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Prevalence, natural history and dynamic nature of chronic headache and medication overuse headache in Italy: The SPARTACUS study

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Abstract

Background: Chronic headaches and medication overuse headache are common and burdening conditions. No studies have evaluated the prevalence of chronic headache and medication overuse headache in an unselected Italian population.
Methods: We performed a three-year cross-sectional and longitudinal population-based study to investigate prevalence, natural history, and prognostic factors of chronic headache. We delivered a self-administered questionnaire to 25,163 subjects. Chronic headache patients were interviewed by General Practitioners. After three years, medication overuse headache patients were invited to undergo a neurological evaluation at our Center.
Results: 16,577 individuals completed the questionnaire; 6878 (41,5%) were episodic headache sufferers and 636 (3.8%) were chronic headache subjects. 239 (1.4%) patients were acute medication over-users. All medication overuse headache patients had migraine or headache with migrainous features. At the three-year follow-up of 98 patients, we observed conversion to episodic headaches in 53 (54.1%) patients. 27 (50.9%) patients remitted spontaneously.
Conclusions: We present the first prevalence data on chronic headache and medication overuse headache in an unselected Italian population and a high rate of spontaneous remission. These data support the interpretation of medication overuse headache as a specific migraine-related disorder that may reflect chronic migraine's dynamic nature, the need for more specific medication overuse headache diagnostic criteria, and highlight the priority of targeted public health policies.

Introduction

Chronic headache (CH) is an umbrella term that encompasses different headache disorders characterized by headache attacks occurring at least 15 days per month (1) among which, chronic migraine (CM)

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and chronic tension-type headache (CTTH) are the most common. Medication overuse headache (MOH) is defined as a CH induced by the overuse of acute headache pain medications above 10 or 15 treatment days depending on medication type (1). Often, medication overuse (MO) represents the underlying putative factor responsible for the chronic conversion of a primary headache (2), especially migraine and tension-type headache; on the other hand, MO could also be an epiphenomenon of headache intensity and/or frequency worsening with a consequent higher need for acute medication intake. Several previous studies revealed a shattering prevalence of both CM and MOH (3–21). Both are remarkably disabling conditions with huge repercussions on individuals and society at large, i.e. MOH has an annual cost of 37 billion euros in the EU among the most productive age group, because of high per capita economic losses (22). Hence, these data assert that CH disorders are among the most burdensome worldwide. Although diagnostic criteria solidly distinguished among episodic and chronic primary headache disorders (1), natural fluctuations of headache days resulting in frequent transitions among distinctive diagnoses have been reported, challenging the current definition of CH (23,24). Conversely, while a similar spontaneous dynamic evolution of MOH might be suggested, no population-based study has specifically addressed this issue.

We conducted a cross-sectional, longitudinal study in the adult general population of the Bologna district, Italy, aiming to investigate the prevalence, natural history, and prognostic factors of chronic headache and MOH, to further enhance knowledge on the social impact and therapeutic management of these conditions.

Methods

A three-year cross-sectional and longitudinal population-based study was conducted to identify patients presenting CH with and without MO. The study was formally named SPARTACUS (Study on the PrevAlence of chRonic headache wiTh And without mediCation overUSe). The study was composed of three major phases.

