BASH
BRITISH ASSOCIATION
FOR THE STUDY OF HEADACHE

Guidelines for All Healthcare Professionals in the

Diagnosis and Management of

Migraine

Tension-Type Headache

Cluster Headache

Medication-Overuse Headache

3rd edition (1st revision) 2010

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British Association for the Study of Headache

Guidelines for All Healthcare Professionals in the Diagnosis and Management of Migraine, Tension-Type, Cluster and Medication-Overuse Headache

Writing Committee: **EA MacGregor, TJ Steiner, PTG Davies**
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1. Introduction

Headache affects nearly everyone at least occasionally. It is a problem at some time in the lives of an estimated 40% of people in the UK. It is one of the most frequent causes of consultation in both general practice and neurological clinics. In its various forms, headache represents an immense socioeconomic burden.

Migraine occurs in 15% of the UK adult population, in women more than men in a ratio of 3:1.[1] An estimated 190,000 attacks are experienced *every day*, with three quarters of those affected reporting disability. Whilst migraine occurs in children (in whom the diagnosis is often missed) and in the elderly, it is most troublesome during the productive years (late teens to 50's). As a result, over 100,000 people are absent from work or school because of migraine every working day.[1] The cost to the economy may exceed £1.5 billion per annum.

Tension-type headache in its episodic subtype affects up to 80% of people from time to time,[2] many of whom refer to it as "normal" or "ordinary" headache. Consequently, they mostly treat themselves without reference to physicians using over-the-counter (OTC) medications and generally effectively. Nevertheless, it can be a disabling headache over several hours[3] and the high prevalence of this disorder means its economic burden through lost work and reduced working effectiveness is similar to that of migraine.[4] In a minority of people, episodic tension-type headache is frequent, whilst up to 3% of adults have the chronic subtype[5] occurring on more than 15 days every month. These people have high morbidity and may be substantially disabled; many are chronically off work.

Cluster headache is much less common, with a prevalence of about 0.05%, but it is both intense and frequently recurring. Medication-overuse headache is usually a chronic daily headache, and may affect 2% of adults as well as some children. Both of these disorders contribute significantly to the disability burden of headache.

Despite these statistics, there is evidence that headache disorders are under-diagnosed and under-treated in the UK, as is the case throughout Europe and in the USA.[6]

1 Steiner TJ, Scher AI, Stewart WF, Kolodner K, Liberman J, Lipton RB. The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. Cephalalgia 2003; 23: 519-527.

2 Rasmussen BJ, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population – a prevalence study. J Clin Epidemiol 1991; 44: 1147-1157.

3 Steiner TJ, Lange R, Voelker M. Aspirin in episodic tension-type headache: placebo-controlled dose-ranging comparison with paracetamol. Cephalalgia 2003; 23: 59-66.

4 Stovner LJ, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher AI, Steiner TJ, Zwart J-A. Headache prevalence and disability worldwide: A systematic review in support of "The Global Campaign to Reduce the Burden of Headache". Cephalalgia 2007; 27: 193-210.

5 Schwartz BS, Stewart WF, Simon D, Lipton RB. Epidemiology of tension-type headache. JAMA 1998; 279: 381-383.

6 American Association for the Study of Headache, International Headache Society. Consensus statement on improving migraine management. Headache 1998; 38: 736.

scope and purpose

2. Scope and purpose of these guidelines

The purpose of these guidelines is to suggest strategies of management for the common headache disorders that have been found by specialists to work well. They are intended for all healthcare professionals who manage headache. Whether in general practice or neurology or headache specialist clinics, or in the community, the approach to management is the same. We recommend that health-care commissioners incorporate these guidelines into any agreement for provision of services.

However, headache management requires a flexible and individualised approach, and there may be circumstances in which these suggestions cannot easily be applied or are inappropriate.

Where evidence exists, these guidelines are based on it. Unfortunately, the formal evidence for much of them is insecure; where this is so, there is reliance on expert opinion based on clinical experience.

2.1 Writing and approval process

The members of the writing group are headache specialists. The task of the writing group is to shoulder the burden of writing, not to promulgate their own opinions. Each edition of these guidelines, and major revisions thereof, are distributed in draft for consultation to all members of the British Association for the Study of Headache (BASH), amongst whom are general practitioners with an interest in headache, and to all neurologist members of the Association of British Neurologists.

Final approval for publication is by Council of BASH.

2.2 Currency of this edition

These guidelines are updated as developments occur or on production of new and relevant evidence.

This edition of these guidelines is current *until the end of December 2013*.

3. Headache classification

Although various schemes preceded it, the 1988 classification of the International Headache Society (IHS)[7] was the first to be widely adopted. This was extensively revised in late 2003 and the new system, the International Classification of Headache Disorders, 2nd edition (ICHD-II), is the international standard.[8] It includes operational diagnostic criteria and classifies headache disorders under 14 headings (table I). The first four of these cover the primary headache disorders.

7 Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia 1988; 8 suppl 7: 1-96.

8 International Headache Society Classification Subcommittee. The International Classification of Headache Disorders. 2nd edition. Cephalalgia 2004; 24 (Suppl 1): 1-160.

Table I*. The International Classification of Headache Disorders, 2nd Edition[9]

Primary headaches	**1.** Migraine, *including:* 1.1 Migraine without aura 1.2 Migraine with aura **2.** Tension-type headache, including: 2.1 Infrequent episodic tension-type headache 2.2 Frequent episodic tension-type headache 2.3 Chronic tension-type headache	**3.** Cluster headache and other trigeminal autonomic cephalalgias, *including:* 3.1 Cluster headache **4.** Other primary headaches
Secondary headaches	**5.** Headache attributed to head and/or neck trauma, *including:* 5.2 Chronic post-traumatic headache **6.** Headache attributed to cranial or cervical vascular disorder, *including:* 6.2.2 Headache attributed to subarachnoid haemorrhage 6.4.1 Headache attributed to giant cell arteritis **7.** Headache attributed to non-vascular intracranial disorder, *including:* 7.1.1 Headache attributed to idiopathic intracranial hypertension 7.4 Headache attributed to intracranial neoplasm **8.** Headache attributed to a substance or its withdrawal, *including:* 8.1.3 Carbon monoxide-induced headache 8.1.4 Alcohol-induced headache	8.2 Medication-overuse headache 8.2.1 Ergotamine-overuse headache 8.2.2 Triptan-overuse headache 8.2.3 Analgesic-overuse headache **9.** Headache attributed to infection, *including:* 9.1 Headache attributed to intracranial infection **10.** Headache attributed to disorder of homoeostasis **11.** Headache or facial pain attributed to disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures, *including:* 11.2.1 Cervicogenic headache 11.3.1 Headache attributed to acute glaucoma **12.** Headache attributed to psychiatric disorder
Neuralgias and other headaches	**13.** Cranial neuralgias, central and primary facial pain and other headaches, *including:* 13.1 Trigeminal neuralgia	**14.** Other headache, cranial neuralgia, central or primary facial pain

**This table is a simplification of the IHS classification*

9 International Headache Society Classification Subcommittee. The International Classification of Headache Disorders. 2nd edition. Cephalalgia 2004; 24 (Suppl 1): 1-160.

diagnosis of headache

4. Diagnosis of headache

4.1 Taking a history

There are no diagnostic tests for any of the primary headache disorders, or for medication-overuse headache. The history is all-important. A headache history requires time to elicit, and not finding the time to take it fully is the probable cause of most misdiagnosis. A simple and helpful ploy when the patient first presents in a busy clinic is to request the keeping of a diary over a few weeks. The pattern of attacks is a very helpful pointer to the right diagnosis, and review can be arranged at a time less rushed. First, of course, it must be ascertained that a condition requiring more urgent intervention is not present (see 5.0).

Table II. An approach to the headache history

1. How many different headache types does the patient experience? Separate histories are necessary for each. It is reasonable to concentrate on the most bothersome to the patient but others should always attract some enquiry in case they are clinically important.	
2. Time questions	a) Why consulting now? b) How recent in onset? c) How frequent, and what temporal pattern (especially distinguishing between episodic and daily or unremitting)? d) How long lasting?
3. Character questions	a) Intensity of pain b) Nature and quality of pain c) Site and spread of pain d) Associated symptoms
4. Cause questions	a) Predisposing and/or trigger factors b) Aggravating and/or relieving factors c) Family history of similar headache
5. Response questions	a) What does the patient do during the headache? b) How much is activity (function) limited or prevented? c) What medication has been and is used, and in what manner?
6. State of health between attacks	a) Completely well, or residual or persisting symptoms? b) Concerns, anxieties, fears about recurrent attacks, and/or their cause

In children, distinctions between headache types, particularly migraine and tension-type headache, are often less clear than in adults.[10]

Different headache types are not mutually exclusive. Patients are often aware of more than one headache type, and a separate history should be taken for each. The crucial elements of a headache history are set out in table II.

10 Viswanathan V, Bridges SJ, Whitehouse W, Newton RW. Childhood headaches: discrete entities or a continuum? Developm Med Child Neurol 1998; 40: 544-550.

4.2 Migraine

Patients with migraine typically give an account of recurrent episodic moderate or severe headaches (which may be unilateral and/or pulsating) lasting part of a day or up to 3 days, associated with gastrointestinal symptoms, during which they limit activity and prefer dark and quiet. They are free from symptoms between attacks.

Diagnostic criteria for ***migraine without aura*** are shown in table III. It is easy to regard these as a check-list, sufficient if ticked by a nurse or even the patient, but they require clinical interpretation. One of the weaknesses of the diagnostic criteria of ICHD-II is that they focus on symptoms, not patients. For migraine, therefore, they do not describe the all-important patterns of occurrence of attacks. Nevertheless, if used as they are meant to be, supplementary to normal enquiry practice, they distinguish effectively between migraine without aura and its principal differential diagnosis, tension-type headache.

Table III. IHS diagnostic criteria for migraine without aura

A	At least 5 attacks fulfilling criteria B-D
B	Headache attacks lasting 4-72 hours* (untreated or unsuccessfully treated)
C	Headache has at least two of the following characteristics: 1. unilateral location* 2. pulsating quality (ie, varying with the heartbeat) 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
D	During headache at least one of the following: 1. nausea and/or vomiting* 2. photophobia and phonophobia
E	Not attributed to another disorder (history and examination do not suggest a secondary headache disorder or, if they do, it is ruled out by appropriate investigations or headache attacks do not occur for the first time in close temporal relation to the other disorder)

***In children,** attacks may be shorter-lasting, headache is more commonly bilateral, and gastrointestinal disturbance is more prominent.

Migraine with aura, which affects about one third of migraine sufferers, is diagnosed relatively easily. The occurrence of typical aura clinches it, but beware of patients who bring "visual disturbance" into their accounts because of what they have read about migraine. Visual blurring and "spots" are not diagnostic. Symptoms of typical aura are progressive, last 5-60 minutes prior to headache and are visual, consisting of transient hemianopic disturbance or a spreading scintillating scotoma (patients may draw a jagged crescent if asked). In some cases visual symptoms occur together or in sequence with other reversible focal neurological disturbances such as unilateral paraesthesia of hand, arm or face (the leg is rarely affected) and/or dysphasia, all manifestations of functional cortical disturbance of one cerebral hemisphere.

Particularly in older patients, typical visual migrainous aura may occur without any further development of a migraine attack. When there is a clear history of earlier migraine with aura, and the description of aura remains similar, this is not alarming. Otherwise it should be remembered that transient ischaemic attack is in the differential diagnosis for older patients.

Patients may, at different times, have attacks of migraine with and migraine without aura. They may, over a lifetime, change from a predominance of one subtype to the other.

Prolonged aura, especially aura persisting after resolution of the headache, and aura involving motor weakness, require referral to specialists for exclusion of other disease. Amongst these cases are a very small number of families expressing recognized genes for familial hemiplegic migraine.[11]

11 Ducros A, Tournier-Lasserve E, Bousser M-G. The genetics of migraine. Lancet Neurol 2002; 1: 285-293.

Migrainous headache occurring every day (chronic migraine) is classified as a complication of migraine; it requires specialist referral because diagnosis and management are difficult.[12]

"Diagnosis" by treatment

It is tempting to use anti-migraine drugs as a diagnostic test for migraine. This is a condition where an empirical approach to management ("Try this and see how it works") is not always unreasonable. However, triptans, despite being the most specific and effective drugs currently available, are at best effective in three quarters of attacks. As a diagnostic test they have rather low sensitivity so this approach is likely to mislead.

4.3 Tension-type headache (TTH)

Episodic tension-type headache also occurs in attack-like episodes, with variable and often very low frequency and mostly short-lasting – no more than several hours. Headache can be unilateral but is more often generalised. It is typically described as pressure or tightness, like a vice or tight band around the head, and commonly spreads into or arises from the neck. Whilst it can be disabling for a few hours, it lacks the specific features and associated symptom complex of migraine (although photophobia and exacerbation by movement are common to many headaches).

TTH may be stress-related or associated with functional or structural cervical or cranial musculoskeletal abnormality, and these are not mutually exclusive. Patients may admit or deny stress. Clinically, there are cases where stress is

12 Boes CJ, Matharu MS, Goadsby PJ. Management of difficult migraine. Adv Clin Neurosci Rehab 2001; 1: 6-8.

obvious and likely to be aetiologically implicated (often in headache that becomes worse during the day) and others where it is not apparent. Equally there are cases with musculoskeletal involvement evident in the history (or on examination) and others where this is not a factor.

What causes people with TTH to consult healthcare professionals is that it is becoming frequent, in which case it may no longer be responding to painkillers. **Chronic tension-type headache** occurs by definition on >15 days a month, and may be daily. This condition is disabling.

Both migraine and TTH are aggravated by stress and, in practice, there are occasions when the distinction is not easily made. Where this is so, especially in patients with frequent headache, the two may co-exist. In such cases, unless both conditions are recognised and dealt with individually, management is unlikely to be successful (see 10.0).

4.4 Cluster headache (CH)

There is another group of disorders, the ***trigeminal autonomic cephalalgias***, where daily occurrence of headache (often several attacks daily) is usual. The most common is cluster headache.

CH affects mostly men (male to female ratio about 6:1) in their 20s or older (very rarely children) and very often smokers. The condition has its name because, typically (although there is a less common chronic subtype), headaches occur in bouts for 6-12 weeks, once a year or two years, often at the same time each year.

The pain of CH is intense, probably as severe as that of renal colic, and strictly unilateral. Although most often focused in one or other eye, it can spread over a larger area of the head, which sometimes misleads the diagnosis. There may, also, be a continuous background headache. The other features should leave no diagnostic doubt, although unusual patterns do occur, especially in women. Typically CH occurs daily, at a similar time each day, and usually but far from always at night, 1-2 hours after falling asleep. The wakened patient, unable to stay in bed, agitatedly paces the room, even going outdoors. He may beat his head on the wall or floor until the pain diminishes, usually after 30-60 minutes. The associated autonomic features of ipsilateral conjunctival injection and lacrimation, rhinorrhoea or nasal blockage, and ptosis as the most obvious feature of a partial Horner's syndrome, may not all be present but almost invariably at least one or two secure the diagnosis. (There are other rare causes of painful Horner's syndrome; referral to specialists is appropriate where doubt occurs.)

4.5 Medication overuse headache (MOH)

This term has displaced the pejorative alternatives of drug, analgesic or medication *abuse* or *misuse* headache. It is estimated that 1 in 50 adults suffer from MOH,[13] 5 women to each man, and some children.

Headache secondary to overuse of medication intended for the treatment of headache was first noted with phenacetin. It became more apparent in patients overusing ergotamine prescribed for migraine.

