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Comparison of chronic daily headache with and without medication overuse headache using ICHD II R and ICHD 3 beta criteria

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ABSTRACT

Objective: : To evaluate the frequency of Medication Overuse Headache (MOH) in the patients with Chronic Daily Headache (CDH) using International Classification of Headache Disorder II Revision (ICHD II R) and International Classification of Headache Disorder 3 Beta (ICHD-3 beta) criteria. We also compare the CHD patients with and without MOH using both the criteria.

Patients and Methods: : Consecutive CDH patients from neurology service between 2014 and 2015 were included. The patients with CDH was categorised to MOH was based on ICHDIIR and ICHD-3 beta criteria. Their demographic and headache characteristics including frequency, duration, severity and disability were noted. Severity of headache was assessed using Visual Analogue Scale (VAS). Predictors of MOH were evaluated by multivariate analysis. Demographic and headache characteristics of CDH patients without MOH were compared with those with MOH.

Results: : 202 patients were included whose median age was 32 (range 18–65) years, and 151(74.8%) were females. 12.3% patients fulfilled ICHDIIR criteria for MOH and 46.5% fulfilled ICHD-3 beta criteria. The predictors of MOH were female gender (OR = 3.72; 95% CI 1.72–8.02, p = 0.001), low education level (OR = 1.07, 95%CI 1.02–1.13; p = 0.007) and higher VAS score (OR = 0.67, 95%CI 0.51-0.88; p = 0.004). MOH patients as per ICHD-3 beta criteria had higher education (p = 0.02) and consumed lesser abortive drugs (p = 0.03) as compared with ICHDIIR criteria.

Conclusion: : The frequency of MOH increases by four-fold when using ICHD-3 beta criteria instead of ICHDIIR criteria. Females with lower education level predispose to MOH.

1. Introduction

Primary daily or near-daily headache is a chronic disabling condition leading to poor quality of life and productivity. Chronic daily headache (CDH) includes all primary headaches presenting with more than 15 (headache days) per month for 3 consecutive months. Primary CDH has been subclassified into short duration (< 4 h/attack) and long duration CDH (≥ 4 h duration/attack). Short duration CDH includes chronic cluster headache, and long duration CDH includes chronic tension-type headache (CTTH), chronic daily migraine (previously called transformed migraine), new daily persistent headache and hemicrania continua [1]. In the general population, the prevalence of CDH is up to 3.2% [2]. The proportions of MOH in a cohort of CDH may vary in different countries. These proportions also vary if different International Classification of Headache Disorders (ICHD) criteria are used. The prevalence of Medication Overuse Headache (MOH) in industrialised countries ranges between 1.4% and 1.7% in the general population [3], while it is nearly 6.1% in developing countries [4]. In Eurolight study, 8,271participants from nine European countries were evaluated using a questionnaire based on ICHD II, and found 1 year prevalence of chronic headache (≥15/month) in 7.2% and probable MOH in 3.1% participants. There was a susceptibility prevalence gradient; females were most susceptible to MOH (4.3% vs 1.8%) followed by migraine (43.6% vs 26.9%) and tension type headache (35.7% vs 40.7%) [5]. In India however, MOH has been less frequently reported. In an Indian study using the ICHD II classification, the frequency of MOH was 3.08% [6]. In another study from India, 24% of 169 CDH patients had MOH while using the ICHD I criteria [7]. The frequency of MOH however will dramatically change as the recent criteria have opened a wider window for the diagnosis. In a systemic review of literature including 27 studies, the prevalence of MOH in adults using ICHD II ranged between 0.5% and 7.2% [8]. The demographic features, migraine characteristics and triggers may be different in patients fulfilling the criteria of MOH as per ICHD II R [9] and ICHD-3 beta criteria

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[10]. A study from China compared MOH according to different criteria, and revealed that 6.1% patients out of 3923 fulfilled the ICHD-3 beta criteria for MOH; of which 55.9% met the MOH criteria according to ICHD II, and 81.2% met the MOH criteria according to ICHD IIR criteria [4]. There is however no report from India categorizing CDH and MOH using the ICHD II R and ICHD-3 beta criteria. The impact of demographic, sociocultural background, headache triggers and severity of headache may be different in the patients with MOH compared to those CDH patients without MOH. In this communication, we evaluate the frequency of MOH in a group of patients with CDH using both the ICHD II R and ICHD-3 beta criteria. We also compare the patients with and without MOH, and report the predictors of MOH using multivariate analysis.

