Identification of Allodynic Migraine Patients with the Turkish Version of the Allodynia Symptom Checklist: Reliability and Consistency Study

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ABSTRACT

Introduction: Cutaneous allodynia is regarded as an expression of central sensitization in migraine. Although the gold standard is quantitative sensory testing, several practical assessment questionnaires have been developed to assess allodynia in migraine. We aimed to establish the first valid Turkish allodynia assessment questionnaire based on a 12-item allodynia symptom checklist and to evaluate the associated factors.

Methods: The first part of the study included the translation and cultural adaptation of a Turkish version of the checklist. The Turkish version of the questionnaire was administered to 344 episodic and chronic migraine patients, who were chosen according to the International Classification of Headache Disorders -III beta criteria.

Results: The total checklist score showed excellent test-retest reliability ($r=0.821$). The internal consistency of the checklist was assessed using

Cronbach alpha values and was found to be acceptable (Cronbach alpha for the checklist=0.767). Data analysis revealed that 10 items of the questionnaire adequately identified allodynic subjects. Cutaneous allodynia was present in 218 (63.4%) migraine patients. Allodynia was more prominent in patients experiencing migraine with aura ($p=0.008$) and in females ($p<0.001$). Multiple logistic regression analysis found that female gender, aura existence, longer headache duration, and higher attack frequency were the major determinants of cutaneous allodynia.

Conclusion: Allodynia is common and has clinical significance in migraine; therefore, establishing a validated Turkish questionnaire for the assessment of allodynia was necessary. In this study, a Turkish version of the allodynia symptom checklist was validated and found to be convenient for the identification of allodynia in migraine patients.

Keywords: Migraine, cutaneous allodynia, checklist, validity

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INTRODUCTION

Cutaneous allodynia (CA) is the perception of pain or discomfort generated by a non-noxious stimulus to the skin (1,2,3,4). Results from population- and clinic-based studies have shown that approximately two-thirds of migraineurs experience CA during attacks (1,4,5). There is accumulated evidence suggesting that CA is associated with chronicity and higher levels of disability (1,3,6). Among migraineurs, CA is often present with frequent attacks and headaches of longer duration (1,7).

CA represents the sensitization of central trigeminal neurons that receive convergent input from the dura and the periorbital skin (1,4,8,9,10). It has been proposed that CA is the result of the repeated sensitization of pain pathways (11,12). After exploring CA as a marker of central sensitization, results of clinical studies have shown that triptans are more effective if administered before the presence of CA (2,13). Consequently, the identification of CA in migraine patients has clinical significance in that it could affect the choice or timing of treatment. Additionally, it might help clinicians be aware of chronicity as a risk factor (14).

Although the gold standard in the assessment of CA is quantitative sensory testing, this requires specialized equipment and training (4,15). For easy and practical use, questionnaires have been developed to assess CA (1,16,17). One of the most widely used and validated questionnaires is the Allodynia Symptom Checklist (ASC) (1). ASC was developed via a large population-based study and provided important data on CA. This study also confirmed that CA is closely related to the duration and frequency of headaches and is proposed as a chronicity-related factor. It contains 12 items and assesses the subtypes (static mechanical, dynamic mechanical, and thermal) and severity of CA (mild, moderate, and severe). ASC has also been translated and adapted into another language (18).

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Because there is no reliable validated Turkish questionnaire for CA assessment, we aimed to develop a Turkish version of ASC via the translation and cultural adaptation of the original checklist. First, we aimed to develop a Turkish version with multiple methods in a way that was concordant with the literature, and second, we tested our final questionnaire with a sample from migraine patients in Turkey.

METHODS

Request permission: The consent of the author of the original questionnaire was obtained, and the ethical committee of İstanbul Training and Research Hospital approved this study (Decision Number: 612/27.02.2015).

Translation and synthesis method: The translation and cultural adaptation of ASC-12 were performed via the consensus of the authors, including language experts and headache specialists, and included six stages (Figure 1):

(I) Initial translations were made by two independent language experts.

(II) The synthesis of translations, performed by headache specialists, and the first Turkish version of the questionnaire were established (ASC-12/T1).

