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Original

Higher frequency of medication overuse headache in patients attended by neurologists in Lima, Peru

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Abstract

Background
The type of medical care received (self-medication and/or medical care provided by a general practitioner or a neurologist) may be associated with differences in the frequency of medication overuse headaches.

Method
This cross-sectional analytical study included 222 records of patients with chronic daily headaches seen at the National Institute of Neurological Sciences Outpatient Unit in Lima, Peru. A pre-designed questionnaire was used to assess and categorize patients with frequent and chronic headaches.

Results
Ninety-four patients (42.34% of those with chronic daily headaches) met the criteria for medication overuse headache. Of these, 19 (28%) self-medicated, 22 (36%) consulted with the general practitioner, and the highest proportion of subjects, 53 (58%), consulted with a neurologist. On bivariate analysis, subjects who had received care from a general practitioner and self-medicated were 38% and 51% less likely to have MOH than the subjects who received medical care from the neurologist (p=0.012; 95% CI 0.42-0.90 and p=0.001; 95% CI 0.32-0.74). On multivariate analysis adjusting by sociodemographic and clinical factors, the association remained significant in regards to self-medication, but became marginal (p=0.055) in regard to being seen by a general practitioner.

Conclusion
In this study, the frequency of the headache due to overuse of medication was higher in patients attending a neurologist than those attending a general practitioner or self-medicated. This cross-sectional design cannot assess whether this reflects more severe cases looking for specialized care or more medication overuse headaches as a result of inappropriate management.

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Medication overuse headache (MOH)
Chronic daily headaches
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Introduction

Headache is a symptom associated with many medical conditions (ICHD-3), and migraine and tension-type headache (TTH) are the most prevalent types of headaches. When migraine or TTH are categorized as episodic migraine (EM) and episodic TTH (ETTH) if attacks occur less than 15 days a month. If attacks occur for 15 or more days per month, they are defined as chronic daily headaches (CDH; chronic migraine [CM] or chronic TTH [CTTH])[1,2]; making up both groups CM and CTTH, the majority of patients with chronic daily headaches CDH.[3] Medication overuse headache (MOH) is a CDH, mostly underlying a pre-existing primary headache, and adding to this, the overuse of symptomatic medication (10 to 15 days/month, depending on the overused drug, equal to or greater than three months) for acute episodes.[2] The prevalence of MOH is 1% to 2% in the general population, predominantly in women in industrialized countries.[4] The global burden of disease lists MOH as the 18th cause of disability. In addition to disability due to migraine (6th cause of disability); together, they represent the 3rd leading cause of disability in the world.[4,5]

Currently, the global campaign to reduce the burden of headache (Lifting the Burden) is assessing known and potential risk factors associated with MOH. Several studies have determined associations with polymorphic variants related to the susceptibility of conversion to MOH[6], psychopathological comorbidities[7], within these, post-traumatic stress events[8], depression, anxiety and insomnia[9], and other sociodemographic factors, such as low education, place of residence, limited medical contact and type of medical care received in the development of MOH.[10-13] Factors that, in addition to transforming EM and ETTH into CM and CTTH[7-9,14,15], induce patients to seek different types of medical attention and to overuse medication in an effort to obtain relief from their pain.[16-19]

There is no clear evidence regarding the association of MOH with the type of medical care received. A 2012 Swedish publication suggested that limited medical care, due to reduced neurological care in rural areas, leads to self-medication with over-the-counter medication, increasing the likelihood of MOH development.[10] Factor similar to the reality of developing countries such as Peru, where specialists are concentrated in metropolitan areas. This study evaluated whether there is a relationship between MOH and the type of medical care received (self-medication, general practitioner or neurologist) in new patients who attended a neurological referral center.

Methods

Clinical interview - In this cross-sectional analytical study, we selected all records with CDH from a previous study that evaluated 419 new patients with headaches in the outpatient clinic of the National Instituto Nacional de Ciencias Neurológicas (INCN), Lima, Peru (a reference tertiary center). In the previous study, the participants were interviewed and examined by an INCN headache specialist, after the application of a complete clinical and demographic questionnaire.

Questionnaire - A questionnaire allowed the diagnosis of episodic and chronic headaches according to ICHD-III-Beta version-2013 criteria.[20] For the study, we included from the primary study, data records with the diagnosis of DCH, excluding records with missing data. The questions: (1) Do you usually take any medication to relieve headaches?, (2) How many times a month do you take any medication?, and (3) How long have you been using the drug? allowed to generate the diagnosis of MOH; while the questions (1) Has a doctor ever treated your headache in your life? and (2) What specialty did the treating physician have? allowed to categorize the type of medical care received.

Ethical aspects - The primary study protocol and informed consent form, as well as this secondary data analysis, were approved by the research and ethics committee of the INCN (N0523-2018-CIEI-INCN).