Phase 1

In December 2009 we mailed an ad hoc self-administered screening questionnaire to 25,163 adult subjects registered on the lists of 20 General Practitioners (GPs) in the Bologna-Casalecchio di Reno district, which includes rural and urban zones (Figure 1). The study population was representative of the general population of Emilia–Romagna Region (Northern Italy). GPs were selected based on the number of patients in their practice and their willingness to contribute to the survey. Local health care agencies provided electronic records with each patient's name and address. We used a questionnaire previously tested in a sample of 133 consecutive patients attending our headache center (sensitivity 97%, specificity 86%). The headache features of interest were assessed
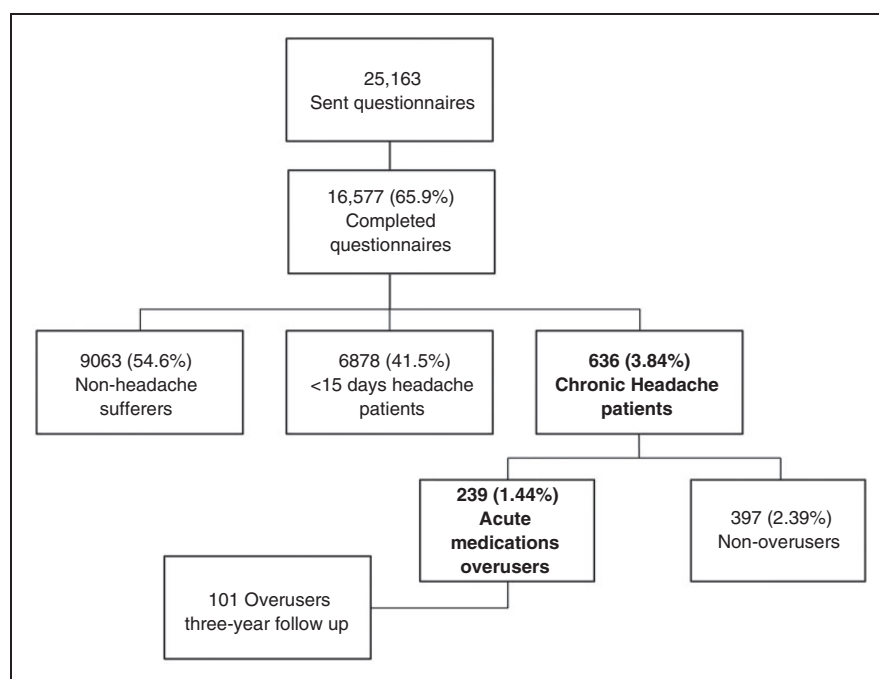

Figure 1. Patients selection flow-chart.

based on three consecutive closed questions: (i) "Have you ever had a headache in the last three months?" ("Yes", "No"); (ii) "How many days per month have you had a headache?" ("Less than 15 days", "15 or more days"); (iii) "How many times in the last month have you used medications to treat a headache?" ("Never", "Less than 15 days", "15 or more days").

Along with the questionnaire, the GPs wrote a cover letter containing information about the project and an invitation to fill out the questionnaire. A self-addressed stamped envelope was enclosed to return the survey. On return, questionnaires were checked for completeness and those containing at least one unanswered question were excluded. We identified chronic headache subjects based on the answers to the first and second screening questions, while acute medications over-users were identified based on responses to the third screening question.

Phase 2

Between November 2010 and June 2011, self-reported CH patients identified during phase 1 were interviewed by their trained GPs through a semi-structured questionnaire, regarding headache, age, sex, Body Mass Index (BMI), marital status, employment, associated medical conditions and medications used. GPs included only patients who met criteria for CM and CTTH; additionally, GPs specified if the subjects were known as patients suffering from CH with or without MO (25). Patients whose GPs' questionnaires were incomplete, were contacted by phone to improve the study sensitivity. CH was defined as a headache occurring at least 15 days per month for at least three months and MOH was defined according to the International Classification of Headache Disorders (ICHD)-2 and ICHD-2R criteria (26) and also, subsequently, confirmed according the new third edition, ICHD-3 (1).

Phase 3

Three years after the initial survey, all MOH patients identified by GPs were invited to undergo a face-to-face semi-structured interview and a neurological examination at our tertiary Headache Center (27). We gathered detailed information about headache clinical features, side and intensity of pain, associated symptoms, age at disease onset, days of headache per month, years of CH, MO characteristics, previous preventive treatment, history of spontaneous remission from MOH, lifestyle (smoking and coffee intake), potential related comorbidities and family history of headache and/or chronic headache.

Statistical analysis

Period prevalence for chronic headache with and without MO were estimated based on the symptom frequencies and medication intake provided in the questionnaire. Ninety-five percent confidence intervals (CIs) for the prevalence were calculated based on previous study (28). The calculated sample size was 4432 patients.

