An Overview of MOH
IHS ASIAN HA MASTERS SCHOOL
MARCH 24, 2013

ALAN M. Rapoport, M.D.
Clinical Professor of Neurology
The David Geffen School of Medicine at UCLA
Los Angeles, California

President-Elect
The International Headache Society (IHS)
DR. RAPOPORT’S DISCLOSURES

SPEAKERS BUREAU
- Allergan
- Impax
- Nautilus Neurosciences

ADVISORY BOARD
- ElectroCore
- MAP
- Nautilus Neurosciences
- NuPathe
- Winston

February 27, 2013
Goals for this lecture

1. Learn an overview of MOH

2. Be able to discuss the pathophysiology of diagnostic criteria of MOH

2. Be able to discuss which medications are more likely to cause MOH
Overview

- Pathophysiology of MOH
- Types of MOH
- Diagnostic Criteria of MOH
- The importance of MOH
- Which medications cause MOH
- Which patients need detoxification
- Conclusions
- An invitation
Diagnosis and Classification of Headache Disorders - ICHD-IIR1

The IHS Classification

2nd edition (1st revision) (ICHD-IIR1)

©International Headache Society 2003/5
8. Headache attributed to a substance or its withdrawal

8.1 Headache induced by acute substance use or exposure

8.2 Medication-overuse headache (MOH)

8.3 Headache as an adverse event attributed to chronic medication

8.4 Headache attributed to substance withdrawal
• **Results.**—Chronic paracetamol administration resulted in a significant decrease in the maximum number of 5-HT 2A binding sites and an increase in the maximum number of 5-HT transporter binding sites in frontal cortical membrane (P = .001). Changes in the central 5-HT system were associated with a rise in platelet 5-HT levels.

• The degree of receptor downregulation, as well as transporter upregulation, became less evident after more prolonged drug administration. Readaptation of serotonin receptors and transporters coincided with the decrease in the analgesic efficacy of paracetamol, as well as a fall in platelet 5-HT levels.

• **Conclusions.**—These findings provide further evidence in support of an involvement of the 5-HT system in the antinociceptive activity of simple nonnarcotic analgesics. Plasticity of this neurotransmitter system after chronic analgesic exposure may lead to the loss of analgesic efficacy and, in its more extreme form, may produce analgesic-related painful conditions, for example, analgesic abuse headache.

The present study was conducted to determine the effect of acute (1 h) and chronic (daily dose for 30 days) paracetamol administration on the development of cortical spreading depression (CSD), CSD-evoked cortical hyperaemia and CSD-induced Fos expression in cerebral cortex and trigeminal nucleus caudalis (TNC).
Results revealed that acute paracetamol administration substantially decreased the number of Fos-immunoreactive cells in the parietal cortex and TNC without causing change in CSD frequency. On the other hand, chronic paracetamol administration led to an increase in CSD frequency as well as CSD-evoked Fos expression in parietal cortex and TNC, indicating an increase in cortical excitability and facilitation of trigeminal nociception.

Alteration of cortical excitability which leads to an increased susceptibility of CSD development can be a possible mechanism underlying medication-overuse headache.
**Pathophysiology of MOH**

Signe B Munksgaard, Lars Bendtsen and Rigmor H Jensen.

**Methods:** We examined pain perception in 35 MOH patients before and two, six and 12 months after detoxification.

**Conclusion:** The central nervous system is sensitised in patients with MOH. For the first time we demonstrate that the pain perception continues to normalise up to a year after detoxification.

• This emphasises the importance of detoxification and follow-up to prevent relapse.

