Evaluation of the new ICHD-III beta cluster headache criteria

IF de Coo¹, LA Wilbrink¹, J Haan¹,², MD Ferrari¹ and GM Terwindt¹

Abstract

Aim: In the revised criteria of the International Classification of Headache Disorders (ICHD-III beta) the following items are added to the diagnostic criteria of cluster headache: ipsilateral sensation of fullness in the ear and ipsilateral forehead/facial flushing. We evaluated the possible additional value of these symptoms for diagnosing cluster headache.

Methods: In this cross-sectional cohort study of (potential) cluster headache patients we investigated these additional symptoms using a Web-based questionnaire. Patients not fulfilling the ICHD-II criteria for cluster headache but fulfilling the ICHD-III beta criteria were interviewed.

Results: Response rate was 916/1138 (80.5%). Of all 573 patients with cluster headache according to ICHD-II criteria, 192 (33.5%) reported ipsilateral ear fullness and 113 (19.7%) facial flushing during attacks. There was no difference in reporting ipsilateral ear fullness and facial flushing between patients who received a diagnosis of cluster headache and patients who did not. None of the patients who did not fulfill all ICHD-II criteria could be categorized as cluster headache according to the ICHD-III beta criteria.

Conclusion: The results of this study do not support the addition of ear fullness and facial flushing to the new ICHD-III beta criteria.

Keywords
Cluster headache, diagnosis, classification, facial flushing, ear fullness, ICHD criteria

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Introduction

As there is no definitive biological marker, a diagnosis of cluster headache is based on patient history, applying diagnostic criteria as offered by the International Classification of Headache Disorders (ICHD) since 1988 (ICHD-I) (1). In the revision of 2004 (ICHD-II), an adjustment was made to these criteria, as a sense of restlessness or agitation as a possible accompanying symptom during a cluster headache attack was added. Furthermore, the duration of remission periods in chronic cluster headache was changed from a maximum of a fortnight to one month (2). Recently, the new ICHD-III criteria beta version was published (3). The following possible accompanying symptoms have been added for the diagnosis of cluster headache in this version: i) the presence of ipsilateral sensation of ear fullness, and ii) ipsilateral forehead and facial flushing. The validity of these new diagnostic criteria remains to be established. The aim of this study was to investigate the presence of these additional symptoms in our Leiden University Cluster headache neuro-Analysis program (LUCA) population, which encompasses self-reported cluster headache patients: patients fulfilling the ICHD-II criteria for cluster headache and patients who fail one or more of the cluster headache criteria. We aimed to assess how many patients who did not fulfill the previous ICHD-II criteria would be diagnosed as cluster headache according to the new ICHD-III beta version.

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Material and methods

Study setting and patient selection

This cross-sectional cohort study was conducted as part of the LUCA program. The LUCA population is a nationwide cohort of self-reported cluster headache patients age 18 years and older. Patients can enroll in the LUCA program through a Web-based database that was promoted through different kinds of media. In addition, patients attending our outpatient headache clinic were also invited to participate in this program.

First, if patients fulfilled a set of screening criteria, they were sent a Web-based extended cluster headache questionnaire, based on the ICHD-II criteria (2). This questionnaire was proven valid and accurate by performing a semi-structured telephone interview in 291 patients who had filled out the extended cluster headache questionnaire (4). Using the interview as the gold standard, the algorithm of the extended cluster headache questionnaire has a specificity of 0.89. We consider the cohort a well-defined Web-based cohort.

Secondly, all patients were asked to fill out an additional questionnaire about ear fullness and facial flushing.

We used Web-based questionnaires, except for patients without the ability to use the Internet, who were allowed to fill out the questionnaires on paper. Only patients who filled out all the necessary items were included in this study.

Approval for the study was obtained by the local medical ethics committee of the Leiden University Medical Center. All participants provided written informed consent.

Classification

Previously, the ICHD-II criteria were used to diagnose cluster headache in the LUCA program. We compared cluster headache patients diagnosed according to the ICHD-II criteria with those diagnosed according to ICHD-III criteria beta version thus adding ipsilateral sensation of ear fullness and ipsilateral forehead and facial flushing as criteria. For a compact overview of the criteria for cluster headache according to the ICHD-II and ICHD-III-beta version, refer to Supplementary Table 1. Patients who did not receive the diagnosis of cluster headache based on ICHD-II but fulfilled a cluster headache diagnosis based on the newly added criteria in the ICHD-III beta version (ear fullness and facial flushing) were directly interviewed (by IFC) for validation.

Statistics

Comparisons between responders and non-responders and subgroups of our LUCA population were performed by using a Mann-Whitney test or Kruskal-Wallis test for ordinal data and \( \chi^2 \)-test for nominal data. Data analyses were performed using SPSS 20.0 (SPSS Inc, IBM, USA). The statistical threshold was set to \( p < 0.05 \).

Results

Of the 1138 LUCA patients who entered our Web-based recruitment system, 916 patients (80.5%) returned our questionnaires on ear fullness and facial flushing (Figure 1). Non-responder analyses showed that non-responders were younger, more often females and were more often diagnosed as “no cluster headache according to the ICHD-II criteria.” The clinical characteristics of the responders and non-responders are summarized in Supplementary Table 2.