2. Material and methods

This is a cross sectional hospital based study conducted at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India. Consecutive patients with primary long duration CDH attending to neurology outpatient service of our institute between 2014 and 2015 were recruited. The study protocol was approved by the Institute Ethics Committee (2014-172-IP-80), and all the patients consented for the study. The diagnosis of primary long duration CDH was made if the headache frequency was ≥15 days/month for 3 months, lasting more than 4 h if untreated, after excluding secondary causes [1]. Children below 18 years, pregnant women and patients with malignancy, stroke, epilepsy, psychiatric disorders, uncontrolled diabetes or hypertension, infections and those on vasodilator therapy were excluded from the study. The patients with CDH due to chronic cluster headache, hemicrania continua and new daily persistent headache were also excluded due to rarity.

2.1. Clinical evaluation

The demographic details (age, gender, and residence, and education level) and duration of illness of the patients were noted. The frequency, duration and severity of headache, associated symptoms and functional disability were recorded. The severity of headache was graded on a 0–4 scale (0 = none, 1 = mild, 2 = moderate, 3 = severe) and a 0–10 Visual Analogue Scale (VAS) [11]. The functional disability was graded on a 0–3 scale (0 = none, 1 = mild, 2 = moderate and 3 = severe) [12]. The Hospital Anxiety and Depression (HAD) score was calculated [13]. Patients were asked about their triggers for migraine using a prefixed questionnaire including various exogenous and endogenous triggers such as physical stress, mental stress, hunger, fasting, sleep deprivation, weather change, menstruation, travel, food, perfume and exposure to bright sun, noise, cold and hot [14,15]. The presence of allodynia and its extent was evaluated by using another questionnaire [16,17]. The allodynia was divided into mechanical, dynamic, static and thermal. Comorbidities such as hypertension and diabetes were also noted.

2.2. Drug intake

The number and types of abortive drugs consumed during the previous 3 months were noted along with treatment response.

2.3. Categorization of patients

Patients with primary long duration CDH were categorised into chronic daily migraine and chronic tension type headache (CTTH) as per the ICHD II R criteria, and details of their diagnostic criteria are summarized in supplementary Table 1 [7]. The diagnosis of MOH was done using both the ICHD II R [9] and the ICHD-3 beta criteria [10], which are summarized in Table 1.

2.4. Statistical analysis

The demographic features, triggers, migraine characteristics, functional impairment and HAD scores between patients with CDH and MOH (diagnosed separately by ICHD II R and ICHD-3 beta criteria) were compared using the Chi-square test for categorical variables, and the student 't' test or Mann-Whitney 'U' test for continuous variables. The predictors of MOH were evaluated using multivariate logistic regression analyses with Bonferroni correction. Variables were considered significant if the two-tailed p value was ≤ 0.05. The statistical analysis was done using the SPSS 16-version software and GraphPad Prism 5.

3. Results

3.1. Patient characteristics

Two-hundred-and-two consecutive patients with CDH were included, of them 151 (74.8%) were females. Their mean age was 33.6 (SD, ± 9.94) years, and 53% were from rural areas. Seventeen patients were illiterate, 10 had been educated up to class five, and the rest were educated more than 6th standard (mean years of education10.37 ± 5.84). The mean duration of illness was 8.5 (SD, ± 6.61) years. 166 (82.2%) patients had chronic daily migraine, 29 (14.4%) had CTTH and seven (3.5%) had mixed features (Fig. 1). Out of 202 patients with CDH, 25 (12.3%) patients fulfilled the criteria of MOH based on the ICHD II R criteria. The number of MOH patients increased to 94 (46.5%), when MOH was diagnosed using the ICHD-3 beta criteria.

3.2. Comparison of clinical characteristics

3.2.1. CDH (without MOH) and MOH (according to the ICHD II R criteria)

Patients with MOH did not differ from CDH with respect to age, duration of illness and demography, but the years of education was significantly lower in patients with MOH (6 ± 5.34 vs 10.89 ± 5.73; p = 0.001). Interestingly, none of the patients with CDH educated to the postgraduate level had MOH. All patients with MOH had migraine as their primary headache diagnosis. The total number of triggers was also significantly higher in chronic daily migraine patients with MOH (8.32 ± 2.13 vs7.25 ± 2.8; p = 0.03). Total duration of headache, associated symptoms and functional disabilities were however not different between the MOH and CDH groups (Table 2).