All data were analyzed using the SPSS software package (version 21- IBM Analytics). T-test or Mann-Whitney test, as appropriate, was used to compare continuous variables, while the Chi-square test was adopted for categorical variables. Results were expressed by mean $\pm$ standard deviation or percentage. The Spearman bivariate test was used to detect the strength of the correlation between selected variables. Values of $p < 0.05$ were considered statistically significant. A Bonferroni correction was applied for multiple comparisons.

Results

Phase 1

During the phase 1 study period, 16,577 individuals returned the completed questionnaire among 25,163 who were invited (65.9% response rate). Specifically, 9063 (54.6% of the responders) were non-headache sufferers; 6878 (41.5% of the responders) reported less than 15 headache days (episodic headache sufferers) and 636 (3.8%) had 15 or more headache days during the previous three months (CH subjects). Among the latter group, 239 (1.4% of the total responders and 37.5% of the CH subjects) patients were acute medications over-users. A female predominance was observed in both CH groups (Females:Males = 3:1).

Phase 2

GP interview was accepted by 435 of the 636 (68.4%) CH patients identified via the screening questionnaire. Baseline epidemiological and anamnestic factors are summarized in Table 1. Through the semi-structured questionnaire, GPs confirmed the diagnosis of MOH for 127 patients (96 females; mean age 49.0 ± 14.3), while 308 (244 females; mean age 53.0 ± 17.7) subjects were confirmed as CH sufferers without MOH. Among the 106 patients who were 65 years or older, 17 were confirmed as MOH patients, while GPs confirmed CH without MO for 89 patients. As shown extensively in Table 1, we observed significant differences between the aforementioned groups, concerning age (49.0 ± 14.3 vs 53.0 ± 17.7; $p = 0.023$), employment ($p = 0.016$), and cardiovascular disease prevalence (22.8% vs 35.1%, $p = 0.013$). Conversely, no statistically significant difference was found regarding sex, BMI, years of education, shift workers, partnership status and other

Table 1. Demographic characteristics of the CH patients.

		Total	MOH	CH without MO	p value
Sample	N	435	127	308	
Age, y	mean ± SD	51.9±16.8	49.0 ± 14.3	53.0 ± 17.7	**0.0230**
Sex					
Males	N (%)	95 (21.8)	31 (24.4)	64 (20.8)	0.405
Females	N (%)	340 (78.2)	96 (75.6)	244 (79.2)	
BMI, Kg/m^2	mean ± SD	25.3 ± 4.7	25.3 ± 4.3	25.3 ± 4.8	0.9934
Marital Status					
Single	N (%)	68 (15.6)	21 (16.5)	47 (15.3)	0.541
Married	N (%)	307 (70.6)	88 (69.3)	219 (71.1)	
Separated/Divorced	N (%)	22 (5.1)	9 (7.1)	13 (4.2)	
Widower	N (%)	38 (8.7)	9 (7.1)	29 (9.4)	
Education					
No degree	N (%)	12 (2.8)	4 (3.1)	8 (2.6)	0.493
Primary school	N (%)	73 (16.8)	14 (11.0)	59 (19.2)	
Lower secondary school	N (%)	133 (30.6)	41 (32.3)	92 (29.8)	
Upper secondary school	N (%)	176 (40.4)	56 (44.1)	120 (39.0)	
Higher education	N (%)	34 (7.8)	10 (7.9)	24 (7.8)	
Other	N (%)	7 (1.6)	2 (1.6)	5 (1.6)	
Years of Education, y	mean ± SD	10.5 ± 5.2	10.6 ± 3.8	10.4 ± 5.7	0.6768
Employment					
Unemployed	N (%)	23 (5.3)	12 (9.4)	11 (3.6)	**0.016**
Student	N (%)	16 (3.7)	4 (3.1)	12 (3.9)	
Employee	N (%)	186 (42.7)	56 (44.1)	130 (42.2)	
Housewife	N (%)	46 (10.6)	13 (10.2)	33 (10.7)	
Retired	N (%)	110 (25.3)	21 (16.6)	89 (28.9)	
Self-employed	N (%)	54 (12.4)	21 (16.6)	33 (10.7)	
Shift workers	N (%)	13 (2.99)	3 (2.4)	10 (3.2)	0.622
Comorbidities					
Gastrointestinal disease	N (%)	89 (20.5)	25 (19.7)	64 (20.8)	0.797
Cardiovascular disease	N (%)	137 (31.5)	29 (22.8)	108 (35.1)	**0.013**
Respiratory disease	N (%)	45 (10.3)	10 (7.9)	35 (11.4)	0.277
Thyroid disease	N (%)	63 (14.5)	13 (10.2)	50 (16.2)	0.106
Immunological disease	N (%)	25 (5.8)	7 (5.5)	18 (5.8)	0.892
Musculoskeletal disease	N (%)	101 (23.2)	22 (17.3)	79 (25.7)	0.061
Trauma history	N (%)	10 (2.3)	2 (1.6)	8 (2.6)	0.518
Psychiatric disease	N (%)	87 (20)	26 (20.5)	61 (19.8)	0.874
Neurological disease	N (%)	22 (5.1)	8 (6.3)	14 (4.6)	0.448
Genitourinary disease	N (%)	27 (6.2)	7 (5.5)	20 (6.5)	0.700

