Chronic frequent headache in the general population

Wiendels, N.J.

Chapter 6

Medication overuse in patients with chronic frequent headache in the general population

Submitted

Natalie J Wiendels[1,2]
Arie Knuistingh Neven[2]
Philip Spinhoven[3,4]
Frans G Zitman[4]
Willem J J Assendelft[2]
Michel D Ferrari[1]

From the departments of [1]Neurology, [2]Public Health and Primary Care,[3]Psychology and, [4]Psychiatry, Leiden University Medical Center, Leiden, The Netherlands

Abstract

We studied patterns and type of medication overuse in patients with chronic frequent headache (CFH: headache on >14 days/month for three months) from the Dutch general population. Patients were identified in a general health survey and were asked questions about headache characteristics and medication use. We compared CFH subjects with medication overuse (as defined by the International Classification of Headache Disorders – II) to those without overuse. Of 177 CFH subjects, 104 (59%) overused medication and 73 (41%) did not. Overuse consisted of analgesics (96%), triptans (2%), opioïds (4%), and various combinations (1%). The majority of subjects with overuse showed signs of drug tolerance; 71% had increased dosage gradually (vs. 41% in the group without overuse, difference 29%, 95% CI 14 to 43), and 64% took medication despite lack of efficacy (vs 27% without overuse, difference 37%, 95% CI 23 to 51). Fourty subjects with overuse (39%) regularly took analgesics to prevent headache, compared to only 14 (19%) in the group without overuse (difference 19%, 95% CI 6 to 33). Only 23 CFH subjects (13%) used prophylactic medication. Distribution of headache types was similar in both groups; we classified 94 (53%) subjects as having chronic tension-type headache, 42 (24%) as chronic migraine, 12 (7%) as miscellaneous, and 29 (16%) could not be classified. We conclude that medication overuse in the general population mainly concerns analgesic overuse. Many subjects show drug tolerance, inappropriate use of analgesics and lack prophylactic medication.

Introduction

Chronic frequent headache is an increasing problem worldwide.[1] Clinical observation suggests that overuse of acute headache medication and caffeine increases headache frequency in susceptible patients. A causal relationship between overuse and chronification of headache is assumed because discontinuation of overused medications and caffeine frequently results in improvement of headache.[2] Moreover, many headache patients with medication overuse fulfil criteria for substance dependence as described in the Diagnostic and Statistical Manual of Mental Disorders, Edition IV (DSM-IV).[3] The International Classification of Headache Disorders – II (ICHD-II) now includes criteria for medication overuse headache (MOH): chronic headache induced by overuse of acute headache medication like analgesics or triptans.[4] The diagnosis of MOH becomes definite only when headache improves after withdrawal. Until then, patients are classified as having *probable* MOH. Most information about MOH comes from headache clinics where the majority of patients are severe migraine patients.[5] Little is known about the clinical characteristics of medication overuse in the general population. Our objective was to study the patterns and type of medication overuse in chronic frequent headache in the general population.

Methods

We conducted a general health survey (Q1) amongst all persons, aged 25-55, registered at 16 general practices in the province of South-Holland in The Netherlands in 2003. This sample represents the general population because in the Netherlands all individuals are registered at a single general practice. The study design and methodology have been described in detail previously.[6] Briefly, we identified subjects with CFH, which was defined as headache on > 14 days per month during the past three months. All CFH subjects received a second, more detailed, questionnaire (Q2) containing questions on headache characteristics and treatment. In total 21,440 subjects received Q1, and 16,232 (76%) completed Q1. Prevalence of CFH was 4% (n = 679). Q2 was sent to 654 CFH subjects and completed by 273 (42%) subjects. The non-respondent analysis showed no relevant differences in age, sex and educational level; non-responders were slightly younger and were more often males than the respondents. Re-assessment of headache frequency in Q2 showed that headache frequency had changed in many subjects. We limited further analyses to the 177 CFH subjects in whom the reported headache frequency had not changed between the two surveys.