13 Diener H-C, Limmroth V. Medication-overuse headache: a worldwide problem. Lancet Neurol 2004; 3: 475-483.

Increasingly in evidence is MOH occurring with triptan overuse.[14] These drugs do not accumulate, but all of them are associated with headache relapse after acute therapy, through mechanisms not yet clear, whilst chronic usage probably results in down-regulation of 5-$HT_{1B/1D}$ receptors.[15]

MOH results also, and *much* more commonly, from chronic overuse of analgesics to treat headache. Combination analgesics containing barbiturates, caffeine, and codeine are the prime candidates for the development of medication overuse headache.[16] This may be a consequence of the addictive properties of these drugs. However, even simple analgesics such as aspirin and paracetamol are implicated in MOH. Whilst the mechanism is again unclear, it is different from those of ergotamine intoxication and triptan-induced MOH, probably involving changes in neural pain pathways. Consequently, it may take a long time (weeks to months) for the headache to resolve after withdrawal.

Many patients with MOH use very large quantities of medication: 35 doses a week on average in one study, and six different agents.[17] Much smaller amounts are sufficient to induce MOH: the regular intake of simple analgesics on 15 or more days a month or of codeine-containing analgesics, ergot or triptans on 10 or more days a month.[18]

Frequency is important: low doses daily carry greater risk than larger doses weekly.

MOH is highly variable but often oppressive, present – and often at its worst – on awakening in the morning. It increases after physical exertion. Associated nausea and vomiting are rarely pronounced. A typical history begins with episodic headache up to years earlier, more commonly migraine than TTH, treated with an analgesic or other acute medication. Over time, headache episodes become more frequent, as does medication intake, until both are daily. Often what brings patients to the GP's attention is that they seek prescriptions for "something stronger". A common and probably key factor in the development of MOH is a switch to pre-emptive use of medication, in anticipation of rather than for headache. In the end-stage, which not all patients reach, headache persists all day, fluctuating with medication use repeated every few hours. This evolution occurs over a few weeks or much, much longer, depending largely but not solely on the medication taken. MOH rarely develops when analgesics are regularly taken for another indication, such as chronic backache or rheumatic disease, except in the presence of primary headache.[19,20,21]

Prophylactic medication added to medication overuse is generally ineffective and can only aggravate the condition, which therefore must be recognised. Any patient complaining of frequently-recurring headache should give a detailed account of medication use (including, and particularly, OTC

14 Limmroth V, Katsarava Z, Fritsche G, Przywara S, Diener H-C. Features of medication overuse headache following overuse of different acute headache drugs. Neurology 2002; 59: 1011-1014.

15 Diener H-C, Limmroth V. Medication-overuse headache: a worldwide problem. Lancet Neurol 2004; 3: 475-483.

16 Bigal ME, Serrano D, Buse D, Scher A, Stewart WF, Lipton RB. Acute migraine medications and evolution from episodic to chronic migraine: a longitudinal population-based study. Headache 2008; 48: 1157-1168.

17 Diener H-C, Dichgans J, Scholz E, Geiselhart S, Gerber WD, Bille A. Analgesic-induced chronic headache: long-term results of withdrawal therapy. J Neurol 1989; 236: 9-14.

18 International Headache Society Classification Subcommittee. The International Classification of Headache Disorders. 2nd edition. Cephalalgia 2004; 24 (Suppl 1): 1-160.

19 Lance F, Parkes C, Wilkinson M. Does analgesic abuse cause headaches de novo? Headache 1988; 28: 61-62.

20 Zwart JA, Dyb G, Hagen K, Svebak S, Stovner LJ, Holmen J. Analgesic overuse among subjects with headache, neck, and low-back pain. Neurology 2004; 62: 1540-1544.

21 Bahra A, Walsh M, Menon S, Goadsby PJ. Does chronic headache arise do novo in association with regular use of analgesics. Headache 2003; 43: 179-190.

medications). If they cannot, or are suspected of having unreliable recall, they should keep a prospective diary over two weeks. Some patients who do not reveal their true extent of medication use need an understanding approach if a practice of which they may be ashamed is to be brought into the open.

The diagnosis of MOH based on symptoms and drug use is initially *presumptive.* It is *confirmed* only when symptoms improve after medication is withdrawn. Sometimes the diagnosis turns out to have been wrong. It is very difficult to diagnose any other headache in the presence of medication overuse which, in any event, must be detected and dealt with lest there be some other condition lurking beneath.

4.6 Differential diagnosis

Headache in almost any site, but often posterior, may arise from functional or structural derangement of the neck **(cervicogenic headache)**, precipitated or aggravated by particular neck movements or positioning and associated with altered neck posture, movement, muscle tone, contour and/or muscle tenderness.

Headache, whether episodic or chronic, should *not* be attributed to ***sinus disease*** in the absence of other symptoms suggestive of it. Chronic sinusitis is not a validated cause of headache unless there is an acute exacerbation. ***Errors of refraction*** may be associated with migraine[22] but are generally widely overestimated as a cause of headache which, if it does occur, is mild, frontal and in the eyes themselves, and absent on waking. Headache should *not* be considered secondary to conditions affecting the ***ears***, ***temporomandibular joints*** or ***teeth*** unless other symptoms are indicative of these.

A number of serious secondary headache disorders should always be kept in mind during diagnostic enquiry (see 5.0).

4.6.1 Warning features in the history

- Headache that is new or unexpected in an individual patient
- Thunderclap headache (intense headache with abrupt or “explosive” onset)
- Headache with atypical aura (duration >1 hour, or including motor weakness)
- Aura occurring for the first time in a patient during use of combined oral contraceptives
- New onset headache in a patient older than 50 years
- New onset headache in a patient younger than 10 years
- Persistent morning headache with nausea
- Progressive headache, worsening over weeks or longer
- Headache associated with postural change
- New onset headache in a patient with a history of cancer
- New onset headache in a patient with a history of HIV infection.

22 Harle DE, Evans BJ. The correlation between migraine headache and refractive errors. Optom Vis Sci 2006; 83: 82-87.

4.7 Undiagnosed headache

A small minority of headaches do not meet recognised criteria and even after the keeping of a diary cannot reliably be diagnosed. The most important requirement in such cases is to exclude (or detect) serious causes (see 5.0).

4.8 Physical examination of headache patients

All of the headaches so far discussed are diagnosed solely on history, with signs present in cluster headache patients if seen during attacks (occasionally, ptosis may persist between). The purpose of physical examination is sometimes debated but, for reasons given below, the optic fundi should always be examined during the diagnostic consultation. Blood pressure measurement is recommended: raised blood pressure is very rarely a cause of headache but patients often think it may be. Several drugs used for migraine prophylaxis affect blood pressure so it is important to have a baseline measurement. Drugs used for headache, especially migraine and cluster headache, affect blood pressure and *vice versa*.

Examination of the head and neck for muscle tenderness (generalised or with tender "nodules"), stiffness, limitation in range of movement and crepitation is often revealing, especially in TTH. Positive findings may suggest a need for physical forms of treatment but not necessarily headache causation. It is uncertain whether routine examination of the jaw and bite contribute to headache diagnosis but may reveal incidental abnormalities.

In children, some paediatricians recommend that head circumference is measured at the diagnostic visit, and plotted on a centile chart.

For many people with troublesome but benign headache, *reassurance* is very much part of successful management. The physical examination adds to the perceived value of reassurance and, within limits, the more thorough the examination the better. The time spent will likely be saved several times over, obviating many future consultations by a still-worried patient.

A recent outpatient study found only 0.9% of consecutive headache patients without neurological signs had significant pathology.[23] This reinforces the importance of physical examination in diagnosing serious causes of headache such as tumour (see 5.0), although the history would probably be revealing in these cases. A prospective study has suggested that isolated headache for longer than ten weeks after initial presentation will only exceptionally be due to a tumour.[24]

4.9 Investigation of headache patients

Investigations, including neuroimaging,[25,26] do not contribute to the diagnosis of migraine or tension-type headache. Some experts, but not all, request brain MRI in patients newly-diagnosed with CH. The risk increases with age, with symptomatic brain abnormalities identified in 1 in 7 of a Rotterdam population over age 45.[27] Investigations

23 Sempere A, Porta-Etessam J, Medrano V, Garcia-Morales I, Concepcion L, Ramos A, et al. Neuroimaging in the evaluation of patients with non-acute headache. Cephalalgia 2005; 25: 30-35.

24 Vazquez-Barquero A, Ibanez F, Herrera S, Izquierdo J, Berciano J, Pascual J. Isolated headache as the presenting clinical manifestation of intracranial tumors: a prospective study. Cephalalgia 1994; 14: 270-272.

25 American Academy of Neurology. Practice parameter: the utility of neuroimaging in the evaluation of headache in patients with normal neurologic examinations. (Summary statement.) Report of the Quality Standards Subcommittee. Neurology 1994; 44: 1353-1354.

26 Detsky ME, McDonald DR, Baerlocker MO, Tomlinson GA, McCory DC, Booth CM. Does this patient with headache have a migraine or need neuroimaging? JAMA 2006; 296: 1274-1283.

27 Vernooij MW, Ikram MF, Tanghe HL et al. Incidental Findings on Brain MRI in the General Population. N Engl J Med 2007; 357: 1821-1828.

are indicated *only* when history or examination suggest headache is secondary to some other condition. They may have the occasional therapeutic value of convincing a patient, who will not be convinced by any other means, that all is well. However, any anxiolytic effects of a normal brain MRI may not be sustained beyond a few months.[28]

Cervical spine x-rays are usually unhelpful even when neck signs suggest origin from the neck as they do not alter management.

Eye tests by an ophthalmic optician are unlikely to contribute to headache diagnosis, although many patients believe they will.

4.10 Conclusion

The great frequency with which complaints of headache are encountered in clinical practice coupled with a very low relative incidence of serious causes (see 5.0) makes it difficult to maintain an appropriate level of suspicion. If headache is approached with a standard operating procedure that supplements history with funduscopic examination, brief but comprehensive neurological examination (which repays the time spent through its therapeutic value) and the use of diaries to record headaches, associated symptoms and medication use, and an awareness of the few important serious causes, errors should be avoided.

The greatest clinical difficulty, usually, is in distinguishing between migraine and TTH, which may coexist. The real concern, on the other hand, is that so much headache is iatrogenic. Many misused drugs are bought OTC. Failure to discover this in the history results in inappropriate treatment.

Headache that defies diagnosis calls for specialist referral.

28 Howard L, Wessely S, Leese M, Page L, McCrone P, Husain K, et al. Are investigations anxiolytic or anxiogenic? A randomised controlled trial of neuroimaging to provide reassurance in chronic daily headache. J Neurol Neurosurg Psychiatry 2005; 76: 1558-1564.

serious causes of headache

5. Serious causes of headache

Non-specialists may worry that these are in the differential diagnosis of primary headache disorders. In a published series of patients presenting in general practice with new-onset headache diagnosed as primary headache, the 1-year risk of a malignant brain tumour was only 0.045%.[29] The reality is that intracranial lesions (tumours, subarachnoid haemorrhage, meningitis) are uncommon, whilst giving rise to histories that should bring them to mind. All healthcare professionals must be alert to warning features in the history (see 4.6.1). *New or recently changed headache calls for especially careful assessment*. Physical signs should then be elicited leading to appropriate investigation or referral.

5.1 Intracranial tumours

Rarely do intracranial tumours produce headache until quite large (although pituitary tumours are an exception to this.[30] Usually they are then evident for other reasons, but 3-4% (that is 3 per million of the population per year)[31] present as headache.[32] Raised intracranial pressure is apparent in the history. Epilepsy is a cardinal symptom of intracerebral space occupying lesions, and loss of consciousness should be viewed very seriously. In all likelihood, focal neurological signs will be present. Problems are more likely to occur with slowly growing tumours, especially those in neurologically "silent" areas of the frontal lobes. Subtle personality change

29 Kernick D, Stapley S, Goadsby PJ, Hamilton WW.What happens to new-onset headache presented to primary care? A case–cohort study using electronic primary care records. Cephalalgia 2008; 28: 1188–1195.

30 Levy M, Jager HR, Powell MP, Matharu MS, Meeran, K, Goadsby PJ Pituitary volume and headache: size is not everything. Archives of Neurology 2004; 61: 721-725.

31 Kurtzke JF. Neuroepidemiology. Ann Neurol 1984; 16: 265-277.

32 Hopkins A. Headache: problems in diagnosis and management. London: WB Saunders 1988: 6.

may result in treatment for depression, with headache attributed to it. Investigation may be prompted eventually by non-response to treatment, but otherwise some of these can be very difficult to pick up, whilst their infrequency does not justify routine brain scanning. *Fundoscopic examination is mandatory* at first presentation with headache, and it is always worthwhile to repeat it during follow-up.

Heightened suspicion is appropriate in patients who develop new headache and are known to have cancer elsewhere, or a suppressed immune system.

5.2 Meningitis

The signs of fever and neck stiffness usually accompany meningitis, in an obviously ill patient. Headache is nearly always progressive over hours or longer, generalised or frontal, perhaps radiating to the neck, and accompanied later by nausea and disturbed consciousness.

The serious implications and urgent need for treatment and investigations demand immediate referral to specialist care.

5.3 Subarachnoid haemorrhage

The clinical diagnosis of subarachnoid haemorrhage (SAH) is often straightforward, although the headache is not always of sudden onset, and neck stiffness may take some hours to develop. The headache of SAH is often described as the worst ever, but some patients are inclined to use such descriptive terms of migraine, rather devaluing them as diagnostic indicators. Even “explosive” features can occur with migraine (so-called “thunderclap headache”). Nevertheless, unless there is a clear history of uncomplicated headaches from which the present one is not particularly different, these characteristics indicate an urgent need for brain imaging, then CSF examination.

The serious consequences of missing SAH call for a low threshold of suspicion. In the elderly particularly, classical symptoms and signs may be absent.

5.4 Giant cell (temporal) arteritis

New headache in *any patient over 50 years of age* should raise the suspicion of giant cell arteritis (GCA).[33] Headache is the best known but not an inevitable symptom of GCA. It is very variable. It is likely to be persistent when present, often worse at night, and it can be very severe indeed. *In only a minority of cases is it localised to the temple(s)*.[34] Jaw claudication is so suggestive that, in its presence, the diagnosis is GCA until proved otherwise. Furthermore, the patient with GCA is systemically unwell. Marked scalp tenderness is common on examination, and may be a presenting complaint. Whilst the temporal artery may be inflamed, and tender, tortuous and thickened to palpation, this is an unreliable sign. Most patients have an ESR >50 mm/hr, but this can be lower[35] or it may be raised in the elderly for other reasons so temporal artery biopsy is usually necessary to secure the diagnosis.

The dilemma is that treatment may be long-term and toxic (steroids in high dosage), and needs to be commenced immediately – but not without very good reason.

33 Jones JG. Clinical features of giant cell arteritis. Baillière’s Clin Rheumatol 1991; 5: 413-430.

34 Ibid.

35 Wise CM, Agudelo CA, Chmelewski WL, McKnight KM. Temporal arteritis with low erythrocyte sedimentation rate: a review of five cases. Arthritis Rheum 1991; 34: 1571-1574.

5.5 Primary angle-closure glaucoma

Non-specific headache can be a symptom of primary angle-closure glaucoma (PACG). This is rare before middle age, when its prevalence is close to 1:1,000. Family history, female gender and hypermetropia are recognised risk factors.[36] PACG may present dramatically with acute ocular hypertension, a unilateral painful red eye with the pupil mid-dilated and fixed, associated nausea and vomiting and, essentially, impaired vision. In other cases, headache or eye pain may be episodic and mild, with the diagnosis of PACG suggested if the patient reports coloured haloes around lights.[37] The diagnosis of PACG is confirmed by skilled slit-lamp examination and gonioscopy.

Glaucoma should not to be missed, and should prompt immediate referral.

5.6 Idiopathic intracranial hypertension

A rare cause of headache that nonetheless should always be in the physician's mind, because it also leads to visual loss, is idiopathic intracranial hypertension (IIH) (formerly termed benign intracranial hypertension or pseudotumor cerebri). IIH is more common in young women, in whom it is strongly associated with obesity.[38] It may not readily be diagnosed on history alone, though this may suggest raised intracranial pressure. The physical sign of papilloedema indicates the diagnosis in adults, but is not seen invariably in children with the condition.

