ORIGINAL ARTICLE

Screening general practice patients for migraine without aura: construction and validation of the Balkan Migraine Screening Questionnaire (BMSQ)

Aziz Šukalo[1], Elma Merdžanović[2], Alma Alic[3]; Muamera Vrabac-Mujčinagić[4], Esad Alibašić[5], Slobodan M. Janković[6]

[1]Bosnalijek JSC, Sarajevo, [2]Health Care Centre of Canton Sarajevo, Hadžići, [3]Health Care Centre Zenica, Zenica, [4]Health Care Centre Tuzla, Tuzla, Health Care Centre, Kalesija; Bosnia and Herzegovina, [6]University of Kragujevac, School of Medical Sciences, Kragujevac, Serbia

ABSTRACT

Aim To develop and validate a screening questionnaire for migraine without aura with sufficient diagnostic accuracy to be used in primary care settings.

Methods The study was designed as cross-sectional, multicentric, diagnostic accuracy trial of new questionnaire for screening patients who visit general practitioners, with an aim to reveal migraine without aura. The instrument was constructed for the purpose of this study, and validated on the sample of 429 primary care outpatients. The gold standard of diagnosing migraine without aura was clinical estimate by a neurologist based on the International Classification of Headache Disorders 3rd edition (ICHD-III) criteria. Diagnostic accuracy of the instrument was tested through construction of the Receiver Operator Curve.

Results The Balkan Migraine Screening Questionnaire (BMSQ) instrument showed good diagnostic accuracy (sensitivity 83.4% and specificity 79.9%) for migraine without aura, with significant screening yield among previously undiagnosed patients of 75.9%. The study also confirmed a high percentage of patients with hidden migraine without aura (MWA) (52.9%) revealed by the BMSQ and the ICHD-III criteria that would otherwise remain undiagnosed.

Conclusion The BMSQ is a valid and reliable clinical instrument for revealing migraine without aura, which could be easily self-administered by patients. It has high screening yield, discovering majority of patients with previously undiagnosed migraine without aura, whose definite diagnosis should later on be confirmed by the attending physicians using the ICHD-III criteria.

Key words: diagnosis, migraine without aura, questionnaire design, screening migraine disorders, validation studies

Corresponding author:
Slobodan M. Janković
School of Medical Sciences,
University of Kragujevac
Svetozara Markovica Street, 69,
34000 Kragujevac, Serbia
Phone: +381 34 306 800;
Fax: +381 34 505 010;
E-mail: slobnera@gmail.com
ORCID ID: http://www.orcid.org/0000-0002-1519-8828

Original submission:
15 March 2019;
Revised submission:
08 April 2019;
Accepted:
10 April 2019.
doi: 10.17392/1021-19

Med Glas (Zenica) 2019; 16(2): 311-316

INTRODUCTION

Migraine is a type of headache which almost completely incapacitates a sufferer during the attack. According to the International Classification of Headache Disorders 3rd edition (ICHD-III) there are two main types of migraine: with and without aura (1). The diagnosis of migraine without aura (MWA) could be ascertained if the following criteria were met: at least 5 atacks of headache in the past; duration of the attack 4-72 hours; at least two of the following - unilateral, pulsating, moderate or severe headache deteriorating with physical activity; and appearance of at least one of these symptoms: nausea and/or vomiting, photophobia and phonophobia. The prevalence of migraine is high, and varies from nation to nation: e.g. in Japan the prevalence is 14% in general population, and about 18% in women (2), while the prevalence in the United States of America amounts to 14.9% in total (20.2% in women and 9.4% in men) (3). About 57% of patients with migraine suffer from 'migraine without aura' type (4).

Although there are clinical criteria for diagnosing migraine without aura, standardized questionnaires with high diagnostic accuracy and administered by the patients themselves could be of great help to reveal patients with undiagnosed MWA in busy and often understaffed primary care settings. Almost 30 to 59% of patients with MWA are undiagnosed and improperly treated, mainly because they were not given enough attention in the primary care (5,6). Although a questionnaire for screening migraine (MS-Q – Migraine Screen Questionnaire) with good diagnostic accuracy (sensitivity 82% and specificity 97%) was developed and validated (7), showing good screening performance (8), it is rather general and not focused on the MWA. Since the role of a general practitioner is crucial for revealing MWA (9), questionnaires that are simple but more focused to the MWA may significantly improve screening results.