Bolded numbers are statistically significant values ($p < 0.05$). y: years, N: number, SD: standard deviation, MOH: medication overuse headache, CH: chronic headache, MO: medication overuse.

comorbidities, including psychiatric disorders such as depression and anxiety.

Phase 3

Ninety-eight of the 127 (77.2%) MOH patients identified by the GPs accepted to be evaluated at our Headache Center for the three-year follow up interview. All MOH patients were diagnosed as migraineurs, with a remarkable predominance of CM diagnosis (94.9%) compared to CCTH with additional episodic migraine (5.1%). The most frequently overused acute medications were non-steroidal anti-inflammatory drugs (NSAIDs) (58%), followed

by triptans (26.6%), combination analgesics (12.2%) and simple analgesics (3.1%).

Clinical conversion to episodic headache with resolution of MOH was reported by 53 (54.1%) patients. Twenty-seven (50.9%) patients achieved remission spontaneously (i.e., without specific pharmacological or educational/behavioral intervention), whereas the remaining patients reported remission in relation to several interventions: preventive pharmacological treatment in 20 patients (37.7%); lifestyle change in three subjects (5.7%); introduction or discontinuation of contraceptive therapy in two (3.8%) and pregnancy in one (1.9%).

Significant positive prognostic factors at baseline for MOH reversal were male sex (males 32.1% vs 13.3%;

p = 0.029), lower headache frequency (19.8 ± 5.8 vs 22.9 ± 6.2; p = 0.0116), and lower number of the concomitantly overused drug (one compound 86.8% vs 37.8%; two compounds 9.4% vs 35.5%; three compounds 3.8% vs 26.7%; p < 0.001). At least one previous period of spontaneous remission from CH status since disease onset was self-reported by both groups, although significantly more frequently in those who achieved remission at the scheduled evaluation (90.6% vs 37.8%, p < 0.001). No statistically significant differences were found between the two groups regarding the other variables of interest (Table 2 and 3).

Discussion

Our large study provides data on the prevalence of CH and MOH, as well as on the natural history and prognosis of MOH in the Italian population. International diagnostic criteria are not always applicable in population-based studies and CH is not an independent diagnosis listed on the international classification (ICHD-3), however, it includes headache disorders occurring at least 15 days per month. We found a prevalence of 3.8% and 1.4% for CH and MOH, respectively, with a persistent female predominant ratio (F:M = 3:1). Although MOH patients might have been mildly overestimated during Phase 1, due to the evaluation of medication overuse only in the previous month (i.e., instead of the actual three months period of evaluation), ensuing GPs diagnosis confirmation may have reduced this bias. A previous study on the elderly population reported a rate of 4.4% CH and 1.7% MOH among 833 Italians aged more than 65 years of age (29). However, no Italian

Table 2. Comparison of baseline characteristics between patients with and without MOH remission.