Suspected cases require referral and diagnostic confirmation by measurement of CSF pressure (>200 mm H2O in the non-obese; >250 mm H20 in obese patients) after brain imaging, which is normal.

5.7 Carbon monoxide poisoning

Carbon monoxide (C0) poisoning is uncommon but an avoidable (and easily overlooked) cause of ill-health and fatalities.[39] The symptoms of subacute C0 poisoning include headaches, nausea, vomiting, giddiness, muscular weakness, dimness of vision and double vision. Not all of these may occur; lethargy may result in misdiagnosis of chronic fatigue syndrome.[40]

In suspected cases, domestic gas appliances should be checked (gas flames should burn blue, not yellow or orange) although Department of Health advice is that the risk of C0 poisoning is higher in households relying on solid fuel.[41] Measurement of blood carboxyhaemoglobin concentration shortly after exposure confirms the diagnosis.

36 Coleman AL. Glaucoma. Lancet 1999; 354: 1803-1810.

37 Ibid.

38 Lueck CJ, McIlwaine GG. Idiopathic intracranial hypertension. Pract Neurol 2002; 5: 262-271.

39 Chief Medical Officer. CMO's update 16. London: Department of Health November 1997: 2.

40 Lader M, Morris R. Carbon monoxide poisoning. J Roy Soc Med 2001; 94: 552.

41 Chief Medical Officer. Carbon monoxide: the forgotten killer. Professional letter PL/CMO/2002/2. London: Department of Health 2002.

management of migraine

6. Management of migraine

6.1 Objectives of management

Cure is not a realistic aim and patients need to understand this. On the other hand, there is evidence that many migraine sufferers have unduly low expectations of what is achievable through optimum management. In the past, physicians’ attitudes have reinforced this. The shared objective should be control of symptoms so that the effect of the illness on a patient’s life and lifestyle is the least it can be.

6.2 Basic principles

To this end, patients should work through the treatment options in a rational order, and continue to do so *until it is certain they have found what suits them best.* In applying the following guidelines, ***follow-up*** should ensure optimum treatment has been established. Denial of best available treatment is difficult to justify for patients generally and, therefore, for individual patients. Unnecessary pain and disability are the result. In addition, increasingly it is being demonstrated that *under-treatment is not cost-effective*: sufferers’ and their carers’ lost time is expensive, as are repeated consultations in the search for better therapy. Never underestimate the benefit of just listening to patients and taking them seriously. It should be remembered that ***needs may change***. Migraine typically varies with time, and concomitant illness including other headaches may develop.

Children often respond to conservative management, which should therefore be the initial approach. Reassurance of parents is an important aspect of treating children. Otherwise, most can be managed as adults, with allowance for different symptom presentation and perhaps different dose-requirements and contraindications.

Children with troublesome migraine not responding to trigger avoidance and simple analgesics taken early with or without anti-emetics *should be seen by a paediatrician with an interest in headache*.

In ***adults***, there are four elements to good migraine management:

- correct and timely diagnosis;
- explanation and reassurance;
- predisposing/trigger identification and avoidance;
- intervention (drug or non-drug).

Diagnosis has been covered above. ***Explanation*** keeps patients' expectations realistic, and fosters appropriate use of therapy. ***Reassurance*** following diagnosis and explanation is all some patients need. In any event the effect of reassurance is added to that of any therapeutic intervention.

6.3 Predisposing and trigger factors

Predisposing factors should be distinguished from precipitating or trigger factors (see 6.3.2). Certain predisposing factors are well recognised. They are not always avoidable but may be treatable (see table).

6.3.1 Predisposing factors

Predisposing factor	Management summary
Stress	Lifestyle change; stress reduction/ coping strategies (see 6.6.2)
Depression/anxiety	Specific therapy
Menstruation	See 6.5.9
Menopause	See 6.5.9
Head or neck trauma	Physiotherapy (see 6.6.1)

6.3.2 Trigger factors

Trigger factors are important in occasional patients but generally less so than is commonly supposed. Dietary sensitivities affect, at most, 20% of migraine sufferers. Many attacks have no obvious trigger and, again, those that are identified may not be avoidable. Clearly they should be avoided where possible, which may involve lifestyle change.

Trigger factor
Relaxation after stress, especially at weekends or on holiday
Other change in habit: missing meals; missing sleep; lying in late; long distance travel
Bright lights and loud noise (both perhaps stress-inducing)
Dietary: certain alcoholic drinks; some cheeses
Strenuous unaccustomed exercise
Menstruation

Diaries (see 6.3.3) may be useful in detecting triggers but the process is complicated as triggers appear to combine, jointly contributing to a "threshold" above which attacks are initiated. Too much effort in seeking triggers causes introspection and may be counter-productive. Enforced lifestyle change is inappropriate management if it adversely affects quality of life by more than is offset by improvement in migraine. Simple advice to patients is to minimise potential triggers: at stressful times eat regularly, for example.

Anxiety and emotion. Most migraineurs cope well with stresses but many have attacks when they relax (so giving rise to weekend migraine, which is common). Stress may induce other triggers such as missed meals, poor sleep and muscle tension. Although stress may be unavoidable, its existence may make it more important to avoid other triggers.

Missing meals may trigger attacks. Regular meals should be encouraged.

Specific foods are less commonly implicated in triggering migraine than is widely believed. A food is a trigger when: a) migraine onset occurs within *6 hours of intake*; b) the effect is reasonably *reproducible*; c) withdrawal leads to *improvement*. Most migraineurs can eat whatever they like as long as they keep up with their energy demands. A few susceptible individuals note a definite relationship between the consumption of certain foods, particularly alcohol, and the onset of migraine. The foods may not always trigger an attack but tip the balance when the person is vulnerable. Dietary triggers, when real, become obvious to patients and are usefully avoided. A suspected food should be excluded for a few weeks. When many foods are suspect, supervision by a dietician is advisable as elimination diets can result in malnutrition. Excluded foods should be reintroduced if there is no significant improvement. There is no case for blanket avoidance of cheese, chocolate or other foods, or for other dietary manipulation.

Cravings for sweet or savoury foods are probably ***premonitory symptoms*** heralding the headache, not triggers.

Food allergy (ie, an immunological process) has ***no part*** in the causation of migraine.

Too much and too little sleep can both play a role. Sleepless nights result in over-tiredness which triggers migraine. Conversely, sleeping in for even half an hour longer than usual, often at the weekend, can trigger migraine. In both cases, the *cause* of the altered sleep pattern (stress, relaxation) may be the true trigger.

Hormonal changes. Migraine is three times more common in women than in men. Attacks in most women start around puberty and continue until the menopause, with respites during pregnancy. Many women are far more susceptible to migraine at the time of their periods and a small percentage have attacks exclusively at or near (±48 hr) the first day of menstruation (***menstrual migraine***). Women with obvious hormonal triggers may benefit from specific intervention (see 6.5.9).

Strenuous exercise can precipitate an attack in a person unaccustomed to it. This puts many people off exercise when in fact regular exercise may help prevent migraine attacks. This is because it improves blood sugar balance, helps breathing, stimulates the body to release its own natural pain killers and promotes a general sense of well-being.

6.3.3 The trigger diary

When migraine attacks are frequent, a trigger diary may be useful in addition to the attack diary. Patients can be given a list of common triggers and record those present each day whether they have a migraine attack or not. The daily trigger diary and attack diary are best reviewed after at least five attacks. The information in each is compared for coincidence of (multiple) triggers with attacks.

6.4 Drug intervention (acute)

The evidence-base for many acute anti-migraine drugs is poor. For aspirin/metoclopramide combination the evidence is better[42] and for the triptans it is generally good. Whilst, logically, drug treatment should be selected for each patient according to his or her need and expected response to it ("stratified management"), little basis other than guesswork presently exists for achieving this. In particular, the superiority of triptans over other treatments in all patients or in any clearly identifiable subgroup of them can be questioned.

Consequently, there is a ***treatment ladder*** which begins with drugs chosen because they are safest and cheapest whilst being known to have efficacy. All patients should *start* on the first step of this ladder ("stepped management"). Stepped management is *not* contrary to the principle of individualised care: on the contrary, it is a reliable strategy for achieving it based on evidence manifestly applicable to the individual patient. Speed is sacrificed only if a better alternative exists, for which a search continues. It is suggested, but not an invariable rule, that ***failure on three occasions*** should be the criterion for progressing from each step to the next. Statistically, three consecutive failures are still compatible with an 80% success rate but, in practice, few patients will persist for longer.

People who recognise attacks of more than one sort, or of differing severity, may apply different steps for each accordingly.

As a general rule, all acute drug therapy should be combined with ***rest and sleep***[43] (promoted if necessary with eg, ***temazepam*** or ***zolpidem***). However, the central objective of treatment for some patients is to be able to carry on with their activities and, for these, this recommendation is inappropriate.

6.4.1 Step one: simple oral analgesic ± anti-emetic

Recommended analgesic doses for acute migraine are typically greater than standard doses to achieve rapid therapeutic levels against a background of gastric stasis.

1a) Over-the-counter analgesic ± anti-emetic:

For pain:

- aspirin 600-900mg,[44,45] or
- ibuprofen 400-600mg[46,47]

42 Tfelt-Hansen P, Henry P, Mulder LJ, Scheldewaert RG, Schoenen J, Chazot G. The effectiveness of combined oral lysine acetylsalicylate and metoclopramide compared with oral sumatriptan for migraine. Lancet 1995; 346: 923-926.

43 Wilkinson M, Williams K, Leyton M. Observations on the treatment of an acute attack of migraine. Res Clin Stud Headache 1978; 6: 141-146.

44 Kirthi V, Derry S, Moore RA, McQuay HJ. Aspirin with or without an antiemetic for acute migraine headaches in adults. Cochrane Database Syst Rev; 4: CD008041.

45 Limmroth V, Katsarava Z, Diener H-C. Acetylsalicylic acid in the treatment of headache. Cephalalgia 1999; 19: 545-551.

46 Kloster R, Nestvold K, Vilming ST. A double-blind study of ibuprofen versus placebo in the treatment of acute migraine attacks. Cephalalgia 1992; 12: 169-171.

47 Havanka-Kannianinen H. Treatment of acute migraine attack: ibuprofen and placebo compared. Headache 1989; 29: 507-509.

in either case best taken in buffered soluble or orodispersible formulations,[48,49] and *early* in the attack when absorption may be least inhibited by gastric stasis. Up to 4 doses can be taken in 24 hours.

These drugs should be used *without* codeine or dihydrocodeine (see 6.4.11).

There is little evidence for the efficacy of paracetamol alone.[50]

For nausea and vomiting (if required):

- ***prochlorperazine 3-6mg buccal tablet***,[51] dissolved between gum and cheek up to twice in 24 hours, or
- ***domperidone 10mg***, up to four times in 24 hours.

1b) OTC or prescription NSAIDs plus a prokinetic anti-emetic:

- ***aspirin 600-900mg***, up to 4 doses in 24 hours or
- ***ibuprofen 400-600mg***, up to 4 doses in 24 hours or
- ***tolfenamic acid rapid release 200mg***,[52] repeated once if necessary after 1-2 hours or
- ***naproxen 750-825mg***,[53,54,55] with a further 250-275mg up to twice in 24 hours or
- ***diclofenac-potassium 50-100mg***,[56,57,58] repeated up to a total of 200mg in 24 hours

In all cases a fast-acting formulation is preferred (avoid slow-release), as is a prokinetic anti-emetic to promote gastric emptying:

- ***metoclopramide 10mg***,[59,60] or
- ***domperidone 20mg***[61]

Domperidone is less sedating than metoclopramide and creates less risk of extrapyramidal side effects.

MigraMax,[62,63] (lysine acetylsalicylate 1620 mg [equivalent to aspirin 900mg] plus metoclopramide 10mg per sachet

48 Ross-Lee L, Heazlewood V, Tyrer JH, Eadie MJ. Aspirin treatment of migraine attacks: plasma drug level data. Cephalalgia 1982; 2: 9-14.

49 MacGregor EA, Dowson A, Davies PTG. A randomised, double-blind, two period crossover study to compare the efficacy of mouth dispersible aspirin 900 mg and placebo in the treatment of migraine. Headache 2002; 42: 249-255.

50 Bandolier, at www.medicine.ox.ac.uk/bandolier/booth/Migraine/Paracute.html

51 Sharma S, Prasad A, Nehru R, et al. Efficacy and tolerability of prochlorperazine buccal tablets in treatment of acute migraine. Headache 2002; 42: 896-902.

52 Myllylä VV, Havanka H, Herrala L et al. Tolfenamic acid rapid release versus sumatriptan in the acute treatment of migraine: comparable effect in a double-blind, randomized, controlled, parallel-group study. Headache 1998; 38: 201-207.

53 Johnson ES, Ratcliffe DM, Wilkinson M. Naproxen sodium in the treatment of migraine. Cephalalgia 1985; 5: 5-10.

54 Sargent JD, Baumel B, Peters K, Diamond S, Saper JR, Eisner LS et al. Aborting a migraine attack: naproxen sodium v ergotamine plus caffeine. Headache 1988; 28: 263-266.

55 Synflex SmPC. April 2009. Available at: http://emc.medicines.org.uk/medicine/1734/SPC/Synflex+275mg+Tablets/

56 The Diclofenac-K/Sumatriptan Migraine Study Group. Acute treatment of migraine attacks: efficacy and safety of a nonsteroidal anti-inflammatory drug, diclofenac-potassium, in comparison to oral sumatriptan and placebo. Cephalalgia 1999; 19: 232-240.

57 McNeely W, Goa KL. Diclofenac-potassium in migraine. Drugs 1999; 57: 991-1003.

58 Dahlöf C, Björkman R. Diclofenac-K (50 and 100 mg) and placebo in the acute treatment of migraine. Cephalalgia 1993; 13: 117-123.

59 Tokola RA The effect of metoclopramide and prochlorperazine on the absorption of effervescent paracetamol in migraine. Cephalalgia 1988; 8: 139-147.

60 Tfelt-Hansen P, Olesen J. Effervescent metoclopramide and aspirin (Migravess) versus effervescent aspirin or placebo for migraine attacks: a double-blind study. Cephalalgia 1984; 4: 107-111.

61 MacGregor EA, Wilkinson M, Bancroft K. Domperidone plus paracetamol in the treatment of migraine. Cephalalgia 1993; 13: 124-127.

62 Chabriat H, Joire JE, Danchot J, Grippon P, Bousser MG. Combined oral lysine acetylsalicylate and metoclopramide in the acute treatment of migraine: a multicentre double-blind placebo-controlled study. Cephalalgia 1994; 14: 297-300.

63 Tfelt-Hansen P, Henry P, Mulder LJ, Scheidewaert RG, Schoenen J, Chazot G. The effectiveness of combined oral lysine acetylsalicylate and metoclopramide compared with oral sumatriptan for migraine. Lancet 1995; 346: 923-926.

(£1.12); up to three sachets in 24 hours) is a convenient preparation. An alternative for those who cannot tolerate aspirin is ***Paramax sachets*** (paracetamol 500mg plus metoclopramide 5mg per sachet; 2 sachets per dose (£0.60); up to 3 doses in 24 hours). These are preferred to ***Paramax tablets***, which are not soluble. There is no other way at present to give metoclopramide in a soluble oral formulation.

Contraindications to step one:

In adults there are no general contraindications, unless it has clearly failed before. There may be specific contraindications to aspirin or to other NSAIDs. In children under 16 years of age aspirin should be avoided. Metoclopramide is not recommended for children or adolescents; prochlorperazine is not recommended for children.

6.4.2 Step two: rectal analgesic ± anti-emetic

Diclofenac suppositories 100mg (up to 200mg in 24 hours) for pain plus ***domperidone suppositories 30-60mg*** (up to 120mg in 24 hours) when needed for nausea or vomiting.

