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Research Article

Evaluation of the relationship between migraine disorder and oral comorbidities: multicenter randomized clinical trial

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Background/aim: Although migraine is a common disorder, there is a lack of research investigating the possible relationship between migraine and oral health. The aim of the present study was to explore the relationship between temporomandibular disorders, bruxism, dental caries, periodontal status, and migraine disorder in a multicenter, parallel, case-controlled clinical study.

Materials and methods: A total of 2001 participants were divided into two groups: migraineurs (nm = 998) and nonmigraineurs (nh = 1003). International Headache Society's Second Edition of International Classification of Headache Disorders and modified Migraine Disability Assessment surveys were administered to evaluate the level of migraine; a pretreatment questionnaire and the World Health Organization oral health assessment form were used to determine the oral comorbidities and their possible effects on DMFT index, gingival plaque index, existence of temporomandibular disorders, bruxism, and consistency of daily oral hygiene habits.

Results: The mean age was 39.6 ± 10.5 years. Female patients seemed to experience migraine attacks more than male patients (64%). The frequency of gastroesophageal reflux was higher in migraineurs in comparison with nonmigraineurs (47%) and tooth wear and abrasion also seemed more frequent (76%). DMFT and plaque index scores showed significant differences for both groups.

Conclusion: There is a strong relationship between migraine and oral health status. The existence of reflux in addition to migraine leads to higher dental problems.

Key words: Migraine, oral health, gastroesophageal reflux disease, dental caries, gingival plaque index

1. Introduction

Migraine headache is one of the primary disabling clinical neurological problems afflicting millions of individuals (1,2). This disorder is most commonly experienced between the ages of 15 and 55 years, and 70% to 80% of sufferers have a family history of migraine (3). A widely accepted neurovascular theory of migraine etiology consists of dural and meningeal vascular dilatation, perivascular inflammation, and nociceptor activation (4). The reflection of migraine pain to the temporomandibular, facial, and maxillary areas has been ascribed to vascular dilatation and inflammation of the trigeminal nerve, which emanates from the brainstem and innervates the orofacial area (5). Although a relationship between the vascular etiology of migraine and orofacial syndrome theoretically exists, the exact nature of the pain remains elusive, as do those of the accompanying symptoms and comorbidities, including nausea, vomiting, gastroesophageal reflux disease

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(GERD), irritation, and fatigue (6,7). These symptoms and comorbidities could possibly affect oral health and care; therefore, a dental professional's evaluation and treatment might be essential for migraineurs (8).

One of the most encountered oral comorbidities is GERD, which is caused by the backflow of acidic gastric juice (pH: 1.0–3.0) into the oral cavity due to the condition itself or to vomiting during acute migraine attacks (9,10). Although the damaging effects of gastric juice depend on the duration of exposure and frequency, it can cause extensive erosions on tooth surfaces, particularly on the lingual side (11). It is a fact that the erosion level of the teeth is much higher in chronic migraine patients and eroded tooth surfaces are more likely to be susceptible to dental caries and periodontal problems (12).

The systemic conditions of migraine patients are also correlated with dental status. The positive correlation between migraine and the presence of gastrointestinal disorders (GIDs) has previously been established in many clinical and epidemiological studies (13). The clinical features of GIDs in migraine patients are most commonly characterized by the effects of acidic gastric juice on mandibular teeth (14). Several studies have demonstrated possible relationship between cardiovascular diseases (CVDs) and migraine (4,15,16). The functional significance of CVDs in migraine patients is that poor oral hygiene could be a predisposing factor for infective endocarditis caused by streptococcal bacteria (17).

Temporomandibular disorder (TMD) is a collective term that encompasses a number of clinical problems that involve the masticatory muscles, the temporomandibular joint (TMJ), and associated structures (18). The most common symptom of TMD is pain, usually located from the temporomandibular region to the retromandibular area through the masticatory muscles, and usually confused with chronic headaches reflected to these areas (19). Although not as well characterized as the prevalence of common headache syndromes, the prevalence of TMD in migraineurs has ranged from 22% to 52% (20).

