

VI

Medication-overuse headache

How is medication-overuse headache diagnosed?

Recommendation

Medication-overuse headache (MOH) is diagnosed according to the diagnostic criteria for “8.2 Medication-overuse headache” described in The International Classification of Headache Disorders, 3rd edition (beta version), which was published in Cephalgia in 2013.

Grade A

Background and Objective

The diagnostic criteria for medication-overuse headache described in the International Classification of Headache Disorders 2nd Edition (ICHD-II)¹⁾ published in 2004 were revised in 2005²⁾ and 2006.³⁾ This section discusses the changes as well as the issues concerning the diagnostic criteria for medication-overuse headache.

Comments and Evidence

In the International Classification of Headache Disorders 2nd Edition (ICHD-II) published in 2004,¹⁾ medication-overuse headache (MOH) is classified within the group of secondary headaches, under 8. *Headache attributed to a substance or its withdrawal*. MOH is characterized by: headache present on at least 15 days of a month, regular overuse of medications for over 3 months, headache developing or exacerbating markedly during medication overuse, and resolution of pain or returning to the previous pattern within 2 months after overuse is stopped. The subforms consist of headaches caused by individual medications: intake of ergotamine, triptan, opioid or combination analgesics on 10 or more days per month for over 3 months; or intake of simple analgesic on 15 or more days per month for over 3 months.

The criteria for medication-overuse headache in ICDH-II were discussed at the International Research Seminar held in March 2004. As a result, a revision (ICHD-II R1) was published in 2005, in which the characteristics of headache were removed and a new subform of headache due to intake of combination of acute medications for 15 days or more (8.2.6 *Medication-overuse headache attributed to combination of acute medications*) was added.²⁾ The Japanese Headache Society promptly incorporated the revisions in time for publication of the Japanese edition of ICHD-II. Therefore the Japanese edition essentially corresponds in the contents of the 2005 revision (R1).⁴⁾

In ICHD-II R1, the criterion “D. Headache resolves or reverts to its previous pattern within 2 months after discontinuation of overused medication” remains. Therefore resolution of pain or reversion to the previous pattern within 2 months after stopping overuse is mandatory. This means that (1) a period of 2 months after cessation of overuse is stipulated, (2) during this period, the diagnosis of probable MOH should be applied, and (3) MOH can be diagnosed only when improvement occurs after cessation of overused medication. However, at that time point, MOH is actually resolved, and the diagnosis would revert to the previous one. Due to the above and other issues, the above-mentioned sentence was eliminated in the 2006 revision,⁴⁾ allowing a diagnosis of MOH to be made before cessation of the overused medication.

Even after the second revision, issues still exist. For example, it is difficult to prove whether medication overuse is caused by frequent headaches, or whether headaches appear or worsen because of medication overuse.⁵⁾⁶⁾ Therefore, in the latest revision, the ICHD 3rd edition (beta version) (ICHD-3beta),⁷⁾ the criterion “headache has developed or markedly worsened during medication overuse” was omitted.

The diagnostic criteria described in ICHD-3beta are shown below.

8.2 Medication-overuse headache

• Diagnostic criteria

- A. Headache occurring on ≥ 15 days per month in a patient with a pre-existing headache disorder.
- B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache.
- C. Not better accounted for by another ICHD-3 diagnosis.

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• Search terms and secondary sources

- Search database: PubMed (2011/12/21)
Medication overuse 825
Medication overuse headache 529
& criteria 141
& diagnosis 267
- Search database: Ichushi Web for articles published in Japan (2011/12/21)
Medication-overuse headache 115
& diagnostic criteria 9

How big is the population of medication-overuse headache patients?

Recommendation

In overseas countries, the 1-year prevalence of medication-overuse headache in the general population is approximately 1 to 2%, and women occupy approximately 70%. In headache clinics or headache centers, the percentage of medication-overuse headache is up to 30% in Europe and over 50% in the United States.

Grade A

Background and Objective

In Japan, no epidemiological study has been conducted to investigate the 1-year prevalence of medication-overuse headache in the general population. This section summarizes the prevalence of medication-overuse headache of overseas countries.

Comments and Evidence

In a review of studies on the prevalence of headache in Europe, which included 49 studies comprising a total of 205,000 adult participants, headache occurred in 54% of the adults and the prevalence of medication-overuse headache (MOH) in the general population was estimated to be 1 to 2%.¹⁾ In Brazil, of 1,631 persons who participated in an interview survey, 23 persons had MOH or probable MOH and the prevalence was 1.4%.²⁾ In a population (1,533 persons) of elderly persons (65 years or older) in Taiwan, the prevalence of MOH was approximately 1%.³⁾ There are no great differences in prevalence of MOH in the general population among various overseas countries.

