7 November 2012

BASH GPwSI Meeting

Treatment Of Medication Overuse Headache

Dr Marcus Lewis

The National
Migraine Centre

International Headache Society Diagnostic criteria for MOH

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:

- Codeine containing painkillers > 10 days per month.
- Triptans > 10 days per month
- Ergotamine >10 days per month
- Combination analgesics [e.g. over the counter medications containing simple analgesia and caffeine] >10 days per month
- Non-opioid analgesics on >15 days per month.
- A combination of any of the above on >15 days per month.

C. Headache has developed or markedly worsened during medication overuse

Why have I chosen this subject?

- It is a common problem in headache practice
  - Under-recognized in Primary Care
  - 25-60% of headache referrals to secondary care
- It can be easily missed unless you think of it as the diagnosis behind the presentation:
  - Treatment failure of abortive and/or preventative drugs
  - Worsening control of migraine
  - Chronic daily headache
- It has a high morbidity - both physical and social:
  - 79% of patients have non-headache symptoms such as fatigue, nausea, restlessness, irritability, depression, concentration difficulties and memory problems.

Why have I chosen this subject?

- Treatment of MOH has a high failure rate:
  - 25% of patients will drop out before completing the initial withdrawal from medication
  - 40% of patients will have relapsed by 1 year
    - the “revolving door” of treating MOH

The history of MOH

- MOH has been known about for a long time:
  - First documented in Swiss pharmaceutical workers given free samples of pain medication containing phenacetin
  - 1950s – observed with ergotamine
  - 1990s – overuse of triptans noted to cause de novo headache and also an increase in "pure" migraine frequency

The mechanisms of MOH

- Pathophysiology poorly understand but thought to involve:
  - Down regulation of 5-HT receptors leading to reduced activity in central pain reducing pathways.
    - The brains of migraineurs already being more "connected" for pain compared to controls (Mainero et al, 2011)
- Physical dependency
  - Caffeine; opioids
- Psychological dependency
  - taking analgesics in anticipation of the possibility that a headache could develop
  - treating mild headaches "just in case" they develop into a more severe, disabling headache
  - the positive reinforcement of reducing pain through taking tablets

Co-morbid psychopathology in MOH

Table 1.—Odds Ratios for Presence of Comorbid Psychiatric Disorder in MOH and Migraine Without Medication Overuse[32]

Disorder	MOH (%)	Migraine (%)	Odds Ratio
All mood disorders	85	51	4.5
Major depressive episode	39	2	21.8
All anxiety disorders	83	54	3.5
Panic disorder	24	2	12.1
Generalized anxiety disorder	42	10	6
Social phobia	34	12	4.3
All substance-related disorders	44	15	7.6

Table 2.—Chronology of Onset of Psychiatric Disorders in Relation to Chronicization of Headaches in MOH Patients—ie, Whether Disorder Precedes or Follows CDH[32]

Disorder	Precedes CDH (%)	Follows CDH (%)
First major depressive episode	76	24
Panic disorder	79	21
Generalized anxiety disorder	80	20
Social phobia	100	0
Substance-related disorders	89	11

(adapted from Radat et al, 2005)

• Personality disorder is more common in MOH [26% compared to 15% in the general US population]:
  – More likely to be overusing opiates than non PD MOH patients
  – Less likely to have a positive outcome following inpatient or outpatient medication withdrawal

(Lake, 2006)

Treatment of MOH

- Withdraw the overused drug
- Support the patient through the withdrawal process
- Reassess the patient as the clinical picture, or their clinical needs, may have changed
- Prevent future relapse

Possible outcomes of treatment of MOH

- Nothing. But MOH has been excluded from the differential diagnosis.
- The patient may become headache-free.
- The patient may have a marked reduction in headache frequency and/or severity.
- A confusing diagnostic picture may become more straightforward leading to a more specific treatment plan.
- A patient who previously responded poorly to treatment may become more responsive to both acute and preventative treatment.
- The patient may generally feel better in themselves.
- The patient may become less psychologically dependant on using painkillers.