(III) ASC-12/T1 was sent to a social–educational sciences expert and then revised (ASC-12/T2). The second version was administered to a group of university students who had English and Turkish language abilities. Students completed the Turkish and English versions of the ASC-12 questionnaire ($n=37$, cross-test). After the test results were obtained, the group discussed the test and their comments were collected. The main objective of this section was to obtain the comments of healthy and educated individuals who have no history of migraine.

(IV) After ASC-12/T2 and the comments of the students were obtained, headache experts evaluated the cross-test results and debated on the written comments. We established the final version, the ASC-12/Turkish. ASC-12/Turkish was re-translated to English by an independent language expert and sent to the original article author (Lipton R).

(V) ASC-12/Turkish was refined via comments and cross-test results. It was administered to a different group of university students ($n=38$) and, concurrently, a group of migraineurs ($n=47$). Two weeks later, a retest was performed, and the results were obtained.

(VI) With the test–retest results in mind, the final version of ASC-12/Turkish was administered to migraine patients at two outpatient neurology clinics.

Patient selection: The participants meeting the inclusion criteria were prospectively enrolled between February and September 2015, after obtaining their written consent. All participants were examined by experienced headache specialists. Migraine without aura (I.1), migraine with aura (MwA) (I.2), and chronic migraine (CM) (I.3) patients were enrolled in the study. Diagnoses were based on the International Classification of Headache Disorders-III beta (ICHD-3 beta) criteria (19). Participants younger than 18 years of age or older than 65 years of age, those who were unable to speak and read Turkish, and those who had less than 5 years of formal education were excluded. Data on sociodemographic and clinical characteristics, including age at onset, headache duration, headache frequency, presence of aura, headache characteristics, localization, pain intensity, triggering factors, associated features, comorbidity, and medical and family history, were gathered from all patients by headache specialists in face-to-face interviews using a structured questionnaire. A clinician performed physical and neurological examinations. Blood pressure, weight, and height measurements were performed by educated nurses using standardized equipment (Riester/Serial Number: 4012835).

ASC-12/Turkish and Migraine Disability Assessment Scale (MIDAS): Participants completed ASC 12/Turkish and MIDAS without any time restrictions. The Turkish version of MIDAS has also been validated and previously reported (20).

Statistical Analysis

The cross-test and test–retest reliabilities and internal consistency of the final version of ASC/Turkish were evaluated Pearson correlation, item-total correlation, and Cronbach alpha coefficients. An exploratory factor analysis with varimax rotation was performed to determine the structure of the scale. Independent samples t-tests and one-way ANOVA or non-parametric alternatives in the form of the Mann–Whitney U and Kruskal–Wallis tests were used to compare groups according to the distribution of dependent variables. Pearson chi-square or Fisher's exact test was used according to the expected count rule for categorical data. Categorical data were summarized as frequency and percentile, n (%), and continuous data were summarized as mean $\pm$ SD or median [IQR] according to distribution. Multiple logistic regression analyses were used to obtain the odds ratio (OR) of variables that significantly related to allodynia. Statistical analyses were performed using the PASW V.18 (SPSS Inc. Released 2009; PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.) statistical package, and p-values less than 0.05 were accepted to be significant.

RESULTS

First part: A total of 37 students were included in the cross-test (Turkish–English), and the results were compatible ($r=0.681$, $p<0.001$). A different university student group ($n=38$) completed the Turkish version of ASC, and two weeks later, a retest was administered. The test–retest reliability was acceptable ($r=0.750$, $p<0.001$). The last version of the test was given to migraine participants ($n=47$) at İstanbul Education and Research Hospital's Neurology Department, and within a two-week interval, retests were administered. The test–retest reliability was excellent ($r=0.821$, $p<0.001$).

Second part: This section of the study was performed using 344 migraine patients (283 females and 61 males) with a mean age of 36.12 ± 12.11 years. The study group comprised episodic migraine (EM) ($n=253$, 73.5%) and CM ($n=91$, 26.5%) patients. The median education of the patients was 8 [5–11] years. Patients had been suffering from migraine headaches for a median of 8 [3–16] years. Their median headache frequency was 7 [4–15] days/month, and the median duration of an attack was 24 [9–48] h.