According to epidemiological studies of adult populations, 50% to 75% of migraineurs have at least one sign of comorbidity, and nearly 35% have at least one symptom of TMD (18). The aim of the present study was to determine the relationships among oral hygiene, dental status, accompanying systemic conditions, and chronic migraine status in a case-control clinical study, to prove the hypothesis that there is a relationship between migraine and oral health and care.

2. Materials and methods

2.1. Study design

Two thousand six hundred and eighty one patients (between 18 and 60 years old and of both sexes) who presented at the neurology clinics of Izmir Ataturk Training and Education Hospital and Ege University and Behcet Uz Training Hospital were invited to participate in this study. A case-control, observational, and multicenter study was designed; the study was approved by the Ethics Committee of Ege University (reg no: 11-10.1/9) and written consent was obtained from all participants. Patients were examined by two neurologists who have experience in the headache field and clinical diagnosis of the neurologist was used as the gold standard. The final diagnosis was made according to the International Headache Society's Second Edition of International Classification of Headache Disorders to evaluate the existence, level, and effects of migraine on daily life (21,22). Prior to the study, Migraine Disability Assessment tests, modified for the present study (MS-Q and MIDAS), were also administered to each participant who was under medication for migraine to determine the systemic, socioeconomic, educational, and habitual statuses and the frequency of comorbid factors affecting the patient's quality of life (Figure) (2,21,23). Some of the comorbid factors such as photophobia, motion sickness, and dizziness were also transferred directly from hospital records to the patients' charts. Both migraine patients and nonmigraineurs were informed about the study design, and the patients who accepted the terms were included in the volunteer pool. The postevaluation stage involved the creation of two groups: Group 1 consisted of patients diagnosed with migraine ($n_m = 998$) and Group 2 consisted of nonmigraineurs as a control group $(n_{\rm b} = 1003)$, according to the block and unregistered randomization type. Therefore, all of the participants in both groups were chosen from similar socioeconomic levels; also, they were university graduates, nonsmokers, and nondrinkers and had average body mass indices (BMI: 25-29). Participants who were unable to complete the questionnaires, smokers, alcohol users, and patients who did not approve of the terms were excluded (n = 40). Patients who were unable to complete oral examinations (9), questionnaires (3.4%), and patients with additional psychological problems (7.1%) that could affect the study results were classified as missing data and also excluded (n = 189).

Each new patient with/without migraine was offered an evaluation by two different restorative dentistry specialists from Ege University at the same health center facility on the same day. To establish a double-blind study, both of the examiners were unaware of which group was being examined, and the interexaminer reliability was assessed with correlation coefficients (ICCs), using mixed effects regression models. The evaluation consisted of the application of a questionnaire (pretreatment form) and an oral examination to evaluate the dental and periodontal status (Figure). The questionnaire had three categories to evaluate oral hygiene habits, previous dental experiences, and common problems/requests in correlation with migraine and subtypes. The oral examinations were performed using the World Health Organization oral health assessment form (Geneva, 2009) to record previous dental treatments, periodontal status, bruxism, dental caries (ICDAS criteria), and TMD. Erosion and abrasions were categorized according to the Bartlett and Shah classification (1).

2.2. Statistical analysis

All of the data acquired from the questionnaires and oral assessment forms, such as the patients' sociodemographic and clinical properties, age, sex, and family history of migraine were descriptively analyzed; means, standard deviations, and 95% confidence intervals were calculated for quantitative variables and frequencies for qualitative variables. Adjustment was made for individual's sex, age, systemic conditions, existence of comorbidities, and