Regarding the gender difference of MOH, women occupied 73% in Denmark,⁴⁾ 93% in Spain,⁵⁾ and 76% in the United States,⁶⁾ showing an overwhelming female preponderance. Mean ages of MOH were reported to be 48 years,⁴⁾ 56 years,⁵⁾ and 42.8 years.⁶⁾ The percentage of MOH in headache clinics and headache centers was up to 30% in Europe and more than 50% in the United States.⁷⁾ The percentage of MOH was 14.6% in a headache center in Japan,⁸⁾ indicating the importance of diagnosis and treatment of MOH in headache centers. A report from Turkey suggests low income and low educational level to be potential risk factors of MOH.⁹⁾

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• Search terms and secondary sources

- Search database: PubMed (2011/12/21)
Medication-overuse headache 529
& epidemiology 157
& prevalence 176
Drug-induced headache 347
& epidemiology 26
& prevalence 33

What are the treatment methods and prognosis of medication-overuse headache?

Recommendation

The treatment principles for medication-overuse headache are: (1) discontinue the overused medication, (2) treat the headache after discontinuing the overused medication, and (3) administer prophylactic medications. However, there is no established treatment method. Discontinuation of the overused medication may be conducted on an outpatient basis, but abrupt discontinuation on an inpatient basis is recommended for severe cases. Simple medication-overuse headache may improve with suitable counseling, but severe cases may require hospitalization. As for prognosis, the relapse rate is approximately 30%. Even after discontinuation, patients should be given suitable counseling, and headache diary should be used to confirm the frequency of using triptans, ergotamine and analgesics.

Grade B

Background and Objective

Even though treatment is important for the frequent headaches in patients with medication-overuse headache, the quality of evidence is low because no randomized controlled trial has been reported. Although there is currently no established treatment, research data is accumulating. This section describes the treatment methods and prognosis.

Comments and Evidence

Regarding the methods of discontinuing the drugs causing medication-overuse headache (MOH), no prospective study has compared abrupt discontinuation of the overused medication and tapering. Clinical studies conducted in Japan reported more relapses of MOH after tapering compared to abrupt discontinuation.^{1,2)}

A prospective randomized open-label study that compared inpatient versus outpatient withdrawal therapies found no difference in response rate at 2 years after withdrawal.³⁾ From the above findings, an outpatient abrupt withdrawal program appears to be the best approach. In patients with severe medication-overuse headache in whom withdrawal symptoms were a concern or who require closer psychological observation, inpatient withdrawal program should be considered.

In the International Classification of Headache Disorders 2nd Edition (ICHD-II),⁴⁾ withdrawal headache attributed to overuse of acute medications for headache is defined as headache that develops within 48 hours after last intake of the overused medication and resolves within 7 days after withdrawal. Improvement is observed after a shorter duration in patients overusing triptans than in patients overusing ergotamine or NSAIDs.⁵⁾ Treatment of withdrawal headache using triptans, naproxen, prochlorperazine, steroids and other drugs have been reported, but they were open-label studies with small numbers of cases. A double-blind study of oral prednisolone given for 6 days (starting with 60 mg/day, increasing by 20 mg every 2 days) reported no difference compared to placebo.⁶⁾ In severe cases, hospitalization and management with hydration, antiemetics, sedatives and steroids should be considered.⁷⁾

Early initiation of prophylactic therapy has been shown to be effective to reduce the number of days with headache by 7.2 days at 3 months and by 10.3 days at 12 months.⁸⁾ Therefore, initiation of prophylactic medications at the time of withdrawal or even before withdrawal of overused medications is recommended. Since most of the MOH patients have migraine prior to MOH, valproic acid, lomerizine, propranolol, amitriptyline (off-label use approved in Japan) and topiramate (currently not covered by health insurance in Japan) may be considered as prophylactic medications.

Evidence for treatment of MOH at the level of randomized controlled trial (RCT) is available for topiramate. In a study conducted in the US comparing topiramate (n = 153) and placebo (n = 153), the change in number of days with headache after withdrawal was -5.6 days in the topiramate group versus -4.1 days in the placebo group, showing a significant improvement in the topiramate group compared to placebo.⁹⁾ In a study conducted in EU, the change in number of days with headache was -3.5 days in the topiramate group (n = 27) versus -0.2 days in the placebo group (n = 32), showing greater decrease in the topiramate group.¹⁰⁾ For amitriptyline also, a double-blind placebo (trihexyphenidyl)-controlled trial showed a significant reduction in headache frequency in the amitriptyline-treated group.¹¹⁾ Moreover, treatment with amitriptyline

in patients who did not respond to withdrawal of misused drugs alone reduced the number of days with headache in 36% of the patients.¹²⁾ These studies suggest the usefulness of amitriptyline in the treatment of MOH.

The relapse rate of MOH after withdrawal therapy is approximately 30% (14-21%).¹³⁾ Therefore, even after discontinuation, use of headache diary to regularly monitor drug intake as well as patient education are important.

The factors predicting poor prognosis for MOH are long duration of migraine, frequent migraine attacks after discontinuation, intake of combination analgesics after withdrawal therapy, frequent drug taking, alcohol consumption, smoking, and taking the former medication again after withdrawal therapy.¹³⁾¹⁴⁾

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• Search terms and secondary sources

- Search database: PubMed (2011/12/21)
Medication overuse 825
Medication overuse headache 529
& withdrawal 118
& advice 4
& risk factor 69
& detoxification 29
& treatment 395
& prognosis 96
& outcome 100
Drug-induced headache 347
& treatment 280
- Search database: Ichushi Web for articles published in Japan (2011/12/21)
Medication-overuse headache 115
& treatment 97