3.2.2. CDH (without MOH) and MOH (according to the ICHD-3 beta criteria)

On comparing patients with MOH and those with CDH, it was found that a significantly higher proportion of females had MOH (88.3% vs 63%; p = 0.001). Patients with MOH had insignificantly fewer years of education (9.48 ± 6.03 vs 11.69 ± 5.35; p = 0.001), a higher VAS score at presentation (6.15 ± 1.20 vs 5.63 ± 1.07, p = 0.002) and higher number of total triggers (7.79 ± 2.67 vs 7.03 ± 2.90, p = 0.05) compared to those with CDH (Table 3).

3.2.3. Comparison of MOH as per ICHD IIR and ICHD 3 beta criteria

There were 94 patients with MOH according to the ICHD-3 beta criteria, of which 25 did not respond to abortive treatment, and formed the MOH group as per the ICHD II R criteria. The remaining 69 patients with MOH according to the ICHD-3 beta criteria responded to abortive treatment. MOH patients as per ICHD-3 beta criteria had higher education (p = 0.02) and consumed lesser abortive drugs (p = 0.03) as compared with ICHDIIR criteria. However, the comparison of their demographic features, migraine characteristics and HAD scores were not significantly different (Table 4).

3.2.4. Abortive drugs used in MOH group

Majority (47.50%) of the MOH patients consumed combination of

Table 1
Diagnostic criteria of medication overuse headache (MOH) using ICHDIIR and ICHD 3 beta criteria.

ICHDIIR criteria of MOH	ICHD 3 beta criteria for MOH
Headache occurring ≥ 15 days / month for ≥ 3 months; Use of 15 single NSAIDS or 10 (combination NSAIDS or ergot or triptans or opiods) abortive drugs /month for ≥ 3 months; Headache either not responding to, or is worsened by abortive drugs, Headache resolving or reverting back to the previous pattern after 2 months of medication withdrawal	Headache occurring ≥ 15 days/month for ≥ 3 months; Use of 15 single NSAIDS or 10 (combination (NSAIDS or ergot or triptans or opiods) abortive drugs/month for ≥ 3 months; No better headache diagnosis according to the ICHD-3 beta criteria

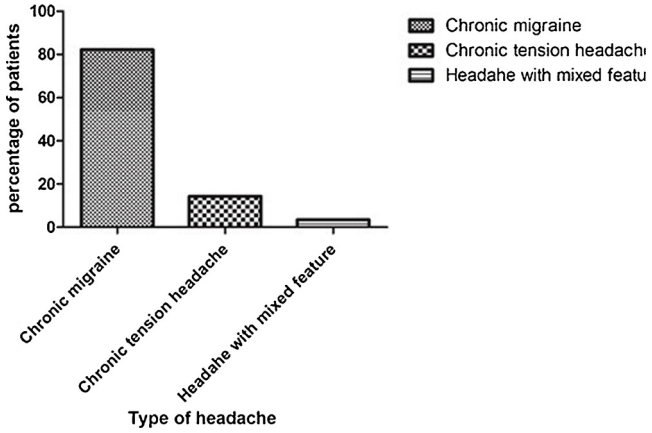

Fig. 1. Bar diagram shows number of patients with chronic migraine (CM), chronic tension headache (CTH) and mixed type of chronic daily headache in a cohort of chronic daily headache (CDH).

NSAIDs (paracetamol + nimesulide /diclofenac/ibuprofen, naproxen + domperidone). This was followed by a single NSAID by 27 (28.7%), opioids (tramadol) by 6 (6.3%), paracetamol, caffeine and propyphenazone combination by 4 (4.2%), homeopathic medications by 4 (4.2%), ergotamine by 1(1.1%), ergotamine-NSAID combination by 4 (4.3%) and triptan-NSAID combination by 1 (1.1%) patient (Fig. 2).

