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World Headache Society's Definition of Refractory Migraine

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ABSTRACT

To expand the current description of refractory migraine, the World Headache Society advocates the use of both simple and complex definitions. Simple would be for the general use of patients and support groups, and complex for research and clinical purposes. These definitions include the roles of preventive and abortive medications, non-medication treatments, medication overuse headache (MOH), and a refractory scale to rate severity. The complex definition provides criteria for the categorization of responses to both abortives and preventives based on the availability of migraine treatments in different countries. It is suggested that refractoriness is defined as failure of adequate trials of at least 3 classes of preventives or 2 classes of abortives. For countries with limited access to both preventive and abortive therapies, the patient should have failed at least half of the available preventive classes, or all of the classes of the available abortive therapies. The rationale behind the definitions is discussed in the subsequent sections.

Keywords: Headache; Refractory; Definition; Classification; Terminology; Syndromes

1 INTRODUCTION

When an individual has persistent headaches that fail to improve after a trial of the standard treatments, the term "refractory migraine" is often used in clinical practice.[(1)] This term was coined by Reisman in 1952.[(2)] Since then, a number of definitions for refractory migraines have been proposed.[(3–7)] However, the current definition is appropriate primarily for countries where there is a wide array of treatments available, including OnabotulinumtoxinA and CGRP medications. There is no mention in the current definitions of abortive approaches. Moreover, the role of medication overuse headache (MOH) is unclear in current definitions. There is no scale to separate milder patients from the more severe refractory migraineurs. It is also noted that current definitions focus on refractory chronic migraine. We have chosen to define refractory migraine.

This paper outlines the proposed definition of refractory migraine and the rationale behind the definition. In addition, other topics such as abortive medications, MOH, and a refractory scale have been included. To expand the current definition of refractory migraine, we would like to suggest both simple and complex definitions. Simple would be for easy general use, and complex for research and headache specialists. In the future, a panel of headache experts from the regional directorates of the World Headache Society will publish a consensus document.

2 OBJECTIVES FOR A REVISED DEFINITION

To standardize terminology and agree on working definitions in order to

1. Provide a clear definition of refractory migraines for:
   (a) Headache specialists
   (b) Researchers in headache medicine
   (c) All clinicians and allied healthcare professionals
   (d) Patients and caregivers
   (e) Policy makers and patient advocacy groups
2. Classify headaches in terms of severity and disability across the lifespan (pediatric, adult, elderly).
3. To include responses to abortives as well as preventive therapies

3 DEFINITION OF REFRACTORY MIGRAINE

3.1 Simple definition

The migraines have not been adequately controlled by medications or non-medication approaches (non-pharmacological).

Note: This definition is drafted for the general use of patients, primary caregivers and patient advocate groups.

3.2 Complex definition of refractory migraine

The migraines have not been adequately controlled by medications or non-medication approaches (non-pharmacological). Migraine is defined according to the International Classification of Headache Disorders-3. In addition, migraine mimics and secondary migraines have been excluded, as discussed in the World Headaches Society's WHIS-MCH1 Classification Group 1, Syndrome of Migraine. [8,9]

The migraines may be refractory to preventives, abortives, or to both. Not all patients have required preventive medications. If they have only been taking abortives, but these have failed, they do have refractory migraine (but just to abortive therapies). In addition, MOH will have been addressed prior to designating the patient as having refractory migraine.

Note: This definition is drafted for the use of clinicians, allied medical professionals, and researchers in the field of headache medicine.

4 EXPLANATORY NOTES

4.1 Non — Medication Approaches

Non-medication approaches have failed to achieve adequate relief. Not all patients are able to utilize most of the non-medication therapies, but attention to the usual lifestyle changes should have been attempted. At least one of the following measures should have been utilized: meditation, biofeedback, other relaxation approaches, psychotherapy, yoga, acupuncture, massage, physical therapy, and others. [10–12]

4.2 Preventive Medications or Preventive Injections

4.2.1. For patients who have had access to almost all migraine medications, including OnabotulinumtoxinA and CGRP monoclonal antibodies:

The preventive approaches have failed to reduce the impact of the migraines by at least 50%, as evidenced by a headache diary. [13,14] The patient should have failed on at least 3 classes of migraine preventives.

Failure was either inadequate relief from an adequate trial of the medication for at least 8 to 12 weeks or discontinuation due to adverse effects or ineligibility due to co-morbidities. The classes of preventives include (certain) anticonvulsants, antidepressants, and antihypertensives. In addition, the patient will have failed on Onabotulinumtoxin A and/or a CGRP preventive (injection or oral).

4.2.2. For patients with limited access to certain migraine medications:

The preventive approaches have failed to reduce the impact of the migraines by at least 50%. The patient should have failed on at least half the classes of migraine preventives that are available. Failure was either inadequate relief from an adequate trial of the medication for at least 8 to 12 weeks, or discontinuation due to adverse effects. The classes of preventives include (certain) anticonvulsants, antidepressants, and antihypertensives. In addition, the patient will have failed on OnabotulinumtoxinA and/or a CGRP preventive (injection or oral), or trials of non-medication therapies such as non-invasive neuromodulation, acupuncture, yoga or CBT.