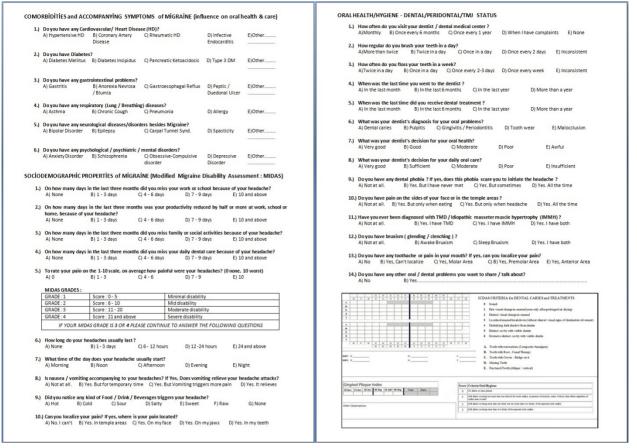


Figure. Modified MS-Q and MIDAS surveys to determine the level of migraine, systemic, socioeconomic, educational, and habitual statuses of the patients and the frequency of accompanying comorbidities.

overall dental health and care status. All analyses were weighted to account for the individual survey sample designs. Analyses considered that observations within each cluster of survey were not independent from each other. The estimation of the sample size was performed with a power analysis test using SPSS software, version 17.0. The evaluation of migraine distribution by age and sex was performed by the chi-square test with a significance level of 0.05. The independent t-test was used to compare the systemic conditions between the patients with migraine and nonmigraineurs. Pearson's correlation test was used to assess the association between oral healthcare and DMFT/ GPI scores and potential confounders.

3. Results

The data collected from 2001 participants were analyzed and revealed nonnegligible differences. Of the participants, 36% were male (n = 720) and 64% were female (n = 1281). The sex distribution in both groups was similar to standardize the research (M/F: 34/66 vs. 38/62). The mean age of the participants was 39.57 \pm 10.49 years old, ranging from 21 to 60 years old. Female

participants suffered from migraine significantly more than male participants (P < 0.05). Systemic diseases and disorders such as cardiovascular and gastrointestinal system diseases, metabolic disorders, and systemic lupus erythematosus, showed no significant differences among the participants (Table 1) (P > 0.05). While photophobia was the most common accompanying symptom, phonophobia, nausea, and gastroesophageal reflux were also found to be high. The other accompanying factors shown in Table 2 in migraineurs were statistically different from nonmigraineurs (P < 0.05).

The frequency of GERD was 42% in the migraine patients and 18% in the control group (P < 0.05). Gastrointestinal problems such as gastritis and ulcers were much more common in nonmigraineurs (12%, P < 0.05) (Table 1). The rate of migraine patients who suffered from bruxism and TMD were relatively high in comparison with the control group (49%, P < 0.05), while correlation analysis showed that the frequency of erosion and abrasions was positively correlated with the existence of bruxism (P < 0.05). Details, including systemic conditions, are also shown in Table 1.

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Table 1.	Evaluation of	patients with	migraine and	l nonmigraineurs	for systemic diseases.
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Systemic conditions	Male	Female	Male	Female	Group 1 vs. Group 2 [#]
Cardiovascular diseases			·		
Hypertension (HTN)	70	161	62	148	0.866
Cardiac dysrhythmia	21	59	30	32	0.582
Respiratory diseases			·		
Chronic obstructive pulmonary disease (COPD)	19	12	17	15	0.299
Asthma	9	13	10	15	0.604
Gastrointestinal system diseases					
Gastroesophageal reflux (GERD)	175	248	82	101	0.000*
Gastritis-gastric ulcer	31	29	22	36	0.348
Endocrine-metabolic diseases					
Diabetes mellitus (DM)	30	107	32	74	0.509
Thyroid disorders	9	61	11	50	0.758
Autoimmune diseases	•				
Systemic lupus (SLE)	28	58	31	49	0.287
Nephrological diseases					
Glomerulonephritis	9	24	10	18	0.410

*: significant difference.

#: Group 1: Migraine patients; Group 2: Nonmigraineurs.

Table 2. The subtypes of migraine in relation to accompanying symptoms.