The aim of our study was to develop and validate a screening questionnaire for migraine without aura with sufficient diagnostic accuracy to be used in primary care settings.

PATIENTS AND METHODS

Patients and study design

The study was designed as cross-sectional, multicentric, diagnostic accuracy trial of new questionnaire for screening patients who visit general practitioners, with an aim to reveal migraine without aura. The instrument was constructed for the purpose of this study, and validated on the primary care outpatients.

The study was conducted in the first half of 2018 on primary care outpatients from the following cities in Bosnia and Herzegovina (B&H): Sarajevo, Hadžići, Zenica, Tuzla and Kalesija. The inclusion criteria were: the patients visiting general practitioners of the public heath care system, of both sex, age between 18 and 65 years, with normal cognition as judged by the attending general practitioners, literate and agreed to sign the informed consent. The exclusion criteria were: pregnancy, schizophrenia, major depression, bipolar disorder, epilepsy, acute diseases that distract the attention of a patient, and reporting any type of aura in relation to the headache.

The study was approved by the Ethics Committee of the Clinical Center of Kragujevac.

The sample was consecutive, i.e. all patients within the study period that fulfilled inclusion criteria and did not meet exclusion criteria were enrolled after signing the informed consent.

Methods

Development of the new questionnaire with a working title „ the Balkan Migraine Screening Questionnaire" (BMSQ) was undertaken according to the guidelines set by Robert F. DeVellis (10,11) in six steps. In the first step (determining object of measurement) migraine without aura was chosen as an object of measurement since it is a separate entity within the framework of headaches and the most frequent among the migraine headache types. The second step, generating an item pool, was conducted at two meetings of the authors one week apart. In the third step (determining format for measurement) the items were formulated as closed, and each item reflected one element of diagnosis of migraine without aura. Each item had two answeres offered, "Yes" or "No". The fourth step (revision and correction

of the -initial pool of items) was made by a five-member expert committee composed of two specialists of neurology and three experienced general practitioners. Every member of the committee evaluated each item in regard to the relevance (1 – not relevant, 2 – the item should be modified, 3 – relevant item, but minimal changes are neccessary and 4 – very relevant item) and clarity (1 – not clear, 2 – the item should be modified, 3 – the item is clear, but minimal changes are neccessary and 4 – very clear item). For each item the content validity index was calculated: number of marks 3 or 4 divided by number of experts, i.e. with 5 in this case. Only the items with the content validity index of 0.8 or more were retained in the final questionnaire (12). Within the fifth step one validation item for discovering socially desirable behavior of respondents was included in the questionnaire: "I always try to help other patients." In the sixth step the initial pool of the BMSQ's items was tested on 10 primary care patients for clarity and comprehension. After the pilot testing certain minor changes were made, and the final version of the BMSQ was copied and prepared for testing diagnostic accuracy on the study sample (Table 1).

Table 1. Items of the final version of the Balkan Migraine Screening Questionnaire (BMSQ) scale

Item	Answers
Is your headache long lasting (4 hours or more)?	Yes No
Is your headache mostly present at one side of the head (left or right)?	Yes No
Does your headache have a pulsating character?	Yes No
Does physical activity aggravate your headache?	Yes No
Do you have an urge to vomit after you get the headache?	Yes No
Do sounds, scents or light bother you after you get the headache?	Yes No

The questionnaire was self-administered by the study subjects. As a gold standard of diagnosing migraine without aura we used clinical estimate by an independent neurologist based on the ICHD-III criteria: at least four of them should be present: at least 5 atacks of headache in the past; duration of the attack 4-72 hours; at least two of the following - unilateral, pulsating, moderate or severe headache deteriorating with physical activity; and appearance of at least one of these symptoms: nausea and/or vomiting, photophobia and phonophobia (1). Diagnostic accuracy of the BMSQ was tested for all possible values of its score (since the answers to each of 6 questions were either "Yes" or "No", which was coded with 1 and 0, respectively, there were in total 7 possible score values: 0, 1, 2, 3, 4, 5 and 6). Based on the calculated values of sensitivity and specificity for each score value we constructed the Receiver Operating Characteristics curve abbreviated as ROC curve, and calculated the area under the curve (13). The ROC curve was drawn by the online software „Cut-off Finder" (available at: http://molpath.charite.de/cutoff/index.jsp). Furthermore, by graphic Manhattan method and Youden's statistics the cut-off value with the highest sensitivity and specificity was found (14), and Cohen Kappa together with diagnostic accuracy indexes (sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio) were calculated for BMSQ using this cut-off point.

