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Medication-overuse headache: epidemiology, diagnosis and treatment

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***Abstract*:** Medication-overuse headache (MOH) is one of the most common chronic headache disorders and a public health problem with a worldwide prevalence of 1–2%. It is a condition characterized by chronic headache and overuse of different headache medications, and withdrawal of the overused medication is recognised as the treatment of choice. However, the strategy for achieving withdrawal is, at present, based on expert opinion rather than scientific evidence, partly due to the lack of randomised controlled studies. This narrative review investigates different aspects of epidemiology, diagnosis, risk factors and pathogenesis as well as management for MOH. We suggest that the first step in the treatment of MOH should be carried out in general practice and should focus primarily on detoxification. For most patients, both prevention and follow up after detoxification can also be performed in general practice, thus freeing resources for referral of more complicated cases to headache clinics and neurologists. These suffering patients have much to gain by an earlier treatment-focused approach lower down on the treatment ladder.

Keywords: chronic headache, dependence, drug safety, medication overuse, migraine

Introduction

Headache is very common and usually occurs episodically, but 3–4% of the general population have chronic headache, defined as 15 or more days of headache per month [Castillo *et al.* 1998; Lantéri-Minet *et al.* 2003; Grande *et al.* 2008; Aaseth *et al.* 2008; Headache Classification Committee of the International Headache Society, 2013]. Headache disorders as a whole are a major public health concern given the large amount of associated disability and financial costs both to the individual and to society [Stovner *et al.* 2007; Jensen and Stovner, 2008; Linde *et al.* 2012; Vos *et al.* 2012]. Patients with chronic headache represent a large population within primary care and in neurologist settings [Patterson and Esmonde, 1993; Latinovic *et al.* 2006; Ridsdale *et al.* 2007]. Headache is often treated with analgesics and is the most common reason for analgesic use in the general population [Eggen, 1993; Antonov and Isacson, 1998; Zwart *et al.* 2003, 2004; Mehuys *et al.* 2012]. In Scandinavia and Scotland, 20–40% had used analgesics over the last 14 days and, in 2007, sales figures of over-the-counter (OTC) analgesics in Denmark were extrapolated to correspond to almost 8% of the general Danish population taking the highest recommended daily dose every day for a whole year [Eggen, 1993; Antonov and Isacson, 1998; Porteous *et al.* 2005; Hargreave *et al.* 2010].

Inappropriate use of symptomatic medication for headaches may paradoxically lead to medication-overuse headache (MOH) [Headache Classification Committee of the International Headache Society, 2013]. This is a condition characterized by chronic headache and overuse of different acute headache medications. Withdrawal headache after excessive intake of ergotamine was described in the early 1950s and 1960s, and from the 1980s studies have shown that frequent intake of all symptomatic headache medication may transform episodic headache to frequent headache [Peters and Horton, 1950, 1951; Horton and Peters, 1963; Kudrow, 1982; Diener *et al.* 1989; Mathew *et al.* 1990]. MOH patients, like other chronic headache sufferers, experience reduced quality of life compared with those do not suffer from headache and episodic headache [Colás *et al.* 2004; Lantéri-Minet *et al.* 2011].

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The treatment of MOH is often complex and withdrawal of the overused medication is recognised as the treatment of choice [Evers and Jensen, 2011]. Though several reviews on MOH have been published previously [Diener and Limmroth, 2004; Katsarava and Jensen, 2007; Rossi *et al.* 2009; Evers and Marziniak, 2010; Russell and Lundqvist, 2012; Katsarava and Obermann, 2013], this review will attempt to give an up-to-date focus on epidemiology, diagnosis and different aspects of the management, treatment and prevention of MOH.

Classification of medication-overuse headache

The International Classification of Headache Disorders 3rd beta edition (ICHD-IIIβ) divides headaches into primary and secondary forms [Headache Classification Committee of the International Headache Society, 2013]. Primary headaches are idiopathic disorders without other known causes, whereas secondary headaches are headaches assumed to be caused by other illnesses or external factors (e.g. trauma, surgery, toxic effects of substances or medications or infection). According to the ICHD-IIIβ:

MOH is headache occurring on 15 or more days per month developing as a consequence of regular overuse of acute or symptomatic headache medication (on 10 or more, or 15 or more days per month, depending on the medication) for more than 3 months. It usually, but not invariably, resolves after the overuse is stopped (Box 1).

