Author's response to reviews

Title: Combination of anxiety and depression is associated with an increased headache frequency in migraineurs: a population-based study

Authors:

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Author's response to reviews: see over
Reviewer: Brad Klein

Major Compulsory Revisions

1. Abstract, under results, you report that 147 patients had migraine, then you broke them into groups noting depression and anxiety, depression, anxiety, or neither depression or anxiety. The sum total of these groups is 138. Can you address the 9 missing subjects? Also based on the study methods, it seems you excluded migraine with aura from consideration. If so, stating that you looked at patients with migraine without aura only would be important when interpreting your migraine prevalence results appropriately.

Authors’ response

Total number of migraine in the present study is 147 (migraine without anxiety and depression=93, migraine with anxiety alone=28, migraine with depression alone 9 and migraine with anxiety and depression=17). The number of migraine participants was described at FIG.1 and RESULTS PAGE 11 line 11–13). I checked again the numbers of migraine participants in each groups. We did not attempt to diagnosis aura and included both migraine with aura and migraine without aura as migraine in the present study. We revised descriptions regarding this issue at MEHODS (PAGE 8 line 18-21) and DISCUSSION (PAGE 16 line 9-16).

2. Abstract, Conclusions: In your background statement, you explain that you wish to understand the clinical implications of comorbid depression and anxiety. However, your conclusion only discusses migraine frequency as affected by depression and anxiety. Other clinical implications not discussed but relevant could be 2 week disability, restriction of activities, poorer QOL, and more mental health care usage. This derives from the referenced article by Jette N. Otherpoints of reference you investigated include the VAS and HIT-6. Presenting some additional findings in the abstract would be useful.

Authors’ response

Thank you for kind comment. We assessed headache characteristics, associated symptoms, headache frequency, associated symptoms and HIT-6 score according to
the occurrence of anxiety and/or depression. We included additional description on headache severity (VAS score) in ABSTRACT (PAGE 3 line 23 – PAGE 4 line 1). At CONCLUSIONS, we included descriptions regarding headache severity and impact of headache (HIT-6 score) (PAGE 18 line 8-11).

3. Methods; Diagnosis of migraine, anxiety, and depression, first paragraph: You diagnose migraine as migraine without aura. Thus it seems you excluded potentially 1/3 of the migraine population. What was the basis for excluding this group? If not included, adding this patient population back in would likely increase your statistical power without tarnishing the results noted.

Authors’ response

We included both migraine without aura participants and migraine with aura participants in the present study. We included additional description regarding migraine with aura diagnosis at METHODS (PAGE 8 line 19-21) DISCUSSION (PAGE 16 line 9-16).

Minor Essential Revisions

4. Background: Paragraph 2: Can you clarify briefly which symptoms and what impact you are referring to? I am also not clear what you mean by “severe.”

Please clarify if you mean chronic migraine versus episodic migraine, intractable, severe pain, etc.

Authors’ response

In most headache studies, the headache frequency were commonly used for investigating severity of symptoms. We revised “the symptoms” as “headache frequency” for better understanding (PAGE 5 line 9-11). We revised as “chronic migraine” instead of “severe form” (PAGE 5 line 12-13) for better understanding.

5. Discussion: Paragraph 4: “Numerous studies have shown a close association
between depression and migraine has been studied.” Please review the grammar.

Authors’ response
We revise properly at PAGE 14 line 3-4.

Discretionary Revisions
1. Abstract, under results, if you state: “147 subjects (5.4%) were classified as having migraine during the previous year.” Adding the word “a” prior to migraine will clarify if you meant the subjects were included if they had a migraine versus they had a diagnosis of migraine.

Authors’ response
We revise properly at PAGE 3 line 14.

2. Methods, Analyses, Paragraph 3, consider deleting the word “groups” from and migraine with anxiety and depression groups.

Authors’ response
We deleted “groups” at PAGE 10 line 7-9.

3. Conclusion: Consider changing “One-third of migraineurs” to “1/3 of migraineurs” for consistency.

Authors’ response
We used one-thirds instead of 1/3 because it was located at the head of a sentence (PAGE 18 line 5).

Reviewer: Ana Recober
1. Explain if the interviews were by phone or in person.

Authors’ response

This study was conducted by door-to-door visit and face-to-face interview using questionnaire. We include additional description at METHODS (PAGE 8 line 13-14).

