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The changing face of chronic migraine: who to treat, how to treat?

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THE CHANGING FACE OF CHRONIC MIGRAINE: WHO TO TREAT, HOW TO TREAT?

Contents

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Paper

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The changing face of chronic migraine

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ABSTRACT

Chronic migraine is the relatively new term that the International Headache Society has adopted to describe patients with frequent headache thought to be biologically migrainous. The strict definition is for the patient to have 15 days or more of headache over each of the previous 3 months and to have 8 or more of these days as typical migraine or treated with a migraine specific agent, such as a triptan. Chronic migraine represents the most disabling spectrum of patients with migraine and such patients could be expected to present to primary care and often be referred for management to secondary care, especially to see neurologists. Many such patients present with concomitant medication overuse, defined as using a compound analgesic, opioid, triptan or ergot derivative on 10 days or more per month. While medicines used typically in the preventive management of migraine will help many patients, some remain refractory to current treatments either due to lack of efficacy or poor tolerability. New treatment strategies for this highly disabled patient cohort are welcome in clinical practice.

INTRODUCTION

Headache is the most common neurological presentation to general practice,¹ and among those who present, migraine is the most common reason for a patient to see their general practitioner for disabling headache.² As a result, headache is the most common presenting problem in neurological practice³ and represents a substantial economic burden.⁴ Given about 4.5% of the population of Western Europe probably has headache on 15 days or more per month,⁵ so-called chronic daily headache,⁶ frequent migraine is certainly a substantial cause of morbidity and cost. After some years of discussion, a consensus has emerged around the nosology of migraine such that, essentially, patients whose migraine affects them on at least 8 days per month together with 15 days or more a month of headaches are described as having *chronic migraine*.⁷ This group presents a very substantial challenge in neurology practice. Here we discuss the diagnosis and management of the problem, including particular attention to medication overuse, which so often complicates this presentation.

WHAT IS CHRONIC MIGRAINE?

According to the International Classification of Headache Disorders—second edition (ICHD-II),⁷ chronic migraine is diagnosed when patients experience headache on 15 days or more per month for

at least 3 months, where 8 of those days meet criteria for typical migraine⁸ or respond to a migraine specific treatment. Migraine specific treatments are currently regarded to be triptans, serotonin 5-HT_{1B/1D} receptor agonists⁹ or ergotamine derivatives.¹⁰ For the diagnosis to be made, patients should not be overusing acute attack medicines, such as triptans, ergots or codeine on 10 days or more per month.¹¹ This terminology has replaced previously used terms that had a similar meaning, such as transformed migraine, mixed headache/migraine or tension-vascular headache, an issue being that previous terms were not so carefully defined and therefore precise comparisons are problematic. How does this official definition stack up in practice?

There are some complexities of the current ICHD-II that should be seen in context. Good research criteria need a degree of inflexibility that good clinicians need to bend. A practical approach to the phenotypic differentiation of migraine and tension-type headache is set out in table 1, and a diagnostic approach in figure 1. The substantial differential diagnostic conundrum between migraine and tension-type headache comes down to considering the biological basis of the patient's presentation versus the phenotypic presentation. The ICHD-II suggests that the biotype should predominate in diagnosis by only insisting on 8 of 15 days with phenotypically clear migraine. Other days may have less features or they may be less troublesome, but this does not mean the patient necessarily has two problems—that is, migraine and tension-type headache. As in most neurological problems it seems desirable to diagnose the underlying issue not just the manifestations. Gowers¹² considered the milder attacks between migraines to be of the same biological nature, and this rather astute clinical wisdom is the forerunner to the modern concept of chronic migraine.

THE ISSUE OF MEDICATION OVERUSE

A frequent complication seen in neurological practice in headache patients is medication overuse.¹³ This currently is considered to be present when a patient takes a triptan, ergot or analgesic, such as codeine, on 10 days or more per month.¹¹ These medicines very often become less effective and certainly overuse predicts increased headache frequency over a 12 month timeframe.¹⁴ There are two very important considerations here: what is the implication of overuse and how does one manage it?