MOH is classified as a secondary chronic headache, but whether MOH is a primary or secondary headache is still under debate, and the concept of medication overuse in other secondary headaches is unclear [Sun-Edelstein *et al.* 2009; Grazzi and Bussone, 2012].

Epidemiological and socioeconomic aspects of MOH

The prevalence of MOH in the general population is 1–2% [Lu *et al.* 2001; Colás *et al.* 2004; Zwart *et al.* 2004; Wiendels *et al.* 2006; Grande *et al.* 2008; Aaseth *et al.* 2008; Straube *et al.* 2010; Jonsson *et al.* 2011]. The male : female ratio is 1 : 3–4 and it is most prevalent in the forties [Straube *et al.* 2010; Jonsson *et al.* 2011]. The prevalence decreases with older age and, among people over 65 years in Taiwan, the prevalence was 1.0% [Wang *et al.* 2000]. The prevalence of MOH in children and adolescents has been suggested to be 0.3–0.5% [Dyb *et al.* 2006; Wang *et al.* 2006]. MOH generally starts earlier in life than other types of chronic headache [Colás *et al.* 2004].

Box 1. International Classification of Headache Disorders, 3rd beta edition (ICHD-IIIß) criteria for medication-overuse headache [Headache Classification Committee of the International Headache Society, 2013].

A. Headache present on >15 days/month.
B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache.
C. Headache has developed or markedly worsened during medication overuse.

(For simple analgesics and for combination of acute medications, the intake must be 15 days or more per month for triptans, ergotamins, opioids and combination analgesics; 10 days per month is enough to get the diagnosis of MOH.)

While OTC drugs are the most commonly overused headache medications in primary care, secondary and tertiary care have a greater proportion of MOH patients who overuse more potent, centrally acting drugs [Lu *et al.* 2001; Meskunas *et al.* 2006; Zeeberg *et al.* 2006; Scher *et al.* 2010; Jonsson *et al.* 2011, Kristoffersen *et al.* 2012; 2013]. The drugs involved in MOH change over time and from region to region [Meskunas *et al.* 2006]. In the US it has been found that 23% of chronic headache sufferers used acute medication on a daily basis in contrast to only 9% in the Norwegian general population [Scher *et al.* 2010; Kristoffersen *et al.* 2012]. In contrast to previously, ergotamine is no longer a large problem in western Europe. However, triptans are now among the most common causes of MOH in the western world. It has been suggested that the mean critical duration of overuse is shortest for triptans (1.7 years), longer for ergotamine (2.7 years) and longest for simple analgesics (4.8 years). The mean critical monthly intake frequency in the same study was lowest for triptans, higher for ergotamine and highest for analgesics [Limmroth *et al.* 2002].

Risk factors

Many psychosocial and socioeconomic factors are associated with MOH. However, it is hard to ascertain if these are directly or indirectly associated as these findings are mainly based on

cross-sectional studies. Thus, many of these factors may merely be markers of a complex situation since many aspects of life may be affected by having chronic headache, as with other chronic conditions.

As for other frequent headaches, MOH patients tend to have a low socioeconomic status with low income and education, but it is uncertain whether this may be a cause of or an effect of headache [Hagen *et al.* 2002; Atasoy *et al.* 2005; Wiendels *et al.* 2006; Jonsson *et al.* 2011, 2012]. A high prevalence of smoking, high body mass index and sleeping problems have also been found among MOH patients [Wiendels *et al.* 2006; Straube *et al.* 2010]. Depression and anxiety was more common among MOH patients than among people with episodic migraine, but in another study this was related to the headache frequency rather than headache diagnosis [Zwart *et al.* 2003; Radat *et al.* 2005]. The risk of developing MOH is greater in individuals with a family history of MOH or other substance abuse [Cevoli *et al.* 2009].

Data from a population-based longitudinal study suggested that those who used analgesics daily or weekly at baseline had a higher risk of developing chronic headache 11 years later [Zwart *et al.* 2003]. This would seem to support a causative role of medication overuse in generating MOH.

A more recent study identified several risk factors for MOH among people with chronic headache (11 years follow up) [Hagen *et al.* 2012]. Regular use of tranquilizers, combination of chronic musculoskeletal and gastrointestinal complaints, and increased Hospital Anxiety and Depression Scale, as well as smoking and physical inactivity increased the risk for MOH. The study was extensive and included over 25,000 people at risk for chronic headache and MOH. However, the mentioned risk factors were just found in a minority of all the MOH patients, and may thus reflect the complex situation for specific subgroups of MOH patients rather than for the MOH patient in general.

