on awakening; and/or temporal headaches. The details of clinical examination as well as duration and frequency of bruxism symptoms were recorded.

Control participants without history of bruxism symptoms were matched to each bruxism patient by age at entry to study ($\pm$ one year) and sex (ratio of controls to cases was 1:1). Control participants were recruited from adults seeking consultation for other oral diseases in the same enrolled sites during the study period.

Additional criteria for all participants were: aged between 18 and 75 years, not pregnant, not during lactation period, not living abroad, not having psychotropic drugs known to affect motor behaviour or sleep such as benzodiazepines, amphetamines, neuroleptics, L-dopa, tricyclic or selective serotonin reuptake inhibitor antidepressants, and not having the following serious medical conditions: cancer, renal dialysis, kidney failure, hyperthyroidism, diabetes, epilepsy, Parkinson's disease or schizophrenia. Participants who were devoid of bruxism symptoms in the past six months but with a history of bruxism symptoms earlier

were excluded.

2.2. Demographic characteristics, medical history and lifestyle factors

The three dentists also served as interviewers in the subsequent interview. Data on age, sex, marital status, place of residence, years of education, height, weight, personal and family medical history, smoking status and consumption of alcohol, tea and coffee were collected during the interview.

The smoking status of participants was evaluated using questions recommended by the World Health Organization [15]. The alcohol consumption profile of the participants in the past year was collected; participants were classified as non-drinkers, moderate drinkers (≤ 15 g/day for women and ≤ 25 g/day for men) and heavy drinkers (had unsafe drinking at least one day a week). "Unsafe drinking" was defined as > 15 g/day for women and > 25 g/day for men based on the recently-revised Chinese Dietary Guidelines [16]. The definition of unsafe drinking was explained to each participant: 0.450 L of beer, 0.15 L of wine, or 37.5 g (40% alcohol) distilled spirits for women; 0.75 L of beer, 0.25 L of wine, or 62.5 g (40% alcohol) distilled spirits for men. The intake frequency of one cup of tea or coffee was confirmed from the following categories (never or hardly ever, < 1 time/week, 1–2 times/week, 3–6 times/week, 1 time/day, 2–3 times/day, 4–5 times/day, and ≥ 6 times/day).

A body mass index (weight divided by the square of heights) of 30 kg/m^2 or greater was designated as obesity [17]. A clinical examination was performed to diagnose pain-related temporomandibular disorder (TMD) in accordance with the Diagnostic Criteria for Temporomandibular Disorders [18].

The following questionnaires were completed by all the participants under the guidance of the three interviewers.

2.3. Evaluation of sleep apnea and sleep quality

The STOP-Bang Questionnaire was used to screen participants for sleep apnea [19]. Participants were asked to complete four yes/no questions regarding snoring, apnea during sleep, tiredness during the daytime and hypertension. Neck circumference of each participant was measured by the interviewers. One point was scored for each of the following criteria: age older than 50 years, male gender, body mass index (weight divided by the square of heights) higher than 35 kg/m^2 , neck circumference wider than 40 cm, and yes to each of the four yes/no questions. A score ≥ 3 on the questionnaire was used to identify participants with high likelihood of obstructive sleep apnea [19]. Participants with a self-reported history of obstructive sleep apnea were also identified with high likelihood of obstructive sleep apnea, irrespective of their scores on the STOP-Bang Questionnaire. Sleep quality of the participants was evaluated using the Pittsburgh Sleep Quality Index questionnaire [20]. Impaired sleep quality was defined as a score ≥ 6 [20].

2.4. Evaluation of anxiety and depression

The 9-item Patient Health Questionnaire [21] and the 7-item Generalized Anxiety Disorder Scale [22] were completed by the participants (Supplementary Material). Each questionnaire was scored on the spot. Participants were diagnosed with depression if they scored ≥ 10 on the 9-item Patient Health Questionnaire [21]. Participants were diagnosed with anxiety if they scored ≥ 10 on the 7-item Generalized Anxiety Disorder Scale [22].

2.5. Evaluation of GERD

A validated questionnaire, GerdQ (Supplementary Material), was used for screening participants for GERD [23]. Participants reporting heartburn, regurgitation, epigastric pain, nausea, disturbed sleep

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