Accompanying syn	mptoms of migraine	e in correlation with	n subtypes					
Photophobia	Status migrainosus	Abdominal migraine	Retinal migraine	Specific migraine with aura	Basilar-type migraine	Hemiplegic migraine	Migraine without aura	n (%)
Phonophobia	4 (100%)	2 (40%)	6 (33%)	271 (86%)	1 (25%)	1 (33%)	409 (63%)	694 (70%)
Phonophobia	3 (75%)	1 (20%)	1 (5%)	216 (69%)	-	-	315 (49%)	536 (54%)
Dizziness	3 (75%)	2 (40%)	-	82 (26%)	1 (25%)	-	248 (38%)	376 (37%)
Motion Sickness	4 (100%)	2 (40%)	1 (5%)	168 (53%)	-	-	87 (13%)	262 (26%)
Nausea	1 (25%)	5 (100%)	-	238 (76%)	-	-	245 (38%)	489 (49%)
Vomiting	-	5 (100%)	-	199 (63%)	-		191 (29%)	394 (39%)
Total cases	4	5	18	315	4		649	998 (100%)

Oral hygiene status was similar in both groups (P > 0.05). Although daily tooth brushing (98% vs. 96%, P > 0.05) and dental flossing (39% vs. 40%, P < 0.05) were similar, as might be expected, regular dental visits were slightly increased to 40%, while dentophobia was increased to 42% in migraine patients, which was significant (P < 0.05). Tooth wear and abrasion seemed more frequent in patients with migraine (76%, P < 0.05). DMFT scores

(mean 3.79 vs. 2.71, P < 0.05) and gingival plaque index scores (mean 1.64 vs. 1.23, P < 0.05) showed significant differences between the groups (Table 3).

The participants' statements revealed that during acute migraine attacks dental care was disrupted for at least 24 h (Table 3). Of the participants, 64% experienced limitations in oral hygiene habits, whereas 2% of participants stopped tooth brushing to avoid triggering pain (P < 0.05).

	Group 1	Group 1		Group 2		
Oral health and dental status	Male	Female	Male	Female	P-value	
Oral health care						
Toothbrush use	330	652	366	594	0.791	
Dental floss use	134	142	111	195	0.921	
Dental visits	201	309	317	334	0.042*	
Dental anxiety and phobia	89	171	67	222	0.037*	
Oral dental status					L.	
Bruxism	121	361	143	150	0.006*	
TME disorders	152	240	118	232	0.045*	
Tooth wear and abrasion	156	367	133	203	0.001*	
Erosions	189	218	80	121	0.005*	
Oral indexes						
DMFT index score [#]	3.8	3.7	2.8	2.6	0.000*	
Gingival plaque index [#]	1.7	1.6	1.4	1.1	0.000*	

Table 3. Oral health and care status amongst patients with migraine.

^I: Overall mean values for the patients.

*: Significant difference.

4. Discussion

The incidence of migraine has been reported to be the highest among middle-aged females (1-3,21,24). Recent studies reported that the prevalence of migraine without aura is higher than migraine with aura, and the more frequent subtype of migraine encountered is of the tension or chronic migraine subtype (25,26). The findings of the present study corroborated the findings of the above mentioned recent studies where it was observed that subtypes of migraine are very rare and do not affect the data. Previous research has addressed the possible associations between migraine and hypertension, hemorrhagic stroke, and CVDs (15,27). For example, Ylöstalo et al. (28) demonstrated that relatively low oral hygiene status among migraine patients was a major underlying factor of infective endocarditis. Our study also revealed a positive relationship between the existence of migraine and oral and dental status. To our knowledge, our study is the first to look at this relationship using correlation analyses, investigating the possible effects of comorbid conditions present to oral hygiene. Although most studies have suggested that migraine patients are more likely to be susceptible to hypertension and to have impaired insulin sensitivity, autoimmune diseases, and several comorbidities related to these diseases, it should be investigated whether oral symptoms are the cause