Data processing - Analysis was performed using Stata 14 StataCorp, (Texas, United States). Descriptive statistics are provided with measures of central tendency, frequencies, percentages, means and standard deviations as appropriate. We consider significance at $p<0.05$ with two-tailed test. We compared proportions using chi-square (X^2) test, after analysis of assumptions, to test the alternative hypothesis, that lack of neurological attention is associated with MOH. Simple and adjusted regressions were performed using generalized linear models (GLM), binomial family to measure prevalence ratios (PR) due to our cross-sectional design. Due to the non-convergence of the binomial GLM model, a robust Poisson generalized linear model (GLM) was also run.

Results

From the primary study consisting of 419 participants (April 2016) (Figure 1), we selected 222 data records with

CDH, the total population of this cross-sectional study.

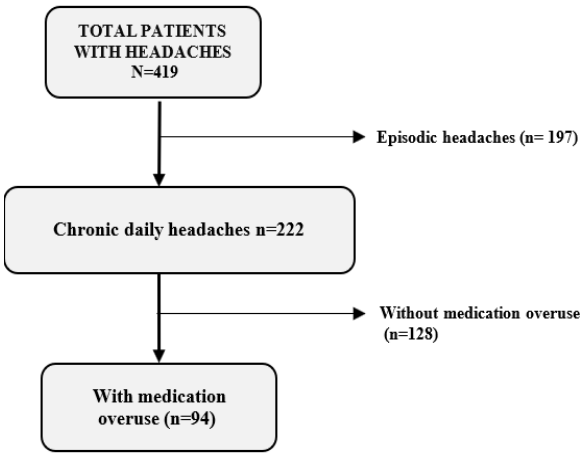

Figure 1. Flowchart for the screening of medication overuse headache patients. CEFAPERU data.

Sociodemographic and clinical variables are described in Table 1. The average age was 46 (±17 SD) years. They were 146 (66%) women and 76 (36%) men. As in other studies, CDH is more prevalent in women; and more patients lived in urban areas, 124 (56%). Migraines (n=122, 55%) were the most frequent type of headache. The order of frequency of drug use was: drugs not remembered, (n=83, 38%), NSAIDs (n=58, 26%), paracetamol (39, 18%), other drugs (24, 11%) and ergotamine (18, 0.8%). Regarding the type of medical care received, neurological care was more frequent, occurring in 92 cases (41%), followed by self-medication in 68 (31%), and care by a general practitioner in 62 (28%) (Figure 2).

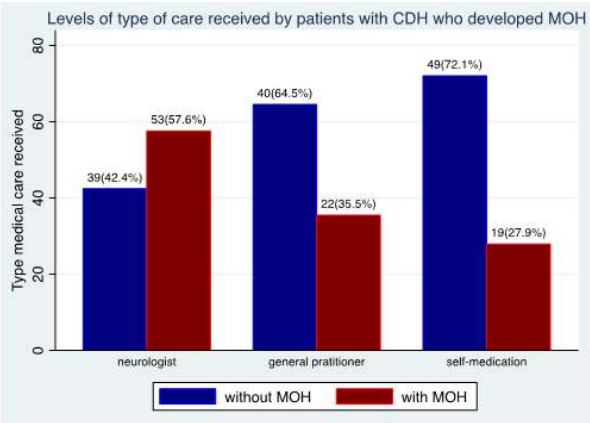

Figure 2. Levels of type of care received by patients with chronic daily headache who developed medication overuse headache (MOH).

While all drug categories were overused; regression adjustment demonstrated that ergotamine were associated with a higher proportion of MOH. Using neurological care as a category of reference in the simple regression, we demonstrated a 38% lower probability of MOH in patients seen by the general practitioner (p=0.012, 95% CI 0.42-0.90), and a 51% lower probability of developing MOH with self-medication (p=0.001, 95% CI 0.32-0.74). Whereas, multiple regression adjusted for other sociodemographic and clinical variables, made the strength of association with general practitioner care marginal (30% less probability, p = 0.053, 95% CI 0.48-1.00), maintaining significant for self-medication (37% less probability, p=0.030, 95% CI 0.42-0.96) (Table 1).

Discussion

In this study, MOH was more frequent in patients seen by neurologists, compared to subjects seen by the general practitioner or self-medicated. In our view, the most plausible explanation is that individuals with MOH sought specialized care, although we cannot rule out that the higher frequency of MOH resulted from inadequate neurological management. Jonsson et al.[10], in Sweden, reported that the high proportion of MOH in their study was due to limited access to medical care. However, in this series the frequency of MOH among those who received medical attention was non-significantly higher with neurological care than with care performed by other physicians. Longitudinal studies are required to confirm this hypothesis.

Most studies report that migraine is the most common underlying headache in MOH, followed by TTH.[18,21,22] Our data have this trend, although there was no significant difference. On the other hand, although psychiatric comorbidities such as anxiety, depression, and others, plus altered hormone levels associated with mood swings in women over 40 years of age[7,23], could lead to CDH and MOH, we found no significant differences for MOH in this subgroup.