According to the ICHD-II criteria, 573/916 (62.6%) patients were diagnosed as having cluster headache. The remaining 343/916 (37.4%) patients did not fulfill the ICHD-II criteria and therefore were not classified as having cluster headache: A total of 216/343 patients were missing one ICHD-II criterion and 127/343 patients were missing more than one ICHD-II criterion (Figure 1). Table 1 shows the demographic characteristics of the patients and reported autonomic symptoms. Patients fulfilling the ICHD-II criteria were significantly more often men (\( p < 0.001 \)), and a higher proportion reported a diagnosis of cluster headache by a physician (\( p < 0.001 \)). The number of autonomic symptoms was significantly higher (\( p < 0.001 \)) among patients with a cluster headache diagnosis.

In 215 out of 216 patients missing one ICHD-II criterion, autonomic symptoms or restlessness was not the
missing criterion. Most often duration or frequency of attacks deviated from the criteria. In one out of 216 patients (0.5%), accompanying autonomic symptoms or restlessness was the missing criterion. This participant reported ear fullness during cluster headache attacks in the additional questionnaire, but failed to recall this in the direct telephone interview. The new version of ICHD criteria did not lead to a diagnosis of cluster headache in this participant (Figure 2).

Of all patients classified with cluster headache according to the ICHD-II criteria, 192/573 (33.5%) reported ipsilateral ear fullness and 113/573 (19.7%) ipsilateral facial flushing as shown in Table 2. Ipsilateral ear fullness was reported in 87/216 (40.3%) patients classified as missing one ICHD-II criterion and 41/216 (19.0%) patients classified as missing two or more ICHD-II criteria for cluster headache. There was no significant difference in the newly added autonomic symptoms between patients diagnosed according to the ICHD-II criteria as having cluster headache and those missing one or more criteria for cluster headache.

**Discussion**

This is the first study that investigated the value of the newly added autonomic accompanying symptoms for diagnosing cluster headache. One-third of cluster headache patients reported ipsilateral ear fullness and 20% ipsilateral facial flushing during attacks. However, there was no significant difference of these reported symptoms compared with patients who did not fulfill cluster headache criteria. Most important, none of the patients who previously did not fulfill all criteria for cluster headache could now be categorized as having cluster headache according to the new ICHD-III criteria.
There is no consensus in the literature about the value of facial flushing in cluster headache. Facial flushing has often been reported during cluster headache attacks (5,6). It was even used for the diagnosis in one of the pre-ICHD criteria (7). After applying these previous criteria, others, however, have suggested that facial flushing is not a symptom of cluster headache because it was not observed at all in their cluster headache population (8).

Ipsilateral ear fullness has been reported only once before as an accompanying symptom in a case of cluster headache. However, in this report the limited description of the symptoms did not allow the application of the ICHD criteria for cluster headache, so a diagnosis remains doubtful (9).

Facial flushing and ear fullness were often reported in our cluster headache population. However, there was no difference in the presence of these autonomic symptoms between the patients diagnosed as having cluster headache and patients missing one or more criteria for the diagnosis of cluster headache according to the ICHD-II criteria in this study. Therefore, the additional diagnostic value for using these newly added symptoms seems low. Comparably, there has been a proposal for alternative diagnostic criteria for migraine without aura in the ICHD-II criteria using at least two of five associated symptoms (nausea, vomiting, phonophobia, photophobia and osmophobia) during an acute migraine attack. Although osmophobia was often reported in these migraine patients, it had a low sensitivity for diagnosing migraine and was therefore not added to the ICHD-III beta version criteria for migraine without aura (10).

None of our patients who missed one ICHD-II criterion to be diagnosed as cluster headache could be diagnosed as having cluster headache according to the new criteria, showing thereby the diagnostic gain of adding the new autonomic features is limited.

The strengths of this study are the large sample size, well-defined cohort and high response rate of more than 80%. A possible limitation is that not all patients received a gold-standard verification of diagnosis by a physician. However, validation of our questionnaire showed high specificity in a previous study (4).

In summary, the results of this study do not support the addition of ear fullness and facial flushing to the new ICHD-III beta criteria.

Table 2. Ipsilateral feeling of ear fullness and facial flushing reported in the responders of the LUCA population according to the ICHD-II.

<table>
<thead>
<tr>
<th></th>
<th>All patients (N = 916)</th>
<th>Cluster headache (N = 573)</th>
<th>No cluster headache Missing 1 criterion (N = 216)</th>
<th>Missing &gt; 1 criterion (N = 127)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear fullness&lt;sup&gt;a&lt;/sup&gt;, n (%)</td>
<td>316 (34.5)</td>
<td>192 (33.5)</td>
<td>87 (40.3)</td>
<td>37 (29.1)</td>
<td>0.080</td>
</tr>
<tr>
<td>Facial flushing&lt;sup&gt;a&lt;/sup&gt;, n (%)</td>
<td>176 (19.2)</td>
<td>113 (19.7)</td>
<td>41 (19.0)</td>
<td>22 (17.3)</td>
<td>0.970</td>
</tr>
</tbody>
</table>

LUCA: Leiden University Cluster headache Analysis program; ICHD-II: the International Classification of Headache Disorders, second edition.
<sup>a</sup>During a cluster headache attack.

Article highlights
- Ipsilateral ear fullness and ipsilateral facial flushing is often reported in patients fulfilling but also in those not fulfilling the International Classification of Headache Disorders, second edition (ICHD-II) criteria for cluster headache. Therefore the additional diagnostic value for using these two newly added symptoms seems low.
- The results of this study do not support the addition of ear fullness and facial flushing to the new ICHD-III beta criteria.

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References