Withdraw the overused drug

- Two month withdrawal of overused medication (Zeeberg et al, 2006):
  - 45% of patients improved
    - 67% median reduction in migraine
  - 48% of patients had no change
  - 7% of patients got more headaches

Withdraw the overused drug

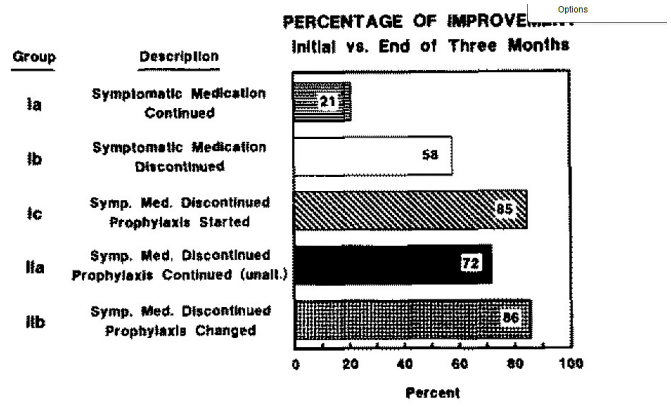
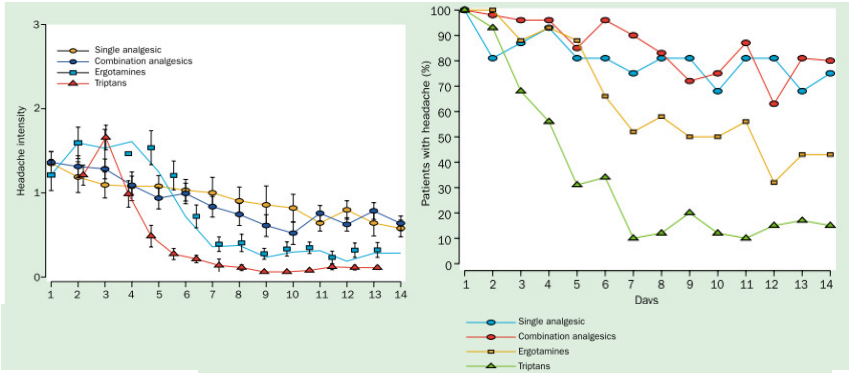


Fig 2.—Percentage of improvement in the headache indices in the five treatment groups. Note the 58% improvement in group I-b by mere discontinuation of symptomatic medications.

(Matthew et al, 1990)

Withdraw the overused drug



Course of headache intensity and percentage of patients with headache during 14 days of withdrawal therapy after medication overuse. (from Diener et al, 2001)

Withdraw the overused drug

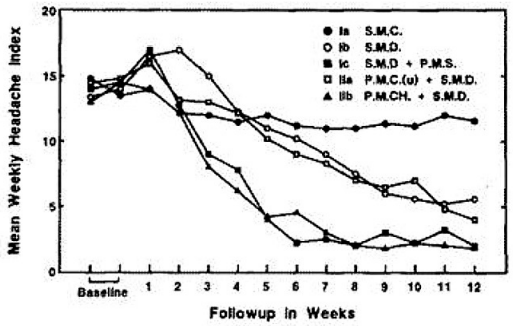


Fig 1.—Headache indices during the base line period and 12 weeks of followup.
S.M.C. Symptomatic Medications Continued
S.M.D. Symptomatic Medications Discontinued
P.M.S. Prophylactic Medications Continued
U Unchanged
P.M.CH Prophylactic Medications Changed

(Matthew et al, 1990)

Withdraw the overused drug

- Detoxification for MOH is not necessary (Diener 2012)
  - "An aggressive detoxification programme is not required as a first step for all patients with evidence of excessive use of medication before the initiation of preventive medication"
  - Studies in migraine prevention in which MOH was not an exclusion criteria have shown benefits:
    - Topiramate – 20% headache reduction compared to placebo
    - Onabotulinum toxin A – 10% headache reduction from baseline

Withdraw the overused drug

- Should medication withdrawal be abrupt or gradual?
  - There is no general evidence whether abrupt or tapering withdrawal treatment should be preferred.
  - For the overuse of analgesics, ergotamine derivatives, or triptans, abrupt withdrawal is recommended.
  - For the overuse of opioids, benzodiazepines, or barbiturates, tapering down of the medication should be offered.

