Medication overuse headache

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Summary

Medication overuse headache is common, affecting at least 1% of the population. It is responsible for the majority of recurrent daily headache and the majority of referrals to headache specialists. A high index of suspicion is warranted especially as there are no specific diagnostic tests. Withdrawal of the inciting medication(s) is the only effective treatment. With large numbers of affected patients and a duration that commonly exceeds 10 years, it is likely that both the economic and psychosocial costs of medication overuse headache are high.

Key words: analgesia, migraine.

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Introduction

Patients commonly take analgesics for headaches. However, chronic use of analgesics for headache can cause headache as a withdrawal phenomenon. Epidemiological data suggest that 4% of the population misuse pain medication, and that a minimum 1% of the general population in Europe, North America and Asia suffer from medication overuse headache.[1]

Classification

In the most recent headache classification (International Classification of Headache Disorders: ICHD-II)[2] medication overuse headache is subdivided according to the drugs involved, such as ergotamine, triptans, opioids, minor analgesics and combination medications. Confusion can arise because these headaches have previously been classified by reference to the preceding headache (transformed migraine, evolved migraine, chronic migraine, status migrainosus), the temporal pattern of the headache (chronic daily headache), the postulated mechanism (analgesia rebound headache) and the likely cause (drug-induced headache, painkiller headache).

It is important that headaches due to overuse of medication are distinguished from those which are caused directly by medication, such as nitrates and related compounds. Although medication overuse headache is associated with tolerance and drug use to prevent withdrawal symptoms, it can usually be distinguished from drug dependency. Patients are less likely to have cravings or to escalate the quantity of drugs they take. Their lives are unlikely to be significantly disrupted by drug-seeking behaviour.

Risk factors

Those 'at risk' for medication overuse headache are patients with frequent migraine or tension-type headache. Patients taking analgesia for other reasons (for example, arthritis) are only at risk of developing medication overuse headache if they also have a history of headaches. Some (particularly migraine) headache is familial and likely to have genetic determinants, so it is possible that medication overuse headache patients may also have some genetic predisposition to the condition.

In a cohort of patients with newly diagnosed migraine, a prospective study documented the development of medication overuse headache in more than 9% of the patients within 12 months.[3] Interestingly, recent data suggest that 'triptans' (serotonin agonists, such as sumatriptan) produce medication overuse headache more quickly, and at a lower frequency of use than either ergotamine or simple analgesics like aspirin or paracetamol.[4] It is believed that analgesics compounded with other substances, such as caffeine, codeine or barbiturates, are more likely to produce the syndrome of medication overuse headache. In the case of caffeine, withdrawal causes tiredness, lowered alertness and poor concentration, providing an incentive to ingest more caffeine, along with the associated analgesic.

Diagnosis

A typical patient is a 30–60-year-old female, with a history of more than a decade of migraine or tension-type headache. There may be a family history of headache and the presentation is often complicated by emotional distress. However, medication overuse headache is certainly not restricted to patients with this profile. It may affect patients from childhood to old age and may arise from apparently infrequent (three times weekly) or relatively short-term treatment. Medication overuse headache is estimated to be responsible for 30% of chronic daily headache, and accounts for 10–60% of patients attending specialist headache clinics. A high index of suspicion is therefore appropriate for any patient presenting with frequent headache.

There are no useful diagnostic tests for medication overuse headache. The history is by far the most important item of information. A critical aspect of the history is the temporal course of the headache, with transformation from intermittent pain or headache to continuous, or frequent (at least second-daily) headache.

The characteristics of medication overuse headache are not uniform.[4] The headache may vary in severity, type and location. In the case of patients with triptan-induced medication overuse headache, the headaches have similar characteristics to the migraines for which treatment was initiated, but may occur on a daily basis. Medication overuse headache developing after a history of tension-type headache is often described as a generalised, dull ache. Ergot-induced medication overuse headache is more likely to have a throbbing component.

Patients who fear headache pain and take prophylactic analgesia are likely to be at higher risk of developing medication overuse headache. A variety of constitutional and dysphoric symptoms may accompany or precede the development of medication overuse headache.

Medication overuse headache is not associated with focal or lateralising neurological symptoms. However, patients with a history of migraine who develop medication overuse headache may experience an aura before the headache emerges. Between episodes neurological examination should be normal. If the patient's symptoms have been stable over months or years, there is no indication for neurological investigation or imaging. Abnormalities on brain imaging are most likely to be incidental. However, atypical features, and particularly fixed abnormal neurological signs, should prompt consideration of the wider differential diagnosis of headache. Such signs include, but are not restricted to, ptosis, pupillary asymmetry, papilloedema, lateralised weakness or sensory disturbance, asymmetrical tendon reflexes and cerebellar inco-ordination. In contrast, signs of migraine aura typically evolve and resolve over 20–30 minutes prior to the development of the headache, and are much less significant.