Signe B Munksgaard, Lars Bendtsen and Rigmor H Jensen. Modulation of central sensitisation by detoxification in MOH: Results of a 12-month detoxification study. *Cephalalgia* 2013; In print on line first.
8.2 Medication-overuse headache

New entrant to classification

8.2.1 Ergotamine-overuse headache
8.2.2 Triptan-overuse headache
8.2.3 Analgesic-overuse headache
8.2.4 Opioid-overuse headache
8.2.5 Combination analgesic-overuse headache
8.2.6 Medication-overuse headache attributed to combination of acute medications
8.2.7 Headache attributed to other medication overuse
8.2.8 Probable medication-overuse headache
8.2 Medication-overuse headache

Notes

• The most common cause of migraine-like or mixed migraine-like and TTH-like headaches on $\geq 15$ d/mo is overuse of symptomatic migraine drugs and/or analgesics.

• Patients with migraine or TTH who develop new headache or whose migraine or TTH is made markedly worse during medication overuse should be coded for that headache + 8.2 Medication-overuse headache.

• Diagnosis of MOH is important because patients rarely respond to preventative medications until withdrawn.

©International Headache Society 2003/5
To be diagnosed with Medication Overuse Headache a patient must be using triptans, ergots, opiates or butalbital containing medication:

A. 15 days per month for 6 months or more
B. 15 days per month for 3 months or more
C. 10 days per month for 6 months or more
D. 10 days per month for 3 months or more
8.2 Medication-overuse headache

A. Headache present on ≥15 d/mo fulfilling criteria C and D

B. Regular overuse for >3 mo 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

D. Headache resolves or reverts to its previous pattern within 2 mo after discontinuation of overused medication

©International Headache Society 2003/5
8.2.1 Ergotamine-overuse headache

A. Headache fulfilling criteria A, C and D for 8.2
   Medication-overuse headache

B. Ergotamine intake on $\geq 10$ d/mo on a regular basis for >3 mo
8.2.2 Triptan-overuse headache

A. Headache fulfilling criteria A, C and D for 8.2 Medication-overuse headache

B. Triptan intake (any formulation) on $\geq 10 \text{ d/mo}$ on a regular basis for $>3 \text{ mo}$
8.2.3 Analgesic-overuse Headache

A. Headache fulfilling criteria A, C and D for 8.2 Medication-overuse headache

B. Intake of simple analgesics on $\geq 15$ d/mo on a regular basis for $>3$ mo

NOTE:
Expert opinion rather than formal evidence suggests that use on $\geq 15$ d/mo rather than $\geq 10$ d/mo is needed to induce analgesic-overuse headache
8.2.5 Combination analgesic-overuse headache

Name-change in ICHD-IIIR1

A. Headache fulfilling criteria A, C and D for 8.2 Medication-overuse headache

B. Intake of combination analgesic medications* on ≥10 d/mo on a regular basis for >3 mo

Note:

*Combinations typically implicated are those containing simple analgesics combined with opioids, butalbital and/or caffeine
8.2.6 MOH attributed to combination of acute medications

New entrant to classification in ICHD-IIIR1

A. Headache fulfilling criteria A, C and D for 8.2 *Medication-overuse headache*

B. Intake of *any combination* of ergotamine, triptans, analgesics and/or opioids on $\geq 10$ d/mo on a regular basis for $>3$ mo without overuse of any single class alone*

*Diagnose 8.2.1-8.2.5 if criterion B is fulfilled in respect of any single class(es) of these medications*
8.2 Medication Overuse Headache (MOH)

- Headache for >15 days/month
- Different drug classes for different periods of time create different medication overuse headache
  - *Triptans, ergots, opiates, butalbital or combinations (often with caffeine) ≥ 10 days/month* for >3 months
  - *Simple analgesics ≥ 15 days/month >3 months*
  - *Headache frequency markedly increases with increased drug use or new type HA develops*
- After detoxification, reversion to episodic headache by 2 months
8.2.8 Probable MOH

Renumbered (from 8.2.7) in ICHD-II R1

A. Headache fulfilling criteria A and C for 8.2 Medication-overuse headache

B. Medication overuse fulfilling criterion B for any one of the subforms 8.2.1 to 8.2.7

C. One or other of the following:
   1. overused medication has not yet been withdrawn
   2. medication overuse has ceased within the last 2 mo but headache has not so far resolved or reverted to its previous pattern

