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Case study

Analysis on the risk factors of medication-overuse headache in Chinese patients

Junxia Li [a,b], Chunfu Chen [a,*], Ligong Zhang [a], Xiaochen Cui [a], Chuanqiao Wei [a], Xiaojun Diao [a]

[a] Department of Neurology, Shandong Provincial Hospital affiliated to Shandong University, No. 324, Jingwu Road, Jinan, China
[b] Department of Neurology, The Second People's Hospital of Liaocheng affiliated to Taishan Medical College, Shandong Linqing, China

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ABSTRACT

Objective: The purpose of this study was to analyze the risk factors of medication-overuse headache in patients with chronic migraine in China.
Materials and methods: 157 patients who were diagnosed as chronic migraine were chosen from headache outpatients of Shandong Provincial Hospital affiliated to Shandong University. Based on a standardized questionnaire, a database was developed and analyzed with 45 indexes.
Results: The independent risk factors of medication-overuse headache identified in this study included the frequency of medicine overuse (OR = 9.575, 95%CI, 3.573–35.659), Allodynia Symptom Checklist scores (OR = 5.846, 95%CI, 2.065–22.856), anxiety disorder (OR = 2.902, 95%CI, 1.601–7.476) and lack or non- standardized preventive treatment (OR = 1.173, 95%CI, 1.073–3.826).
Conclusions: The frequency of medicine overuse, Allodynia Symptom Checklist scores, anxiety disorder and lack or non-standardized preventive therapy were the independent risk factors for medication-overuse headache in patients with chronic migraine.

1. Introduction

Chronic migraine is one of the most common chronic encephalopathies in Neurology Department in the clinic. Most patients lack of appropriate knowledge of the primary headache and just treat it as a symptom rather than a disease, which leads to the occurrence of medication overuse. The medication overuse not only blocks the systematic and standardized treatment process of medical staffs, but easily causes drug resistance and dependence. Gradually, the primary headache could evolve into a new type of headache. The Headache Classification Committee of the International Headache Society (IHS) named it as medication-overuse headache (MOH) officially in the International Classification of Headache Disorders in the second edition (ICHD-II) in 2004, which belongs to the chronic daily headache (CDH). The IHS revised the diagnosis criteria in 2005 and 2006 respectively. Most of the scholars in China and abroad use the ICHD-ⅢR revised in 2005 [1].

MOH is the third most common headache type after migraine and tension-type headache and counts about 11%–70% of CDH, which is much higher than in the general population [2]. Epidemiological studies show the prevalence of MOH in general population is about 1%–2% [3] and has a tendency to increase steadily. MOH can attack in all age groups, even in the childhood [4]. In China, Qiu et al. [5] reported 102 CDH patients, of which 91 patients (about 89.2% of them) were conformed or probably conformed to the diagnostic criteria of MOH. The population-based headache study in Taiwan of adults found 3.2% of the participants fulfilled the criteria for CDH, 34%of the CDH participants overused analgesics [6]. Another epidemiological study in Taiwan of adolescents found a prevalence of 1.5% for CDH, and MOH was present in 20% of the CDH group, representing 0.3% of the study population [7]. Therefore, we can see MOH is common in China.

MOH is a type headache that frequently attacks medication users after the appearance of the chronic process, which is generated by the therapeutics treated regularly and excessively in the acute phase of headache. All classes of symptomatic medications, both migraine-specific (such as ergots and triptans) and nonspecific analgesics (such as opiates and non-narcotic analgesics) can able to cause MOH if they are used excessively (on 10 or more, or 15 or more days per month) [8].

MOH usually occurs in the patients who have primary headaches, or who have headache past history or family history. One study in patients attending a rheumatology-monitoring clinic of second-line agents found that individuals with primary headache, specifically migraine, were predisposed to developing chronic headache in association with regular use of analgesics [9]. The

* Corresponding author.
E-mail address: chencf301@163.com (C. Chen).

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most common primary headache in the medical history of MOH patients is migraine and (or) tension-type headache. Other primary headaches account for only a small proportion. MOH strongly affects the living quality of patients, resulting in disability and decline of labor, which would not only cause patients lots of trouble, but also promote the occurrence of adverse events such as substance abuse and mass medical resource consumption, therefore brings heavy social burden. The economic losses of MOH in Europe are immense [10]. MOH has become an inevitable global problem in the headache field.