Because the study was conducted in 2003, we reclassified our subjects according to the new ICHD-II criteria for MOH in 2005.[4] Overuse is present when patients use simple analgesics on ≥ 15 days/month or other acute headache medication like triptans on ≥ 10 days/month. Because withdrawal had not been attempted at the time subjects completed the questionnaire, we could only diagnose probable MOH. Clinical features of CFH subjects with overuse were compared to CFH subjects without overuse. We asked subjects which headache pattern fitted their situation best: a) headaches come in attacks, in between there is no headache at all, b) a continuous headache which is present almost daily, and does not vary much in intensity, or c) a continuous headache which is present almost daily, with superimposed attacks of moderate to severe headache (Figure 1). We classified CFH into three subgroups: chronic tension-type headache (CTTH), chronic migraine (CM), and new daily persistent headache (NDPH), according to the ICHD-II. Associated symptoms were considered present when subjects answered to be nauseated or suffer from photo- and/or phonophobia most of the time when having headaches. For the diagnosis CTTH, mild nausea or mild photo- and/or phonophobia were allowed. Vomiting excluded CTTH. NDPH was diagnosed when headaches had started suddenly or had evolved into a daily headache in only a few days, with CTTH characteristics. If subjects reported that daily headaches started after an accident with head or neck trauma or whiplash injury, we classified them accordingly.

Descriptive statistics were performed with SPSS, version 12.0.1. Differences between groups are presented with 95% confidence intervals (95% CI). The Medical Ethics Committee of Leiden University Medical Centre approved this study.

Results

Demographic characteristics of 177 subjects with CFH are presented in table 1. There were slightly more subjects with a high educational level in the group without overuse. Of the 177 CFH subjects, 145 (82%) subjects used analgesics, 12 (7%) subjects used triptans, only one used ergotamine, and nine (5%) used opioïds. Overuse was present in 104 CFH subjects (59%), 73 (41%) had no overuse.

Table 1 Characteristics of CFH subjects with overuse vs. CFH subjects without overuse

	Total N = 177	Overuse N = 104	No overuse N = 73	mean difference (95%CI)
Mean age, y (SD)	43 (8)	44 (8)	42 (9)	2 (-0.3 to 4.8)
Female, n (%)	127 (72)	78 (75)	49 (67)	8% (-6 to 22)
Educational level				
Low, n (%)	62 (35)	37 (36)	25 (34)	2% (-13 to 17)
Medium, n (%)	70 (40)	47 (46)	23 (32)	15% (0 to 29)
High, n (%)	43 (25)	18 (18)	25 (34)	-17% (-30 to -4)
Age at onset headache, y (SD)	19 (11)	18 (10)	20 (13)	-2 (-5 to 2)
Age at onset CFH, y (SD)	25 (12)	24 (11)	26 (13)	-2 (-5 to 2)

Table 2 shows use and percentage of overuse per drug. Overuse consisted mainly (96%) of analgesics; 83 subjects overused simple analgesics, and 17 overused combination analgesics. Only two subjects (2%) overused triptans, and these two also overused analgesics. Four (4%) overused opioïds, two in combination with analgesic overuse. Two subjects (1%) overused various combinations of acute medication. There was no ergotamine overuse.

Table 2 Use and overuse per drug in 177 CFH subjects

	Analgesics	Triptans	Ergotamine	Opioïds
Number of users in total CFH group	145	12	1	9
Number of overusers	100	2	0	4
Percentage overuse in total CFH group	56%	1%	0%	2%
Percentage overuse in users	69%	17%	0%	44%

Differences in intake behaviour between CFH subjects with overuse and those without overuse are presented in Table 3. The majority of overusing subjects had gradually increased dosage of acute medication and took medication despite lack of efficacy. Many admitted to take analgesics regularly to prevent headache. Few used prophylactic medication.