©International Headache Society 2003/5
8.2.8 Probable MOH

8.2.8.1 Probable ergotamine-overuse headache
8.2.8.2 Probable triptan-overuse headache
8.2.8.3 Probable analgesic-overuse headache
8.2.8.4 Probable opioid-overuse headache
8.2.8.5 Probable combination analgesic-overuse headache
8.2.8.6 Headache probably attributed to overuse of acute medication combinations (new in ICHD-II R1)
8.2.8.7 Headache probably attributed to other medication overuse
8.4 Headache attributed to substance withdrawal

8.4.1 Caffeine-withdrawal headache

8.4.2 Opioid-withdrawal headache

8.4.3 Oestrogen-withdrawal headache

8.4.4 Headache attributed to withdrawal from chronic use of other substances
Excessive acute migraine medication use and migraine progression

• 1) Opiates are associated with migraine progression; critical dose of exposure is around 8 days per month, and the effect is more pronounced in men.

• 2) Barbiturates are also associated with migraine progression. Critical dose of exposure is around 5 days per month and the effect is more pronounced in women.

• 3) Triptans induced migraine progression in those with high frequency of migraine at baseline (10–14 days per month), but not overall.

4) Anti-inflammatory medications were protective in those with <10 days of headache at baseline, and, as triptans, induced migraine progression in those with high frequency of headaches.

Accordingly, specific classes of medications are associated with migraine progression, and high frequency of headaches seems to be a risk factor for chronic migraine regardless of medication exposure.

Bigal, ME, Lipton RB Neurology 2008;71:1821-1828
Marja is a 46 year old Dentist with frequent HAs

- 46 year-old, married, female dentist, mother of 3
- Headaches since childhood, age 6
- History of asthma and breast cancer
- HA #1 in her 20s: 3 episodes/mos lasting up 12 hours: right temporal, severe intensity (9/10), throbbing pain with nausea, phonophobia and photophobia.
- HA #2 in her 40s, after using sumatriptan tablets 100 mg 3 or 4 days per week: 18 days per month of moderate intensity (6/10), bilateral, non-throbbing, TTHA without photophobia or nausea
- Total 21 days per month of headache
- Medications: 12-16 days per month of sumatriptan and opiates
- Examinations and MRI of the head normal except for deep white matter hyperintensities
What are Marja’s Diagnoses?
Marja

How should we treat Marja?
Case Presentation (Cont)  
Migraine without aura  

Treatment

- Behavioral Medicine consultation for biofeedback and relaxation techniques
- Have her keep a headache calendar
- Detoxify gradually from opiates and sumatriptan, gradually
- Consider clonidine for withdrawal symptoms from opiates
- Consider sleeping medication
- Bridge therapy with prednisone 60 mg day one and decrease and stop over 5 days
- In the first month acute treatment with naproxen sodium 500 mg up to 2 times per day, up to 3 days per week
- Trial zolmitriptan nasal spray 5 mg early in the migraine attack, after detoxification from sumatriptan. May repeat in 2 hours. Maximum use 2 days per week
- Frequent office visits for evaluation and fine tuning therapy
Conclusions

• Take a complete and careful history of over the counter and prescription acute care medication

• Make an accurate diagnosis of headache types and presence or absence of MOH

• **Detoxify**, if patient has MOH. **Preventive** medication started first to reach therapeutic level

• Select acute care medications and limit use to 2 days per week

• Behavioral Medicine techniques (Biofeedback Training, relaxation, cognitive restructuring)

• Arrange for frequent office visits
Welcome to BOSTON

IHC 2013

In Boston, MA

June 27-30, 2013

American Headache Society

(2015 – Valencia, Spain)
Thanks for your attention!