3.2.5. Predictors of MOH

On univariate analysis, MOH (ICHD-3 beta criteria) was more frequent in females (p = 0.001). In comparison to the CDH patients without MOH, the MOH patients were less educated (years of education 9.48 ± 6.03 vs 11.69 ± 5.35; p = 0.001), and had a higher VAS score at presentation (6.15 ± 1.20 vs 5.63 ± 1.07; P = 0.002). On multivariate analysis, the best predictors of MOH amongst patients with CDH were female gender (OR = 3.72; 95% CI 1.72–8.02, p = 0.001), lower education level (OR = 1.07, 95% CI 1.02–1.13; p = 0.007) and higher VAS score (OR = 0.67, 95% CI 0.51–0.88; p = 0.004) (Fig. 3).

4. Discussion

In this study, only 12.3% patients with CDH had MOH as per ICHD II R criteria which had increased to 46.5% when the ICHD-3 beta criterion was used. This four-fold increase in the frequency of MOH in the same cohort of CDH patients highlights the greater sensitivity of ICHD-3 beta criteria in the diagnosis of MOH. This may be due to less stringent

Table 2
Comparison of demographic, migraine triggers, and migraine characteristics between the patients of CDH with medication overuse headache (MOH) as per ICHD IIR and chronic daily headache (CDH).

Characteristics		MOH (N = 25)	CDH (N = 177)	P value
Age in years		34.68 ± 9.01	33.49 ± 10.08	0.54
Gender (female)		22(88%)	129(72.9%)	0.14
Dwelling	Rural	13(52.0%)	94(53.1%)	1.00
	Urban	12 (48.0%)	83(46.9%)	
Total years of education		6 ± 5.34	10.89 ± 5.73	0.001
Total duration of headache (in years)		8.52 ± 5.69	8.56 ± 6.74	0.97
Headache triggers		25(100%)	171(96.6%)	1.00
Total no of triggers		8.32 ± 2.13	7.25 ± 2.8	0.03
Years to develop MOH/CDH(Duration of CDH)		1.64 ± 2.23	1.95 ± 2.06	0.51
Headache frequency in days		21.20 ± 6.10	21.48 ± 6.86	0.83
Duration of headache in hrs		21.88 ± 15.00	21.48 ± 6.86	0.83
Severity of headache	Severe	10(40%)	49(27.7%)	
	Moderate	15(60%)	128(72.3%)	
Nausea		17(80%)	114(64.4%)	0.82
Vomiting		12(48.0%)	69(39.0%)	0.39
Photo/phonophobia		24(96%)	165(93.2%)	0.50
Allodynia		20(80.0%)	119(67.2%)	0.25
VAS score		6.40 ± 1.29	5.80 ± 1.13	0.03
HADS (total)		7.76 ± 5.54	7.78 ± 5.21	0.98
HADS(anxiety)		3.76 ± 2.60	4.07 ± 2.69	0.57
HADS(depression)		3.92 ± 3.60	3.68 ± 3.18	0.75
Type of abortive drugs used	Single NSAID	7(28%)	62(35%)	
	Combination NSAID	10(40.%)	86(48.5%)	
	PCM + caffeine + phenazone	2(8%)	7(3.9%)	
	Ergotamine + NSAID	4(16.0%)	3(1.7%)	
	Opiates + NSAID	2(8%)	5(2.8%)	
	Triptan + NSAID	0	3(1.7%)	
	Ergotamine	0	3(1.7%)	
	Homeopathic	0	4(2.3%)	

HADS = Hospital Anxiety and Depression Scale.

Table 3
Comparison of demographic, migraine triggers, and migraine characteristics between the patients of CDH with medication overuse headache (MOH) as per ICHD IIIβ criteria and chronic daily headache (CDH).