(EFNS Guidelines, 2011)

Support the patient through the withdrawal process

- In uncomplicated MOH, effective drug withdrawal can be achieved through the imparting of advice alone.
- More complicated patients may need replacement therapy. The evidence is limited, of poor quality and difficult to apply to a Primary Care setting:
  - Prednisolone 60mg [tapered over 6 days] – not effective compared to placebo in reducing withdrawal symptoms
  - Prednisolone 100mg for 5 days – reduced number of hours with severe or moderate headache over the first 72 hours
  - Naproxen 250mg TDS or 500mg BD or tapering course – little evidence to support use

Support the patient through the withdrawal process

Rossi et al	120 patients randomized to:	a) Advice to withdraw overused medications b) Outpatient withdrawal programme with steroids in week 1 and prophylaxis started in week 2 c) Inpatient withdrawal programme as per (b) but with close personal support and IV fluids
Krymchantowski and Moreira	150 outpatients randomized to:	a) 6 day course of Prednisolone b) Regular Naratriptan c) No medication All groups were given advice; rescue medication (Indometacin or Chlorpromazine); and started on prophylaxis on Day 7
Boe et all	100 inpatients:	Prednisolone or placebo plus advice plus PRN use of rescue treatment (antiemetics; antihistamines; antipsychotics)

• With follow up ranging from 8 days to 2 months, none of these studies show any differences in:
  – The percentage of patients achieving successful withdrawal
  – Headache frequency
  – Headache intensity

(Slide is adapted from Rossi et al, 2009)

Preventing future relapse

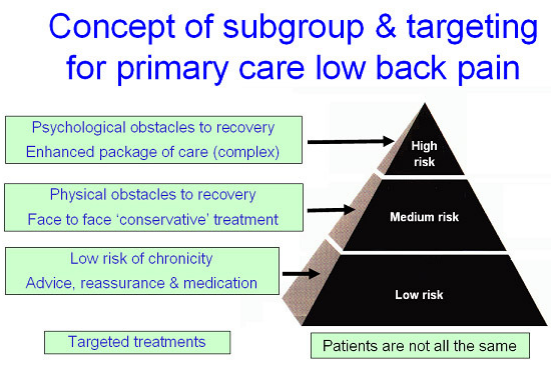
- In various studies, the relapse rate of MOH at 1 year is 14% to 41%:
  – Irrespective of whether inpatient or outpatient treatment, or advice alone, was offered
- Most studies indicate that relapse occurs within the first few months after withdrawal
- Evidence from limited, poor quality studies do not show that starting prophylactic treatment reduces the chance of future relapse

Preventing future relapse

- In simple MOH patients, the decision on whether or not to start a preventive treatment may be postponed until a follow-up visit performed 2–3 months after the start of the withdrawal treatment .
  - This approach may help patients to feel more in control of their headache, and it also fits better with what is known about the natural history of the disease.
- An alternative approach is to start preventive and withdrawal treatments simultaneously, or to start preventive therapy during the washout period, making it clear to the patient that the treatment may not become fully effective until MOH has been eliminated.
  - This approach has two potential advantages: first, it may help to reduce reliance on symptomatic medications, and, second, the prophylactic treatment may improve the withdrawal symptoms and headache frequency.

(Rossi et al, 2009)

Subgroup targeting for back pain



STarT Back Screening Tool Website

Subgroup targeting for back pain

Patient name: _____ Date: _____

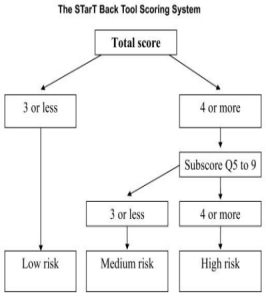
Thinking about the **last 2 weeks,** tick your response to the following questions:

		Disagree 0	Agree 1
1	My back pain has **spread down my leg(s)** at some time in the last 2 weeks	☐	☐
2	I have had pain in the **shoulder** or **neck** at some time in the last 2 weeks	☐	☐
3	I have only **walked short distances** because of my back pain	☐	☐
4	In the last 2 weeks, I have **dressed more slowly** than usual because of back pain	☐	☐
5	It is not really safe for a person with a condition like mine to be physically active	☐	☐
6	**Worrying thoughts** have been going through my mind a lot of the time	☐	☐
7	I feel that **my back pain is terrible** and **it is never going to get any better**	☐	☐
8	In general I have **not enjoyed** all the things I used to enjoy	☐	☐

9. Overall, how **bothersome** has your back pain been in the **last 2 weeks**?

Not at all	Slightly	Moderately	Very much	Extremely
☐ 0	☐ 0	☐ 0	☐ 1	☐ 1

Total score (all 9): _____ **Subscore (Q5 to 9):** _____



Subgroup targeting for MOH

Table 1 Proposed criteria for simple or complex medication overuse headache (see references [3, 4])

