Medication overuse headache in Spain

EPIDEMIOLOGY AND DEMOGRAPHICS

Spain has been a pioneer in the study of chronic daily headache (CDH) epidemiology. One of the main reasons for our interest in carrying out this kind of study is the way in which our health system is organized. In Spain > 95% of people only have public health insurance, and we all have one specific and stable family doctor in a Health Centre, a necessary intermediary for referral to a specialist in case of necessity. Therefore, it is easy to perform true epidemiological studies from Health Centres in such a country where people move infrequently.

Almost a decade ago, we published the first CDH epidemiological study, in which we personally interviewed 1883 randomly selected subjects > 14 years old in the Health Centre of Camargo, in the region of Cantabria, in the north of Spain (1). CDH prevalence (according to Silberstein et al.'s criteria) was 4.7% (89 subjects). By diagnoses, 2.6% met chronic tension-type headache criteria, 2% transformed migraine criteria and only 0.1% had new daily persistent headache. These diagnoses were done after filling in a headache diary for 1 month and after examination and at least two interviews by a neurologist experienced in headache. Contrary to what happens in headache clinics, only a quarter of CDH subjects (22 of 89 subjects) met Silberstein et al.'s criteria, very similar to current International Headache Society (IHS) criteria, for overuse of symptomatic medication. Analgesic overuse was more frequent in those patients with transformed migraine (31%) compared with those with chronic tension-type headache (19%). Even though the numbers for the interviewed subjects were rather low to define prevalence, according to these data, prevalence of CDH with analgesic overuse or medication overuse headache (MOH) would be 1.3% of the general population. To better define the epidemiology of MOH we conducted a second survey with the same methodology (personal interview and diary for 1 month) in the Health Centre of Santoña in the same region. A total of 4855 unselected subjects were interviewed, using a quota sampling approach. Prevalence of MOH was 1.41%, confirming our previous results. Again, overuse was more frequent in migraineurs (prevalence 0.9%) than in subjects fulfilling chronic tension-type headache (0.4%) or new daily persistent headache criteria (0.1%) (Fig. 2). These data concur with those of other epidemiological studies and show that MOH is a common disorder in the general population. Quality of life was also assessed in this study by using the Short Form-36 Health Survey (SF-36) questionnaire. In the general population, MOH induces a remarkable decrease in all quality of life aspects studied by the SF-36 test, with Body pain and Role physical being the most affected items (2).

General population data cannot necessarily be extrapolated to clinical practice. What is the 'epidemiology' of MOH in our neurological clinics in Spain? Headache is the most common reason for consultation, accounting for 24–32% of new neurological visits, according to two recent unpublished surveys among > 800 neurologists. Migraine is the most frequent diagnosis in our clinics, accounting for around half of consultations due to headache. In a very recent study, 13.5% of new out-patients attending a general neurological service in Spain had migraine (3). In our general neurological clinics, around 40–45% of migraine patients meet chronic migraine criteria. Of these, 30–70%, depending on the criteria and on the range of the hospital, overuse symptomatic medications. That means that MOH accounts for 2–5% of new consultations in general neurological services in our country. In our headache clinics, however, up to 40% of patients meet MOH criteria.

DEMOGRAPHICS

A clear female predominance has been the rule in all studies carried out in Spain. In the survey analysing the prevalence of CDH in the general population, with only one-quarter having MOH, 89.9% of the CDH patients were women (1). In our MOH prevalence study, 94.6% were women (2). That gave a prevalence of MOH in women of 2.6% [95% confidence interval (CI) 2.0, 3.3] and of only 0.2% (95% CI 0.1, 0.5) in men. The prevalence of CDH and analgesic overuse according to age at diagnosis is illustrated in Figs 1 and 2. The mean age of these subjects in the general population fulfilling MOH criteria was 56 years (range 19–82 years). The mean (subjective) age at onset of MOH was 38 years (range 9–82 years), whereas the mean age at onset of the primary episodic headache was 22 years (range 5–60 years). As regards the very recent study carried out using the current IHS criteria in a general neurological service, 85% of patients consulting due to chronic migraine and 75% of patients with MOH were female. The mean age of these patients was 38 and 43 years, respectively (3).