Characteristics		MOH (N = 94)	CDH (N = 108)	P value
Age in years		34.01 ± 9.62(median = 32)	33.31 ± 10.24(median = 33)	0.62
Gender (female)		83(88.3%)	68(63%)	< 0.001
Dwelling	Rural	53(56.4%)	54(50%)	0.39
	Urban	41(43.6%)	54(50%)	
Total years of education		9.48 ± 6.03(med = 9.50) (0-20)	11.69 ± 5.35(med = 12) (0-23)	0.001
Total duration of headache in yrs		9.48 ± 5.99(med = 8)	7.75 ± 7.03(med = 5)	0.06
Duration of CDH in years		1.97 ± 2.02(med = 1)	1.85 ± 2.14(med = 1)	0.67
Headache triggers		92(97.9%)	104(96.3%)	0.68
Total no of triggers		7.79 ± 2.67(median = 8)	7.03 ± 2.90(median = 7)	0.05
Migraine aura		3(3.2%)	12(11.15)	0.05
Type of abortive drug used	Simple NSAID	27(28.7%)	42(38.9%)	
	Combination NSAID	47(50.0%)	49(45.3%)	
	Opiates + PCM	6(6.3%)	1(0.9%)	
	PCM + caffeine + phenazone	4(4.2%)	5(4.6%)	
	Ergotamine	1(1.06%)	2(1.9%)	
	Ergotamine + NSAID	4(4.3%)	2(1.9%)	
	Triptan + NSAID	1(1.06%)	2(1.8%)	
	Homeopathic/alt medicine	4(4.2%)	0	
Frequency of headache in days/mo		20.59 ± 6.18(median = 16)	22.19 ± 7.16(median = 17)	0.08
Duration of headache in hrs		19.76 ± 12.23(median = 24)	16.90 ± 14.29	0.12
Severity of headache	Moderate	65(69.1%)	78(72.2%)	
	Severe	29(30.9%)	30(27.8%)	
VAS score		6.15 ± 1.20(median = 6)	5.63 ± 1.07(median = 6)	0.002
Nausea		70(74.5%)	61(56.5%)	0.008
Vomiting		41(43.6%)	40(37%)	0.26
Photo/phonophobia		90(95.7%)	99(91.7%)	0.26
Allodynia		72(76.6%)	67(62.0%)	0.87
HAD score (total)		7.71 ± 5.03(median = 7)	7.83 ± 5.43(8.00)	0.87
HAD score(anxiety)		3.87 ± 2.68	4.18 ± 2.6	0.42
HAD score (depression)		3.78 ± 3.22	3.65 ± 3.24	0.77

HAD = Hospital Anxiety Depression.

Table 4
Comparison of demographic and clinical characteristics of patients of CDH with medication overuse headache (MOH) as per ICDH IIR and ICDH IIIβ criteria who did not fulfilled ICDH IIR criteria.

Characteristics		MOH (ICHDIIR) (N = 25)	MOH (ICHD3β) (N = 69)	P value
Age in years		34.68 ± 9.01	33.77 ± 9.88	0.68
Gender (female)		22(88%)	61(88.4%)	1.00
Dwelling	Rural	13(52%)	40(58%)	0.64
	Urban	12 (48%)	29(42%)	
Total years of education		6.64 ± 5.34	9.64 ± 6.1	0.02
Total duration of headache (in years)		8.52 ± 5.69	9.83 ± 6.10	0.33
Headache triggers		25(100%)	67(97.1%)	1.00
Total no of triggers		8.32 ± 2.13	7.59 ± 2.83	0.18
Years to develop MOH/CDH		1.64 ± 2.23	2.10 ± 1.94	0.36
Total no of drugs /month		34.04 ± 21.30	24.09 ± 12.92	0.03
Headache frequency in days		21.20 ± 6.10	20.36 ± 6.24	0.56
Duration of headache in hrs		21.88 ± 15.00	18.99 ± 11.09	0.38
Severity of headache	Severe	10(40%)	50(72.5%)	
	Moderate	15(60%)	19(27.5%)	
Nausea		17(68%)	53(76.8%)	0.55
Vomiting		12(48.2%)	29(42%)	0.64
Photo/phonophobia		24(96%)	66(95.7%)	1.00
Allodynia		20(80%)	352(75.4%)	0.78
VAS score		6.40 ± 1.29	6.06 ± 1.17	0.25
HADS (total)		7.76 ± 5.54	7.70 ± 4.88	0.95
HADS(anxiety)		3.76 ± 2.60	3.91 ± 2.72	0.80
HADS(depression)		3.92 ± 3.60	3.72 ± 3.09	0.81
Type of abortive drugs used	Single NSAID	7(28%)	20(29.0%)	
	Combination NSAID	10(40%)	37(39.36%)	
	PCM + caffeine + phenazone	2(8.0%)	2(2.12%)	
	Ergotamine + NSAID	4(16%)	0	
	Opiates + NSAID	2(8.0%)	4(4.2%)	
	Triptan + NSAID	0	1(2.0%)	
	Ergotamine	0	1(1.06%)	
	Homeopathic	0	4(5.8%)	

HADS = Hospital Anxiety and Depression Scale.