		Total	Remitted from MOH	Unremitted from MOH	p value
		N = 98	N = 53	N = 45	
Age, y	mean ± SD	49.2 ± 12.9	47.4 ± 14.2	51.4 ± 11.0	0.1229
Sex					
Males	N (%)	23 (23.5)	17 (32.1)	6 (13.3)	**0.029**
Females	N (%)	75 (76.5)	36 (67.9)	39 (86.7)	
BMI, Kg/m²	mean ± SD	25.7 ± 4.9	25.3 ± 4.7	26.0 ± 5.2	0.4945
Marital Status					
Single	N (%)	17 (17.3)	9 (17.0)	8 (17.8)	0.887
Married	N (%)	68 (69.4)	37 (69.8)	31 (68.9)	
Separated/Divorced	N (%)	8 (8.2)	5 (9.4)	3 (6.7)	
Widower	N (%)	5 (5.1)	2 (3.8)	3 (6.7)	
Employment					
Student	N (%)	3 (3.1)	3 (5.7)	0 (0.0)	0.127
Housewife	N (%)	12 (12.2)	5 (9.4)	7 (15.6)	
Self-employed	N (%)	13 (13.3)	10 (18.9)	3 (6.7)	
Employee	N (%)	49 (50.0)	22 (41.5)	27 (60.0)	
Unemployed	N (%)	7 (7.1)	5 (9.4)	2 (4.4)	
Retired	N (%)	14 (14.3)	8 (15.1)	6 (13.3)	
Years of Education, y	mean ± SD	10.7 ± 3.6	10.9 ± 3.6	10.5 ± 3.5	0.5312
Coffee intake					
No	N (%)	14 (14.3)	7 (13.2)	7 (15.6)	0.710
Occasionally	N (%)	3 (3.1)	1 (1.9)	2 (4.4)	
Daily	N (%)	81 (82.6)	45 (84.9)	36 (80.0)	
Smokers	N (%)	51 (52.0)	28 (52.8)	23 (51.1)	0.865
Family history					
Headache	N (%)	84 (85.7)	46 (86.8)	38 (84.4)	0.741
Chronic headache	N (%)	39 (39.8)	24 (45.3)	15 (33.3)	0.228
Age at Headache Onset, y	Med (IQR)	15 (12–20)	14 (12–18)	16 (12.20)	0.2936
Migraine with Aura	N (%)	13 (13.3)	6 (11.3)	7 (15.6)	0.538
Age at Headache Chronification, y	mean ± SD	32.1 ± 12.7	30.9 ± 13.9	33.5 ± 11.2	0.3089
Duration of Chronification, y	Med (IQR)	13.5 (6–26)	12 (4–26)	16 (8–26)	0.1526
Diagnosis of Chronic Headache					
Chronic Migraine	N (%)	93 (94.9)	52 (98.1)	41 (91.1)	0.116
CTTH + EM	N (%)	5 (5.1)	1 (1.9)	4 (8.9)	

Bolded numbers are statistically significant values (p < 0.05). y: years, SD: standard deviation, N: number, MOH: medication overuse headache, CTTH: chronic tension type headache, EM: episodic migraine, Med: median, IQR: interquartile range.

Table 3. Comparison of baseline characteristics between patients with and without MOH remission.