Statistical analysis

Characteristics of the study sample were described using descriptive statistics by rates and percentages when categorical in nature, and by means and standard deviations when continuous.

RESULTS

In total 429 patients visiting general practitioners in primary health care centres of Bosnia and Herzegovina took part in the study. Mean age of patients was 46.4 ± 12.7 years. Female patients were more numerous and somewhat younger (46.0 ± 12.7 years) than male patients (47.6 ± 12.6 years). According to the ICHD-III, the criteria for migraine without aura were met in 195 (62.5%) females and in 70 (59.8%) males, based on clinical judgement (Table 2).

The area under the ROC curve for BMSQ was 0.89 (Figure 1).

The cut-off point of the BMSQ score with maximal sensitivity and specificity calculated by Manhattan graphical method and Youden's statistics was 3.5, i.e. four or more responses „Yes" to the items of the BMSQ. Sensitivity and specificity of the BMSQ for this cut-off point were higher and equal to 80%, respectively, indicating satisfactory accuracy (Table 3).

The Cohen Kappa coefficient of agreement between diagnosis of migraine without aura by

Table 2. Characteristics of 429 study participants

Variable	No (%) of participants
Gender	
Females	312 (72.7)
Males	117 (27.3)
Education	
Elementary school	50 (11.7)
High school	265 (61.8)
Higher education	114 (26.5)
Primary reason for visiting a general practitioner	
Cardiovascular disorder	78 (18.2)
Respiratory disorder	9 (2.1)
Psychiatric disorder	11 (2.6)
Neurological disorder	226 (52.7)
Gastrointestinal disorder	10 (2.3)
Musculoskeletal disorder	26 (6.1)
Endocrinological disorder	17 (4.0)
Infection	37 (8.6)
Other	15 (3.5)
Previous diagnosis of migraine without aura	
Yes	117 (27.3)
No	312 (72.7)
Family diagnosis of migraine	
Yes	142 (33.1)
No	287 (66.9)
Smoking	
Yes	151 (35.2)
No	278 (64.8)
Drinking coffee	
Yes	370 (86.2)
No	59 (13.8)
Diagnosis of migraine without aura according to the International Headache Society (IHS) criteria	
Yes	265 (61.8)
No	164 (38.2)

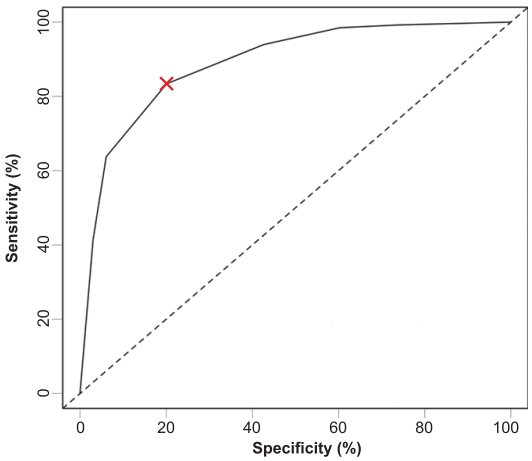

Figure 1. The Receiver Operator Curve (ROC) for the Balkan Migraine Screening Questionnaire (BMSQ) score as a positive marker for the diagnosis of migraine without aura according to the International Headache Society criteria
X, cut-off point

the BMSQ score ≥ 4 and diagnosis by the ICHD-III criteria (gold standard) was 0.625 (standard error 0.039; p=0.000).

Among the patients who did not have diagnosis of migraine without aura before participation in the study (n = 312), 154 (49.4%) met the ICHD-III criteria and were newly diagnosed („de novo“) as having the MWA. The BMSQ with cut-off score of 4 correctly made diagnoses of the MWA in 117 (75.9%) newly diagnosed patients suggesting a significant screening yield. On the other hand, six (5.1%) patients from those who had diagnosis of migraine without aura before the study did not meet the ICHD-III criteria; the BMSQ correctly classified these patients as not having the MWA, but it also wrongly classified five (4.3%) patients as not having the MWA, while they actually met the ICHD-III criteria.