MOST COMMON ACUTE DRUGS OF OVERUSE

The distribution of overuse in the first epidemiological study in our country was as follows: combinations of different analgesics (46%), ergotics (36%) and non-steroidal anti-inflammatory drugs (NSAIDs) (18%) (1). In the second epidemiological study, devoted specifically to MOH, the distribution was as follows: 34.7% of patients overused simple analgesics, 22.2% ergotamine-containing medications, 12.5% opioids and 2.7% triptans, whereas the remaining 27.8% were overusing different combinations of these pharmacological groups (see Fig. 3) (2). The most consumed drugs were paracetamol (52.2% of subjects), caffeine (48.6%), ergotics (37.5%), propifenazone (34.7%), aspirin (18.1%) and codeine (12.5%). The mean number of units per subject and month was 50 (range 10–180 units). Patients were taking, on average, 2.5 different pharmacological

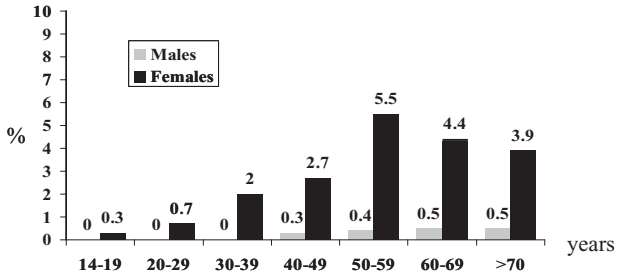

Figure 1 Prevalence of medication overuse headache (MOH) in men and women according to age at diagnosis (taken from (2)).

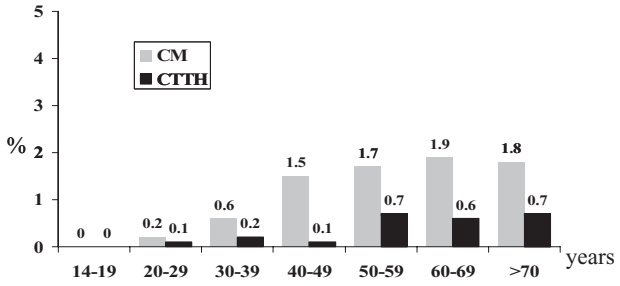

Figure 2 Prevalence of medication overuse headache (MOH) according to age at diagnosis and type of primary headache. CM, chronic migraine; CTTH, chronic tension-type headache (modified from (2)).

components simultaneously (range 1–6). In the recent study in a general neurological clinic, 67% of patients overused different combinations, 26% only analgesics and 7% NSAIDs. As in the general population studies, triptan overuse was seen in only 7% of these patients and always in combination with other symptomatic medications.

TREATMENT

Patients suffering from MOH are difficult to treat. Two years ago, the Headache Group of the Spanish Society of Neurology published the local guidelines for the treatment of these headache patients (4). Recommendations in the guidelines include a combination of general measures and specific pharmacological treatments. General measures include: (i) promoting good communication between patient and physician; (ii) reassurance, excluding secondary headaches; (iii) identifying comorbid medical/psychiatric conditions; (iv) recognizing the subtype of MOH (i.e. coming from migraine or tension-type headaches); and (v) concomitant behavioural intervention.

When possible, pharmacological management should be planned on an out-patient basis. The general protocol should include: (i) abrupt discontinuation of the offending symptomatic medications; (ii) specific treatment of detoxification; (iii) daily NSAIDs (e.g. sodium naproxen 550 mg/8 h with gastric protection) for about 15–30 days; (iv) triptans only for moderate–

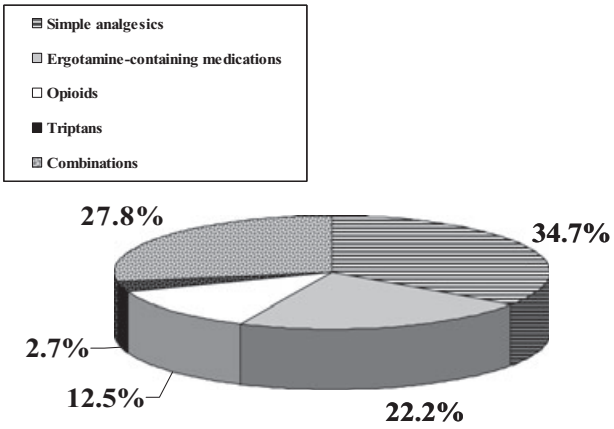

Figure 3 Distribution of overuse in the general population of Spain (data taken from (2)).

severe headache only if they are not the overused drug and up to 2 days (two doses per day) per week; and (v) preventive treatment.