		Total	Remitted from MOH	Unremitted from MOH	*p* value
Type of Medication overused drugs					
Simple analgesics	*N (%)*	3 (3.1)	1 (1.9)	2 (4.4)	0.579
Combination analgesics	*N (%)*	12 (12.2)	6 (11.3)	6 (13.3)	
NSAIDs	*N (%)*	57 (58.2)	34 (64.2)	23 (51.1)	
Triptans	*N (%)*	26 (26.5)	12 (22.6)	14 (31.1)	
Number of medication overused drugs					
1	*N (%)*	63 (64.3)	46 (86.8)	17 (37.8)	
2	*N (%)*	21 (21.4)	5 (9.4)	16 (35.5)	**<0.001**
3	*N (%)*	14 (14.3)	2 (3.8)	12 (26.7)	
Headache Frequency at Screening, days	*mean ± SD*	21.2 + 6.1	19.8 + 5.8	22.9 + 6.2	**0.0116**
Past Spontaneous Remission from MOH	*N (%)*	65 (66.3)	48 (90.6)	17 (37.8)	**<0.001**
Past Preventive Treatment	*N (%)*	46 (46.9)	25 (47.2)	21 (46.7)	0.911
Comorbidities		87 (88.8)	45 (84.9)	42 (93.3)	0.188
Hypertension	*N (%)*	20 (20.4)	10 (18.9)	10 (22.2)	0.681
PCOS	*N (%)*	5 (5.1)	3 (5.7)	2 (4.4)	0.785
Fibrocystic mastopathy	*N (%)*	3 (3.1)	0 (0.0)	3 (6.7)	0.056
Hypothyroidism	*N (%)*	12 (12.2)	8 (15.1)	4 (8.9)	0.305
Raynaud Phenomenon	*N (%)*	4 (4.1)	1 (1.9)	3 (6.7)	0.233
Allergies	*N (%)*	23 (23.5)	11 (20.8)	12 (26.7)	0.491
Asthma	*N (%)*	3 (3.1)	2 (3.8)	1 (2.2)	0.657
Previous Head trauma	*N (%)*	28 (28.6)	15 (28.3)	13 (28.9)	0.949
Diabetes	*N (%)*	2 (2.0)	1 (1.9)	1 (2.2)	0.907
Sleep Problems	*N (%)*	41 (41.8)	23 (43.4)	18 (40.0)	0.734
History of Cancer	*N (%)*	0 (0.0)	0 (0.0)	2 (4.4)	0.121
Depression	*N (%)*	13 (13.3)	6 (11.3)	7 (15.6)	0.538
Anxiety	*N (%)*	30 (30.6)	13 (24.5)	17 (37.8)	0.156

Bolded numbers are statistically significant values ($p < 0.05$). MOH: medication overuse headache, NSAIDs: non-steroideal anti-inflammatory drugs, N: number, SD: standard deviation, PCOS: polycistic ovarian syndrome.

epidemiological study on an unselected adult population has been conducted so far, whereas worldwide previous epidemiological studies showed consistently high prevalence ranging between 1% to 10.5% for CH and 1% to 7.2% for MOH (3–21,30). Our study reinforces previous findings and provides highly reliable prevalence data, because of our multiple-level design, in which initially self-reported CH and MO diagnoses were secondarily confirmed by trained GPs.

We extensively evaluated the clinical features and evolution of MOH patients detected in our cohort. We found that all patients had headache with migrainous features, either suffering from CM (94.9%) or episodic migraine associated with CTTH (5.1%). Whereas MOH is considered a potential complication of all primary headaches, 80% of these patients have CM and the remaining patients have a migraine background or familial history of Migraine (30,31). Additionally, individuals who take medication for non-headache pain can develop MOH only if they suffer also from migraine (32). These data and our results support the hypothesis that MOH could be a specific migraine complication, rather than a headache secondary to pharmacologic overuse itself (24). However, we cannot exclude that

we have missed chronic non-migraine headache patients because they were less likely to participate due to a lower disability. Considering the overused acute medications, the most reported were NSAIDs (58%) and triptans (26.6%), while few patients used combination analgesics (12.2%) or simple analgesics (3.1%). None of our patients used opioids that are not widely used in Italy in accordance with current guidelines (33). Notably, a relatively high percentage of patients were triptans users, which correlates with previous Italian data (34). We extensively discussed the high rate of unknown primary headaches in primary care in a previous work (25), since 64.3% of CH sufferers were not known as such by their GPs (25). These data shed further light on the need for public health education and awareness policies for primary headaches and their proper management in the Italian primary care system, in order to provide better diagnostic accuracy and management, as well as resulting in a potential reduction in indirect social costs (22). After three years (Phase 3), we observed a 54.1% remission from both CH and MOH in a sample of 98 patients. Thirty-eight percent of patients reverted from MOH following preventive treatments, and 50% experienced spontaneous remission. Albeit debatable in

a three-year period, GPs were informed about the risks of medication overuse and their involvement in the study both during phase 1 and phase 2 may have played a role. Furthermore, 66% of MOH patients reported a previous period of spontaneous remission in their lifetime, supporting the conceivable dynamic nature of the disease. Natural fluctuations above and below the 15 headache days barrier for CM have been extensively reported (4–7,23,35–37). Whereas a similar spontaneous dynamic evolution of MOH was suggested, no study has specifically addressed this issue prospectively.

