Role of Anxiety and Depression in Association with Migraine and Myofascial Pain Temporomandibular Disorder

Abstract

Background: Previous studies have demonstrated a strong association between primary headaches (HAs) and temporomandibular disorders (TMDs), specifically the myofascial pain subtype of TMD (MP TMD). The role of anxiety and depression in presentation and maintenance of MP TMD and migraine is previously demonstrated. Therefore, the objective of the current study was to evaluate the modification effect of anxiety and depression on the possible association of MP TMD and migraine.

Methods: In this retrospective case–control study, individuals between 15 and 45 years old who were diagnosed with migraine HA according to the international classification of headache disorder-II (ICHD-II) were selected as case subjects (n = 65). Non-HA control subjects were matched by sex and age (n = 63). Research diagnostic criteria (RDC/TMD) (Axis I) was used to diagnose patients with MP TMD; other subtypes of RDC/TMD Axis I were excluded from the study. Subjects’ anxiety and depression were screened using Persian version of Hospital Anxiety and Depression Scale-14. Chi-square and Mantel–Haenszel tests were used to analyze the data. P < 0.05 was considered statistically significant. Results: A significant association was found between migraine and MP TMD so that subjects with MP TMD had a five times chance of developing HA (P < 0.001). Further analysis using stratification method revealed that anxiety and depression have a modification effect in the association of MP TMD and HA and MP TMD patients with anxiety or depression had more chance of developing migraine HA (P = 0.003). Conclusion: Association between HA and TMD was observed in this study. Besides, we depicted that anxiety and depression interact in this association so that patients who did not have anxiety or depression did not demonstrate an association between TMD and HA. We suggest further studies to confirm the modifying effects of anxiety and depression.

Keywords: Anxiety, depression, primary headache, research diagnostic criteria/temporomandibular disorders

Introduction

Headache (HA) disorders are a number of conditions characterized by recurrent attacks of head pain and associated symptoms. The most common type of HA in general population studies is tension type HA, wherein migraine is the most common type among patients who seek medical attention. Migraine affects about 12% of the population, with an annual cost of $16.6 billion for America.

Temporomandibular disorder (TMD) is a group of signs and symptoms affecting masticatory muscles, temporomandibular joints, or both. TMD is also a common disorder affecting 8–15% of women and 3–10% of men.

Some clinical and epidemiological studies have revealed an association between TMD and primary HAs. Patients suffering from migraine are more prone to develop tenderness in TMJ and masticatory muscles. Besides, signs and symptoms of TMD are more common in migraine patients. On the other hand, HA disorders are more common in TMD patients in comparison to healthy subjects’ representative of the normal population. Anxiety and depression (A/D) are one of the most common psychological symptoms in patients suffering from HA and TMD. On the other hand, patients suffering from anxiety or depression are more susceptible to experience recurrent pain. Since the introduction of research diagnostic criteria (RDC/TMD) by Dworkin and LeResche in 1992, the role of A/D in the pathogenesis of TMD has been under investigation. Recent publications have revealed the role of A/D in myofascial pain (MP) subtype of TMD. It has demonstrated that symptoms

Access this article online

Website: www.ijdr.in
DOI: 10.4103/0970-9290.244932

How to cite this article: Nazeri M, Gahrechahi HR, Pourzare A, Abareghi F, Samiee-Rad S, Shabani M, et al. Role of anxiety and depression in association with migraine and myofascial pain temporomandibular disorder. Indian J Dent Res 2018;29:583-7.
of anxiety are specific for patients with muscle pain, while the symptoms of depression present in patients suffering from joint pain.\\(^{[29]}\)

Depression and anxiety might contribute to the MP TMD and migraine through interacting with pain modulating networks and decreasing pain threshold or altering the perception of pain in patients suffering from anxiety or depression, though the exact mechanism is not yet clear.\\(^{[26]}\)

Despite the study by List et al. regarding the association of TMD and HA in the context of A/D,\\(^{[27]}\) there are still controversies as to the effect of A/D on the association of TMD with HA. Therefore, we first tested to see whether MP TMD and migraine are associated in the subjects of study and then using stratification method, we evaluated to see whether A/D have a modification effect on this association. Findings of our study would help clinicians in treating migraine patients with comorbid MP TMD who also show symptoms of A/D.

**Methods**

This age- and sex-matched case–control study was conducted semiannually from September 2011 to February 2012 in Kerman, Iran. This study was approved by the Kerman Medical University’s Ethics Committee (ethics code: KMU/EC/92-7).