Table 1 Differentiating migraine and tension-type headache—a practical approach

	Migraine	Tension-type headache
Attack characteristics	Lateralised/generalised Throbbing Made worse by movement Associated with <ul style="list-style-type: none"> ▶ Nausea ▶ Photophobia ▶ Phonophobia 	Generalised Non-throbbing No effect of movement Associated with <ul style="list-style-type: none"> ▶ Nil
Patient characteristics	Family history: present Triggers <ul style="list-style-type: none"> ▶ Sleep ▶ Eating ▶ Stress/relaxation ▶ Exertion ▶ Hormonal change ▶ Weather change 	Family history: absent Triggers <ul style="list-style-type: none"> ▶ Stress

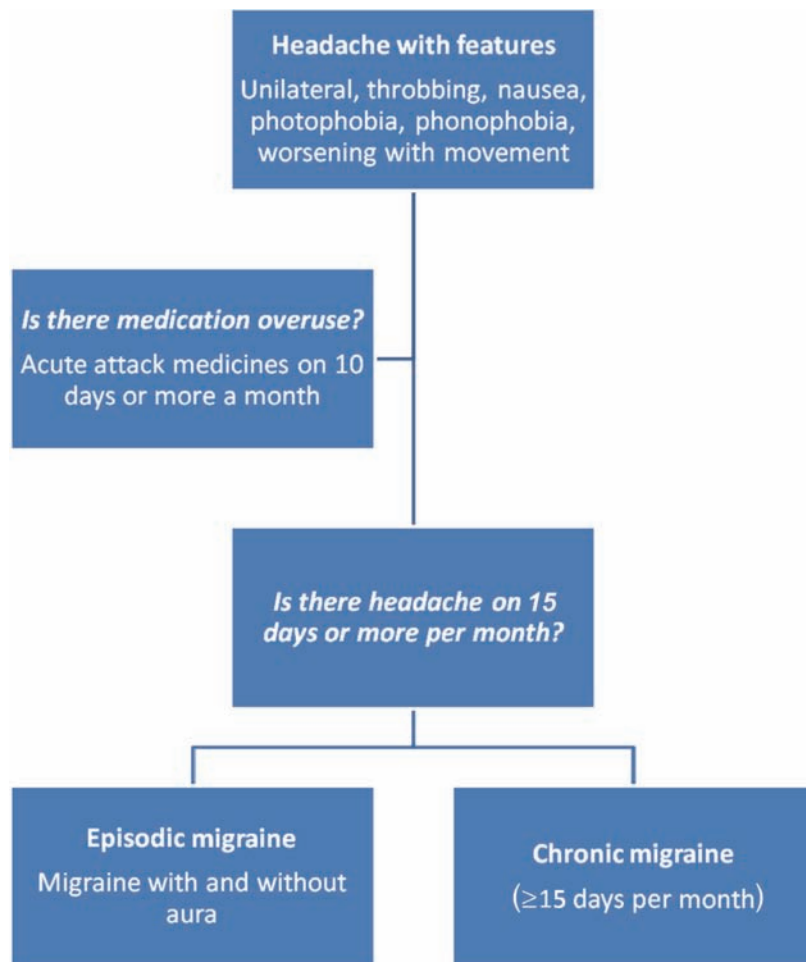


Figure 1 Practical classification of migraine.

Implications of medication overuse

Medication overuse and medication overuse headache (MOH) are terms sometimes used interchangeably although the clear intent of the current diagnostic criteria is to capture the concept that medication overuse causes headache.¹¹ Cross-sectional studies in patients treated with analgesics for another indication, arthritis¹⁵ or a gastrointestinal indication,¹⁶ demonstrate that about 10% of patients who are taking such medicines have daily or near daily headache. These

patients also have a personal or family history of migraine or troublesome headache. More interesting perhaps is that another 20% have a personal or family history of migraine or troublesome headache and do not have daily headache even though their analgesic consumption is no different. These data suggest that some migraineurs may be especially at risk of headache induction from analgesics.¹⁷ This is borne out by the fact that in other primary headache disorders, such as cluster headache, it is those with a personal or family history of migraine or troublesome headache who are at risk for MOH.¹⁸ The data are also consistent with clinical experience that while some patients do very well in terms of headache frequency reduction when they undergo analgesic medication withdrawal, many do not.