Previous primary headache such as migraine and tension-type headache are also risk factors and seems to be required for the development of MOH [Bahra *et al.* 2003; Colás *et al.* 2004; Bigal and Lipton, 2008].

Societal consequences of MOH

MOH is probably the most the most costly headache disorder for both society and the sufferer [Linde *et al.* 2012]. In a recent assessment of direct and indirect costs of headache disorders in Europe, indirect loss due to reduced productivity and absenteeism accounts for about 90% of the costs [Linde *et al.* 2012]. The individual costs of MOH were higher than for migraine, and the total national costs for headache disorders in some countries were estimated to be higher for MOH than for migraine. Total national costs for MOH were estimated at €5–10 billion in Italy, Spain and France [Linde *et al.* 2012]. Thus, the worldwide personal and economic costs are enormous.

Pathogenesis

Approximately half of those with headache on more than 15 days per month have MOH [Grande *et al.* 2008; Aaseth *et al.* 2008]. Most headache experts regard the association between overuse of acute medication and development of MOH as causal [Bigal and Lipton, 2009; Evers and Jensen, 2011]. Improvement for two-thirds to three-quarters of patients upon removal of the overused medication supports its causative role in generating or maintaining a chronic headache.

However, it is still a matter of debate whether the overuse is a consequence of living with chronic headache or the other way round [Dodick, 2002; Tepper, 2002]. Furthermore, not all headache patients with medication overuse develop MOH, and the mechanism how chronic exposure to abortive medication leads to MOH remains unclear.

Virtually all acute headache medication may cause MOH and since the different medications have different pharmacological actions, it is unlikely that MOH is caused by the specific action of any single agent. Mechanisms may differ from one class of overused drug to another and different possible pathogeneses have been suggested. It is of course possible that there is a common, but still unknown, mechanism by which pharmacologically different medications leads to MOH. However, at present it is possible only to describe mechanisms (mostly from preclinical studies) that appear to be associated with, or may predispose people to develop MOH.

A pre-existent headache disorder seems to be required to develop MOH [Bahra *et al.* 2003]. Migraine and tension-type headache have a higher potential for developing MOH than other

primary headaches, but also patients with cluster headaches may develop MOH [Colás *et al.* 2004; Paemeleire *et al.* 2006; Bigal and Lipton, 2008]. However, MOH does not develop in persons without a history of headache when medication is taken regularly for other conditions such as arthritis or inflammatory bowel disease [Wilkinson *et al.* 2001; Bahra *et al.* 2003]. Thus, a connection between headache-specific pain pathways and headache medication effects seems to be a central factor in generating a more chronic pain.

A hereditary susceptibility to MOH has been suggested as the risk of developing MOH is greater in individuals with a family history of MOH or other substance abuse [Cevoli *et al.* 2009]. A few small-scale studies have found some molecular genetic factors that are possibly associated with MOH, but these results are from small studies in selected groups and the generalizability of the findings is difficult to ascertain [Cevoli *et al.* 2006; Di Lorenzo *et al.* 2007, 2009]. Thus, further studies are required.

Alteration of cortical neuronal excitability, central sensitization involving the trigeminal nociceptive system, and changes in serotonergic and dopaminergic expressions and pathways including the endocannabinoid system have been suggested to play a part in the pathophysiology of MOH [Cevoli *et al.* 2006; Di Lorenzo *et al.* 2009; Cupini *et al.* 2010; De Felice *et al.* 2010; Meng *et al.* 2011; Bongsebandhu-Phubhakdi and Srikiatkhachorn, 2012].

Low serotonin (5-HT) levels with reduction of 5-HT in platelets and upregulation of a pronociceptive 5-HT_{2A} receptor have been demonstrated in MOH [Srikiatkhachorn *et al.* 1998; Srikiatkhachorn and Anthony, 2006]. A higher frequency of cortical spreading depression (CSD) has been found in animals with low 5-HT levels suggesting an association with sensitization processes [Supornsilpchai *et al.* 2006; Le Grand *et al.* 2011] Furthermore, chronic, but not acute, paracetamol administration led to an increase in CSD frequency in another rat model which may indicate that chronic analgesic exposure leads to hyperexcitability in cortical neurons and an increase in CSD [Supornsilpchai *et al.* 2010]. A 5-HT_{2A} receptor antagonist blocked this increased CSD susceptibility in the rats which had been exposed to chronic paracetamol [Supornsilpchai *et al.* 2010].