The so-called „hidden migraine without aura“ was found in 58.1%, i.e. there were 154 patients with *de novo* diagnosis out of total 265 migraine patients without aura diagnosed by both ICHD-III criteria and BMSQ.

DISCUSSION

The BMSQ instrument showed good diagnostic accuracy (sensitivity 83.4% and specificity 79.9%) for migraine without aura, with significant screening yield among previously undiagnosed patients of 75.9%. The study also confirmed a high percentage of patients with hidden MWA (58.1%) revealed by the BMSQ and ICHD-III criteria that would otherwise remain undiagnosed.

The diagnosis of migraine without aura is usually established by checking compliance with the ICHD-III criteria of patients with frequent headaches, either through interviewing them or using headache diaries or structured input forms for headaches (15). However, these methods take considerable time to complete and require familiarity of attending physicians with the ICHD-III criteria, which makes them unsuitable for the use in primary care settings. Unfortunately, to date

Table 3. Accuracy of the Balkan Migraine Screening Questionnaire (BMSQ) instrument when used for screening of migraine without aura

Questionnaire	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ratio	Accuracy
BMSQ	83.4% (78.4% - 87.7%)	79.9% (72.9% - 85.7%)	87.0% (83.1% - 90.1%)	74.8 % (69.2% - 79.7%)	4.1 (3.0 - 5.6)	0.2 (0.2 - 0.3)	82.1% (78.1% - 85.6%)

*95% confidence intervals are shown in parenthesis

only two short questionnaires were developed and validated for rapid diagnosis and screening of migraine in general, the three-item ID-Migraine (focusing to headache disability, nausea, and photophobia) (15) and the five-item MS-Q (referring to the ICHD-III criteria) (7). Both questionnaires have solid diagnostic accuracy (sensitivity and specificity 0.82 and 0.75 for ID-Migraine, and 0.82 and 0.97 for MS-Q, respectively), but are not targeted to migraine without aura. The items of the BMSQ are somewhat more corresponding to the ICHD-III criteria for diagnosing the MWA, although it did not result with much higher sensitivity and specificity. However, this could have been the consequence of unusually high prevalence of MWA in the study sample (61.8%), which was not representative of the general population in Bosnia & Herzegovina.

There is an ongoing debate whether migraine with and without aura are separate clinical entities, or just two variations of the same one. Proponents of the second opinion stress commonalities in the pathophysiology of both migraine types (16), while the opponents underline differences in epidemiology, clinical picture, patient behaviour during attacks, age at onset and age at resolution, the pattern of attacks, risk factors, comorbidities and response to drugs (17). However, even if pathophysiology is common, the two migraine types do produce different symptoms and signs, which are accompanied by differences in the patients' perception of their disorder. These differences require separate communication patterns when taking the patients' history, and this explains why questionnaires for diagnosing migraine with and without aura should differ. Like the MS-Q and the ID-Migraine, the BMSQ is not differentiating between the two migraine types, but may reveal the MWA cases which, due to the absence of aura, could be misdiagnosed as some other type of headache. The fact that the BMSQ was targeted to the MWA is further confirmed by a relatively high value of Cohen's Kappa coefficient (0.625), which corresponds to moderate agreement (18) between the BMSQ score ≥ 4 and the diagnosis of the MWA by the ICHD-III criteria specific for this migraine type.

Besides having considerable validity and reliability, the BMSQ has a significant screening yield, since positive predicted value was high (87%) in our study, and the test correctly recognized 75.9% of previously undiagnosed MWA cases. The prevalence of the MWA was higher in our patient sample than that in general population, which may explain so high yield, but according to general recommendations for screening tests, prevalence of migraine without aura is high enough to justify the use of the BMSQ for screening purposes (19). It is illustrated by overall accuracy of the BMSQ, which was 82.1% in our study sample, but decreased just a little to 79.6% when actual prevalence of MWA (8.5%) in general population was taken into account (19).

The main limitation of our study was the use of an unrepresentative sample with high prevalence of MWA to test reliability, validity and screening yield of the BMSQ, but it was dictated by availability of the study sites, some of them being linked to neurology departments of nearby hospitals more than average primary care facilities. It could contribute to overestimation of the screening yield, which should be taken into account when utility of the BMSQ for screening purposes is judged upon.