Figure 1. Study flow

Table 1. Characteristics of migraine patients who suffer from allodynia versus those without allodynia

	Total (n=344)	ASC of 0-2 (n=126)	ASC of >2 (n=218)	p
Age*	36.12±12.11	35.06±12.78	36.73±11.69	0.216
BMI*	26.41±5.48	26.23±5.06	26.52±5.72	0.631
Systolic BP*	121.64±18.24	120.93±18.73	122.04±17.99	0.596
Diastolic BP*	77.48±12.57	76.93±11.82	77.79±12.99	0.551
Male/Female [#]	61/283	41/85	20/198	<0.001
MwA/MwoA [#]	115/229	31/95	84/134	0.008
Family history [#]	233 (67.7)	84 (66.7)	149 (68.3)	0.748
Illness duration (years) ⁺	8 [3–16]	6 [3–12]	10 [4–18]	0.008
Headache frequency (days/month) ⁺	7 [4–15]	5 [3–10]	8 [4–15]	0.001
Headache duration (h) ⁺	24 [9–48]	24 [8–48]	24 [12–48]	0.014
Headache intensity (VAS) ⁺	8 [7–9]	8 [7–9]	9 [8–10]	<0.001
Throbbing headache [#]	317 (92.2)	113 (89.7)	204 (93.6)	0.196
Smoking [#]	122 (35.5)	44 (34.9)	78 (35.8)	0.873
Nausea [#]	291 (84.6)	96 (76.2)	195 (89.4)	0.001
Vomiting [#]	143 (41.6)	44 (34.9)	99 (45.4)	0.057
Photophobia [#]	286 (83.1)	99 (78.6)	187 (85.8)	0.085
Phonophobia [#]	288 (83.7)	107 (84.9)	181 (83.0)	0.647
Medication overuse [#]	64 (18.6)	21 (16.7)	43 (19.7)	0.483
MIDAS ⁺	22 [12–45]	16 [10–35]	25 [12–55]	0.010

*Independent samples t, ⁺Mann–Whitney U, and [#]Chi-square tests were performed; data were summarized as *Mean±SD, ⁺Median [IQR], and [#]n (%). BMI: body mass index; BP: blood pressure; MwA: migraine with aura; MwoA: migraine without aura; VAS: visual analog scale; MIDAS: Migraine Disability Assessment Scale

Table 2. Item-total correlations and internal consistency coefficients

(Cronbach α) Scale	Item-total correlation	0.767 Cronbach α
1. Combing your hair	0.528	0.734
2. Pulling your hair back	0.564	0.727
3. Shaving your face	---	---
4. Wearing eyeglasses	0.496	0.739
5. Wearing contact lenses	---	---
6. Wearing earrings	0.445	0.749
7. Wearing a necklace	0.360	0.758
8. Wearing tight clothing	0.346	0.759
9. Taking a shower (when shower water hits your face)	0.412	0.750
10. Resting your face or head on a pillow	0.556	0.729
11. Exposure to heat (e.g., cooking, washing your face with hot water)	0.365	0.756
12. Exposure to cold (e.g., using an ice pack, washing your face with cold water)	0.279	0.767

According to clinical examinations, the frequencies of migraine-associated symptoms were as follows: aura in 33.4%, nausea in 84.6%, phonophobia in 83.7%, photophobia in 83.1%, and vomiting in 41.6% of the patients. Medication overuse headache was present in 18.6% of the patients. A family history of migraine or undiagnosed recurrent headache was present in 67.7% of the patients. The ICHD-III beta diagnosis and demographic characteristics of the study population are demonstrated in Table 1. If we

assume patient to be allodynic when the ASC-12 score is >2, as in the original article, the frequency of CA was 63.4% (n=218).

ASC-12 factor analysis: The internal consistency of the checklist was assessed via the Cronbach alpha value and was found to be acceptable (0.767). The item-total correlation coefficients for each question ranged from 0.279 to 0.564, except for the items shaving your face (Q3) and wearing contact lenses (Q5). Items Q3 and Q5 were answered positive by only three and five patients, respectively, and their effects on the checklist could not be calculated (Table 2). These items did not affect allodynia frequency (Table 3). The most commonly identified symptoms of allodynia were “pulling your hair” (Q2), “combing your hair” (Q1), and “resting your face or head on a pillow” (Q10) (Table 3).

Three factors emerged from the 10-item factor analyses (KMO=0.792, Barlett's $p<0.001$). Similar to the original checklist, these factors were mechanical dynamic (Q1 and Q2), static (Q4, Q6, Q7, and Q8), and thermal allodynia (Q9, Q10, Q11, and Q12).