Chronic use of opioids and triptans has been shown to increase calcitonin gene related peptide (CGRP) levels which is involved in neurogenic inflammation and headache pain [Belanger *et al.* 2002; De Felice *et al.* 2010]. In addition, chronic morphine infusion may alter the diffuse noxious inhibitory controls (DNICs) and impaired DNICs are also found in MOH [Perrotta *et al.* 2010].

Another important phenomenon related to MOH is central sensitization which has for a long time been suggested to play an important role and has recently been described clinically in MOH patients with normalization after withdrawal of the overused medication [Ayzenberg *et al.* 2006; Munksgaard *et al.* 2013].

The endocannabinoid system is involved in modulating pain and plays a role in the common neurobiological system underlying drug addiction and reward [Cupini *et al.* 2008]. Both an endocannabinoid membrane transporter and levels of endocannabinoids in platelets were reduced in MOH and chronic migraine patients compared to controls [Cupini *et al.* 2008; Rossi *et al.* 2008].

In MOH patients, increased levels of orexin-A and corticotrophin-releasing hormone were found in the cerebrospinal fluid compared with patients with chronic migraine and these levels were correlated to monthly drug intake [Sarchielli *et al.* 2008]. In addition, neuroimaging studies suggest changes in the orbitofrontal cortex and the mesocorticolimbic dopamine circuit [Fumal *et al.* 2006; Ferraro *et al.* 2012].

In conclusion, the complex pathophysiology behind MOH is still only partly known. However, it is clear that many of these phenomena are similar to and thus may involve mechanisms seen in dependence processes [Calabresi and Cupini, 2005; Cupini *et al.* 2010] and it is equally clear that more research in these areas is needed.

Medication dependence or not?

Although triptans and simple analgesics are not regarded as psychotropic agents, patients with MOH do share some characteristics with dependence and some authors have advocated the division of MOH into two subgroups depending on the type of overused medication and on co-morbidity [Lake, 2006; Saper and Lake, 2006].

Codeine and opioids are not recommended in the treatment of tension-type headache or migraine. Regardless of this, it is well known that many MOH patients use these agents [Evers *et al.* 2009; Bendtsen *et al.* 2010]. Furthermore, many countries have codeine (which is metabolised to opioids) and caffeine-containing analgesics available as OTC drugs. Codeine, opioids and caffeine are known to be psychotropic drugs; thus abuse and dependence on headache drugs may be a problem [Abbott and Fraser, 1998; Cooper, 2013a, 2013b].

Theoretical considerations also show many similarities between MOH and drug addiction [Calabresi and Cupini, 2005]. Previous studies from Norway have revealed that MOH can easily be detected in a population using a screening instrument for behavioural dependence – the Severity of dependence scale (SDS) [Gossop *et al.* 1995; Grande *et al.* 2009; Lundqvist *et al.* 2010]. The SDS has high sensitivity, specificity, positive and negative predictive values for detecting persons with MOH among chronic headache patients [Grande *et al.* 2009; Lundqvist *et al.* 2010, 2011]. In addition, the SDS score has been shown to predict likelihood of successful detoxification in a general population [Lundqvist *et al.* 2012]. The SDS has not been validated against other measurements of dependency in MOH sufferers.

In two studies, approximately 70% of MOH patients fulfilled criteria for dependence according to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) [Fuh *et al.* 2005; Radat *et al.* 2008]. However, the use of DSM-IV criteria in patients with MOH has been criticised since it may overestimate dependence [Lauwerier *et al.* 2011]. Another study found that the dependency score based on the Leeds Dependency Questionnaire (LDQ) was similarly increased in MOH patients and illegal drug addicts [Ferrari *et al.* 2006]. However, in contrast to drug addicts, it was not the type of drug that was most important for the MOH patients but the effect of the drug [Ferrari *et al.* 2006].

Based on today's knowledge, it is impossible to ascertain whether dependency-like behaviour seen in those with MOH represents a real dependence or whether it is a form of 'pseudo-addiction' secondary to frequent headache [Saper *et al.* 2005; Lake, 2006; Saper and Lake, 2006; Radat and Lantéri-Minet, 2010; Fuh and Wang, 2012].