Table 3 Medication use characteristics of CFH subjects with overuse vs. without overuse

	Total N = 177	Overuse N = 104	No overuse N = 73	mean difference (95%CI)
Gradual increase dosage	105 (59)	74 (71)	31 (42)	29% (14 to 43)
Intake despite lack of efficacy	87 (49)	67 (64)	20 (27)	37% (23 to 51)
Intake to prevent headache	54 (31)	40 (39)	14 (19)	19% (6 to 33)
Prophylactic medication*	23 (13)	17 (16)	6 (8)	8% (-2 to 18)
Headache indication	15 (8)	11 (11)	4 (6)	5% (-4 to 13)
Comorbid indication	8 (5)	6 (6)	2 (3)	3% (-4 to 10)

*Prophylactic medication can be either used for prevention of chronic headache, or for a comorbid disorder (e.g. propanolol for migraine or hypertension).

Headache patterns were similar in both the overuse group and the group without overuse; in 22 of the 177 subjects (12%) headaches came in attacks, with no headache in between (figure 1, pattern A), in 62 subjects (35%) headache was continuous without attacks (figure 1, pattern B), and 91 subjects (51%) experienced their headaches as continuous with superimposed attacks of moderate to severe headache (figure 1, pattern C). Two subjects did not answer the question on headache patterns.