4.3 Abortive Therapies

4.3.1. For patients who have access to almost all abortives, including gepants:

The abortives have not provided consistent relief at least 50% of the time (trial in at least 4 consecutive headaches). Relief is defined as pain-freedom (or "near" pain-freedom) at 2 hours, after medication overuse headache has been addressed. [15–18] Alternatively the medication may have been discontinued due to intolerable adverse effects. The patient should have utilized simple analgesics (paracetamol and NSAIDs) and at least 2 of the following categories: triptans, gepants, DHE, or injectables (ketorolac, etc).

4.3.2. For patients with limited access to certain abortive medications:

Refractoriness may be defined as non-responsiveness to all of the available classes of abortive therapies.

Note: It is important to note if the patient is refractory to preventives, abortives, or both preventives and abortives.

4.4 The Role of Medication Overuse Headache (MOH)

Medication overuse headache (MOH): The patient should have been assessed for MOH. MOH is defined according to ICHD-3 with the modifications as follows:

- It is important that MOH not be conflated or confused with medication overuse (MO)
- To determine whether MOH is truly present, a careful history regarding the offending medication must be obtained. Based on the history and assessment of headache diaries, it should be more likely than not that the offending medication is actually triggering more migraines. Ideally, the subsequent medication should be withdrawn, and the effect on the patient's migraines

observed. This is not always possible.

- After observing the results of the offending medication having been discontinued, a definite determination of MOH may be made. If it is determined that the patient most likely is suffering from MOH, the designation of refractory migraine will be withheld until the MOH situation is resolved.

*4.5 **Refractory Migraine Rating Scale***

It is useful to separate patients into mild, moderate, and severe refractory. This is helpful for research purposes. In addition, our clinical approach and expectations are different for a patient with mild refractory migraine versus severe refractory migraine.[17,19]

4.5.1. Refractory Rating Scale for adult patients, age 20+: The scale consists of eight items, with 10 possible points. Points are added if the patient is:

Refractory to preventive approaches	2 points
Refractory to abortive medications	2 points
Duration (number of years) of migraine occurrence; if greater than 10 years	1 point
Number of headaches per month; if 25 or more days, on average	1 point
Two or more diagnosed comorbid central sensitization syndromes (irritable bowel syndrome [IBS], chronic regional pain syndrome (CRPS), temporomandibular joint disorder [TMD], fibromyalgia, chronic pelvic pain, burning mouth syndrome); in addition: chronic fatigue syndrome, or visual snow	1 point
Psychiatric comorbidities, whether a severe Axis I disorder (ie, an affective disorder) or any definite Axis II disorder (ie, a personality disorder), as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)	1 point
Disability (work/school and/or home)	1 point
Medication overuse headache (not simply medication overuse)	1 point

After totaling the points, the scale helps clinicians to categorize patients as follows:

To 4 points= mild refractory migraine

To 7 points= moderate refractory migraine

To 10 points= severe refractory migraine

4.5.2. Refractory Migraine Rating Scale for Adolescents, Ages 11 to 19

The point system for the adolescent patient would be as follows:

Refractory to preventives (which may include OnabotulinumtoxinA)	1 point
Refractory to abortives	1 point
Headache occurrence greater than one year	1 point
Number of headaches per month; if 25 or more days, on average	1 point
Significant comorbidities; if at least one is present (IBS, TMD, fibromyalgia, or chronic fatigue)	1 point
Psychiatric comorbidities: severe Axis I (affective disorders), or a strong indication that Axis II (personality disorders) may be present	1 point
Disability defined as an inability to go to school for at least 2 months due to headache (either homebound, or a greatly modified schedule), or a significant decrease in functioning	1 point
Severe family dysfunction, which may include personality disorder pathology in the primary parent (usually the mother)	1 point

With this scale, a total of 8 points would be possible, ranking as such:

2 to 4 points = mild refractory migraine.

5 to 6 points = moderate refractory migraine.

7 to 8 points = severe refractory migraine.

5 FUTURE PERSPECTIVES AND CONCLUSION

This is a continuous work in progress. We have attempted to revise and add to existing refractory definitions. Our primary changes include: including abortives in a refractory definition, separating a simple from a more complex definition, adding a section that applies to patients with limited access to more advanced approaches, adding to the existing MOH definition, and adding a refractory rating scale for adults and adolescents.

In the future, we may use biomarkers to identify refractory patients, but until then we must use our clinical criteria.

6 KEY POINTS

Simple Definition

The migraines have not been adequately controlled by medications or non-medication approaches.

Complex Definition of Refractory Migraine

>The migraines have not been adequately controlled. Non-medication approaches had not sufficiently alleviated the headaches. It is important to note if the patient is refractory to preventives, abortives, or both. Not all patients will have required preventive therapies.
>If preventives have been used, they have failed to reduce the impact of the migraines by at least 50%. At least 3 classes of preventives will have had an adequate trial.
>Abortive medications will have failed to achieve adequate relief of 50% for at least 4 episodes.
>Medication overuse headache will have been adequately addressed.
>For countries with limited access to both preventive and abortive therapies, the patient should have failed at least half of the available preventive classes or all of the classes of the available abortives.

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