Treatment

MOH is a heterogeneous and complex condition which includes both simple and complicated overuse [Saper *et al.* 2005; Lake, 2006; Rossi *et al.* 2011]. A further challenge in the treatment is the fact that there is no worldwide consensus for the management of these patients other than that termination of medication overuse is desirable. How this should be addressed is frequently discussed. This may be mainly due to the lack of controlled studies, but also reflects the differences in use of the headache classification and nondocumented treatment strategies across the world. Although debated, withdrawal of the overused medication(s) is the treatment of choice, since withdrawal of the overused medication(s) in most cases leads to an improvement of the headache [Linton-Dahlöf *et al.* 2000; Zeeberg *et al.* 2006; Evers and Jensen, 2011; Diener, 2012; Olesen, 2012].

Most patients experience withdrawal symptoms lasting 2–10 days after detoxification. The most common symptom is an initial worsening of the headache, accompanied by various degrees of nausea, vomiting, hypotension, tachycardia, sleep disturbances, restlessness, anxiety and nervousness. The duration of withdrawal headaches have been found to vary with different drugs, being shorter in patients overusing triptans (~4 days) than in ergotamine (~7 days) or analgesics (~10 days) [Katsarava *et al.* 2001].

The procedures for detoxification vary substantially and include both in-patient (2 days to 2 weeks) and out-patient withdrawal [Krymchantowski and Moreira, 2003; Grazzi *et al.* 2008; Creac'h *et al.* 2011; Gaul *et al.* 2011; Rossi *et al.* 2011, Munksgaard *et al.* 2012]. The different strategies include: just simple advice; multidisciplinary approaches; use of antiemetics, tranquilizers, neuroleptics, rescue medication (another analgesic than the overused); intravenous hydration; and/or administration of oral, nasal or intravenous ergotamines. Steroids have for a long time been expected to alleviate withdrawal headache in the acute phase, but two placebo-controlled studies did not find prednisolone (60 or 100 mg for 5 days) superior to placebo [Boe *et al.* 2007; Rabe *et al.* 2013]. However, it may be useful in subgroups.

Regardless of the strategy, the main aims of the treatment are:

(i) Withdrawal of the overused drug(s)
(ii) To provide the patient with pharmacological and nonpharmacological support
(iii) To prevent relapse.

Clinical studies of treatment results from headache centres often have treatment success rates of around 70%. These results are commonly based on in-patient treatment, rescue medication and continued support. In addition, the 70% success rate is based on very variable outcome measures and therefore difficult to compare [Hagen *et al.* 2010]. No randomised controlled trials have been conducted in the general population or in primary care. However, some studies have suggested effect of simple advice for MOH in both a research setting in the general population and in a headache clinic [Rossi *et al.* 2006, 2011, 2013; Grande *et al.* 2011]. In a previous population-based study from Norway, simple information on medication use led to improvement with 42% of patients reverting to episodic headache and 76% being free of medication overuse after 1.5 years. The study was observational and lacked a control group, but the effect of simple information was supported by the fact that the participants had had MOH for 8–18 years prior to the interview during which the information was given [Grande *et al.* 2011]. Two Italian studies from neurologist settings have reported 78–92% of simple MOH patients and 60% of complicated MOH to be without chronic headache and medication overuse two months after simple advice [Rossi *et al.* 2006, 2011, 2013].

There is still some debate as to whether or not initially to detoxify MOH patients and whether prophylactic medication should be initiated immediately at withdrawal or after completed withdrawal therapy [Evers and Jensen, 2011; Diener, 2012; Olesen, 2012].

Placebo-controlled studies of prophylactic medication (onabotulinumtoxin A and topiramate) for chronic migraine with medication overuse have found a significant reduction in migraine and headache days per month compared with placebo [Diener *et al.* 2007, 2009, 2010; Dodick *et al.*, 2010; Aurora *et al.* 2010; Sandrini *et al.* 2011]. However, these results are not superior to detoxification without prophylactic medication in both simple and complicated MOH in the general population and neurologist setting, or in treatment-resistant MOH patients in a tertiary headache centre [Grande *et al.* 2011; Rossi *et al.* 2011; Munksgaard *et al.* 2012].

Therefore, based on today's knowledge we suggest that initial withdrawal is the treatment of choice. In addition, prophylactic headache medication should be restricted to patients that do not benefit sufficiently from simple advice or other means of withdrawal of medication overuse for the following reasons:

1. Removing offending medication is a logical primary aim for patients with headache partly due to medication side effects.
2. Removal of the distorting effect of medication overuse and assessment in an overuse-free state may be expected to show the characteristics of remaining headache and enable a rational choice of prophylactics, should they be needed.
3. A period free of medication overuse has been suggested to lead to recovery of prophylactic responsiveness [Zeeberg *et al.* 2006].