or consequence of migraine (8,18,29,30). None of the systemic conditions in migraineurs differed from those of nonmigraineurs in the present study except for GERD. This difference could be explained by disturbances in migraine patients of the parasympathetic branch of the autonomic nervous system, which controls the gastrointestinal reflexes (31). In migraineurs, nausea and bulimia, in addition to GERD, are well-known accompanying symptoms that affect the oral health (7). Volitional vomiting can provide short-term relief of pain, but consistent vomiting can lead to serious complications such as tooth erosion (9,32,33). The abrasion, thus caused, could explain the low caries risk but high tooth wear and high fracture incidences in dental restorations (8,34). The results of our study show that the presence of migraine was associated with an increased erosion and abrasion intensity, which leads to dental tissue susceptibility to dental caries.

TMDs have frequently been associated with both head and jaw pain; therefore, it is easy to confuse TMDs with acute migraine attacks (18,35). The pain is usually localized in the temporomandibular region, and the type, frequency, and predisposing factors of this pain are referred to TMDs (36). Although not all migraine patients suffer from TMDs, the relationship between malocclusion and migraine cannot be overestimated. It is, however, unclear whether the cause of malocclusion is TMD or skeletal problems (37). In addition, it is not known whether TMD is one of the main causes of migraine or the effect of neuropathic muscle contraction during acute migraine attacks (27,38). In contrast, some parafunctional habits such as bruxism and masseter hypertrophy are secondary oral consequences of migraine attacks originating from TMDs, resulting in extensive tooth wear and abfraction, which affects oral health dramatically (33). According to our findings, bruxism caused by TMD resulted in tooth wear on occlusal surfaces and caused malocclusion, which has been associated with migraine attacks; it initiated non-TMD-related (masseter muscle-related) bruxism, initiating a vicious cycle. This deduction is consistent with the study by Pistoia et al. (39). In addition, correlation analysis proved that migraineurs who suffered from TMDs also had tooth wear, but no positive correlation was found unless accompanied by bruxism. However, an association between migraine and TMD has been previously observed (36), and our results may support the notion that DMFT and periodontal status are most likely to stem from comorbid factors such as GERD and vomiting, which lead to extensive dental hard tissue loss.

Pearson's analysis also showed a strong correlation between migraine and DMFT and plaque index scores, as stated in previous studies. This could be the result of either susceptible tooth surfaces caused by erosion and abrasion or a significant increase in dental anxiety and phobias, which can lead to decreased regular dental visits (40,41).

The importance of migraine headaches in the population lies in its disability potential (23). Intermittent dental care leads to significant changes in oral hygiene; hence, dental and periodontal tissues can suffer. In addition, the medication used for migraine attacks can exacerbate these conditions (41). Although there have

been many previous studies showing the relationship between migraine and oral health, few of these studies have mentioned the possible effects of migraine attacks on daily oral health care (42). Along with the discomfort caused by the headache, the results of our study showed major effects of interruption of daily dental care routines. Our research could be useful because it offers the opportunity to evaluate the possible effects of migraine on oral hygiene and daily oral care.

According to its intensity and dispersion, pain is referred from the TMJ to the maxillary and mandibular posterior areas, as well as the teeth in those areas (43). According to our findings, the evidence corroborated our hypothesis of a relationship between migraine and oral health care, particularly the erosions and tooth abrasions caused by the stress of upcoming migraine attacks, supporting the results of the study conducted by Nixdorf et al. (44). Dental plaque can easily accumulate on eroded and abraded tooth surfaces, which can cause dental caries and gingivitis. Within the limitations of this crosssectional study, further investigations and evaluations must be performed to establish causal relationships between migraine and oral comorbidities.

In conclusion, patients with migraine headaches who consulted dental professionals were usually misdiagnosed and received unnecessary treatments. Most dental clinicians are unfamiliar with this headache disorder and its associated oral health problems. In addition, most of the patients are unaware of their oral health condition because of chronic migraine disease. The cervical erosions caused by GERD and the occlusal tooth wear caused by bruxism are the main problems that must be managed concomitantly to achieve improved treatment outcomes.

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