Pathophysiology

At least some of the characteristics of medication overuse headache may be understood by considering the mechanism of action. Triptans are agonists at serotonin 5-HT_{1B} and 5-HT_{1D} receptors. These receptors are rapidly downregulated following drug exposure (within 24–96 hours). By contrast, aspirin and non-steroidal anti-inflammatory medications act on the enzymes cyclo-oxygenase 1 and 2. These enzymes are also downregulated following drug exposure, but much more slowly. Triptan usage therefore results in tachyphylaxis (less effect for the same dosage) more quickly, at a lower frequency of use, and at a lower dosage than other non-narcotic analgesics. Receptor and enzyme downregulation in structures responsible for the transmission and reception of nociceptive input creates increased sensitivity to such input, resulting in a lowered threshold for pain perception.

Management

The essential treatment of medication overuse headache is withdrawal of the offending medication, but in most cases that is easier said than done. Some patients find it very difficult to accept that the medication they use to treat their headaches is actually making their situation worse. Drug withdrawal can be undertaken by general practitioners with patients who are motivated and overuse triptans or other single drugs, excluding barbiturates, benzodiazepines or opioids. However, if the patient has failed a trial of outpatient withdrawal, overuses barbiturates, benzodiazepines, opioids or multiple drugs, and particularly if there is significant anxiety or depression complicating the presentation, inpatient withdrawal or specialist consultation should be considered (see box).

Prophylactic medication can be commenced before drug withdrawal. Migraine prophylactics and other previously ineffective drugs can become effective following drug withdrawal. This information can be used to encourage reluctant patients (particularly those who argue 'only drug X is effective in my case').

The withdrawal from triptans will be complete for almost all patients after four days so additional medication is usually not required. However, after four days only a minority of patients overusing standard analgesics will have completed withdrawal. Response in this group may be gradual. In some cases it may take three months before there is a two-thirds reduction in headache frequency. It may be six months before the patient has six consecutive days free of headache. To assist in the transition period, other drugs can be used. In hospital, some specialists use intravenous lignocaine[5], although risks include cardiac dysrhythmia and seizures. In the short term, steroid therapy[6], and over the medium term naproxen, may diminish withdrawal headache.

For patients overusing compound analgesics or ergot compounds, withdrawal symptoms may also include nausea and vomiting, as well as tachycardia and hypotension. These symptoms may require additional treatment with intravenous fluids, antiemetics and vasoactive drugs such as clonidine or propranolol.

Management hints

- Triptans, ergot and non-opioid medications can be ceased abruptly
- Non-steroidal anti-inflammatory drugs may be used for withdrawal headache (e.g. naproxen 500 mg twice a day)
- Prophylactic drugs in migraine may be commenced prior to triptan or ergot withdrawal (e.g. propranolol 10–40 mg thrice a day)
- Tricyclic antidepressants can be a useful 'prophylactic' drug to cover withdrawal of treatment for tension-type headaches (e.g. amitriptyline 10–25 mg at night)
- Benzodiazepines, barbiturates and opioids may require dose reduction prior to withdrawal (particularly if high doses have been used for years)

Relapse

Following successful withdrawal of the overused medication, migraine prophylaxis, careful assessment of precipitants, counselling, a headache management plan and clear limits on the use of analgesia may all be required in order to prevent relapse. Studies suggest that following withdrawal of the offending drug, medication overuse headache will relapse in approximately 40% of patients. This relapse is most likely to occur in the first 12 months following withdrawal. Patients with a prior history of tension-type headache are three times more likely to relapse than those with migraine precursor headaches. Those overusing analgesics (especially combination) are more likely to relapse than those using triptans or ergot (these may not be independent observations as patients with tension-type headache are less likely to be using triptans and ergot than patients with migraine).

Although supporting evidence is limited, behavioural interventions may help prevent headaches. Examples include relaxation therapy, stress management, meditation, regular aerobic exercise, or movement disciplines such as t'ai chi or yoga. Specific recommendations need to be mindful of patient preference and likely compliance, as well as local availability.

Conclusion

The prevalence of medication overuse headache is high and the condition is usually present for a long time before it is recognised and treated. Consider medication overuse headache as a possible cause in all patients with daily or second-daily headache, particularly among those with a prior history of migraine or tension-type headache. Medication must be withdrawn to treat the condition. A comprehensive management plan should be implemented to prevent relapse.

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false
(answers on page 159)

1. Patients who complain of daily headaches with no obvious cause may have medication overuse headache.
2. The aura of migraine can occur in medication overuse headache.