CA-associated factors: We examined the associations of CA with headache symptoms and migraine characteristics and found statistically significant differences between patients with and without CA. CA was more common among MwA patients ($p=0.008$) and among females ($p<0.001$). CA was also associated with the presence of nausea ($p=0.001$), headache duration ($p=0.014$), headache frequency ($p=0.001$), headache severity ($p<0.001$), and MIDAS scores ($p=0.010$). There were no differences in terms of age, blood pressure, body mass index, or family history for migraine (Table 1).

Allodynia severity based on checklist scores: According to the original article, we classified CA severity as follows: no CA (scores of 0–2), mild CA (scores of 3–5), moderate CA (scores of 6–8), and severe CA (scores of ≥ 9). Using these scores, we found that 63.4% of the mi-

Table 3. Prevalence of cutaneous allodynia symptoms in the patient group

Questions (1–12)	Total (n=344)	ASC of 0–2 (n=126)	ASC of >2 (n=218)	p
1. Combing your hair	178 (51.7)	12 (9.5)	166 (76.1)	<0.001
2. Pulling your hair back	198 (57.6)	16 (12.7)	182 (83.5)	<0.001
3. Shaving your face	5 (1.5)	1 (0.8)	4 (1.8)	0.656
4. Wearing eyeglasses	95 (27.6)	2 (1.6)	93 (42.7)	<0.001
5. Wearing contact lenses	3 (0.9)	0 (0.0)	3 (1.4)	0.302
6. Wearing earrings	33 (9.6)	0 (0.0)	33 (15.1)	<0.001
7. Wearing a necklace	27 (7.8)	0 (0.0)	27 (12.4)	<0.001
8. Wearing tight clothing	36 (10.5)	1 (0.8)	35 (16.1)	<0.001
9. Taking a shower (when shower water hits your faces)	66 (19.2)	3 (2.4)	63 (28.9)	<0.001
10. Resting your face or head on a pillow	188 (54.7)	15 (11.9)	173 (79.4)	<0.001
11. Exposure to heat (e.g., cooking, washing your face with hot water)	71 (20.6)	5 (4.0)	66 (30.3)	<0.001
12. Exposure to cold (e.g., using an ice pack, washing your face with cold water)	78 (22.7)	7 (5.6)	71 (32.6)	<0.001

Pearson-chi square or Fisher's exact test were used according to the expected count rule data were summarized as n (%)

Table 4. Severity of cutaneous allodynia as measured by the ASC-Turkish and Headache Features and Disability

	ASC of 3–5 (mild CA) (n=74)	ASC of 6–8 (moderate CA) (n=87)	ASC of ≥9 (severe CA) (n=57)	p
Age*	37.35±12.15	36.09±11.53	36.91±11.49	0.787
BMI*	26.27±5.40	26.47±6.28	26.93±5.31	0.806
Systolic BP*	123.44±19.02	122.12±17.26	120.14±17.93	0.593
Diastolic BP*	77.76±13.76	77.62±12.44	78.09±13.07	0.978
Male/Female [#]	6/68	13/74	1/56	0.025
MwA/MwoA [#]	20/54	36/51	28/29	0.028
Family history [#]	51 (68.9)	53 (60.9)	45 (78.9)	0.075
Illness duration (years) ⁺	9 [4–17]	10 [3–17]	10 [4–20]	0.590
Headache frequency (days/month) ⁺	7 [4–15]	8 [4–15]	9 [4–20]	0.265
Headache duration (h) ⁺	24 [9–48]	24 [12–48]	48 [12–72]	0.174
Headache intensity (VAS) ⁺	8 [7–10]	9 [8–10]	9 [8–10]	0.008
Throbbing headache [#]	70 (94.6)	78 (89.7)	56 (98.2)	0.110
Smoking [#]	24 (32.4)	35 (40.2)	19 (33.3)	0.533
Nausea [#]	64 (86.5)	76 (87.4)	55 (96.5)	0.130
Vomiting [#]	29 (39.2)	33 (37.9)	37 (64.9)	0.003
Photophobia [#]	62 (83.8)	73 (83.9)	52 (91.2)	0.391
Phonophobia [#]	55 (74.3)	74 (85.1)	52 (91.2)	0.031
Medication overuse [#]	15 (20.3)	15 (17.2)	13 (22.8)	0.707
MIDAS ⁺	16 [9–39]	25 [16–55]	30 [20–78]	0.015