Contraindications to step two:

Peptic ulcer (misoprostol 800µg or omeprazole 20-40 mg daily may give limited gastroduodenal protection,[64,65]) or lower bowel disease. The occurrence of diarrhoea during acute migraine may prevent effective use. Some patients will not accept suppositories.

64 Gøtzsche PC. Non-steroidal anti-inflammatory drugs. BMJ 2000; 320: 1058-1061.

65 Lazzaroni M, Bianchi Porro G. Prophylaxis and treatment of non-steroidal anti-inflammatory drug-induced upper gastrointestinal side-effects. Digest Liv Dis 2001; 33 (Suppl 2): S44-S58.

6.4.3 Step three: specific anti-migraine drugs

The marketed triptans differ in ways that might rationally suggest one rather than another for a particular patient. Clinical trials indicate that they range in comparative efficacy.[66] They also range in cost, suggesting that they might be ranked according to their cost-effectiveness (in the accounts of each below, prices are basic NHS costs per dose for branded triptans).[67] However, there are unpredictable individual variations in response to different triptans. About 30% of patients fail to respond to any particular one, with non-response attributable to a variety of factors including low and inconsistent absorption, use of the medication at the wrong time (too early or too late in an attack), inadequate dose and individual biological variability.[68] Evidence from several trials confirms the common clinical observation that patients with a poor response to one triptan can benefit from another in subsequent attacks. Ideally, each triptan should be tried in three attacks before it is rejected for lack of efficacy. Not only a different triptan but also dosage and a different route of administration should be considered.

66 Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT1B/1D agonists) in acute migraine treatment: a meta-analysis of 53 trials. Lancet 2001; 358: 1668-1675.

67 Belsey, J. The clinical and financial impact of oral triptans in the management of migraine in the UK: a systematic review. J Med Econ 2000; 3: 35-47.

68 Dodick D. Triptan nonresponder studies: implications for clinical practice. Headache 2005; 45: 156-162.

Triptans should be taken at the start of the headache phase. There is increasing evidence of greater efficacy when taken whilst pain is still mild,[69] but triptans appear to be ineffective if administered during aura.[70,71]

All triptans are associated with return of symptoms within 48 hours in 20-50% of patients who have initially responded (*relapse*). This is a troublesome limitation (see 6.4.7).

When triptans are taken orally, concomitant administration of a prokinetic anti-emetic, metoclopramide or domperidone, is suggested on theoretical grounds: there is some evidence to support the former.[72]

Sumatriptan was first launched, and clinical experience of its use is greatest. The ***50mg tablet*** (£4.20-£4.42 [generic versions available at £0.21-0.32]) and the rapidly-dispersing ***RADIS 50mg tablet*** (£3.98) are equally appropriate for first use of a triptan. When response to these is inadequate, the ***100mg tablet*** (£7.15 [generic versions available at £0.46]), ***RADIS 100mg tablet*** (£7.15) or 20mg ***nasal spray*** (£5.90) may be used according to preference.[73,74] Total dosage per 24 hours should not exceed 300mg orally or 40mg intranasally. The nasal spray is not useful if vomiting precludes oral therapy since its bioavailability depends largely on ingestion.

Sumatriptan 50mg tablet is available from pharmacies, without prescription, as ***Imigran RECOVERY*** (£3.99) or ***Migraleve ULTRA*** (£3.91).

If a rapid response is important above all, ***6mg subcutaneously (autoinject device)*** (£20.21-£21.24) is the triptan of choice.[75] Only sumatriptan offers this option. The total dose per 24 hours should not exceed 12mg.

For adolescents (12-17 years), sumatriptan ***10mg nasal spray*** (£5.90) is a specifically licensed formulation.

Zolmitriptan 2.5mg tablet[76] (£3.00) and ***2.5mg RAPIMELT***[77] (orodispersible tablet placed on the tongue) (£2.98) are also equally appropriate for first use of a triptan. A second dose may be taken for lack of effect after two hours if needed. When this is usually the case, a first dose of ***5mg RAPIMELT*** (£3.80) is recommended.[78] Total dose per 24 hours should not exceed 10mg. Zolmitriptan ***5mg nasal spray***[79] (£6.08) produces a rapid response, and may be useful if vomiting is already occurring since up to 30% is absorbed through the nasal mucosa.[80]

69 Goadsby PJ. The 'Act when Mild' (AwM) study: a step forward in our understanding of early treatment in acute migraine. Cephalalgia 2008; 28 Suppl 2: 36-41.

70 Bates D, Ashford E, Dawson R, et al. Subcutaneous sumatriptan during the migraine aura. Sumatriptan Aura Study Group. Neurology 1994; 44: 1587-1592.

71 Olesen J, Diener HC, Schoenen J, Hettiarachchi J. No effect of eletriptan administration during the aura phase of migraine. Eur J Neurol 2004; 11: 671-677.

72 Schulman EA, Dermott KF. Sumatriptan plus metoclopramide in triptan-nonresponsive migraineurs. Headache 2003; 43: 729-733.

73 Pfaffenrath V, Cunin G, Sjonell G, Prendergast S. Efficacy and safety of sumatriptan tablets (25mg, 50mg and 100mg) in the acute treatment of migraine: defining the optimum doses of oral sumatriptan. Headache 1998; 38: 184-190.

74 Salonen R, Ashford E, Dählof C, Dawson R, Gilhus NE, Lüben V et al. Intranasal sumatriptan for the acute treatment of migraine. J Neurol 1994; 241: 463-469.

75 The Subcutaneous Sumatriptan International Study Group. Treatment of migraine attacks with sumatriptan. N Engl J Med 1991; 325: 316-321.

76 Rapoport AM, Ramadan NM, Adelman JU, Mathew NT, Elkind AK, Kudrow DB. Optimizing the dose of zolmitriptan (Zomig, 311C90) for the acute treatment of migraine. A multicenter, double-blind, placebo-controlled, dose range-finding study. Neurology 1997; 49: 1210-1218.

77 Dowson AJ, MacGregor EA, Purdy RA, Becker WJ, Green J, Levy SL. Zolmitriptan orally disintegrating tablet is effective in the acute treatment of migraine. Cephalalgia 2002; 22: 101-106.

78 Rapoport AM, Bigal ME, Tepper SJ, Sheftell FD. Zolmitriptan (Zomig). Expert Rev Neurother 2004; 4: 33-41.

79 Charlesworth BR, Dowson AJ, Purdy A, Becker WJ, Boes-Hansen S, Färkkilä M. Speed of onset and efficacy of zolmitriptan nasal spray in the acute treatment of migraine. CNS Drugs 2003; 17: 653-667.

80 AstraZeneca: Data on file.

Although zolmitriptan is not licensed for use in children or adolescents (12-17 years), there is evidence to suggest efficacy in adolescents.[81,82]

Rizatriptan 10mg tablet (£4.46) and ***10mg MELT*** (orodispersible wafer placed on the tongue) (£4.46) are alternatives to sumatriptan 100mg.[83,84] The total dose per 24 hours should not exceed 20mg. *Metabolism is affected by propranolol* and patients on this drug should take ***5mg tablet*** (£4.46) with a maximum dose per 24 hours of 10mg.

Naratriptan 2.5mg tablet[85] (£4.09) is well tolerated but its relatively low efficacy and slow onset of effect limit its use in patients seeking a rapid response. It is recommended when side-effects to other triptans are troublesome. The evidence for less relapse is not convincing. The total dose per 24 hours should not exceed 5mg.

Almotriptan 12.5mg tablet (£3.02) has shown similar efficacy and relapse rates to sumatriptan 100mg in clinical trials, and it is well tolerated.[86,87] These features suggest it is a strong candidate for first-line use as a triptan. The total dose per 24 hours should not exceed 25mg.

Eletriptan is unlike other triptans in exhibiting a clear dose-response relationship for efficacy in the range 20-80mg.[88,89] The standard starting dose is ***40mg tablet*** (£3.75). Those who find this dose well-tolerated but not efficacious may benefit from ***80mg*** (two tablets; £7.50). A ***20mg tablet*** (£3.75) is marketed for those with mild or moderate renal impairment, but may be used if side-effects occur at higher doses. This dose-flexibility makes eletriptan another strong candidate for first-line use as a triptan. The total dose per 24 hours should not exceed 80mg.

Frovatriptan 2.5mg tablet (£2.78) has a substantially longer half-life (26 hours) than all other triptans, but this does not appear to translate into markedly lower relapse rates.[90] In comparative clinical trials, frovatriptan 2.5mg was less efficacious than sumatriptan 100mg[91] but with fewer adverse events.[92] The total dose per 24 hours should not exceed 5mg. Post-marketing experience is needed to establish the position of frovatriptan amongst other triptans.

Ergotamine tartrate 1-2 mg, in clinical trials in which it has been used as a comparator, has shown significantly lower relapse rates which may be due to its prolonged duration of action.[93] Ergotamine may therefore still have a place if relapse is a particular problem (see 6.4.7), but *toxicity* and

81 Dixon R, Engleman K, Kemp J, Ruckle JL. A comparison of the pharmacokinetics and tolerability of the novel antimigraine compound zolmitriptan in adolescents and adults. J Child Adolesc Psychopharmacol 1999; 9: 35-42.

82 Linder SL, Dowson AJ. Zolmitriptan provides effective migraine relief in adolescents. Int J Clin Pract 2000; 54: 466-469.

83 Gijsman H, Kramer MS, Sargent J, Tuchman M, Matzura-Wolfe D, Polis A et al. Double-blind, placebo-controlled, dose-finding study of rizatriptan (MK-462) in the acute treatment of migraine. Cephalalgia 1997; 17: 647-651.

84 Krymchantowski AV, Bigal ME. Rizatriptan in migraine. Expert Rev Neurother 2005; 5: 597-603.

85 Mathew NT, Asgharnejad M, Peykamian M, Laurenza A. Naratriptan is effective and well tolerated in the acute treatment of migraine: Results of a double-blind, placebo-controlled, crossover study. Neurology 1997; 49: 1485-1490.

86 Dodick DW. A review of the clinical efficacy and tolerability of almotriptan in acute migraine. Expert Opin Pharmacother 2003; 4: 1157-1163.

87 Dowson AJ. Oral almotriptan: practical uses in the acute treatment of migraine. Expert Rev Neurother 2004; 4: 339-348.

88 Stark R, Dahlof C, Haughie S, Hettiarachchi J. Efficacy, safety and tolerability of oral eletriptan in the acute treatment of migraine: Results of a phase III, multicentre, placebo-controlled study across three attacks. Cephalalgia 2002; 22: 23-32.

89 Diener HC. Eletriptan in migraine. Expert Rev Neurother 2005; 5: 43-53.

90 Ryan R, Géraud G, Goldstein J, Cady R, Keywood C. Clinical efficacy of frovatriptan: placebo-controlled studies. Headache 2002; 42 (suppl 2): S84-S92.

91 Ibid.

92 Géraud G, Spierings ELH, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache 2002; 42[suppl 2]: S93-S99.

93 Tfelt-Hansen P, Saxena PR, Dahlof C, Pascual J, Lainez M, Henry P et al. Ergotamine in the acute treatment of migraine - a review and European consensus. Brain 2000; 123: 9-18.

misuse potential are greater risks with ergotamine than with triptans. It has very poor bioavailability and is better taken rectally. Each suppository contains 2mg (plus caffeine 100mg) (£0.27) and a half suppository is adequate for some people. The total dose per 24 hours should not exceed 4mg.

Ergotamine should not be taken *concomitantly* with any triptan, but is probably safe 12 hours after all but frovatriptan (see 6.4.6).

Contraindications to step three:

a) Uncontrolled hypertension.

b) Risk factors for coronary heart disease or cerebrovascular disease: past history; strong family history (the significance of this is age-related); advanced age; signs of either. The cardiovascular risk of triptans is very low in the absence of these contraindications.[94] In cases of uncertainty, cardiological referral and/or exercise ECG are recommended.

c) Children under 12 years:
no experience has been reported and neither safety nor efficacy are established.

There are additional specific contraindications to some triptans. Ergotamine taken with beta-blockers, which impair nutrient flow to the skin, can cause digital gangrene.

If step three fails:

Review the diagnosis. Review compliance and manner of use of medication. Steps four and five *may* be worth trying. Consider prophylaxis (see 6.5).

94 Dodick D, Lipton RB, Martin V, Papademetriou V, Rosamond W, MaassenVanDenBrink A et al. Consensus statement: cardiovascular safety profile of triptans (5-HT1B/1D agonists) in the acute treatment of migraine. Headache 2004; 44: 414-425.

6.4.4 Step four: combinations

There is some evidence that the combination of sumatriptan 50mg and naproxen 500mg is superior to either drug alone.[95] Other combinations of ***steps one + three*** may be worth trying, followed by ***steps two + three***.

Although it is not common practice, ***diclofenac 75mg intramuscularly***[96] may be self-injected. It is difficult: the intramuscular volume is 3ml, requiring two injection sites.

6.4.5 Emergency treatment

These recommendations apply to emergency treatment of patients at home or of those visiting accident and emergency departments. Treatment offered will depend on the availability of medication and the possibilities for observing the patient after treatment.

In all cases, ***narcotics*** are **NOT** recommended for the emergency treatment of migraine and their use can be associated with delayed recovery (see 6.4.11).[97]

Patients who have not already taken a triptan for the current attack, and in whom enquiry as to potential contra-indications is possible, may benefit from ***sumatriptan 6mg subcutaneously***. Some specialists favour ***diclofenac 75mg intramuscularly***[98] which can be given alone or in combination with ***chlorpromazine 25-50mg***

95 Smith TR, Sunshine A, Stark SR, Littlefield DE, Spruill SE, Alexander WJ. Sumatriptan and naproxen sodium for the acute treatment of migraine. Headache 2005; 45: 983-991.

96 Bigal ME, Bordini CA, Speciali JG. Intramuscular diclofenac in the acute treatment of migraine: A double-blind placebo controlled study. Arquivos Neuro-Psiquiat 2002; 60: 410-415.

97 Tornabene SV, Deutsch R, Davis DP, Chan TC, Vilke GM. Evaluating the use and timing of opioids for the treatment of migraine headaches in the emergency department. J Emerg Med 2009; 36: 333-337.

98 Engindeniz Z, Demircan C, Karli N, Armagan E, Bulut M, Aydin T, et al. Intramuscular tramadol vs. diclofenac sodium for the treatment of acute migraine attacks in emergency department: a prospective, randomised, double-blind study. J Headache Pain 2005; 6: 143-148.

intramuscularly or intravenously.[99] ***Metoclopramide 10-20mg***[100] or ***prochlorperazine 12.5mg intramuscularly*** or ***intravenously***[101] are alternative options but can cause acute dystonia including oculogyric crisis, particularly in young and elderly people. This effect can be reversed by ***procyclidine*** 5-10mg ***intramuscularly*** or ***intravenously***. For patients at high future risk of needing emergency treatment, it is worth providing ***chlorpromazine 25-50mg*** suppositories for home use, although there are no data regarding efficacy of this route of delivery.

In hospital, rehydration with intravenous normal saline may be advisable.

Early follow-up is suggested.

6.4.6 Treatment of relapse within the same attack after initial efficacy

Symptomatic medications (steps one and two) may, and if needed should, be repeated within their dosage limitations.

In the case of triptans, there is good evidence that a second dose is effective for relapse but very little to show that it is the most appropriate treatment. In most people it is the sensible option, with a minimum of 2 hours between doses and within the total daily dose limitation for the particular triptan. But, in some, relapse appears to be a manifestation of rebound and *repeated dosing can give rise to repeated rebound over several days*.[102] There is no clear consensus on the best management of these people, but ***naproxen 500mg*** or ***tolfenamic acid 200mg***[103] may be preferable for the first or second relapse.

Ergotamine tartrate may be an alternative but efficacy has not been formally established; it should not be used within 12 hours after any triptan.

6.4.7 Patients who consistently experience relapse

There is some evidence that this occurs more in those whose untreated attacks last longer than 24 hours.