2. Provide the surveys or questionnaires used for the interviews.

Authors’ response

We revised description regarding survey procedure at METHODS (PAGE 8 line 6-14). We submitted Korean and English-translated questionnaire in this revision.

3. Discuss limitations of low participation as well as diagnoses based on questionnaires.

Authors’ response

We include descriptions regarding low participation issue at DISCUSSION (PAGE 15 line 24 – PAGE 16 line 8).

4. Discuss further the low migraine prevalence in this population sample.

Authors’ response

We included description on migraine prevalence rate of the present study at DISCUSSION (PAGE 13 line 8 – 14). Briefly, the 1-year migraine prevalence rate in the present study (5.4%) was somewhat lower than those of European (10-25%) and North American (9-16%) countries and was similar to those of eastern and southeastern Asian countries. The 1-year prevalence rate in Asian countries are mostly ranging from 4.7% to 9.1%.

5. Correct typos (page 13 line 9 – sentence needs revision; page 15 line 7 – “diagnosis” should be “diagnose”)

Authors’ response

We properly revised sentence at PAGE 14 line 3 and corrected as “diagnose” at PAGE 16 line 11.
Reviewer: Todd Smitherman

Minor Essential Revisions. The authors refer to "anxiety" throughout the manuscript, but the Goldberg, a measure with which I am generally unfamiliar, seems to map closely to the diagnostic criteria for Generalized Anxiety Disorder specifically. The authors should consider qualifying their use of the term "anxiety" or at least addressing what anxiety disorders (as anxiety is not one "thing") the Goldberg is useful for screening.

Authors' response

Goldberg Anxiety Scale was developed in 1988 for detecting anxiety in general medical setting to assess anxiety symptoms of various diagnoses listed in DSM-III (Ref No. 28). Goldberg Anxiety Scale was validated in Korean population and showed a good correlation with State-Trait Anxiety Inventory, a well-known tool for assessing anxiety (Ref No. 30 and Ref No.31).

The authors should better specify how participants were recruited and justify the very high refusal rate. It is striking that such a large proportion refused to complete surveys--how were individuals approached/recruited/identified for potential participation?

Authors’ response

We revised descriptions about recruitment of participants and survey procedure at METHODS (PAGE 8 line 6 – 14). We also revise description for low participation rate at DISCUSSION (PAGE 15 line 24 – PAGE 16 line 8).

The authors indicate that the diagnostic criteria for migraine without aura were used--does this mean that no individuals with aura were included or that aura was simply not assessed? Were any efforts made to distinguish between episodic and chronic migraine? From the attack frequency distributions it appears as though only those of those with both depression and anxiety had attacks at a frequency suggestive of chronic migraine--the frequency analysis addresses this to some extent, but I am
curious if the authors can indicate how many individuals met criteria for chronic migraine.

Authors’ response

We included both migraine without aura participants and migraine with aura participants in the present study. We included additional description regarding migraine with aura diagnosis at METHODS (PAGE 8 line 19-21) and DISCUSSION (PAGE 16 line 9-16). We did not attempted to diagnose chronic migraine in the present study because the diagnostic criteria for chronic migraine is currently not definitive and investigating chronic migraine in epidemiological study was very difficult. We included descriptions regarding CM at DISCUSSION (PAGE 16 line 17 – PAGE 17 line 1).

The authors should more clearly indicate what these data add to existing literature. They acknowledge in the Discussion that the effects of depression and anxiety on disability and quality-of-life are well-documented, and thus many of the findings replicate what is already established. Is the main contribution the analysis of migraine symptoms as a function of depression/anxiety?

Authors’ response

Both anxiety and depression are common comorbidity in general population and migraineurs. Anxiety or depression was associated with exacerbation of symptoms of migraineurs has been well-known. The main contribution of this manuscript is investigating both anxiety and depression in migraineurs and assessing clinical characteristics of migraine according to detailed status of anxiety and depression. We found that: 1) Combination of anxiety and depression was associated with an increased headache frequency; 2) Anxiety was associated with exacerbation of headache intensity 3) Impact of headache increased with the accompaniment of anxiety and depression. We revised description regarding main contribution of this study at CONCLUSIONS (PAGE 18 line 4-12) for better understanding.

On page 13, line 23, there appears to be a numerical error--"174/147" should be
changed to "17/147"

Authors' response

We revised as 17/147 (PAGE 14 line 17).