*One-way ANOVA, ⁺Kruskal–Wallis, and [#]chi-square tests were used; data were summarized as *Mean±SD, ⁺Median [IQR], and [#]n (%). BMI: body mass index; BP: blood pressure; MwA: migraine with aura; MwoA: migraine without aura; VAS: visual analog scale; MIDAS: Migraine Disability Assessment Scale

graineurs had CA. Allodynia was mild in 21.5%, moderate in 25.3%, and severe in 16.6% of the study group. Severe CA was nearly doubled for MwA patients when compared to migraine without aura patients (24.3% vs. 12.7%, respectively). Severe CA was also strongly related to CM when compared to EM patients (25.3% vs. 13.4%, respectively) (Figure 2). Severe CA was significantly more common in female patients ($p=0.025$). Severity of attack ($p=0.008$), vomiting ($p=0.003$), and phonophobia ($p=0.031$) and higher MIDAS scores ($p=0.015$) were also associated with severe CA (Table 4).

Multiple analysis of CA: We examined the determinants of CA in a multiple logistic regression model. The following determinants were associated with the presence of CA: (i) female gender [OR=4.45 (95% CI, 2.40–8.25), $p<0.001$], (ii) MwA [OR=1.82 (95% CI, 1.08–3.08), $p<0.026$], (iii) higher migraine attack frequency (for separate ORs, see Table 5), and (iv) longer disease duration (for separate ORs, see Table 5).

DISCUSSION

To our knowledge, this is the first study to evaluate the reliability of

an allodynia questionnaire in a Turkish-speaking population. The translation and cultural adaptation of a self-administered test to new languages are challenging. To cope with this challenge, we concurrently used multiple methods in the translation and cultural adaptation stages. At this part of the study, we used a unique method and administered the original and Turkish version of the test to healthy individuals who were capable of speaking and reading English and Turkish. With their comments, the Turkish version was re-evaluated by headache experts (Table 6). All patients were examined via face-to-face interviews by the study authors. We identified CA in 63.4% of the migraine patients if we assumed that a score of >2 is the cutoff value (1,5). The distributions of the study group reflected those in population-based studies (1,5,21). The prevalence of allodynia was reported to be 63.2% by Lipton, and it has ranged between 50% and 80% in other studies (4,5,15,16,17,22). Variations between studies could be the result of different evaluation methods. The results of a study from Turkey have shown an allodynia frequency of 61.3% among EM patients (23). Recently, Baykan et al. (24) evaluated allodynia in a large population-based study using ASC. They reported similar CA in 61.1% of migraineurs in Turkey and significant associations with duration and severity of attacks, photophobia, and phonophobia (24). Our study results are compatible with this large

population-based study. ASC has also been used to evaluate allodynia in other headache disorders such as idiopathic intracranial hypertension (25) and to investigate changes in neuronal excitability in headache patients with allodynia (26).

Factor analysis revealed a moderate accordance (0.767), and the most frequently observed symptoms of allodynia were "combing your hair," "pulling your hair," and "resting your face or head on a pillow." The items Q3 and Q5 were occasionally answered positively and did not affect the types of patients who could be excluded from the Turkish version of the checklist. Similarly, Askhenazi et al. (16) reported that the shaving-your-face item does not have an additive effect in terms of identifying allodynic patients. Lipton et al. (1) also reported the low prevalence of these items in the original study to develop the checklist. Finally, this study revealed that the 10-item version of ASC is also convenient for use in identifying allodynic patients.

CA was more common among CM and MwA participants. The results were compatible with the literature supporting the association of CA with chronicity. In a longitudinal study, CA was found to be a risk factor of chronification (3).