Naratriptan, ***eletriptan*** and ***frovatriptan*** are associated with relatively low recurrence rates.[104] The differences are not marked. ***Ergotamine*** is associated with significantly less relapse and is a fall-back option (see 6.4.3).

Naproxen or ***tolfenamic*** acid may be used pre-emptively if relapse is anticipated.

6.4.8 "Long-duration migraine"

Migraine lasting longer than 3 days (***status migrainosus***) is uncommon. Apparently long-duration attacks may be migraine with a superseding tension-type headache for which ***naproxen*** or ***diclofenac*** are preferable to specific anti-migraine drugs.

Multiple relapses over days following repeated doses of a triptan are a well-recognised complication (see 6.4.6).

99 Loga P, Lewis D. Chlorpromazine in migraine. Emerg Med J 2007; 24: 297-300.

100 Colman I, Brown MD, Innes GD, Grafstein E, Roberts TE, Rowe BH. Parenteral metoclopramide for acute migraine: meta-analysis of randomised controlled trials. BMJ 2004; 329: 1369-1373.

101 Friedman BW, Esses D, Solorzano C, Greenwald P, Radulescu R, Change E, Hochberg M et al. A randomized controlled trial of prochlorperazine versus metoclopramide for treatment of acute migraine. Ann Emerg Med 2008; 52: 399-406.

102 Limmroth V, Katsavara Z, Fritsche G, Przywara S, Diener H-C. Features of medication overuse headache following overuse of different acute headache drugs. Neurology 2002; 59: 1011-1014.

103 Krymchantowski AV, Adriano M, Fernandes D. Tolfenamic acid decreases migraine recurrence when used with sumatriptan. Cephalalgia 1999; 19: 186-187.

104 Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT1B/1D agonists) in acute migraine treatment: a meta-analysis of 53 trials. Lancet 2001; 358: 1668-1675.

6.4.9 Slowly developing migraine

Patients whose attacks develop slowly may initially be uncertain whether their headache is migrainous or not. If treatment is required at this stage, ***simple analgesics*** are recommended and may prevent further development. ***Triptans*** should not be used, if at all, until it is certain that the headache is migrainous.

6.4.10 Menstrual migraine

The diagnosis of menstrual migraine (migraine attacks that occur regularly on day 1 of menstruation ± 2 days)[105] is confirmed using contemporaneous diary cards for a minimum of three menstrual cycles. Acute treatment of menstrual attacks of migraine is the same as for non-menstrual attacks but, because the former may have longer duration, it may be necessary to repeat treatment over several consecutive days. Provided that this does not lead to treatment on 15 or more days a month with simple analgesics or on 10 or more days a month with codeine-containing analgesics, ergot or triptans, there is no concern regarding medication overuse.

6.4.11 Migraine in pregnancy and lactation[106]

Paracetamol in moderation is safe throughout pregnancy. ***Aspirin*** and ***NSAIDs*** are safe except in the third trimester. For nausea, ***metoclopramide*** or ***domperidone*** are unlikely to cause harm throughout pregnancy and lactation.

Many women ask whether they can continue to use triptans whilst pregnant. Most of the available information relates to ***sumatriptan***, and suggests that exposure during pregnancy leads to no higher risk of birth defects than is recorded in the general population.[107] Women who have inadvertently taken triptans and then find themselves pregnant can be reassured that the outcome of the pregnancy is very unlikely to be adversely affected by the triptan. However, since present knowledge is still limited, triptans cannot be recommended as a routine.

A number of drugs can be used by breastfeeding women to treat migraine. These include the painkillers ***ibuprofen***, ***diclofenac***, and ***paracetamol***, which may be combined with ***domperidone***. The manufacturers of ***almotriptan***, ***eletriptan***, ***frovatriptan*** and ***rizatriptan*** all recommend avoiding breast-feeding for 24 hours after treatment, and the manufacturer of ***sumatriptan*** recommends 12 hours, although studies on ***eletriptan*** and ***sumatriptan*** show that only negligible amounts enter breast milk. In contrast, the manufacturers' advice for ***naratriptan*** and ***zolmitriptan*** state only "Caution should be exercised when considering administration… to women who are breast-feeding." However, the American Academy of Pediatrics (AAP) Committee on Drugs advises that use of ***sumatriptan*** is compatible with breast-feeding.[108]

Ergotamine and ***dihydroergotamine*** are contraindicated during pregnancy and lactation.

6.4.12 Drugs to avoid in acute intervention

Opiates and ***opioids*** (including diamorphine, morphine, pethidine, dextropropoxyphene, buprenorphine, tramadol.

105 International Headache Society Classification Subcommittee. The International Classification of Headache Disorders. 2nd edition. Cephalalgia 2004; 24 (Suppl 1): 1-160.

106 MacGregor A. Management of migraine during pregnancy. Progress in Neurology and Psychiatry 2009; 13 (5): 21-23.

107 Sumatriptan/Naratriptan/ Treximet Pregnancy Registry August 2009: available at: http://pregnancyregistry.gsk.com/sumatriptan.html

108 American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. Pediatrics 2001; 108: 776-789. Available at: http://www.aap.org/healthtopics/breastfeeding.cfm

codeine and dihydrocodeine) increase nausea, promote systemic shut-down and have addictive potential. ***Buprenorphine*** is particularly emetic. ***Codeine*** and ***dihydrocodeine*** are used extensively in OTC combination analgesics; they provide small additional benefit in a range of painful conditions but evidence of this does not extend to headache and it is at the expense of increased side-effects.[109] Furthermore, when these drugs are implicated in MOH, management is significantly more difficult (see 9.0).

6.4.13 Limits to acute therapy: frequency of use

Over-frequent use of drugs for acute intervention may be one criterion for prophylaxis (see below). On a regular basis:

a) use of ***triptans on 10 or more days a month*** or ***analgesics on 15 or more days a month*** is inappropriate for migraine and is associated with a clear risk of MOH;

b) use of either on ***two or more days every week*** calls for close enquiry into how it is used, and review of the diagnosis.

6.5 Drug intervention (prophylactic)

6.5.1 Indications for prophylaxis

Prophylaxis is used to reduce the ***number*** of attacks in circumstances when acute therapy, used appropriately, gives ***inadequate symptom control***. The judge of this is usually the patient. *In children*, an index of this is frequency of absence from school because of migraine.

Over-frequent use of acute therapy is also a criterion for migraine prophylaxis, but prophylactic drugs are inappropriate and will be ineffective for medication overuse headache. This condition must first be excluded.

When indicated, prophylactic therapy is used *in addition* to acute therapy, not in place of it.

6.5.2 Dose-titration

Most prophylactics are used within a dose range, and in general must be up-titrated slowly to an effective dose (or to the maximum dose) in order to avoid side-effects that will precipitate premature discontinuation. This can lead to a delay in efficacy which itself, unfortunately, sometimes triggers discontinuation (see 6.5.3). Careful explanation is needed.

6.5.3 Duration of use

Migraine is cyclical: treatment is required for periods of exacerbation and uninterrupted prophylaxis over very long periods is rarely appropriate.

Drugs that are *effective* should be continued for ***4-6 months***, then withdrawal considered to establish continued need. Withdrawal is best achieved by tapering the dose over 2-3 weeks.

Prophylactic drugs that are apparently *not effective* should not be discontinued too soon since efficacy may be slow to develop, particularly when dose-titration is necessary (see 6.5.2). In practice patients usually decide when they stop medication, so careful explanation is needed lest they be labelled non-responders inappropriately (eventually, perhaps, to all drugs). There is no absolute guide but, in the absence of unacceptable side-effects, ***6-8 weeks*** is a reasonable trial following dose-titration, and ***3 cycles*** in the case of specific therapy for hormone-related migraine (see 6.5.9).

109 de Craen AJM, Di Giulio G, Lampe-Schoenmaeckers AJEM, Kessels AGH, Kleijnen J. Analgesic efficacy and safety of paracetamol-codeine combinations versus paracetamol alone: a systematic review. Brit Med J 1996; 313: 321-325.

6.5.4 First-line prophylactic drugs

The criteria for preferring one prophylactic drug to another are based upon:

- evidence of efficacy;
- comorbidity and the anticipated effect of the drug upon it;
- contraindications, including risks in pregnancy;
- good evidence that poor compliance is a major factor impairing efficacy of migraine prophylactics and that once-daily dosing is preferable.[110]

The formal evidence-base for efficacy is good for beta-blockers,[111,112] topiramate,[113,114,115] and valproate,[116] and adequate for amitriptyline,[117] but poor for other prophylactic drugs. The following recommendations are based on this evidence coupled with expert clinical experience.

Beta-adrenergic blockers without partial agonism are first-line if not contraindicated by asthma, heart failure, peripheral vascular disease or depression. Cardioselectivity and hydrophilicity both improve the side-effect profile; on this basis, ***atenolol* 25-100mg bd*** is to be preferred over ***metoprolol 50-100mg bd*** and this over ***propranolol LA 80mg od-160mg bd***. On the same basis plus the knowledge that once-daily dosing is associated with significantly better compliance,[118] ***bisoprolol* 5 10mg od*** may be the beta-blocker of choice but better evidence of its efficacy is needed. Commonly reported adverse events include cold extremities, reduced exercise tolerance and dizziness.

Amitriptyline* 10-150mg daily, at or 1-2 hours before bedtime, is first-line when migraine coexists with:

- troublesome tension-type headache (see 6.7);
- another chronic pain condition;
- disturbed sleep;
- depression

Except in the last case it is wise to explain the choice of this drug to patients who do not consider themselves depressed or they may reject it. Commonly reported adverse events include dry mouth, sedation, dizziness and nausea. These are most apparent in the first couple of weeks and usually settle with continued use.

Desipramine*, ***nortriptyline**** and ***protriptyline**** are less sedative alternatives with no formal evidence of efficacy.

6.5.5 Second-line prophylactic drugs

Topiramate 25mg od-50mg bd and sodium valproate* 300-1000mg bd are second-line.

Topiramate was licensed for migraine prophylaxis in 2005. Clinical trials suggest equivalent efficacy with sodium

110 Mulleners WM, Whitmarsh TE, Steiner TJ. Noncompliance may render migraine prophylaxis useless, but once-daily regimens are better. Cephalalgia 1998; 18: 52-56.

111 Holroyd KA, Penzien DB, Cordingley GE. Propranolol in the management of recurrent migraine: a meta-analytic review. Headache 1991; 31: 333-340.

112 Ramadan NM, Schultz LL, Gilkey SJ. Migraine prophylactic drugs: proof of efficacy, utilization and cost. Cephalalgia 1997; 17: 73-80.

113 Silberstein SD et al. Topiramate in migraine prevention: results of a large controlled trial. Arch Neurol 2004; 61: 490-495.

114 Brandes JL et al. Topiramate for migraine prevention: a randomized controlled trial. JAMA 2004; 291: 965-973.

115 Bussone G, Diener HC, Pfeil J, Schwalen S. Topiramate 100 mg/day in migraine prevention: a pooled analysis of double-blind randomised controlled trials. Int J Clin Pract 2005; 59: 961-968.

116 Rothrock JF. Clinical studies of valproate for migraine prophylaxis. Cephalalgia 1997; 17: 81-83.

117 Couch JR, Hassanein RS. Amitriptyline in migraine prophylaxis. Arch Neurol 1979; 36: 695-699

*unlicensed indication.

118 Mulleners WM, Whitmarsh TE, Steiner TJ. Noncompliance may render migraine prophylaxis useless, but once-daily regimens are better. Cephalalgia 1998; 18: 52-56

*unlicensed indication.

valproate.[119] Hence, in the event of failure or poor tolerability of one treatment, the other is worth trying. These drugs, but particularly sodium valproate, are not safe during pregnancy and therefore contraindicated when pregnancy may occur. Sodium valproate does not reduce the efficacy of hormonal contraception. Topiramate is an enzyme-inducer and reduces the efficacy of hormonal contraception in anti-epileptic doses. However, it is unlikely to have a clinically significant effect on hormonal contraception at doses not exceeding 100mg daily.[120]

Adverse events reported for sodium valproate include nausea, asthenia, somnolence, weight gain and alopecia. Blood cell count, platelet count, bleeding time and coagulation tests are recommended prior to starting treatment and in case of spontaneous bruising or bleeding. Liver dysfunction is reported rarely.

About 50% of patients taking topiramate for migraine experience tingling sensations, like 'pins and needles', which usually resolve with continued use. Around a quarter report relative anorexia and loss of more than 10% of their body weight, and almost as many experience some degree of cognitive dysfunction. Use of topiramate has been associated with nephrolithiasis, depression and mood alterations. Secondary angle-closure glaucoma has been reported.

6.5.6 Third-line prophylactic drugs

There is some clinical justification for considering other antiepileptics such as ***Gabapentin* 300mg od-800mg tds***,[121] although evidence of efficacy is far from robust. The most common adverse events reported are dizziness and sedation.

Methysergide 1-2mg tds[122] is generally considered (on limited formal evidence) to be the most effective prophylactic, but is held in reserve. This is partly because of its association with retroperitoneal fibrosis although it is said not to have this side-effect in courses of less than 6 months (see 6.5.3). Perhaps more importantly, methysergide has 5-$HT_{1B/1D}$ agonist activity which may be responsible for the severe rebound headache experienced by many patients attempting to withdraw from this drug after several months of usage. There is no consensus on managing this problem, although some experts provide cover with prednisolone 60mg od reducing over 2-3 weeks. Commonly reported side-effects of methysergide are gastrointestinal intolerance and sedation, and can be minimised by taking it with food.

Beta-blockers and amitriptyline can be used together, and a synergistic effect is claimed for this combination without formal evidence. It is logical if there may be a depressive trait.

6.5.7 Other drugs used in prophylaxis but with limited or uncertain efficacy

Pizotifen[123] and ***clonidine***[124] have been widely used for many years but with little clinical trials evidence of efficacy.

119 Shaygannejad V, Janghorbani M, Ghorbani A, Ashtary F, Zakizade N, Nasr V. Comparison of the Effect of Topiramate and Sodium Valporate in Migraine Prevention: A Randomized Blinded Crossover Study. Headache 2006; 46: 642-648.

120 Doose DR. Effect of topiramate or carbamazepine on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinylestradiol in healthy obese and non obese female subjects. Epilepsia 2003; 44: 540-549.

121 Mathew NT, Rapoport A, Saper J, Magnus L, Klapper J, Ramadan N, Stacey B, Tepper S. Efficacy of gabapentin in migraine prophylaxis. Headache 2001; 41: 119-128.

122 Pedersen E, Møller CE. Methysergide in migraine prophylaxis. Clin Pharm Ther 1966; 7: 520-526.

123 Cleland PG, Barnes D, Elrington GM, Loizou LA, Rawes GD. Studies to assess if pizotifen prophylaxis improves migraine beyond the benefit offered by acute sumatriptan therapy alone. Eur Neurol 1997; 38: 31-38.

124 Clonidine in migraine prophylaxis-now obsolete. Drug Ther Bull 1990; 28: 79-80

*unlicensed indication.

They should now be superseded.

Verapamil* MR 120-240mg bd has limited clinical-trials evidence of efficacy. Headache is sometimes a side-effect.

Selective serotonin reuptake inhibitors are of uncertain value. ***Fluoxetine* 20mg alter die to 40mg od*** is best studied with inconclusive evidence of efficacy against migraine.[125]

Other drugs, including ***lisinopril***,[126] ***montelukast***,[127] ***candesartan***,[128] ***riboflavin***[129] and ***co-enzyme Q10***[130] show potential benefit from randomised controlled trials but further research is necessary before they can be recommended.

OnabotulinumtoxinA is licensed for prophylaxis of patients with more than 15 headache days per month, of which at least eight days are with migraine. The difference between active and placebo treatments was small in reported clinical trials, although statistically significant.[131]

125 Steiner TJ, Ahmed F, Findley LJ, MacGregor EA, Wilkinson M. S-fluoxetine in the prophylaxis if migraine: a phase II double-blind randomised placebo-controlled study. Cephalalgia 1998; 18: 283-286.