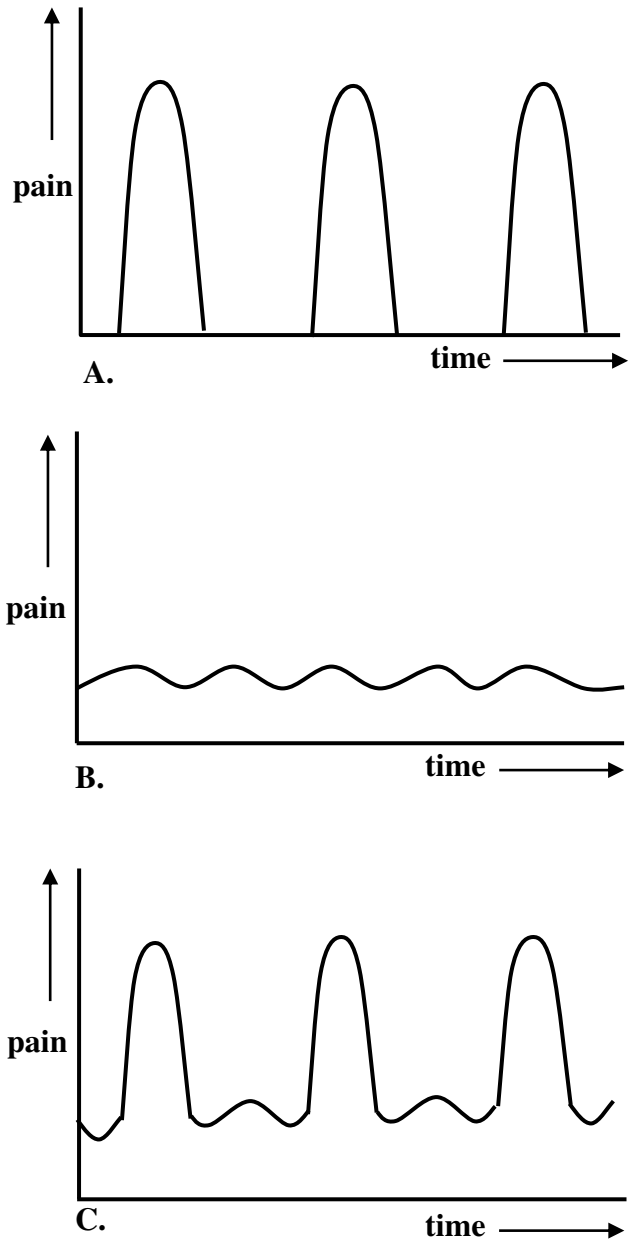

Figure 1 *Headache patterns*

Headache type according to ICHD-II is presented in table 4. There were no relevant differences in diagnosis between the overuse group and the group without overuse. Most subjects could be classified as chronic tension-type headache, of which 21 (22%) also had migraine attacks without aura, and six (6%) migraine with aura. A considerable number could not be classified, mostly (in 72%) due to a combination of tension-type headache characteristics with vomiting or photo- and phonophobia, and to a lesser extent (in 21%) due to migraine headache characteristics without associated symptoms. The diagnostic category "miscellaneous" consisted of chronic posttraumatic headache (n=3) and chronic headache due to whiplash injury (n=2).

Table 4 Headache diagnosis according to ICHD-II

	Total N = 177	Overuse N = 104	No overuse N = 73	mean difference (95%CI)
CTTH*	94 (53)	56 (54)	38 (52)	2% (-13 to 17)
CM*	42 (24)	25 (24)	17 (23)	1% (-12 to 14)
NDPH*	7 (4)	1 (1)	6 (8)	-7% (-13 to -2)
Miscellaneous	5 (3)	1 (1)	4 (5)	-4% (-10 to 1)
Not classifiable	29 (16)	21 (20)	8 (11)	9% (-2 to 20)

Values are number (%). CTTH = chronic tension-type headache, CM = chronic migraine, NDPH = new daily persistent headache. * In case of overuse, the headache diagnosis should be preceded by *probable,* until causation by medication can be refuted after withdrawal.

Discussion

In our population-based study the majority (56%) of CFH subjects overused analgesics, only a few (2%) overused triptans or opioïds. When expressed as percentage of medication users, the pattern was the same: 69% of analgesic users were overusers, 17% of triptan users and 44% of opioïd users. Overuse of analgesics is likely to be more prevalent in the general population than triptans, because analgesics are over-the-counter products. Twelve CFH subjects (7%) currently used triptans. Only two of them overused triptans and in combination with analgesic overuse. The low percentage of triptan overuse, despite high headache frequency, suggests that the risk of overuse in triptan users is low.

The majority could be classified as chronic tension-type headache. This is in contrast to studies in headache clinics where the majority of patients with MOH are migraine patients and many overuse triptans.[1] The different distribution of headache type and overuse illustrates that referred patients in headache clinics comprise a totally different, selected, population. One cannot extrapolate conclusions from studies conducted in headache clinics to the general population without accounting for differences in clinical characteristics. Although the distribution of headache types was similar in both the overuse group and the group without overuse, almost twice as many subjects with overuse could not be classified. It is possible that overuse obscures typical features and that the underlying headache type becomes apparent only after withdrawal.

Some general aspects of our study should be taken into account when interpreting our results. First, our sample consisted of non-consulting patients who are possibly different from consulting patients in general practice. Our results therefore apply to the general population, not to general practice. Secondly, our study is questionnaire based. Although headache diagnosis is always more reliable when obtained by interview, our questionnaire was based on diagnostic criteria of the International Headache Society, and the distribution of chronic headache types is in agreement with other population-based studies.[7,8] Lastly, because of the cross-sectional design, we did not study the direction of a possible causal relation between overuse and chronic headache. However, many overusers showed characteristics of dependence, which makes a diagnosis of MOH more likely. The majority had noticed a gradual increase in dosage over time and took medication despite lack of efficacy suggesting development of drug tolerance. This is in accordance with the clinic-based study by Fuh et al.,

where over 70% of patients with probable MOH fulfilled DSM-IV criteria of tolerance.[3] Another mechanism for the development of overuse could be inappropriate use of analgesics; many took analgesics to prevent headache. The use of prophylactic medication in a population with chronic headaches is remarkably low, leaving room for improvement of treatment.

We conclude that medication overuse headache in the general population in the Netherlands mainly concerns analgesic overuse. To prevent overuse in the general population, public information should be primarily aimed at appropriate use of analgesics and the possibility of prophylactic treatment when headache frequency increases.

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