Management of medication overuse

While it is easy with a simple diary to count the days of consumption and determine if a patient has medication overuse, it is very much more complex to manage it. A careful history and a careful diary, which quantifies the problem, and acts as a good baseline, are good starting points. In the history, often patients do not immediately recognise analgesics bought in the supermarket as medicines as such, so it is important to tease apart carefully the contribution of such sources to the problem. The patient can then elect to abruptly withdraw the medicine or taper by, for example, 10% per week. This can be facilitated by a long acting non-steroidal anti-inflammatory drug, such as naproxen 500 mg twice daily for 6 weeks. Although there is some evidence that preventive treatment may work in the context of ongoing medication overuse,¹⁹ its effectiveness is less than half that achieved when medication overuse is not present. Previously ineffective preventive treatments may in fact work when medication overuse is treated.²⁰

BURDEN OF DISEASE

The impact of chronic migraine can be very severe and lead to significant burden, more time off work, a higher risk of unemployment, relationship difficulties and family problems.²¹ Indeed, compared with patients with episodic migraine, those with chronic migraine are severely burdened by their disease and suffer an increased level of disability (figure 2). Appropriate intervention with acute or prophylactic treatments could therefore reduce the impact of chronic migraine on patients and society.

Some patients will recover from chronic migraine either through treatment or due to natural history while other patients with episodic migraine will develop chronic migraine. The number of patients with chronic migraine, however, remains static at between 2.5% and 4.6%.²² Patients at an increased risk of developing chronic migraine are those who experience frequent attacks, have a high migraine disability score and tend to overuse acute medications, especially opioids and barbiturates.^{14, 23} Patients who are obese

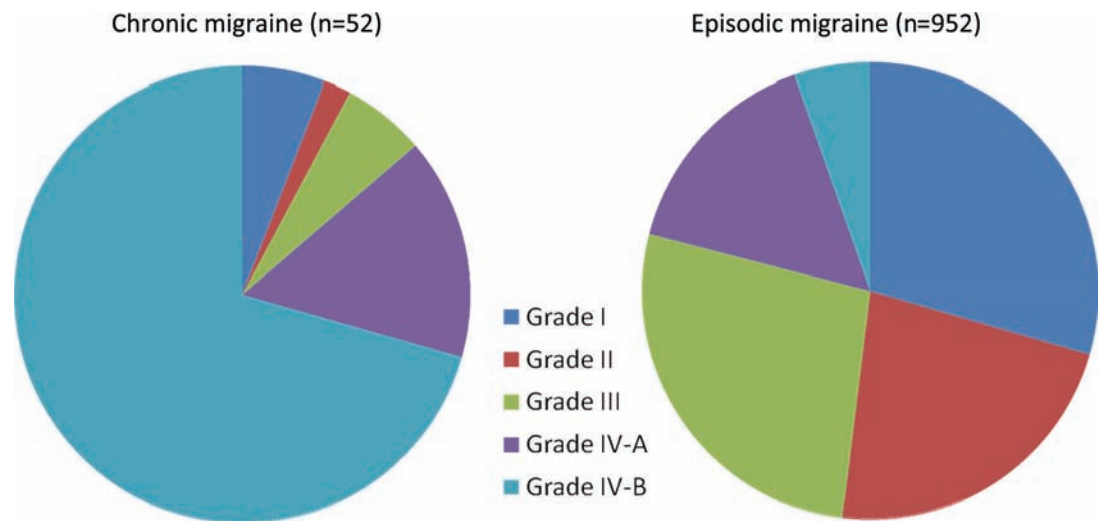


Figure 2 Difference in disability experienced by patients with chronic compared with episodic migraine.³⁴

and those that experience allodynia and sleep disturbances are also at an increased risk of developing chronic migraine.