126 Schrader H, Stovner LJ, Helde G, Sand T, Bovim G. Prophylactic treatment of migraine with angiotensin converting enzyme inhibitor (lisinopril): randomised, placebo controlled crossover study. BMJ 2001; 322: 19-22.

127 Brandes JL, Visser WH, Farmer MV, Schuhl AL, Malbecq W, Vrijens F, Lines DR, Reines SA. Montelukast for migraine prophylaxis: a randomized, double-blind, placebo-controlled study. Headache 2004; 44: 581-586.

128 Tronvik E, Stovner LJ, Helde G, Sand T, Bovim G. Prophylactic treatment of migraine with an angiotensin II receptor blocker: a randomized controlled trial. JAMA 2003; 289(1): 65-69.

129 Schoenen J, Jacquy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis. A randomized controlled trial. Neurology 1998; 50(2): 466-470.

130 Sandor PS, Di Clemente L, Coppola G, Saenger U, Fumal A, Magis D, et al. Efficacy of coenzyme Q10 in migraine prophylaxis: a randomized controlled trial. Neurology 2005; 64(4): 713-715.

131 Dodick DW, Turkel CC, Degryse RE, Aurora SK, Silberstein SD, Lipton RB, et al. OnabotulinumtoxinA for Treatment of Chronic Migraine: Pooled Results From the Double-Blind, Randomized, Placebo-Controlled Phases of the PREEMPT Clinical Program. Headache 2010; 30: 804-814.

*unlicensed indication

It has not shown efficacy for episodic migraine.[132]

6.5.8 Prophylaxis in children

There is little formal evidence of efficacy of prophylactic drugs in children. For the few children who need prophylaxis, ***beta-blockers*** or ***pizotifen*** (available as an elixir) may be tried. Paediatric headache specialists employ the full range of treatments used in adults, often with benefit.

Dosage is adjusted according to age.

6.5.9 Prophylaxis for hormone-related migraine

An effect of hormones on migraine is common, and greater for migraine without aura.[133] Evidence suggests estrogen withdrawal triggers migraine in some women.[134,135]

More than 50 percent of women report an association between migraine and menstruation.[136] ***Menstrually-related migraine***, defined as attacks of migraine without aura that occur regularly on day 1 of menstruation ± 2 days with additional attacks at other times of the cycle, is common; ***pure menstrual migraine*** with attacks solely occurring with menstruation, affects fewer than 10% of women with migraine.[137] Correct diagnosis of menstrual migraine is essential for successful hormonal management.

132 Schulte-Mattler WJ, Martinez-Castrillo JC. Botulinum toxin therapy of migraine and tension-type headache: comparing different botulinum toxin preparations. Eur J Neurol 2006; 13 Suppl 1: 51-54.

133 Rasmussen BK, Olesen J. Migraine with aura and migraine without aura: an epidemiological study. Cephalalgia 1992; 12: 221-228.

134 Somerville BW. Estrogen withdrawal migraine. Neurology 1975; 25: 239-250.

135 MacGregor EA, Frith A, Ellis J, Aspinall LJ, Hackshaw A. Incidence of migraine relative to menstrual cycle phases of rising and falling estrogen. Neurology 2006; 67: 2154-2158.

136 MacGregor EA, Brandes J, Eikermann A, Giammarco R. Impact of migraine on patients and their families: the Migraine And Zolmitriptan Evaluation (MAZE) survey - Phase III. Curr Med Res Opin 2004; 20(7): 1143-1150.

137 MacGregor EA. "Menstrual" migraine: towards a definition. Cephalalgia 1996; 16(1): 11-21.

The diagnosis is clinical and confirmed by diary card evidence over three months.

Depending on need for contraception, several options can be tried in whatever order seems appropriate. Prophylaxis should be tried for a *minimum of three cycles* at maximum dose before it is deemed ineffective.

A) Non-hormonal prophylaxis does not depend on regular menstruation. ***Mefenamic acid* 500mg tds-qds*** can be given from the onset of menstruation until the last day of bleeding. It is recommended as *first-line in migraine occurring with menorrhagia and/or dysmenorrhoea.*[138]

B) Triptans have been studied in clinical trials of short-term prophylaxis of menstrual attacks of migraine. The greatest evidence of efficacy is for ***frovatriptan* for 6 days (5mg bd on day 1; 2.5mg bd on days 2-6)*** starting 2 days before the expected onset of migraine.[139,140]

C) Hormones for menstrual migraine are ***supplements***: if the women has an intact uterus and is menstruating regularly, no progestogens are necessary. ***Transdermal estrogen* 100µg***[141] is used from *3 days before onset of menses for 7 days*, preferably using a 7-day patch. When this is effective but not well tolerated, ***50µg*** may be tried. Alternatively, ***estradiol* 1.5mg in 2.5g gel***,[142,143144] is applied daily from ***day -3 for 7 days***. The gel produces higher, more stable levels of estrogen and may be better.

D) ***Combined hormonal contraceptives*** (CHCs)(pills, patches, vaginal ring)(also see 6.5.10), and the progestogen-only ***oral desogestrel*** (Cerazette), ***subdermally implanted etonogestrel*** (Implanon) and ***injectable depot progestogens*** inhibit the natural ovarian cycle, which can benefit menstrual migraine. *Migraine in the hormone-free interval* is best managed by continuous hormone use, without a break.[145,146] If persistent breakthrough bleeding occurs, continuous use for 9-12 weeks ("tricycling"), followed by a 3-4-day hormone-free interval, can be considered.[147] For women who prefer a regular monthly 'period', estradiol supplements can be used during the seven-day pill-free interval in the same doses as stated for menstrual migraine above.[148] With the exception of desogestrel, standard doses of ***oral progestogen-only contraception*** do not inhibit ovulation and have no place in the management of migraine.

138 MacGregor EA. Menstrual migraine: a clinical review. J Fam Plann Reprod Health Care 2007; 33(1): 36-47.

139 Silberstein SD, Elkind AH, Schreiber C, Keywood C. A randomized trial of frovatriptan for the intermittent prevention of menstrual migraine. Neurology 2004; 63: 261-269.

140 Brandes JL Poole AC, Kallela M, Schreiber CP, MacGregor EA, Silberstein SD, Tobin J, Shaw R. Short-term Frovatriptan for the Prevention of Difficult-to-Treat Menstrual Migraine Attacks. Cephalalgia 2009; 29: 1133-1148.

141 Pradalier A, Vincent D, Beaulieu PH, Baudesson G, Launay JM. Correlation between oestradiol plasma level and therapeutic effect on menstrual migraine. In: Rose FC (ed). New advances in headache research, 4th ed. London: Smith-Gordon 1994: 129-132

*unlicensed indication.

142 De Lignières B, Vincens M, Mauvais-Jarvis P, Mas JL, Touboul PJ, Bousser MG. Prevention of menstrual migraine by percutaneous oestradiol. BMJ 1986; 293: 1540.

143Dennerstein L, Morse C, Burrows G, Oats J, Brown J, Smith M. Menstrual migraine: a double-blind trial of percutaneous estradiol. Gynecol Endocrinol 1988; 2: 113-120

144 MacGregor EA, Frith A, Ellis J, Aspinall LJ. Estrogen and migraine: a double-blind placebo-controlled crossover study. Neurology 2006; 67: 2159–2163.

145 Sulak P, Willis S, Kuehl T, Coffee A, Clark J. Headaches and oral contraceptives: impact of eliminating the standard 7-day placebo interval. Headache 2007; 47(1): 27-37.

146 Edelman A, Gallo MF, Nichols MD, Jensen JT, Schulz KF, Grimes DA. Continuous versus cyclic use of combined oral contraceptives for contraception: systematic Cochrane review of randomized controlled trials. Hum Reprod 2006; 21(3): 573-578.

147 Sulak PJ, Carl J, Gopalakrishnan I, Coffee A, Kuehl TJ. Outcomes of extended oral contraceptive regimens with a shortened hormone-free interval to manage breakthrough bleeding. Contraception 2004; 70(4): 281-287.

148 MacGregor EA, Hackshaw A. Prevention of migraine in the pill-free week of combined oral contraceptives using natural oestrogen supplements. J Family Planning Reproduct Healthcare 2002; 28: 27-31

*unlicensed indication.

6.5.10 Migraine and hormonal contraception

Headache is a common side-effect of CHCs and many women report onset of migraine after starting them. Others report improvement of pre-existing migraine.[149] There is concern that migraine with aura and CHCs are both *independent risk factors for stroke in young women*, in the latter case related to the ethinylestradiol component. This has led to the development of opinion-based recommendations for the use of CHCs in migraineurs,[150,151,152] although not all experts agree.

Relative or absolute contraindications to contraceptive use of CHCs:

a) Migraine with aura (experts disagree over whether this is an absolute contraindication).

b) Migraine treated with *ergot derivatives* but not triptans (relative).

Progestogen-only contraception is acceptable with any type of migraine contraindicating synthetic estrogens as its use is not associated with increased thrombotic risk.[153,154]

149 Epstein MT, Hockaday JM, Hockaday TDR. Migraine and reproductive hormones throughout the menstrual cycle. Lancet 1975; 1: 543-548.

150 Faculty of Sexual and Reproductive Healthcare. UK Medical Eligibility Criteria for Contraceptive Use. London: FSRH; 2009.

151 World Health Organization. Medical eligibility criteria for contraceptive use. Fourth ed. Geneva: WHO; 2009.

152 Bousser M-G, Conard J, Kittner S, de Lignières B, MacGregor EA, Massiou H, Silberstein SD, Tzourio C. Recommendations on the risk of ischaemic stroke associated with use of combined oral contraceptives and hormone replacement therapy in women with migraine. Cephalalgia 2000; 20: 155-156.

153 World Health Organization. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Contraception 1998; 57: 315-324.

154 Heinemann LA, Assmann A, DoMinh T, Garbe E. Oral progestogen-only contraceptives and cardiovascular risk: results from the Transnational Study on Oral Contraceptives and the Health of Young Women. Eur J Contracept Reprod Health Care 1999; 4: 67-73.

The standard progestogen-only pill has a higher failure rate but desogestrel, etonogestrel, injectable depot progestogens and the levonorgestrel intrauterine system both have lower failure rates than CHCs. Women can switch immediately from CHCs to progestogen-only contraception.

6.5.11 Migraine in pregnancy and lactation

Most women with migraine improve during pregnancy and a need for prophylaxis does not commonly arise. When it does, ***propranolol**** has best evidence of safety during pregnancy and lactation.[155] ***Amitriptyline**** in the lowest effective dose may also be used.[156] ***Atenolol*** is not recommended for migraine prophylaxis during pregnancy.[157]

As always, women should be counselled with regard to the relative risks and benefits.

6.5.12 Migraine and hormone replacement therapy (HRT)

Hormone replacement therapy is ***not*** contraindicated: there is no evidence that risk of stroke is elevated or reduced by the use of HRT in women with migraine, with or without aura. The menopause itself commonly exacerbates migraine and symptoms can be relieved with optimised replacement therapy. Nevertheless, in practice, a number of women on HRT do find their migraine becomes worse. This is often no more than a problem of formulation or dosage.

155 National Teratology Information Service. Use of propranolol in pregnancy. 2009; Available at: www.toxbase.org

156 National Teratology Information Service. Use of amitriptyline in pregnancy. 2009; Available at: www.toxbase.org

157 National Teratology Information Service. Use of atenolol in pregnancy. 2009; Available at: www.toxbase.org

*unlicensed indication

Adequate, stable levels of estrogen are best provided by percutaneous or transdermal delivery systems used continuously.[158] Headache associated with cyclical progestogens may be controlled by changing the type of progestogen, using transdermal progestogens or the levonorgestrel intrauterine system, or changing to progesterone (vaginal gel pessary or suppository).

After hysterectomy, estrogen implants are an option.

6.5.13 Drugs to avoid in prophylactic intervention

Combined hormonal contraceptives (see 6.5.10) often improve migraine; but they may exacerbate it[159] and should be changed or discontinued if they do. They are contraindicated if exacerbation includes the development of focal neurological signs.[160]

The active ingredient of ***feverfew*** is sometimes claimed to be parthenolide but standardised formulations of this drug do not have proven efficacy.[161] Other marketed preparations of feverfew are variable in what they contain. Furthermore, feverfew contains potential carcinogens; its toxicity is not well understood and its long-term effects are unknown. *It is particularly unsuitable for children*.

6.5.14 If prophylaxis fails

Review the diagnosis. Review both compliance with treatment (often poor, especially with multiple daily doses) and concordance, which may not have been achieved. Review other medication, especially for medication overuse. Consider combinations (no formal evidence for any).

If prophylaxis still fails to have measurable benefit, *discontinue* it.

6.6 Non-drug intervention

6.6.1 Physical therapy

Improving ***physical fitness*** may reduce susceptibility to migraine.[162]

Physical therapy may be helpful where a specific indication (eg, neck dysfunction) exists. In other cases it may be useful as adjunctive therapy.[163] A therapist with specific training is more likely to achieve good results than a generalist.

Acupuncture may provide additional benefit to routine care.[164]

Dental treatment, including the fitting of splints or bite-raising appliances and other procedures to correct malocclusion, is of unproven benefit in migraine but occasional patients claim benefit. It may improve temporomandibular joint dysfunction and secondary head pain. The importance of ***bruxism*** in headache causation is undetermined.

158 Nappi RE, Cagnacci A, Granella F, et al. Course of primary headaches during hormone replacement therapy. Maturitas 2001; 38: 157–163.

159 Aegidius K, Zwart JA, Hagen K, Schei B, Stovner LJ. Oral contraceptives and increased headache prevalence: the Head-HUNT Study. Neurology 2006; 66: 349-353.

160 Faculty of Sexual and Reproductive Healthcare. UK Medical Eligibility Criteria for Contraceptive Use. London: FSRH; 2009.

161 Pittler MH, Ernst E. Feverfew for preventing migraine. Cochrane database of systematic reviews 2004: CD002286.

162 Neususs K, Neumann B, Steinhoff BJ, Thegeder H, Bauer A, Reimers D. Physical activity and fitness in patients with headache disorders. Int J Sports Med 1997; 18: 607-611.

163 Marcus DA, Scharff L, Mercer S, Turk DC. Nonpharmacological treatment for migraine: incremental utility of physical therapy with relaxation and thermal biofeedback. Cephalalgia 1998; 18: 266-272.

164 Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for migraine prophylaxis. Cochrane Database Syst Rev 2009(1): CD001218.

6.6.2 Psychological therapy

Relaxation therapy, ***stress reduction*** and ***coping strategies*** are *first-line treatments* where a specific indication exists (*eg*, anxiety, stress), since migraine treatments may fail unless these underlying problems are dealt with. In other cases they may be useful as adjunctive therapy, particularly the simple device of relaxation tapes. They need formal evaluation. ***Yoga*** and ***meditation*** are said to enhance stress management and appeal to some people.

Biofeedback techniques have some support from clinical trials; being operator-dependent, they are difficult to standardise. ***Hypnotherapy*** is of unproven value.

6.6.3 Homoeopathy

This appears to be of no value.[165,166,167] Its basis calls for expert prescribing if it is to be used, so there is no case for over-the-counter sales of homoeopathic remedies for migraine.

6.6.4 Other alternative remedies

Reflexology has no scientific basis.

Many ***devices*** are on the market, some at considerable cost and promoted with specific but unsupportable claims of efficacy. “Testimonials” can be attributed to placebo effect and should be disregarded. Any of these that may have efficacy should be formally evaluated in clinical trials. Unless that has been done, and evidence of efficacy adduced, patients encouraged to buy them are done a disservice.

165 Whitmarsh TE, Coleston-Shields DM, Steiner TJ. Double-blind randomized placebo-controlled study of homoeopathic prophylaxis of migraine. Cephalalgia 1997; 17: 600-604.

166 Ernst E. Homeopathic prophylaxis of headaches and migraine: A systematic review. J Pain Symptom Management 1999; 18: 353-357.