Simple MOH	Complex MOH
Short duration of MOH (3 months–1 year)	Long duration of MOH (>1 year)
Relatively modest doses of drugs[a]	Daily opioids or combination medication with more than one prescription drug
Minimal psychiatric contribution[b] (one or two axis I clinical syndromes)	Multiple psychiatric comorbidities including personality disorders
No history of relapse after withdrawal	History of relapse following withdrawal

[a] Up to two triptans and three analgesics per day

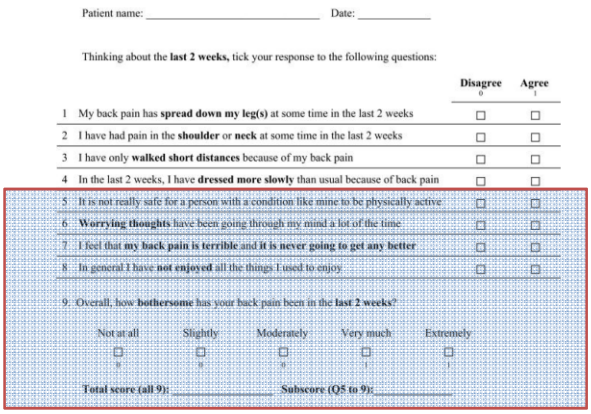
[b] Psychological issues contributing to the perpetuation of MOH include: (a) the belief that drug(s) is(are) the only solution, (b) anticipatory fear of pain (cephalalgiophobia), (c) difficulty tolerating discomfort, (d) sedation seeking, (e) outside pressure, need to function, (f) axis I, clinical syndrome, (g) axis II personality disorders

(Rossi et al, 2009)

Subgroup targeting for MOH

- Should we routinely be thinking in terms of "simple" and "complex" MOH?
- How can we easily screen for and identify the "complex" MOH patients?

Subgroup targeting for MOH



Patient name: _____ Date: _____

Thinking about the **last 2 weeks,** tick your response to the following questions:

		Disagree 0	Agree 1
1	My back pain has **spread down my leg(s)** at some time in the last 2 weeks	☐	☐
2	I have had pain in the **shoulder** or **neck** at some time in the last 2 weeks	☐	☐
3	I have only **walked short distances** because of my back pain	☐	☐
4	In the last 2 weeks, I have **dressed more slowly** than usual because of back pain	☐	☐
5	It is not really safe for a person with a condition like mine to be physically active	☐	☐
6	**Worrying thoughts** have been going through my mind a lot of the time	☐	☐
7	I feel that **my back pain is terrible** and **it is never going to get any better**	☐	☐
8	In general I have **not enjoyed** all the things I used to enjoy	☐	☐

9 Overall, how **bothersome** has your back pain been in the **last 2 weeks?**

Not at all	Slightly	Moderately	Very much	Extremely
☐ 0	☐ 0	☐ 0	☐ 1	☐ 1

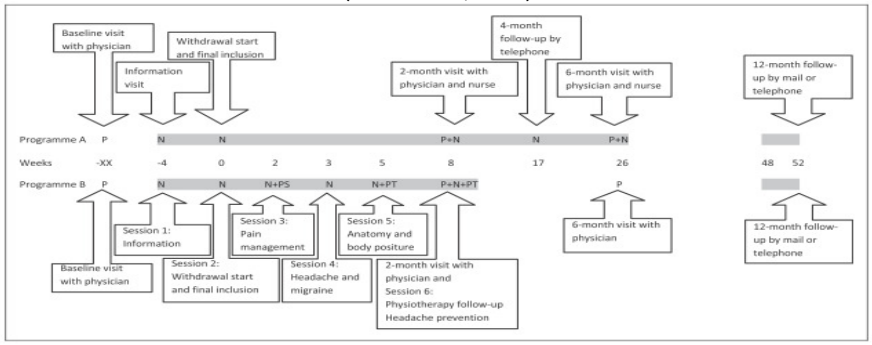
Total score (all 9): _____ **Subscore (Q5 to 9):** _____

Subgroup targeting for MOH

- Should we routinely be thinking in terms of "simple" and "complex" MOH?
- How can we easily screen for and identify the "complex" MOH patients?
- How can we more effectively manage these patients?
  - Especially given limited resources
- Is a more intensive withdrawal programme the answer?