**Sample selection, headache diagnosis, and exclusion criteria**

Sampling for this study was done through consecutive patients referred to a general clinic in Kerman who were diagnosed with a migraine for the first time. Patients were selected from subjects between 15 and 45 years old. The rationale for this inclusion criterion was the fact that this range is the most common age range for migraine headaches.\\(^{[28]}\) Subjects were examined by an expert neurologist based on international classification of headache disorders-II (ICHD-II) criteria and they were diagnosed with migraine if they had the following criteria: Recurrent throbbing HAs that often affected one side of the head and are of moderate intensity which could also cause nausea, photophobia, and phonophobia (ICHD-II). After being diagnosed with migraine, if subjects were willing to participate in the study, their informed consent was taken by the examiner. Then, they were examined by one trained and experienced dentist for the TMD status according to RDC for TMDs Axis I (RDC/TMD Axis I).\\(^{[29]}\) Patients diagnosed with MP TMD were included in the study and subjects with other Axis I diagnosis (disc displacements with and without reduction, arthralgia, osteoarthritis, and osteoarthrosis) were excluded from the study. The rationale for including only MP TMD patients was the fact that previous studies\\(^{[19,21,23]}\) have shown a strong association between A/D and MP TMD, while such a strong association has not been reported for other Axis I diagnosis.\\(^{[24]}\) The other exclusion criteria were as follows: (1) History of trauma to the face or jaw, (2) history of orthodontic treatment, (3) neuropathy, (4) chronic pain syndromes (not HA) such as fibromyalgia or arthritis, (5) odontalgia, (6) isolated Axis I Group II (disk displacements), (7) acute pain, (8) osteoarthritis without other TMD signs and symptoms, (9) any disability in language and cognition (10) intraoral lesions, and (11) previous medication taken for migraine.

Subsequently, patients were classified into two groups: (1) Myofascial pain (MP) TMD patients and (2) non-TMD patients. In the next step, included subjects were asked to complete a standardized Persian version\\(^{[30]}\) of the Hospital Anxiety and Depression Scale-14 (HADS-14)\\(^{[30]}\) to measure the level of A/D. HADS-14 is made of 14 questions, 7 related to depression level and the other 7 questions measure the anxiety level of the subject. Each question can be scored from 0 to 3, so in each subscale (depression or anxiety) the maximum score will be 21. According to prior studies, any subject with depression ≥8 or anxiety ≥8 was considered to have anxiety or depression (A/D).\\(^{[30]}\)

To provide socioeconomic homogeneity, individuals who accompanied patients and did not have a history of primary HA and were qualified according to the inclusion criteria were used for the control group. Patients in the control group were group-matched with the case group in gender and age and underwent the same examination procedures as in case subjects.

The sample size was calculated according to previous studies.\\(^{[31]}\) 65 migraine patients and 63 healthy controls were enrolled for the analysis according to the strict inclusion/exclusion criteria. Data were summarized by using descriptive statistics. The initial sample size was fifty for each group, but since we did want to evaluate the modification effect of A/D, a 10% increase for each independent variable was considered in the analysis to reach the required confidence interval (CI).\\(^{[31]}\)

In the first step of analysis, the possible association between HA and TMD was evaluated using Chi-square test. Then, controlling for anxiety and/or depression, Mantel–Haenszel analysis followed by Breslow–Day test, was recruited to evaluate the possible modification effect of anxiety and or depression on the association of migraine and TMD. \(P < 0.05\) was considered statistically significant.

**Results**

Case subject were 65 migraine patients, 52 (80%) of them were female and 13 (20%) were male (mean age: 29.32 ± 8.97). Control subjects matched with the case subjects in gender and age (mean age: 28.63 ± 9.14) comprised 46 (73%) females and 17 (27%) males. Regarding TMD condition, the case group consisted of 50 (76.9%) TMD and 15 (23.1%) non-TMD subjects while there were 25 (39.7%) TMD and 38 (60.3%) non-TMD subjects in the control group [Table 1].
To investigate whether there was a significant association between HA and TMD, a number of TMD patients in the case (HA) and control (non-HA) group were compared using Chi-square test and significant difference was observed between HA and non-HA patients. Fifty out of 65 cases were diagnosed with TMD (76.9%), while 25 subjects from 63 healthy controls (39.7%) were diagnosed with TMD [Table 1] \( (\chi^2, P < 0.001, \text{odds ratio [OR]} = 5.067 \ [CI = 2.354–10.906]) \) indicating a five times chance of TMD in HA patients compared to normal subjects.

Regarding the A/D condition, patients were stratified in both case and control groups. Association of TMD and HA was evaluated in each A/D classified subgroup to test the possible modification effect of A/D in the association of TMD and HA. In HA patients who were not anxious or depressed (non-A/D), 5 out of 55 (9.1%) were diagnosed with TMD, while in HA patients with A/D, 45 out of 73 (61.6%) were diagnosed with TMD [Table 2].

To understand the role of A/D in the association of TMD and HA, Mantel–Haenszel test was performed (Mantel–Haenszel test, \( \chi^2 = 8.04, P = 0.003 \)). Patients who were diagnosed with only TMD and not A/D had a 1.36-fold chance of developing HA which was not statistically significant \( (P > 0.05, \ [CI = 0.347–5.404]) \), while patients with A/D and TMD had a 9-fold chance of developing HA \( (P = 0.001, \ [CI = 2.72–29.75]) \) suggesting a synergistic role for TMD and A/D in development of HA. Interestingly, the chance of HA occurrence (evaluated by Mantel–Haenszel analysis) was significantly different between two tests (Breslow–Day test, \( P = 0.039 \)) showing that A/D are not just confounding factors in the association of TMD and HA.