167 Straumsheim P, Borchgrevink C, Mowinckel P, Kierulf H, Hafslund O. Homeopathic treatment of migraine: a double blind, placebo controlled trial of 68 patients. Br Homeopath J 2000; 89(1): 4-7.

management of tension-type headache

7. Management of Tension-type headache

7.1 Objectives of management

Episodic TTH is self-limiting, non-disabling, and rarely raises anxieties about its causation or prognosis. Reassurance, if needed, and intermittent symptomatic treatment are often quite sufficient. Provided that patients are not at risk of escalating consumption, little more may need to be done.

Long-term remission is the objective of management of very frequent episodic or chronic TTH. It is not always achievable, particularly in long-standing chronic TTH. In such cases, avoidance of aggravation by medication overuse remains important, as do recognition and appropriate treatment of contributory factors.

7.2 Basic principles

As with migraine, ***reassurance*** is important and often effective on its own; it should never be omitted.

Underlying contributory factors are of greater potential importance in TTH than in migraine. Effective treatment is likely to depend on successfully identifying these, particularly when headaches are frequent.

The distinction between episodic and chronic TTH, based on frequency, is somewhat arbitrary but it has practical importance for two reasons. One arises from the potential for overuse of symptomatic medication, to the extent that long-term harm outweighs short-term benefit. ***Medication overuse*** must always be discovered and remedied

because it can mask the diagnosis, causes illness and markedly reduces the effectiveness of all forms of headache treatment.[168] The other relates to likely comorbidity. ***Clinical depression*** must be diagnosed and treated appropriately. In the background of chronic TTH, either of these will defeat management unless recognised and adequately dealt with.

7.3 First measures

TTH is more common in sedentary people. Regular ***exercise*** is of general and potentially considerable benefit and always worth recommending.[169]

Physiotherapy may be appropriate, and the treatment of choice, for musculoskeletal symptoms. A therapist with specific training is more likely to achieve good results than a generalist. Physiotherapy may include massage, mobilisation, manipulation and, particularly in those with sedentary lifestyles, correction of posture. Regular home exercises are often prescribed. Mobilisation and manipulation sometimes aggravate symptoms before they improve, and cervical spine manipulation is not risk-free.[170]

Physiotherapy may help symptoms secondary to trauma such as whiplash injury but is less useful in degenerative disease of the neck. It is unlikely to be beneficial in stress-related illness for which ***lifestyle changes*** to reduce stress and ***relaxation therapy*** and ***cognitive training*** to develop stress-coping strategies are the mainstays of treatment.[171]

168 Mathew NT. Transformed migraine. Cephalalgia 1994; 14: 162-167.

169 Rasmussen BK. Migraine and tension-type headache in a general population: precipitating factors, female hormones, sleep pattern and relation to lifestyle. Pain 1993; 53: 65-72.

170 Stevinson C, Honan W, Cooke B, Ernst E. Neurological complications of cervical spine manipulation. J Roy Soc Med 2001; 94: 107-110.

171 Nigl AJ. Biofeedback and behavioural srategies in pain treatment. Lancaster: MTP press 1984.

Yoga and meditation are said to enhance stress management and appeal to some people.

7.4 Drug therapy

This is of limited scope but effective nevertheless in many patients. Symptomatic treatment is appropriate for episodic TTH occurring on fewer than 2 days per week. Over-the-counter analgesics (***aspirin 600-900mg, ibuprofen, 400mg***)[172] are usually sufficient; other NSAIDs (***ketoprofen 25-50mg, naproxen 250-500mg***) are sometimes indicated.[173,174] ***Paracetamol 500-1000mg*** appears less effective.[175]

Children, and adolescents under 16 years, are not advised to use aspirin.

As the frequency of headaches increases, so does the risk of medication overuse. Therefore, these treatments are *inappropriate* in chronic TTH, whether they appear to give short-term benefit or not.[176] Nevertheless, a 3-week course of ***naproxen 250-500mg bd***, taken regularly, may break the cycle of frequently recurring or unremitting headaches and the habit of responding to pain with analgesics. If it fails, it should not be repeated.

172 Steiner TJ, Lange R, Voelker M. Aspirin in episodic tension-type headache: placebo-controlled dose-ranging comparison with paracetamol. Cephalalgia 2003; 23: 59-66.

173 Lange R, Lentz R. Comparison of ketoprofen, ibuprofen and naproxen sodium in the treatment of tension-type headache. Drugs Exp Clin Res 1995; 21: 89-96.

174 Steiner TJ, Lange R. Ketoprofen (25mg) in the symptomatic treatment of episodic tension-type headache: double-blind placebo-controlled comparison with acetaminophen (1000mg). Cephalalgia 1998; 18: 38-43.

175 Steiner TJ, Lange R, Voelker M. Aspirin in episodic tension-type headache: placebo-controlled dose-ranging comparison with paracetamol. Cephalalgia 2003; 23: 59-66.

176 Schnider P, Aull S, Feucht M et al. Use and abuse of analgesics in tension-type headache. Cephalalgia 1994; 34 (suppl): S2-S7.

Amitriptyline is otherwise the drug treatment of choice for frequently recurring episodic TTH or for chronic TTH.[177] Its use in chronic pain syndromes is not dependent on its antidepressant activity. Clinical trials evidence does not establish how best to use this drug, or in what dose. Intolerance is relatively common but greatly reduced by starting at a low dose (***10-25mg at night***). Increments of 10-25mg should be as soon as side-effects permit, perhaps each 1-2 weeks and usually into the range ***75-150mg*** at night. Withdrawal may be attempted after improvement has been maintained for 4-6 months.

Failure of tricyclic therapy may be due to subtherapeutic dosage, insufficient duration of treatment or non-compliance. Patients who are not informed that they are receiving medication often used as an antidepressant, and why, may default when they find out.

Some experts offer alternatives, eg, ***dothiepin***, if amitriptyline fails. ***Nortriptyline*** and ***protriptyline*** may be better tolerated but their usefulness is less certain. There is no evidence that ***SSRIs*** reduce headache in chronic TTH, though they may be indicated for underlying depression.[178] ***Anxiolytics*** may be appropriate when specifically indicated but ***beta-blockers*** may promote depression whereas the high risk of dependence generally rules out prolonged use of ***benzodiazepines***.

7.4.1 Drugs to avoid in TTH management

Codeine and ***dihydrocodeine*** are not indicated, and there is no place for stronger opioids.

Botulinum toxin is ineffective for TTH.[179]

7.5 If all else fails

Chronic TTH in particular is often refractory. Its association with personality factors and psychosocial dysfunction that militate against effective treatment is often suspected but not consistently demonstrated. Some of these patients end up in pain management clinics where ***cognitive therapies*** are more readily available and where non-specific therapies such as ***transcutaneous electrical nerve stimulation*** (TENS) may be offered.

The role of ***acupuncture*** is unproven but it may be worth trying in the absence of other options.[180] Detection of tender muscle nodules on palpation, with needling aimed at these, is said to offer a good prospect of at least limited success but evidence to support this is poor. As with physiotherapy, symptoms may at first be aggravated by acupuncture. It is sometimes claimed that early exacerbation is prognostic of later improvement.

Homoeopathy is of unknown value. Its basis calls for expert prescribing if it is to be used. There is *no case* for over-the-counter sales of homoeopathic remedies for TTH.

177 Bendtsen L, Jensen R, Olesen J. A non-selective (amitriptyline), but not a selective (citalopram), serotonin reuptake inhibitor is effective in the prophylactic treatment of chronic tension-type headache. J Neurol Neurosurg Psychiat 1996; 61: 285-290.

178 Ibid.

179 Silberstein SD, Göbel H, Jensen R et al. Botulinum toxin type A in the prophylactic treatment of chronic tension-type headache: a multicentre, double-blind, randomized, placebo-controlled, parallel-group study. Cephalalgia 2006; 26: 790-800.

180 Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for tension-type headache. Cochrane Database Syst Rev 2009(1): CD007587.

8.0 Management of Cluster headache

Cluster headache management is usually better left to experienced specialists who see this disorder frequently.

8.1 Objectives of management

Although short-lasting, CH is excruciatingly painful and patients suffer badly. Because of the frequency of attacks, disability during a cluster period can be considerable. Whilst CH may spontaneously enter long-term remission, there is no present prospect of curative medical intervention. The ultimate attainable goal of treatment is total attack cessation or suppression – but only until the next episode. More conservatively, and usually more realistically, its aim is to shorten the cluster period in episodic CH and to reduce the frequency and/or severity of attacks in both episodic and chronic CH.

As the biological nature of the underlying mechanism of CH is poorly understood, prophylactic methods are empirical.

8.2 Basic principles

Patients experiencing their first attacks will be greatly concerned, and need reassurance.

Drug treatment, which includes oxygen, is always necessary for effective control. In most cases, prophylactic drugs are the mainstay of treatment as symptomatic treatment alone is rarely sufficient to achieve adequate control. Exceptions are cluster periods of short-duration (<2-3 weeks), when this can be anticipated from past experience, and cases where prophylaxis has failed.

Prophylactic drugs should be commenced as early as possible after the start of a new cluster period, since there is some evidence of their greater effectiveness then.[181] Treatment found effective in a previous cluster period should be rapidly reintroduced at the start of the next. To facilitate this, patients may benefit from being given a supply before the next cluster period is anticipated. Early review is recommended in such cases. Unfortunately, what has worked well before does not invariably do so again.

Failure of one drug does not predict failure of others. All those recommended below should be tried if necessary. There is no consensus on what level of benefit should be considered satisfactory. Many treatments in use are potentially toxic, and risk/benefit evaluation is often central to decision-making. Partial relief presents an obvious dilemma, with no clear rules of guidance. Not uncommonly, two or more prophylactic drugs are needed in combination,[182] although the potential for toxicity is obviously high.

For most drugs, dosage should be escalated as quickly as tolerability permits, and often to the maximum tolerated dose. When benefit is not apparent within 1 week of achieving the maximum tolerated dose of a drug, it should be discontinued and replaced, or supplemented. Acute therapy may be used in addition in the period until prophylactic drugs become effective, and/or if breakthrough attacks still occur.

Alcohol should be wholly avoided during active cluster periods. Other contributory factors are of little importance to management. Many patients with CH have been heavy smokers. Advice to stop smoking is always good advice, but there is no evidence that this affects the prognosis of CH.

181 Mathew NT. Cluster headache. Neurology 1992; 42: 32-36.

182 Kudrow L. Treatment of cluster headache. Headache Quart 1993; 4: 42-47.

8.3 Prophylactic drug intervention

The formal evidence base for all drugs listed below is limited, with a very small number of published trials, but expert opinion strongly supports their use. Not all experts use them in the same order, but the following is recommended.

8.3.1 Drugs with efficacy

Verapamil* is a reasonable first-line choice for both episodic and chronic CH.[183,184] Doses of ***80mg tds or qds*** may be effective but up to ***960mg daily*** is sometimes required. Some experts believe that standard preparations of verapamil are more useful than modified-release formulations.

Verapamil is usually well tolerated: constipation (which may be severe) and flushing are common side-effects. Gingival hyperplasia is heralded by gum bleeding that should trigger referral for dental review. The ECG should be checked for AV-block before the dosage reaches 480mg daily and whenever it is increased beyond that.[185] Beta-blockers should not be given concomitantly.

Prednisolone* may be preferred because, unlike all other treatments, it is commenced in high dosage.[186] A starting

183 Gabai IJ, Spierings ELH. Prophylactic treament of cluster headache with verapamil. Headache 1989; 29: 167-168.

184 Bussone G, Leone M, Peccarisi C, Micieli G, Granella F, Magri M, Manzoni GC, Nappi G. Double blind comparison of lithium and verapamil in cluster headache prophylaxis. Headache 1990; 30: 411-417.

185 Cohen AS, Matharu MS, Goadsby PJ. Electrocardiographic abnormalities in patients with cluster headache on verapamil therapy. Neurology 2007; 69(7): 668-675.

186 Couch JR, Ziegler DK. Prednisone therapy for cluster headache. Headache 1978; 18: 219-221.

*unlicensed indication

dose of ***60-100mg***, ***once daily*** for 2-5 days, will, if this treatment will work at all, most often produce marked, almost immediate relief. Because of the potential otherwise for serious side-effects, treatment is limited to a very short and intensive course. Dose reduction is initiated after 2-5 days and continued, in 10mg decrements each second or third day, so that treatment is discontinued after 2-3 weeks.

Relapse may occur as the dose is reduced. Second (and sometimes third) courses, administered with due caution, can consolidate efficacy of the first following relapse but are not indicated otherwise. Prednisolone may be used as an initial add-on therapy to other prophylactics until the latter are effective (*see Combinations below*).

Gastric intolerance is the most likely side-effect in short-term use. Standard contra-indications to steroid therapy apply. Usual counselling should be given to patients, but short courses of steroids do not seriously risk suppression of endogenous steroid production.

Lithium carbonate* should be considered in episodic or chronic CH if verapamil is not effective.[187,188] In the episodic form, with short-duration treatment courses (<12 weeks) expected, higher doses of ***800-1600mg daily*** may be needed and serum concentrations pushed if necessary into the range 1.0-1.4 mmol/l. Tolerance may develop, and efficacy be lost, after two or three clusters periods treated with lithium. Patients with chronic CH, needing long-term treatment, may benefit from lower daily doses in the range ***600-900mg***, and serum concentrations of 0.3-0.8 mmol/l.[189]

Serum concentrations *must* be frequently monitored, both to ensure adequacy of dosing in the absence of symptom remission and to guard against over-dosing. Symptoms of early toxicity (nausea, diarrhoea, polyuria, polydipsia) without benefit mandate abandonment of this therapy. Serious long-term side-effects include tremor, oedema, electrolyte disturbance, muscle weakness, central nervous system disturbance, ECG abnormality and hypo- or hyperthyroidism. Renal, cardiac and thyroid functions should be monitored. NSAIDS should not be taken concomitantly.

Methysergide 1-2mg tds may be effective in up to 70% of patients with episodic CH[190] and is worth trying when other treatments fail. Tolerance may develop after two or three treatment periods.[191]

The short-term side-effects are few but may include nausea, abdominal discomfort and leg cramps. Potential long-term side-effects of retroperitoneal, endomyocardial or pulmonary fibrosis are serious.[192] Treatment should therefore be interrupted every 6 months for at least one month. As the usual duration of cluster periods is 6-12 weeks, this limitation is seldom a practical problem in episodic CH. Although ergotamine should not be taken during methysergide therapy because of increased risk of ergotism, there is no evidence against concomitant use of triptans.

187 Kudrow L. Lithium prophylaxis for chronic cluster headache. Headache 1977; 17: 15-18.

188 Ekbom K. Lithium for cluster headache: review of the literature and preliminary results of long-term treatment. Headache 1981; 21: 132-139.

*unlicensed indication

189 Manzoni GC, Bono G, Lanfranchi M, Micieli G, Terzano MG, Nappi G. Lithium carbonate in cluster headache: assessment of its short- and long-term therapeutic efficacy. Cephalalgia 1983; 3: 109-114.

190 Curran DA, Hinterberger H, Lance JW. Methysergide. Res Clin Stud Headache 1967; 1: 74-122.

191 Lovshin LL. Treatment of histaminic cephalgia with methysergide (UML-491). Dis nerv Syst 1963; 24: 3-7.

192 Graham JR. Cardiac and pulmonary fibrosis during methysergide therapy for headaches. Am J Med Sci 1967; 245: 23-34.

Ergotamine tartrate* 1-2mg rectally (half to one Cafergot suppository) is rarely a suitable preventative drug in chronic CH but still useful in short-term management of episodic CH when attacks occur predictably during the day or at night. Nocturnal attacks are prevented by taking it at bedtime. Expected daytime attacks may be prevented by a dose at least one hour before they are due, but are sometimes only delayed. The maximum total daily dosage is 3-4 mg. Treatment should be omitted from time to time (every 7th day is common practice) to establish continued need.