In analogy with other substance overuse, it is an aim in itself to achieve a behavioural change from 'have pain – take tablet' thinking to other, alternative and in the long run less detrimental ways of handling headache. Based on our clinical experience most patients overusing simple analgesics as well as codeine-containing combination medications and triptans manage abrupt detoxification from their offending medication without tapering. Patients overusing heavier drugs with physical abstinence profiles may be a different matter. However, in Norway as in most countries in Europe, the prior drug classes clearly dominate [Colás *et al.* 2004; Zeeberg *et al.* 2006; Jonsson *et al.* 2011; Kristoffersen *et al.* 2012, 2013].

Based on the lacking evidence base regarding detoxification strategies we are presently completing a randomised controlled trial of a behavioural-based, nonpharmacological short intervention in primary care. The results of this trial may contribute more firm evidence regarding whether detoxification in primary care can be achieved in primary out-patient care and whether it leads to lasting improvement of the headache situation of these patients [Kristoffersen *et al.* 2012].

Follow up and relapse

Studies from clinical settings have reported a 20–40% relapse rate of detoxified patients within the first year after withdrawal. Only few relapse after 12 months [Katsarava *et al.* 2003, 2005;

Grazzi *et al.* 2004; Zidverc-Trajkovic *et al.* 2007; Rossi *et al.* 2008; Boe *et al.* 2009a, 2009b; Andrasik *et al.* 2010]. There are conflicting results regarding at what time during the first year patients relapse with some suggesting that most patients relapse within the first 6 months while others suggest between 6 and 12 months [Katsarava *et al.* 2003, 2005; Grazzi *et al.* 2004; Ghiotto *et al.* 2009; Andrasik *et al.* 2010]. The literature is not clear regarding to what degree pre-existent headache type or type of overused medication predicts successful withdrawal [Limmroth *et al.* 2002; Katsarava *et al.* 2003, 2005; Grazzi *et al.* 2004; Zidverc-Trajkovic *et al.* 2007; Rossi *et al.* 2008; Boe *et al.* 2009a, 2009b; Andrasik *et al.* 2010].

In addition, these results on relapse should be compared with some caution, since the studies varied in the use of different headache classification systems, different withdrawal and prophylaxis as well as follow up and criteria for improvement.

Prevention

Some studies have found that most MOH patients do not know about the relationship between medication overuse and headache chronification [Bekkelund and Salvesen, 2002; Rossi *et al.* 2006; Jonsson *et al.* 2012]. The authors suggest that it is possible that the patients had been informed, but that they did not remember or had not fully understood the information. A brochure on medication overuse was preventive of development of MOH in people with migraine and frequent medication use [Fritsche *et al.* 2010].

Since most MOH patients have been in contact with their general practitioner (GP) for headache (80%), and almost half have had such contact in the previous year, primary care is probably the ideal setting for prevention and treatment of MOH [Jonsson *et al.* 2012; Kristoffersen *et al.* 2012, 2013]. Therefore, the GP has a key role in providing patient education and, in some cases, prophylactic headache medication before headaches become chronic.

It would be worthwhile to consider whether these MOH patients may benefit as much from a GP as they do from a neurologist. Taking care of uncomplicated cases in primary care may also free more resources for referrals to neurologists for complicated cases. Most follow-up studies are conducted in tertiary care centres and may reflect a selected population. However, one Norwegian study supports that patients initially detoxified as inpatients, can be followed up by their GP [Boe *et al.* 2009].

The improvement after withdrawal of the overused medication may potentially be augmented by a greater awareness by doctors, pharmacists and society in general regarding the dangers associated with inappropriate use of painkillers for headache. Considering that possibly anyone with primary episodic headache may be at risk of developing MOH, the number of people at risk is high. New information campaigns and strategies to target the people under risk have to be developed since the potential benefit of information and prevention of MOH is thus also high.

Conclusion

MOH is a worldwide public health problem. The treatment may be complex, but improvements seen in two out of three MOH patients after withdrawal suggest detoxification to be the treatment of first choice. Prevention as well as primary detoxification is possible and should probably be attempted in primary care. The gain from treating patients with MOH is potentially high, and may lead to substantial economic savings for society as well as large benefits for the individual patients.

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Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

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