**Discussion**

In this study, we have shown that primary HA and TMD (MP subgroup according to RDC/TMD Axis I) are associated and patients with TMD are more prone to develop HA in comparison to healthy controls. By using HADS-14 as a screening tool, we stratified patients and interestingly patients who were not anxious or depressed did not show a significant association between HA and TMD, while in A/D patients, TMD patients were more prone to develop HA. Further analysis revealed that anxiety or depression has a modification effect in the association of HA and TMD, which is a new finding.

It was previously shown that TMD patients exhibit a higher prevalence of HA compared to healthy subjects, and interestingly TMD is significantly more common among patients with primary HA \[^{[10,11,14–16]}\]. Franco et al. showed that migraine is the most common primary HA in TMD patients, and the prevalence of HA in TMD patients is 85.5%, whereas it is 45.6% in controls. In their study, they evaluated the prevalence of primary HA in TMD patients, \[^{[15]}\] while we evaluated the prevalence of TMD in primary HA patients which is similar to Stuginski-Barbosa et al.’s study. \[^{[14]}\] In their study, Stuginski-Barbosa et al. evaluated the prevalence of TMD signs in primary HA patients using Helkimo’s protocol for the evaluation of TMD signs and symptoms. They showed that HA patients are more likely to develop TMD signs in comparison to normal controls, which is consistent with our crude OR calculated for the association between HA and TMD without considering A/D. Two limitations of their study were (1) Helkimo protocol instead of gold standard (RDC/TMD) and (2) no evaluation of anxiety or depression. These mentioned drawbacks were resolved in our designed study, and yet, our findings are consistent with their study.

The role of A/D in pain perception has been studied before, and it is demonstrated that TMD or HA patients suffering from anxiety or depression report more severe pain. \[^{[19–21,23,24]}\]

We have shown that TMD and HA are associated only in the context of anxiety or depression. It is known for more than 20 years that A/D play an important role in the initiation and maintenance of TMD and HA, and since the introduction of RDC/TMD as a diagnostic tool for TMD by Dworkin and LeResche, \[^{[4]}\] psychological factors have been proposed to play an important role in the pathogenesis of TMD. Although previous studies \[^{[14,15]}\] have shown a strong association between HA and TMD, the possible role of A/D have not been evaluated in this association except for a recently published study by List et al. \[^{[27]}\] List et al. demonstrated that HA frequency is correlated with TMD and emotional functioning (A/D) and HAs are precipitated by jaw function. \[^{[27]}\] Consistent with this study, we have shown that the association between TMD and HA is only meaningful in patients presenting with anxiety or depression.

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**Table 1: On-headache (control) patients classified by their gender, temporomandibular disorder, and anxiety/ depression condition**

| Group          | Gender (%) | TMD condition OR=5.06* (%) | Anxiety and depression condition (%) |
|----------------|------------|---------------------------|-------------------------------------|
|                | Male       | Female                    | MP                                  | Hx        | OR A/D     | Normal    |
| Case (29.32±8.97 year) | 13 (20) | 52 (80) | 50 (76.9) | 15 (23.1) | 55 (84.6) | 10 (15.4) |
| Control (28.36±9.14 year) | 17 (27) | 46 (73) | 25 (39.7) | 38 (60.3) | 18 (28.6) | 45 (71.4) |
| Total          | 30 (23.4) | 98 (76.6) | 75 (58.6) | 53 (41.4) | 73 (57)   | 55 (43)   |

A strong association was found between headache and TMD (OR=5.06, \( P=0.001, \ [CI=2.35–10.90]) \). TMD=Temporomandibular disorder, MP=Myofascial pain, A=Anxiety, D=Depression, OR=Odds ratio, CI=Confidence interval.
A meaningful association was found between headache and TMD only in patients with anxiety or depression (OR=9, *: P < 0.05, significantly different from the Control, CI=2.72-29.75). Further analysis revealed a significant difference between two ORs, showing a modification effect for anxiety and depression in association of TMD and headache (P=0.039, Breslow-Day test). TMD=Temporomandibular disorder, A=Anxiety, D=Depression, MP=Myofascial pain, OR=Odds ratio, CI=Confidence interval.

One limitation of our study is the low number of cases in some of the subgroups. Another limitation is the nature of case–control studies. We only have evaluated the association of TMD and HA but not their possible relationships with each other. A prospective study would solve the aforementioned limitation, while our study might give initial documentation for the modification effect of A/D in the association of TMD and HA. We suggest a prospective study with a larger sample size to evaluate the association of TMD and HA considering the possible role of A/D.

Conclusion

We have shown that A/D have a modification effect in the association of HA and TMD and should be considered in the rehabilitation of patients with concurrent MP TMD and migraine HA. Although our sample size was not large enough, it might provide evidence for further epidemiological studies regarding the modifying effect of A/D in the association of myofascial TMD and HA.

Acknowledgment

This study was conducted by a grant from Kerman Neuroscience Research Center, Neuropharmacology Institute, Kerman, Iran.

Financial support and sponsorship

This study was conducted by a grant from Kerman Neuroscience Research Center. Grant number: /KNRC/92-7.

Conflicts of interest

There are no conflicts of interest.

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