Is a more intensive withdrawal programme the answer?

Detoxification of medication-overuse headache by a multidisciplinary treatment programme is highly effective: A comparison of two consecutive treatment methods in an open-label design. (Jensen et al, 2012)



At 1 year follow up both Programme A [80%] and Programme B [85.4%] were "cured" of MOH [>50% reduction in headache frequency]

My personal reflections

- How can we improve the recognition of MOH in Primary Care?
- How can we help GPs to follow up patients with MOH who we discharge to their care?
- How can we identify the more problematic cases of MOH?
  - Could an existing screening tool be useful? Or is there scope to develop one?
- What do we do with them?
- What is the role of psychological/ behavioural management?
  - Would that be more effective handed back to the patient's GP and community Psychology services?

The Danish recipe for withdrawal from MOH

Detoxification of medication-overuse headache by a multidisciplinary treatment programme is highly effective: A comparison of two consecutive treatment methods in an open-label design. (Jensen et al, 2012)

"From days 1–7, patients were allowed three days with either naproxen 500 mg up to two times a day or acetaminophen 1 g up to three times a day. Additionally, the patients were allowed to take rescue medication: promethazine 25 mg or levomepromazine 25 mg up to three times a day, and metoclopramide 20 mg up to three times a day (2). From day 8, the patients were allowed two days/week with symptomatic medications prescribed by the physician at the baseline visit.

Symptomatic medications included simple analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), triptans, and combination analgesics, all except the previously overused drugs.

Prophylactic treatment was prescribed by the physician at the base line visit according to the patients' primary headache, efficacy and side effects of previous treatments, co-morbid disorders and preferences, and was started from day 1."

Further reading and references

- Munksgaard SB, Bendtsen L, Jensen RH. Detoxification of medication-overuse headache by a multidisciplinary treatment programme is highly effective: a comparison of two consecutive treatment methods in an open-label design. Cephalalgia. 2012 Aug;32(11):834-44. Epub 2012 Jun 29.
- Diener HC. Detoxification for medication overuse headache is not necessary. Cephalalgia. 2012 Apr;32(5):423-7. Epub 2011 Nov 29. Mainero C, Boshyan J, Hadjikhani N. Altered functional magnetic resonance imaging resting-state connectivity in periaqueductal gray networks in migraine. Ann Neurol. 2011 Nov;70(5):838-45. doi: 10.1002/ana.22537.
- Evers S, Jensen R; European Federation of Neurological Societies. Treatment of medication overuse headache--guideline of the EFNS headache panel. Eur J Neurol. 2011 Sep;18(9):1115-21. doi: 10.1111/j.1468-1331.2011.03497.x.
- Management of medication overuse headache. BMJ. 2010 Apr 28;340:c1305. doi: 10.1136/bmj.c1305.
- Rossi P, Jensen R, Nappi G, Allena M; COMOESTAS Consortium. A narrative review on the management of medication overuse headache: the steep road from experience to evidence. J Headache Pain. 2009 Dec;10(6):407-17. Epub 2009 Oct 3. Review. Erratum in: J Headache Pain. 2010 Feb;11(1):85.
- Katsarava Z, Holle D, Diener HC. Medication overuse headache. Curr Neurol Neurosci Rep. 2009 Mar;9(2):115-9. Review
- Zeeberg P, Olesen J, Jensen R. Probable medication-overuse headache: the effect of a 2-month drug-free period. Neurology. 2006 Jun 27;66(12):1894-8. Epub 2006 May 17.
- Saper JR, Hamel RL, Lake AE 3rd. Medication overuse headache (MOH) is a biobehavioural disorder. Cephalalgia. 2005 Jul;25(7):545-6.
- Radat F, Creac'h C, Swendsen JD, Lafittau M, Irachabal S, Dousset V, Henry P. Psychiatric comorbidity in the evolution from migraine to medication overuse headache. Cephalalgia. 2005 Jul;25(7):519-22.
- Diener HC, Limmroth V. Medication-overuse headache: a worldwide problem. Lancet Neurol. 2004 Aug;3(8):475-83. Review.
- Mathew NT, Kurman R, Perez F. Drug induced refractory headache--clinical features and management. Headache. 1990 Oct;30(10):634-8.