For reasons unknown, CH patients appear relatively resistant to the toxic effects of ergotamine that limit its use in migraine. Nevertheless, because of its systemic vasoconstrictor action, this treatment is contra-indicated in those with any vascular disease or significant hypertension, and in the presence of multiple risk factors for vascular disease (most cluster headache patients are smokers). Beta-blockers or methysergide should not be used concomitantly, nor should sumatriptan as acute therapy.

8.3.2 Drugs with uncertain efficacy

Open-label studies suggest that ***topiramate* ≥100mg daily*** may be effective. Other anti-epileptics, including sodium valproate*, gabapentin* and carbamazepine* are all of little or no value. A single small RCT suggests potential benefit from ***melatonin* 10mg daily***.[193]

Frovatriptan* 2.5mg bd has been tried by some experts as a presumed safer alternative to ergotamine. This is the only triptan with a long half-life (26 hours). Experience is limited and, anecdotally, results have not been uniformly good.

Pizotifen* 1.5-3mg daily is of limited value.

8.3.3 Combinations of prophylactic drugs

Therapeutic delay as verapamil is up-titrated can be avoided by early short-term concomitant use of prednisolone. This is an option when rapid control is a high priority because of frequent severe attacks.

Otherwise, monotherapy is recommended initially, but resistance to monotherapy is not rare in both episodic and chronic CH. In these cases, combinations can be recommended.[194] Verapamil should be the basic treatment to which ergotamine, or methysergide is added. Lithium can be combined with verapamil but with caution because there is increased risk of toxicity without increase in the plasma concentration of lithium. In severe chronic cases, all of verapamil, lithium and ergotamine may be required, but the potential for toxicity is obviously high.

8.3.4 Duration of use

With the exception of prednisolone, prophylaxis should be continued in episodic CH until the patient has been headache-free for at least 14 days. This is probably sufficient to minimise the risk of relapse, although no formal proof exists that this is so. Drugs should be withdrawn by progressive dosage reduction rather than ceased abruptly. If relapse does occur, treatment must be resumed but, unfortunately, control is not always quickly re-established.

Prophylaxis sometimes converts chronic CH into the

193 Leone M, D'Amico D, Moschiano F, Fraschini F, Bussone G. Melatonin versus placebo in the prophylaxis of cluster headache: a double-blind pilot study with parallel groups. Cephalalgia 1996; 16(7): 494-496.

*unlicensed indication

194 May A. Cluster headache: pathogenesis, diagnosis and management. Lancet 2005; 366: 843-855.

*unlicensed indication

episodic sub-type, and can be withdrawn according to the same criterion of 14 days symptom-free. Otherwise, medication may need to be continued indefinitely.

8.4 Acute drug intervention

8.4.1 Drugs with efficacy

Sumatriptan 6mg subcutaneously (£20.21-£21.24) is the treatment of choice, unless contra-indicated. It is the only proven highly-effective acute treatment.[195,196] In a high proportion of cases it aborts the attack in 5-10 min.

Sumatriptan is contra-indicated in uncontrolled hypertension or the presence of risk factors for coronary heart disease or cerebrovascular disease.

Oxygen* 100% at 10-15 l/min for 10-20 min helps some people.[197] Its advantage, when it works, is its safety, allowing multiple daily uses. The high flow-rate requires a special regulator and non-rebreathing mask.

Oxygen can be prescribed using the Home Oxygen Order Form, which is sent to the supplier who has the contract in that region. All cylinders (1,360 litre, and 460 litre portable) come with integral high regulators allowing up to 15 litres per minute. The oxygen supplier will also provide non-rebreathing masks.

Zolmitriptan 5-10mg nasal spray (£6.08-£12.16) has delayed bioavailability compared with sumatriptan subcutaneously. It was effective in a placebo-controlled trial, but achieved lower response rates than injectable sumatriptan.[198] Although it may suit some people, it should not be preferred on grounds of cost. Despite one trial suggesting efficacy,[199] ***sumatriptan 20mg nasal spray**** (£5.90) has little place in clinical practice.

Sumatriptan and zolmitriptan are contra-indicated in uncontrolled hypertension or the presence of risk factors for coronary heart disease or cerebrovascular disease. Zolmitriptan is contraindicated in patients with Wolff-Parkinson-White syndrome.

8.4.2 Drugs to avoid in acute intervention

Analgesics have no place in treating CH. Ergotamine tartrate, and all orally-administered triptans are of no use as acute therapy.

8.5 Non-drug intervention

When prophylactic therapy is commenced and until doses considered to be therapeutic are achieved, transitional therapy using occipital nerve blockade is often used but without good evidence of efficacy.[200,201] Surgical options include implantation of occipital nerve or deep brain

195 Gregor N, Schlesiger C, Akova-Ozturk E, Kraemer C, Husstedt IW, Evers S. Treatment of cluster headache attacks with less than 6 mg subcutaneous sumatriptan. Headache 2005; 45: 1069-1072.

196 Law S, Derry S, Moore RA. Triptans for acute cluster headache. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD008042. DOI: 10.1002/14651858.CD008042.pub2.

197 Cohen AS, Burns B, Goadsby PJ. High-flow oxygen for treatment of cluster headache: a randomized trial. JAMA 2009; 302(22): 2451-2457.

*unlicensed indication

198 Cittadini E, May A, Straube A, Evers S, Bussone G, Goadsby PJ. Effectiveness of intranasal zolmitriptan in acute cluster headache. Arch Neurol 2006; 63: 1537-1542.

199 van Vliet JA, Bahra A, Martin V, et al. Intranasal sumatriptan in cluster headache: randomized placebo-controlled double-blind study. Neurology 2003; 60: 630-633.

200 Peres MFP, Stiles MA, Siow HC, Rozen TD, Young WB, Silberstein SD. Greater occipital nerve blockade for cluster headache. Cephalalgia 2002; 22: 520–522.

201 Ambrosini A, Vandenheede M, Rossi P, Aloj F, Sauli E, Pierelli F, et al. Suboccipital injection with a mixture of rapid- and long-acting steroids in cluster headache: a double-blind placebo-controlled study. Pain 2005; 118(1-2): 92-96.

*unlicensed indication.

stimulators, and are under clinical investigation at specialist centres.

9. Management of medication-overuse headache

9.1 Objectives of management

There are four separate objectives in the complete management of MOH, and all are important.

The ***first*** is to achieve withdrawal from the overused medication. The ***second***, which should follow, is recovery from MOH. The ***third*** is to review and reassess the underlying primary headache disorder (migraine or tension-type headache), which will probably become unmasked and may or may not need a treatment plan according the the principles above. The ***fourth*** is to prevent relapse, which has a rate of around 40% within five years and is most likely to occur within the first year after withdrawal.[202,203]

9.2 Basic principles

Prevention is preferred to management. Patients with primary headaches should be educated about the risk of medication overuse and be encouraged to keep a diary to monitor headache frequency and drug use.

Once MOH has developed, early intervention is important. The long-term prognosis depends on the type of primary headache and the type of overused medication.[204]

202 Schnider P, Aull S, Baumgartner C, et al. Long-term outcome of patients with headache and drug abuse after inpatient withdrawal: five-year follow-up. Cephalalgia 1996; 16: 481-485

203 Katsarava Z, Muessig M, Dzagnidze A, Fritsche G, Diener HC, Limmroth V. Medication overuse headache: rates and predictors for relapse in a 4-year prospective study. Cephalalgia 2005; 25: 12-15.

204 Katsarava Z et al. Clinical features of withdrawal headache following overuse of triptans and other headache drugs. Neurology 2001; 57: 1694–1698.

The *only* treatment of established MOH is withdrawal of the suspected medication(s).[205]

Some patients are psychologically dependent upon their medication. They will be difficult to manage successfully unless this is dealt with.

9.3 Management of withdrawal

Patients must be motivated. Clear understanding that their "treatment" for headache is actually the cause of it is vital to success. They may be told that the outcome of withdrawal is usually good, whereas the alternative to withdrawal is ever-worsening headache.

They should be forewarned that withdrawal initially aggravates symptoms, so should be planned in advance to avoid unnecessary lifestyle disruption. Sick leave for 1-2 weeks may be needed. A diary to record symptoms and medication use during withdrawal is strongly recommended and good hydration should be maintained.

Ergots, triptans, and non-opioid drugs can be stopped abruptly. Outpatient and inpatient settings can provide the same results, if sufficient advice is given. Abrupt withdrawal can lead to withdrawal headache usually lasting from 2 to 10 days (average 3.5 days), which can be accompanied by nausea, vomiting, arterial hypotension, tachycardia, sleep disturbances, restlessness, anxiety and nervousness. The type of drug overused also affects the response to withdrawal. Patients overusing triptans or ergots generally show improvement more rapidly (within 7-10 days) than patients taking simple analgesics (2-3 weeks) or narcotics (2-4 weeks).[206]

Opioids or barbiturates usually need to be withdrawn slowly, sometimes under inpatient supervision, in order to treat withdrawal symptoms.[207] Patients who have previously failed outpatient withdrawal or who suffer from depression and anxiety should also be considered for inpatient detoxification.

Withdrawal headache can be managed with naproxen, 250mg tds or 500mg bd.[208] It should be taken regularly for a while in order to break the habit of responding to pain with medication. Some specialists recommend a course of 3-4 weeks, and not repeated; others suggest a six week course of 250mg tds for two weeks, 250mg bd for two weeks, then 250mg od for two weeks. There are no studies to support or refute these strategies.

9.4 Follow-up

Review is advised after 2-3 weeks to ensure withdrawal has been achieved.

Recovery continues slowly for weeks to months. Further follow-up is necessary. Most patients revert to their original headache type (migraine or tension-type headache) within 2 months. Overused medications (if appropriate) may be reintroduced after 2 months, with explicit restrictions on frequency of use.

Relapse is common, and many patients require extended

205 Hering R, Steiner TJ. Abrupt outpatient withdrawal of medication in analgesic-abusing migraineurs. Lancet 1991; 337: 1442-1443.

206 Katsarava Z et al. Rates and predictors for relapse in medication overuse headache: a 1-year prospective study. Neurology 2003; 60: 1682–1683.

207 Diener H-C, Limmroth V. Medication-overuse headache: a worldwide problem. Lancet Neurol 2004; 3: 475–483.

208 Dodick DW. Clinical practice. Chronic daily headache. N Engl J Med 2006; 354: 158-165.

support to prevent it. The majority of relapses occur within the first year after withdrawal. The main risk factors for relapse are male sex, intake of combined analgesic drugs and tension-type headache as the primary headache disorder.[209] Behavioural therapies (CBT, stress reduction, biofeedback) may help.[210]

9.5 Management of failure to withdraw

This may have several explanations. Lack of commitment should be addressed by further explanation. Evidence of psychological dependence may require referral for cognitive behavioural therapy. In either of these cases, there is a potential role for counselling,[211] but this has not been formally explored in the context of MOH.

9.6 When recovery does not follow withdrawal

The diagnosis of MOH is presumptive. Sometimes withdrawal of overused medication (which is necessary anyway) does not lead to recovery. This situation, in which chronic daily headache persists more or less unabated, requires a new diagnosis to be made and is an indication for specialist referral.

In all cases, enquiry should confirm, as far as possible, that medication overuse is not continuing. Once medication overuse has been eliminated, preventative drugs may become effective. Dependent upon the symptoms, these may include migraine prophylactics. Alternatively, management should be as for mixed headache (*see below*).

Persistent daily headache after withdrawal may be refractory, and may be associated with personality factors and psychosocial dysfunction that militate against effective treatment.[212] Referral to a pain management clinic may be indicated.

209 Suhr B et al. Drug-induced headache: long-term results of stationary versus ambulatory withdrawal therapy. Cephalalgia 1999; 19: 44–49.

210 Rapoport AM. Medication overuse headache: awareness, detection and treatment. CNS Drugs 2008; 22: 995–1004.

211 Counselling in general practice. Drug Ther Bull 2000; 38: 49-52.

212 Lake AE, 3rd. Medication overuse headache: biobehavioral issues and solutions. Headache 2006; 46 Suppl 3: S88-S97.

management of multiple coexisting headache disorders

10. Management of multiple coexistent headache disorders

Symptomatic medication should be restricted to no more than 2 days per week. Where migraine coexists with episodic tension-type headache and prophylaxis is considered, ***amitriptyline 10-150mg daily*** is the drug of choice (see 6.5.4 and 7.4). Some specialists are using ***sodium valproate 0.6-2.5g daily***, ***topiramate 25mg od-50mg bd*** or ***gabapentin 300-800mg tds*** as alternatives.

Where migraine occurs in association with other, more troublesome headache (usually chronic tension-type headache or medication overuse headache), that headache should be treated first. Improvement in migraine often occurs concomitantly.

11. Costs of implementing these guidelines

It is predicted that fully implementing these guidelines will:

a) *improve* diagnosis, *reducing* the rate of inappropriate treatment;

b) *increase* the number of consultations per patient initially, to find the best treatment for each individual;

c) *increase* the number of patients with migraine using triptans;

d) *reduce* misuse of medication, including triptans, and *reduce* iatrogenic illness;

e) *improve* the overall effectiveness of management;

f) *raise* expectations, and lead to *more* patients consulting in primary care;

g) *reduce* the need for specialist referral, with opportunity gain for other neurological disorders;

h) *reduce* the overall burden of illness, with *savings* elsewhere.

Whereas some of these outcomes will increase NHS costs, at least initially, others will reduce them. Management costs *may* rise overall, but there is no good financial argument for treating headache disorders suboptimally. In the case of migraine, evidence is accruing that under-treatment is not cost-effective, although figures are not yet available to show the levels of savings overall that better management can achieve. Troublesome and inadequately managed TTH is also costly. Whilst not all cases can be treated effectively, there is considerable potential for making things worse by inappropriate management. Again, it is not known what savings might result from better care. It should be a priority to find out. Inadequately treated cluster headache causes considerable disability. Indirect costs per individual are likely to be high, although they have not yet been well estimated. Medication-overuse headache wastefully consumes resources unless correctly managed.

12. Audit

Audit should aim to measure headache burden in the target population and its diminution over time after implementation of these guidelines. Measurements may be made in random samples of patients large enough to represent the target population and to show change. It is not sufficient to assess outcome only in those with known headache: this will not measure success or failure in identifying and diagnosing those not complaining of headache, who are likely to be numerous and in whom burden may nevertheless be significant.[213]

Within the population of a primary care trust, it may be appropriate to assess burden annually in random samples of 1,000 adults reselected at each audit. Of these, about 150 will have migraine, more will have tension-type headache and 20-30 will have chronic daily headache. Instruments such as MIDAS[214] or HIT-6[215] may be useful. These self-administered questionnaires, which can be mailed, measure limitations on work, other chores and social activity attributable to headache over the preceding 1-3 months. Although developed for migraine, MIDAS appears to be applicable to any headache and regardless of whether any headache condition has been diagnosed. Both instruments have yet to be validated for this purpose but, as a measure of change, those people who are significantly affected by headache seem more likely to complete the assessment and those who do not can probably safely be discounted.

In addition, audit should measure direct treatment costs: consultations, referrals and prescriptions.

213 Lipton RB, Scher AI, Steiner TJ, Bigal ME, Kolodner K, Liberman JN, Stewart WF. Patterns of health care utilization for migraine in England and in the United States. Neurology 2003; 60: 441-448.

214 Stewart WF, Lipton RB, Kolodner K, Sawyer J, Lee C, Liberman JN. Validity of the Migraine Disability Assessment (MIDAS) score in comparison to a diary-based measure in a population sample of migraine sufferers. Pain 2000; 88: 41-52.

215 Kosinski M, Bayliss MS, Bjorner JB, et al. A six-item short-form survey for measuring headache impact: the HIT-6. Qual Life Res 2003; 12(8): 963-974.

BASH
BRITISH ASSOCIATION
FOR THE STUDY OF HEADACHE

The British Assoiciation for the Study of Headache,
Department of Neurology, Hull Royal Infirmary,
Anlaby Road, Hull HU3 2JZ

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