MANAGEMENT OF PATIENTS WITH MIGRAINE

Managing patients with frequent headache of any type is facilitated by encouraging them to keep a careful diary. The diary will monitor headache frequency and very clearly demonstrate issues of medication overuse. The diary can also be used to identify whether there are any clear triggers, such as menses, precipitating the migraine attack. If these are present then it may be possible to reduce the frequency of migraine attack by giving the patient some advice about their lifestyle and by removing these triggers, such as strategies for dealing with weekend let-down headaches.

Acute attack treatment

There is considerable tension in practice between advocating the probable benefit of early treatment of migraine, when the pain is still mild,^{24–26} versus the concern that such an approach promotes medication overuse. Perhaps the most tangible benefit from the treatment is reduced headache recurrence that probably leads to reduced medication use. The issue is complex and when present usually means the patient really needs a preventive to reduce attack frequency altogether. In secondary care it is exceptional to see patients who have not been exposed to simple analgesics, non-steroidal anti-inflammatory drugs and even codeine containing treatments although often at inadequate doses or with the benefit of concomitant antiemetics.

Preventive treatment

In general terms, once the patient is having more than 4–6 attacks per month, preventive treatments need to be considered. Unfortunately, in secondary care many patients arrive with many more attacks and already with medication overuse. An important current issue in preventive treatment is the extent to

which one needs to stop medication overuse before starting a preventive. The only controlled trial evidence in chronic migraine in which patients who had medication overuse had the same response rate to topiramate as those who did not.¹⁹ However, the absolute response rate in that study was about a third of what one sees in practice with topiramate or indeed in clinical trials.^{27–29} It is generally accepted by clinicians that for many patients medication overuse does impede the effect of preventives. It could be observed that if a patient comes with a history of having failed several preventives while overusing acute medicines this suggests there is a problem, while if they have never had a preventive, perhaps one course of preventive first is reasonable. This area is a matter of practice, not evidence, at this time. Given the fact that opioids, triptans and ergots have a considerable unwanted side effect burden when used on 10 days or more per month, it seems reasonable to recommend their initial withdrawal before commencing preventive therapy.

Current licensed options available for episodic migraine are β blockers, topiramate (an antiepileptic), pizotifen (a serotonin antagonist) and methysergide (a serotonin antagonist). Having listed these, it is highly likely that the pharmacological characterisation is simplistic and the licensing is not consistent as, for example, valproate has a reasonable base of clinical trial evidence^{30–33} but is not licensed. Tricyclic antidepressants have also been used but their use is off-label. The type of migraine prophylaxis prescribed for each patient depends on many factors, including the presence of contraindications or comorbidities, the potential effect of the drug on any concomitant conditions and any issues that relate to compliance, such as frequency of dosing. This is particularly important as low adherence can reduce the effectiveness of migraine prophylaxis. It is also important that the patient's expectations are managed so that these are realistic as the current options available are not suitable or effective in all patients.

SUMMARY AND CONCLUSIONS

Many patients who present with chronic daily headache, headache on 15 days per month or more, have chronic migraine, a condition that is responsible for much disability and may be challenging to treat in the clinic. Patients with chronic migraine require careful management with acute medications due to their risk of developing MOH. This is a complication that can develop in patients who need to take regular pain relief for their migrainous headaches. Patients at risk of developing MOH and those who experience frequent or disabling migraine attacks are candidates for migraine prophylaxis. Although not specifically licensed for use in chronic migraine, medicines licensed in episodic migraine can reduce the frequency of attacks in some patients but adherence might be low and these treatments may not be suitable for all. As such, patients' expectations need to be managed carefully.

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