Shand et al.[11] reported that the overused drugs that led to the development of MOH in Argentina and Chile were combined ergotamine (70%) and NSAIDs (33.8%). Johnson et al.[10], however, showed a higher proportion of MOH (66%) with overuse of psychotropic drugs. While Find et al.[12], in a multicenter study on MOH, reported that ergotamine was greatly overused in Latin America (72% compared with 4% in Europe, p<0.001). Our findings support these data, MOH was 2.5 times more frequent in patients with ergotamine overuse compared to those who overused drugs that they did not remember (reference category). In Peru, as in other Latin America countries ergotamine is extremely cheap and available over the counter.

Our study has several limitations. Self-report could create inaccuracies in the estimation of the exposure to the studied factors, affecting the reliability. However, a study on the validity of the self-report on MOH dependency severity

Table 1. Analysis of the association between medication overuse headache and (MOH) sociodemographic and clinical characteristics.

Variables	N (%)	Without MOH (n = 128)	With MOH (n = 94)	p-value	Simple model PR (95% CI)	p-value	Adjusted model PR (95% CI)	p-value
Sex				0.533				
Male	76 (34.2)	46 (60.5%)	30 (39.5%)		Ref.		Ref.	
Female	146 (65.8)	82 (56.2%)	64 (43.8%)		1.11 (0.79-1.55)	0.539	1.01(0.72-1.38)	0.955
Age	45.7±17.0	-	-		-		-	-
Categorized age (years)				0.905				
18-40	87 (39.19)	51(58.6%)	36(41.4%)		Ref.		Ref.	
41-60	86 (38.74)	48(55.8%)	38(44.2%)		1.11 (0.79-1.57)	0.554	1.21(0.87-1.68)	0.251
61-93	49 (22.07)	29(59.2%)	20(40.8%)		1.00 (0.66-1.53)	0.986	1.31(0.87-1.97)	0.204
Residence				0.219				
Rural	98 (44.14)	61 (62.2%)	37 (37.8%)		Ref.		Ref.	
Urban	124 (55.9)	67 (54.0%)	57 (46.1%)		1.22 (0.89-1.67)	0.226	1.16(0.86-1.57)	0.324
Types of Headache				0.192				
Tension-type headache	49 (22.1)	30 (61.2%)	19 (38.8%)		Ref.		Ref.	
Indeterminate headache	51 (22.6)	34 (66.7%)	17 (33.3%)		0.86 (0.51-1.45)	0.572	0.79 (0.48-1.31)	0.355
Migraine	122 (55.0)	64 (52.5%)	58 (47.5%)		1.23 (0.82-1.83)	0.317	1.15 (0.79-1.67)	0.459
Overused drugs				<0.001				
Forgotten drug	83 (37.4)	67 (80.7%)	16 (19.3%)		Ref.		Ref.	
Paracetamol	39 (17.6)	23 (59.1%)	16 (41.0%)		2.13 (1.19-3.80)	0.011	2.21 (1.21-4.03)	0.010
Other drugs	24 (10.8)	11 (45.8%)	13 (54.2%)		2.81 (1.58-4.99)	<0.001	2.78(1.54-5.00)	0.001
NSAIDs	58 (26.1)	21 (36.2%)	37 (63.8%)		3.31 (2.04-5.36)	<0.001	3.08(1.88-5.04)	<0.001
Ergotamine	18 (8.1)	6 (33.3%)	12 (66.7%)		3.46 (1.99-5.99)	<0.001	2.76(1.58-4.84)	<0.001
Type medical care received				0.001				
Neurologist	92 (41.4)	39 (42.4%)	53 (57.6%)		Ref.		Ref.	
General practitioner	62 (27.9)	40 (64.5%)	22 (35.5%)		0.62 (0.42-0.90)	0.012	0.70 (0.48-1.00)	0.053
Self-medication	68 (30.6)	49 (72.1%)	19 (27.9%)		0.49 (0.32-0.74)	0.001	0.63 (0.42-0.96)	0.030

scales suggests that a self-reported version provides valuable information as a screening tool after a headache consultation.[23] There are studies that provide greater security in this context, reporting concordance between what is reported by patients and medical prescription and diagnosis records, using telephone lines or online platforms for interviews. The cross-sectional design of this study limits the estimation of causality, as well as the fact that this study was carried out in a tertiary referral center, where the most serious cases arrive, limiting the representativeness of MOH in the population.

We determined that subjects who arrived at this third-level center, with a higher proportion of MOH, had already been seen by neurologists. These results could reflect that headaches as severe as MOH, came in search of more specialized care than they received and are the result of improper prior, non-specialized management. However, we cannot prove this from our data; longitudinal studies are required to clarify this and complement our findings. However, the high frequency of occurrence of MOH attended by neurologists, should lead to awareness regarding its diagnosis and management, as well as the prompt and adequate training of specialists in its diagnosis and management.

Conflict of interest: None
Author Contributions: MEN, Study conception and design, Data acquisition and interpretation, Revised the manuscript and final approval; CAB, Critically revised the manuscript and final approval.

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