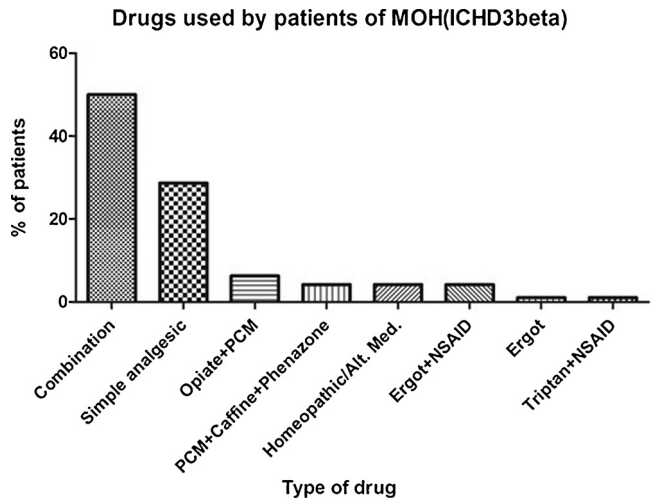

Fig. 2. Bar diagram shows types of abortive drugs in the patients with medication overuse headache.

criteria for the diagnosis of MOH in ICHD-3 beta criteria as reversal of headache to baseline after withdrawal of drug for 2months, and worsening or non-responsiveness of headache to abortive dugs are not required. Amongst the patients with CDH, the best predictors of MOH were female gender, lower education and higher VAS scores. About 80% of MOH patients overused single or multiple NSAID combinations.

This study comprehensively evaluated the frequency of MOH in Indian CDH patients and its predictors using two diagnostic criteria. There are reports from different countries about the frequency of MOH and its predictors, but majority of these studies were based on earlier criteria, resulting in a lower frequency of MOH [18,19]. In a study from South America, 80% of MOH patients were females, and 96.4% had migraine as the primary diagnosis. 43.8% of MOH patients reported emotional stress, and 43.8% had insomnia. Ergotamine (70%) was the most frequently consumed drug, followed by NSAIDs (33.8%) and triptans (5.4%) [20]. Another study reported a higher disability and anxiety score in MOH patients, when compared with healthy controls [21]. In our study, HAD score and functional disability were not significantly different in MOH and CDH patients. In a study on CDH from Eastern India, 82.4% patients had chronic or transformed migraine, 16.1% had CTTH, while 15.5% were new persistent headache. The factors associated with chronic or transformed migraine were psychological stress (44.4%), ergot (41%) and analgesic overuse (28.4%) [7]. In the present study also, a majority of patients with CDH had migraine, and only 14.4% had CTTH. The lower frequency of ergotamine use may be due to rising concerns regarding its toxicity in recent years. In a population-based study on 7417 adults with headache, 0.2% had chronic migraine, and half of them fulfilled the HIS (International Headache society) criteria for MOH. Smokers and patients with body mass index more than 30 were more susceptible to chronic migraine and MOH [2].

The predictors of MOH in our study were female gender, fewer years of education and a higher VAS score. Patient with severe headache is likely to consume abortive medication which may result in MOH. Ignorance about the side effects of excessive NSAID and other abortive medication intake may make these patients vulnerable to medication overuse. Patients from lower socioeconomic strata may be unable to avail specialized medical care due to pre-existing poor health infrastructure. Association of MOH with lower education and socioeconomic status was reported in a large randomly-selected population from Sweden [3].

There is only few studies reporting the incidence of MOH based on ICHD-3 beta criteria. In a study, out of 240 patients with MOH, 55.8% fulfilled the ICHD II criteria, while 81.2% fulfilled the ICHD II R