With the cessation of overuse, the headache gradually ease or revert to its previous pattern [11]. It is a primary intervention approach to inform the patients of the reasons and possible results of MOH. It is noteworthy that medication overuse and MOH is not necessarily a cause-and-effect relationship, overuse drugs to prevent headache does not cause MOH in every individuals. As time goes on, the investigation methods of the epidemiology in the headaches field continue to be improved, which have promoted the epidemiological investigation of MOH groups. The risk factors of the occurrence of MOH have been reported by literatures [12], but not been researched in China. Our study will explore the risk factors of medication-overuse headache in patients with chronic migraine in China, and provide epidemiological reference data for the prevention of medication-overuse headache for migraine patients in clinic.

2. Materials and methods

2.1. Object

2.1.1 Subjects

patients who were firstly diagnosed as chronic migraine by the Headache Specific Outpatient of Shandong Province Hospital were followed up between January 2013 and December 2015. The study was approved by the Ethic Committee of Shandong Provincial Hospital, and written informed consent was obtained from the participants after they became acquainted with all the procedures (reference number: 20140321). The patients were informed with the consent and recorded their headache diary.

2.1.2 Case inclusion criteria

The patients met the criteria of chronic migraine in the ICHD-IIIβ made by the IHS [8]. Meanwhile, the MOH patients met the criteria of ICHD-IIR [1] modified by the IHS.

2.1.3 Case exclusion criteria

(1) Other types of primary headache; (2) Secondary headache; (3) The patients who combined with other system diseases and needed long-term to take painkillers; (4) The patients who combined other serious chronic diseases; (5) The patients who had medication cessation history; (6) The patients who had obvious organic complications; (7) The patients who rejected detoxification treatment (overused medication withdrawal);(8) The patients whose medical records were not complete; (9) The patients who refused to enter the group and accept the survey and did not complete the 2-month follow-up.

The patients who successfully completed the cessation of medications overuse after two months and headache resolved absolutely or reversed to its previous pattern or headache days reduced by 50% per month were chosen as the case group. The patients who successfully finished the cessation of medications overuse but headache did not resolve or got worse were chosen as the control group.

2.2. Methods

The survey adopted unified survey forms and a database was built based on the data collected from the survey with Excel 2015. We finished surveying in 45 dominant terms and 57 sub-items according to the headache medical records and headache diary of the patients and all the items were digital coded according to the unified method.

2.3. Date analysis

The observations and clinic data collected were recorded into computer and a database was built with Office Excel 2015, and the statistical analysis was performed with the Statistical Package for the Social Science 19.0 software. The research data was analyzed with univariate analysis firstly. The categorical data was analyzed with chi-square test and Fisher exact probability. The measurement data with normal distribution was analyzed by *t* test, and the non-normal distribution measurement data was analyzed by Wilcoxon rank test. The indicators with statistical significance ($P < .05$) were screened as risk factors, and these variables were included into the unconditional multivariate logistic regression analysis. The significant standard was defined as $\alpha = 0.05$.

3. Results

3.1. General basic data analysis

After the outpatient service or telephone interview, 157 chronic migraine patients with complete survey data were recruited. There were 44 male patients (28.0%) and 113 female patients (72.0%) and their age was between 18 and 52 (average 34.4 ± 10.3). Among them, 63 (40.1%) patients were in the MOH group, 94 (59.9%) patients in the control group. The ratio of female patients to male patients was 3.8:1 in MOH group.

3.2. Univariate analysis

3.2.1. The analysis of the categorical data

The results were shown in Table 1.

3.2.2. The analysis of measurement data

The results were shown in Table 2.

After the univariate analysis, 14 risk factors ($P < .05$) were screened from 46 factors, including headache family history, headache side number, headache associated symptoms, relieving factors, lacking of headache healthy education, MIDAS scores, OTC, failure to comply with medical advice to take medicine during headache attacks, ASC scores, anxiety disorder, depressive disorder, sleep disorder, lack or non-standardized preventive treatment, the cumulative use time of drugs in acute phase per month (the use frequency of drugs).

3.3. Multivariate analysis

Fourteen risk factors were analyzed with the multivariate unconditional Logistic regression. Four indicators (drug use frequency, ASC scores, anxiety disorder, and preventive treatment without or non-standardized) were applied to the regression equation and were found to be the independent risk factors for MOH. The results were shown in Table 3.

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