Previously, an 11-year follow-up population-based study reported a 74.5% CH remission rate in 605 patients interviewed with a lower likelihood of remission for MOH patients (37), corroborating the evidence of MO as a poor prognostic factor for CH (38). Nevertheless, our results suggest that MOH may also have a high remission rate, further promoting the idea that MOH is a fluctuating complication of migraine. In addition, 5.7% of patients identified lifestyle change as a key factor for remission, confirming the connection between behavioral patterns and risk for headache chronification and the need to encourage a multi-level approach with these patients (39).

Considering baseline characteristics, we observed that males are more likely to revert from MOH, as well as those who overuse a single type of acute medication; while those who are over-users of two or more compounds are less likely to achieve remission from MOH. Although this result may be secondary to a more frequent need for acute medications and a more difficult-to-treat headache, it also underlines the need for more specific and effective acute headache medication. Interestingly, the class of acute medications used did not influence remission.

Moreover, patients with lower headache frequency were more likely to revert spontaneously from MOH, compared to patients with a higher headache frequency, with the cut-off value being 22.9 headache days. Interestingly, a very similar finding was highlighted in a recent trial that described how patients with 23 or more acute medication intake days represented a subgroup who achieved better outcomes if they were switched off the overused medication (40). These data could support the need for more specific MOH diagnostic criteria in order to efficiently identify a subgroup of patients characterized by a distinct natural history and possibly, a distinct therapeutic approach. Contrary to what we would have expected, BMI, partnership status, and years of education did not appear to be negative prognostic factors for MOH. Interestingly, MOH and CH without MOH patients differ in cardiovascular disease prevalence and employment status,

probably due to the older age of non-over-users. Among other comorbidities, it is still unclear whether psychiatric diseases are real risk factors or consequences of MOH. In the present study, we found a relatively low rate of psychiatric diseases (20% of CH subjects interviewed by GPs; 13% of MOH suffered from depression and 30% from anxiety). Depression and anxiety did not differ between MOH and CH without MO patients. Moreover, psychiatric comorbidities did not affect MOH remission.

The strengths of our study are the following: (i) the large adult unselected population evaluated; (ii) the multiple level design which involved 20 GPs, allowing the good rate of answers (65.9% response rate) to our screening survey; (iii) collection of population data about MOH and CH without MO patients and confirmation of survey diagnosis by an expert physician and; (iv) the long three-years follow-up of MOH patients. Nonetheless, some limitations should be considered. Patients were initially selected and defined according to ICHD-2, even though all diagnoses of included patients were subsequently confirmed according to ICHD-3 whose definitions of MOH and CH overlap with previous criteria. At the screening survey, we used a cut-off of 15 day/month during the last month to define medication overuse, whereas ICHD allows medication overuse definition above 10 treatment days per month for triptans (1) and an evaluation period of three months. Hence, on one hand, we may have included some transient over-user patients in Phase 1; on the other hand, we may have missed a proportion of milder triptan over-users, yet the validity of MOH spontaneous remission may be considered even more impressive. Finally, although minimized by the high initial response rate, we cannot exclude a mild selection bias in those that returned the screening survey, those that accepted GPs interview and attended our Headache Center.

Conclusions

CH and MOH represent highly prevalent disorders with 3.8% and 1.4% respectively. Among MOH patients, 54% experienced remission from MOH after three years and 50% of them remitted spontaneously. We also found that the male sex, lower number of concomitantly used acute medications, and lower headache frequency are positive prognostic factors for spontaneous MOH remission, advocating a conceivable fluctuating nature of this condition and a need for current diagnostic criteria improving. Finally, our results highlight the priority of multi-level public health awareness and education policies, to provide better diagnostic accuracy and standard of care.

Key Findings

- CH and MOH represent highly prevalent disorders with 3.8% and 1.4% respectively.
- The high rate of spontaneous MOH remission after three years supports the dynamic nature of this condition and the need for more specific diagnostic criteria.
- Public health awareness and education policies should be empowered to provide better diagnostic accuracy and prevent complications of acute medication overuse.

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