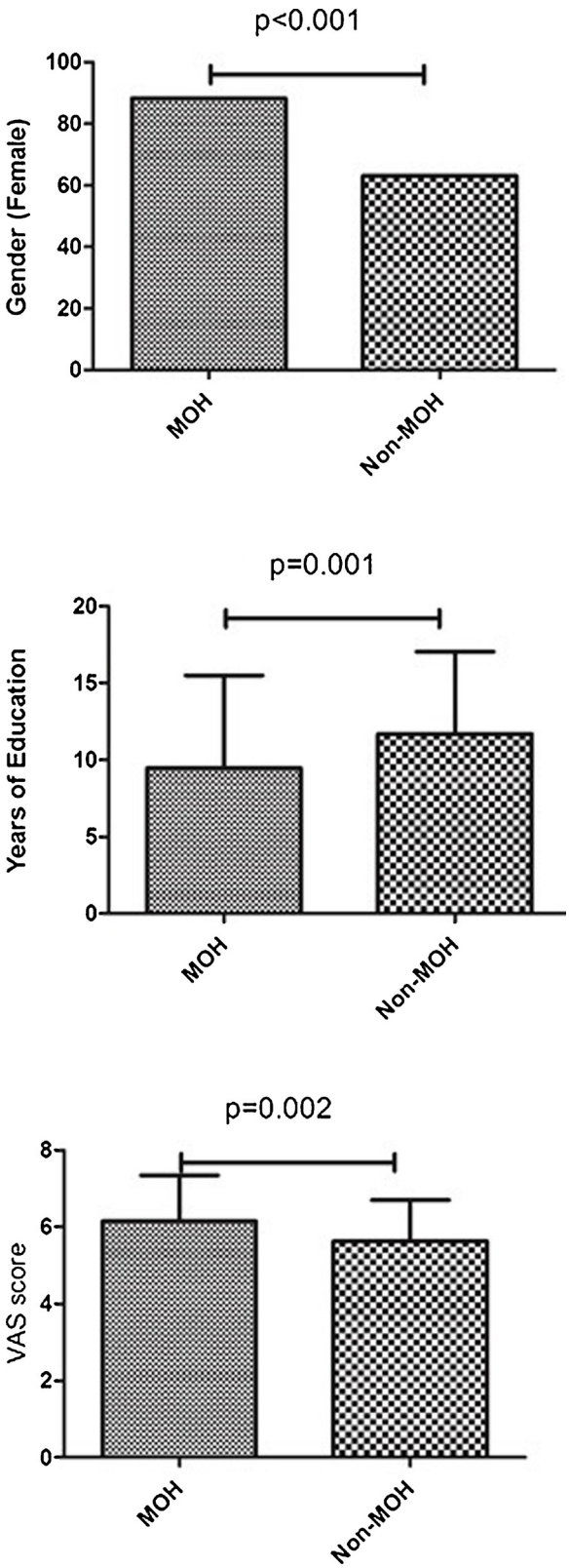

Fig. 3. Error bar diagrams showing predictors of medication overuse headache (MOH) in the cohort of chronic daily headache.

criteria. This study also reported an association of MOH with lower education and lower socioeconomic status [4]. Females may have an inherent susceptibility to migraine, due to the influence of female hormones. After the onset of the menarche, the prevalence of migraine is higher in girls than in boys, and nearly 50% of migraine attacks in

girls appear to be associated with the menstrual cycle. The higher prevalence of migraine at puberty may be due to resetting of hypothalamic neuroendocrine circuits which determine sexual dimorphism. Resetting of hypothalamic hormones in migraine may also alter the trigeminovascular system, a key player of neural pathway in migraine. In females, there may be enhanced excitability and sensitization of neurons through estrogen-driven mismatch in homeostatic gene regulation and the resultant mitogen-activated membrane hyperexcitability [22].

Migraine characteristics, its triggers and allodynia were not different between chronic migraine and MOH groups, suggesting a similar pathophysiological basis. Following triptan use, increased CGRP (calcitonin gene-related peptide), endogenous facilitation of pain, and impaired endogenous pain inhibition have been reported in patients with MOH [23]. The mechanism of MOH following NSAID overuse is however not well known. There may be a rebound phenomenon of release of pain-mediating substances following frequent and prolonged NSAID and ergotamine use.

The present study is limited by a small sample size, lack of follow up to evaluate the effect of withdrawal of abortive medicine and lack of biochemical markers for the possible pathophysiology of MOH. The strength of this study is detailed evaluation of all the patients by an experienced neurologist.

5. Conclusion

From this study, it can be concluded that the frequency of MOH increases by four-fold when the ICHD-3 beta criteria is used compared with the ICHD IIR criteria. The best predictors of MOH are female gender, higher VAS score and lower education status according to ICHD 3 beta criteria.

Ethical approval

This study was approved by the SGPGI Institute Ethics Committee (2014-172-IP-80). The patient consented for the study.

Conflict of interest

None.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Acknowledgement

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.clineuro.2019.105382.

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