In conclusion, the BMSQ is valid and reliable clinical instrument for revealing migraine without aura, which could be easily self-administered by the patients. It has high screening yield, discovering majority of patients with previously undiagnosed migraine without aura, whose definite diagnosis should be later on confirmed by the attending physicians using the ICHD-III criteria.

ACKNOWLEDGEMENTS

The authors want to thank the following colleagues for their precious help in regard to recruiting patients and collecting the study data: Prof. Siniša Miljković, MD, DSc, Neurology Clinic, University Clinical Centre Banja Luka, Bosnia & Herzegovina, Merita Tirić Čampara, MD, DSc, Neurology Clinic, University Clinical Centre Sarajevo, Bosnia & Herzegovina, and Nataša Pejanović Škobić, MD, MSc, Neurology Clinic, University Clinical Hospital, Mostar, Bosnia & Herzegovina.

FUNDING

No specific funding was received for this study.

TRANSPARENCY DECLARATION

Conflicts of interest: None to declare.

REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders. 3rd edition. Cephalalgia 2018; 38:1–211.
2. Katsarava Z, Buse DC, Manack AN, Lipton RB. Defining the differences between episodic migraine and chronic migraine. Curr Pain Headache Rep 2012; 16:86-92.
3. Burch RC, Loder S, Loder E, Smitherman TA. The prevalence and burden of migraine and severe headache in the United States: updated statistics from government health surveillance studies. Headache 2015; 55:1-34.
4. Rasmussen BK, Olesen J. Migraine with aura and migraine without aura: an epidemiological study. Cephalalgia 1992; 12:21-8.
5. Di Piero V, Altieri M, Conserva G, Petolicchio B, Di Clemente L, Hettiarachchi J, "General Practitioners' Co-operative" of the Casilino district of Rome. The effects of a sensitisation campaign on unrecognised migraine: the Casilino study. J Headache Pain 2007; 8:5–8.
6. De Diego EV, Lanteri-Minet M. Recognition and management of migraine in primary care: influence of functional impact measured by the headache impact test (HIT). Cephalalgia 2005; 25:184–90.
7. Láinez MJ, Domínguez M, Rejas J, Palacios G, Arriaza E, Garcia-Garcia M, Madrigal M. Development and validation of the Migraine Screen Questionnaire (MS-Q). Headache 2005; 45:1328-38.
8. Láinez MJ, Castillo J, Domínguez M, Palacios G, Díaz S, Rejas J. New uses of the Migraine Screen Questionnaire (MS-Q): validation in the Primary Care setting and ability to detect hidden migraine. MS-Q in Primary Care. BMC Neurol 2010; 10:39.
9. Lantéri-Minet M. The role of general practitioners in migraine management. Cephalalgia 2008; 28 Suppl 2: 1–8.
10. DeVellis RF. Scale Development, Theory and Applications. 2nd Ed. London: SAGE Publications, 2003.
11. Streiner DL, Norman GR. Health Measurement Scales - a Practical Guide to Their Development and Use. 4th Ed. Oxford: Oxford University Press, 2008.
12. Zamanzadeh V, Ghahramanian A, Rassouli M, Abbaszadeh A, Alavi-Majd H, Nikanfar A-R. Design and Implementation Content Validity Study: Development of an instrument for measuring Patient-Centered Communication. J Caring Sci 2015; 4:165–78.
13. Janković S. Dizajn istraživanja. 1st Ed, Kragujevac: Medrat, 2016.
14. Budczies J, Klauschen F, Sinn BV, Győrffy B, Schmitt WD, Darb-Esfahani S, Denkert C. Cutoff Finder: A comprehensive and straightforward Web application enabling rapid biomarker cutoff optimization. PLoS One 2012; 7:e51862.
15. Peng KP, Wang SJ. Migraine diagnosis: screening items, instruments, and scales. Acta Anaesthesiol Taiwan 2012; 50:69-73.
16. Purdy RA. Migraine with and without aura share the same pathogenic mechanisms. Neurol Sci 2008; 29:44-6.
17. Manzoni GC, Torelli P. Migraine with and without aura: a single entity?. Neurol Sci 2008; 29 Suppl 1: S40-3.
18. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med 2012; 22: 276-82.
19. Alberg AJ, Park JW, Hager BW, Brock MV, Diener-West M. The use of "overall accuracy" to evaluate the validity of screening or diagnostic tests. J Gen Intern Med 2004; 19:460-5.