Figure 2. Cutaneous allodynia severity association with the ICHD-3 beta diagnosis
EM: episodic migraine; CA: cutaneous allodynia; CM: chronic migraine; MwA: migraine with aura; MwOA: migraine without aura

Table 5. Logistic associations of allodynia and possible determining factors

	Multivariate logistic analysis		
	OR	95% CI	p
MwA/MwOA	1.821	1.075–3.084	0.026
Female/Male	4.449	2.400–8.247	<0.001
Frequency (days/month)			0.004
6–14/≤5	2.300	1.302–4.061	0.004
≥15/≤5	2.198	1.207–4.000	0.010
Illness duration (years)			0.021
6–14/≤5	1.709	0.969–3.015	0.064
≥15/≤5	2.210	1.224–3.989	0.009
MwA: migraine with aura; MwOA: migraine without aura			

Table 6. Allodynia symptom checklist Turkish version (ASC/T)

Soru: Yaşadığınız şiddetli baş ağrısı sırasında aşağıdakileri yaparken cildinizde ne sıklıkta artan bir ağrı veya rahatsızlık hissi yaşarsınız?	Benim için geçerli değil	Hiçbir zaman	Nadiren	Yarısından azında	Yarısı veya yarısından daha sık
Saçınızı tararken	☐	☐	☐	☐	☐
Saçınızı toplarken (örneğin at kuyruğu yaparken)	☐	☐	☐	☐	☐
Yüzünüzü tıraş ederken	☐	☐	☐	☐	☐
Gözlük takarken	☐	☐	☐	☐	☐
Lens takarken	☐	☐	☐	☐	☐
Küpe takarken	☐	☐	☐	☐	☐
Kolye takarken	☐	☐	☐	☐	☐
Dar kıyafet giyerken	☐	☐	☐	☐	☐
Duş alırken/banyo yaparken (su yüzünüze çarptığında)	☐	☐	☐	☐	☐
Yüzünüzü veya kafanızı yastığa koyduğunuzda	☐	☐	☐	☐	☐
Isıya maruz kaldığınızda (örneğin yemek yaparken, sıcak su ile yüzünüzü yıkarken)	☐	☐	☐	☐	☐
Soğuğa maruz kaldığınızda (örneğin buz kıracağı kullanırken, soğuk su ile yüzünüzü yıkarken)	☐	☐	☐	☐	☐

We observed higher MIDAS scores in migraine patients with allodynia. Moreover, MIDAS score was associated with the severity of allodynia. Similarly, Lipton et al. (1) reported higher MIDAS scores in allodynic subjects.

We assessed the possible determinants of CA in a logistic association model and showed that female gender, MwA, headache frequency, and disease duration independently increased in the presence of CA. Our data are compatible with those from previous reports (1,3). The novel findings of the present study were that we estimated that patients experiencing >5 days/month of headache were at a 2.3-fold higher risk of developing CA and that those with ≥ 15 days/month of headache were at a 2.2-fold higher risk of developing CA. Those patients who had suffered from migraine headaches for more than 5 years were at a 1.7-fold higher risk of developing CA and those with ≥ 15 years of migraine history were at a 2.2-fold higher risk of developing CA.

CA commonness among females could be explained by the effects of gonadal hormones on pain modulating systems (27). It has been suggested that the repeated activation of trigeminal neurons and modulatory pain pathways throughout the years cause structural changes, thus leading to chronification (3,6,22). This theory is supported by evidence of iron deposition in the periaqueductal gray mater in patients with a long history of migraine (28). In addition, chronicity is associated with a greater degree of impairment in the cortical processing of sensory stimuli (29). Therefore, proposed structural changes in trigeminovascular pathway excitability and/or other brainstem pain-modulating systems also seem to be responsible for the development of allodynia.

The strengths of this study are as follows: the test–retest, cross-test, and correlation of the study group characteristics and associated factors can be used to evaluate the psychometric properties of the questionnaire. In this study, we used almost all these methods together. Although the patient group comprised neurology clinic patients, the group distributions are consistent with those in population-based studies (MwA ratio and CA prevalence). This could have resulted from the selection of consecutive patients from a general neurology outpatient clinic as opposed to a specialized headache clinic. In addition, face-to-face examinations by headache specialists provided accurate diagnoses according to the ICHD-III beta criteria.

This study has certain limitations. It is not population-based study, which is in contrast to the original study, and it might not represent the original population. The study group is small compared with that of the original study.

In this study, we established a reliable and validated self-administered CA checklist for a Turkish-speaking population. There is a growing tendency to use self-administered tests in headache clinics worldwide. We encourage the use of ASC-Turkish to assess CA in clinical practice, and it could also be helpful in the standardization of international research.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Istanbul Training and Research Hospital approved this study (Decision Number: 612/27.02.2015).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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