In the opinion of the vast majority of headache specialists involved in the elaboration of the guidelines, MOH patients are frequently lost for follow-up if only detoxification is recommended. One possible exception in our experience are those migraine patients overusing ergotics, who usually respond just to detoxification. Regarding the controversial use of triptans as rescue medication, we recommend triptans in this indication at restricted doses, as in Spain the proportion of patients overusing triptans is very low (see above). In addition, in this particular indication the guidelines favour using preferably triptans with very low central nervous system penetrance, such as almotriptan or sumatriptan, as—at least theoretically—they would have a lower possibility of rebound headache, if we consider this phenomenon as a central one. With the possible exception of those patients overusing ergotics, we recommend preventive treatment from the beginning. The choice depends on the subjacent headache. Amitriptyline, 20–50 mg at night, is indicated in those patients with pure tension-type headache with overuse. For migraine patients, the guidelines recommend either combining a standard β-blocker with nocturnal amitriptyline or an antiepileptic, topiramate or valproic acid. Topiramate is the preferred drug locally, as there is no need for blood tests and as controlled data in this indication are available. For patients with no response, the next steps we recommend are: (i) combining a β-blocker with an antiepileptic; and (ii) adding pericranial botulinum toxin type A (100 U BOTOX).

We indicate in-patient management when: (i) the out-patient protocol has failed; (ii) in the presence of high depression scores; or (iii) if the patient takes significant doses of tranquillizers, opioids of barbiturates. The general pharmacological protocol for these patients includes: (i) i.v. methylprednisolone, at least 80 mg/24 h, for 5–7 days; (ii) i.v. valproate 400–800 mg/12 h for 3–5 days, then oral prophylaxis with 500–1000 mg/daily; (iii)

i.v. metoclopramide; (iv) short treatment with either benzodiazepines or neuroleptics (1–2 weeks); and (v) NSAIDs (after the steroids) and triptans as mentioned above. Parenteral dihydroergotamine is not available in our country.

PROGNOSIS

Prospective data on the long-term prognosis of MOH are very scarce in the medical literature. Most papers offer the results obtained within the first semester of treatment and in selected patients attending headache clinics. In the studies in Spain, and using the treatment protocol outlined above, about 50–60% of MOH patients attending our local neurological clinics move from a daily/almost-daily headache to an episodic migraine or tension-type headache and do not meet overuse criteria at the end of the first year of treatment.

The subjects who participated in the epidemiological study of MOH published in 2004 were offered standard pharmacological treatment for 6–12 months. After the treatment period, they were discharged to their respective general physicians, with written instructions regarding their headache treatment. All these subjects have been contacted, interviewed and followed up again by us recently. After 4 years, 56% of these subjects had episodic migraine or tension-type headache and did not meet overuse criteria, whereas the remaining 44% continued to suffer from MOH. Even though we do not know the spontaneous evolution of MOH, these data suggest that such an intervention in the general population, especially in middle-aged women, is highly justified. Age, sex or socio-economic status did not influence prognosis, whereas patients who followed our recommendations of taking just NSAIDs (and triptans up to 2 days/week as acute treatment) and who had taken preventive treatment had a significantly better prognosis (Pascual and Fontanillas, in preparation).

PERSONAL REFLECTIONS

Local epidemiological data confirm that MOH is a serious problem in Spain, mainly in middle-aged women. MOH clearly decreases quality of life, even in unselected subjects in the general population. Regarding local treatment guidelines, in general we recommend using preventatives from the beginning, with NSAIDs as the standard symptomatic medication and allowing a reasonable number of triptan doses as rescue medication. Even though combined analgesics (usually containing caffeine, ergotics or barbiturates) and opioids seem to be involved in the development of MOH, it is our general view that many patients with primary headache seem to be biologically (possibly genetically) predisposed to develop CDH regardless of analgesic overuse, which can be a consequence and not the reason for daily headache. There are many arguments supporting this contention, for example: (i) the fact that CDH exists in children and adolescents, with no time for overuse to develop; (ii) the finding that almost three-quarters of those with daily/near-daily headache in the general population does not overuse analgesics; (iii) the experience that at least 40% of patients who are detoxified do not improve; or (iv) the recent demonstration that preventatives work even in the presence of overuse. To conclude, we also favour an active detection and treatment approach to these patients, whose condition can highly improve long-term in more than half of cases if managed adequately.

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