

Acute Treatment of Migraine

**Headache Cooperative of New England
(HCNE) Topnotch at Stowe, VT
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Dr. Rapoport's Potential Conflicts



SPEAKER'S BUREAU

Endo Pharmaceuticals (yearly)

GlaxoSmithKline (yearly)

Merck (yearly)

Pfizer

Valeant

ADVISORY BOARDS

Allergan

Endo

NuPathe

Pfizer

Roxro

Overview



- **General principles of treatment**
- **Frequent comorbid states**
- **What meds to use**
- **What meds to avoid**
- **How to treat and when to treat**
- **How to modify therapies to optimize success**
- **Drug-drug interactions**
- **Future acute migraine treatment**
- **Conclusions**

Acute Treatment Strategies: General Principles



- Proper treatment begins with accurate diagnosis of all headache types
- A therapeutic partnership is essential
- Pts should participate in their own care
- Patient education and behavioral management
 - Strategies for identifying triggers
 - Trigger avoidance
 - Regular sleep, meals and exercise routines
 - Stress management, biofeedback

Acute Treatment Strategies: General Principles



- Review past treatments in detail
 - Successes and failures + AEs
- **Attack frequency, duration and disability determines Rx plan**
- Think about the “entire” migraine complex
- Treatment needs to encompass pain relief *and* associated symptoms
- Specifically ask about ***disability***
- Consider co-morbid and co-occurring conditions

Migraine Co-Morbidity



- Raynaud's disease
- Mitral valve prolapse
- Stroke
- **Sleep Disorders**
- **PFO**
- Epilepsy
- **Depression**
- **Anxiety/panic disorder + others**
- Irritable bowel syndrome

Consider Co-Occurring Conditions



- Hypertension/ Hypotension
- Angina/MI
- Ulcer disease/reflux
- **Vertigo/dizziness**
- **Current or prior medication overuse**
- Allergies
- **Asthma**
- ? Hypothyroidism

Goals of Acute Migraine Treatment



- Treat attacks **rapidly** and consistently without recurrence →→ ***Pain Free State***
- ***One and done***
- Restore the patient's **ability to function**
- Prevent adverse events
- Minimize the use of rescue and backup medications
- Optimize self-care and reduce resource utilization (avoid ER)
- Be cost-effective

ASSESSING TREATMENT SUCCESS



The new goal: **Migraine free at 2 hours, no recurrence**

Severity of **disability** (MIDAS or HIT-6)

Duration, intensity, and frequency of attacks

Use of medical resources

- frequency of second dosing
- frequency of rescue medication
- frequency of emergent care / clinic visits

Incidence of adverse events

Level of patient satisfaction

Strategies for Initial Acute Therapies



- Step care across attacks
- Step care within attacks
- Stratified care (**THE RIGHT TREATMENT FIRST TIME**)

Lipton RB, et al. *Neurology*. 2000;54(suppl 3):A14
(The Disc Study)

Headache Therapeutic Options



- Nonpharmacologic approaches
- *Acute (abortive, symptomatic) therapy*
- Preventive therapy
- Adjunctive therapies (Vitamins, Minerals, Supplements, Herbs): Vitamin B-2, Magnesium, Feverfew, Petasites, Melatonin and Coenzyme Q 10
- Physical Techniques

Classes of Medications for Acute Treatment of Migraine



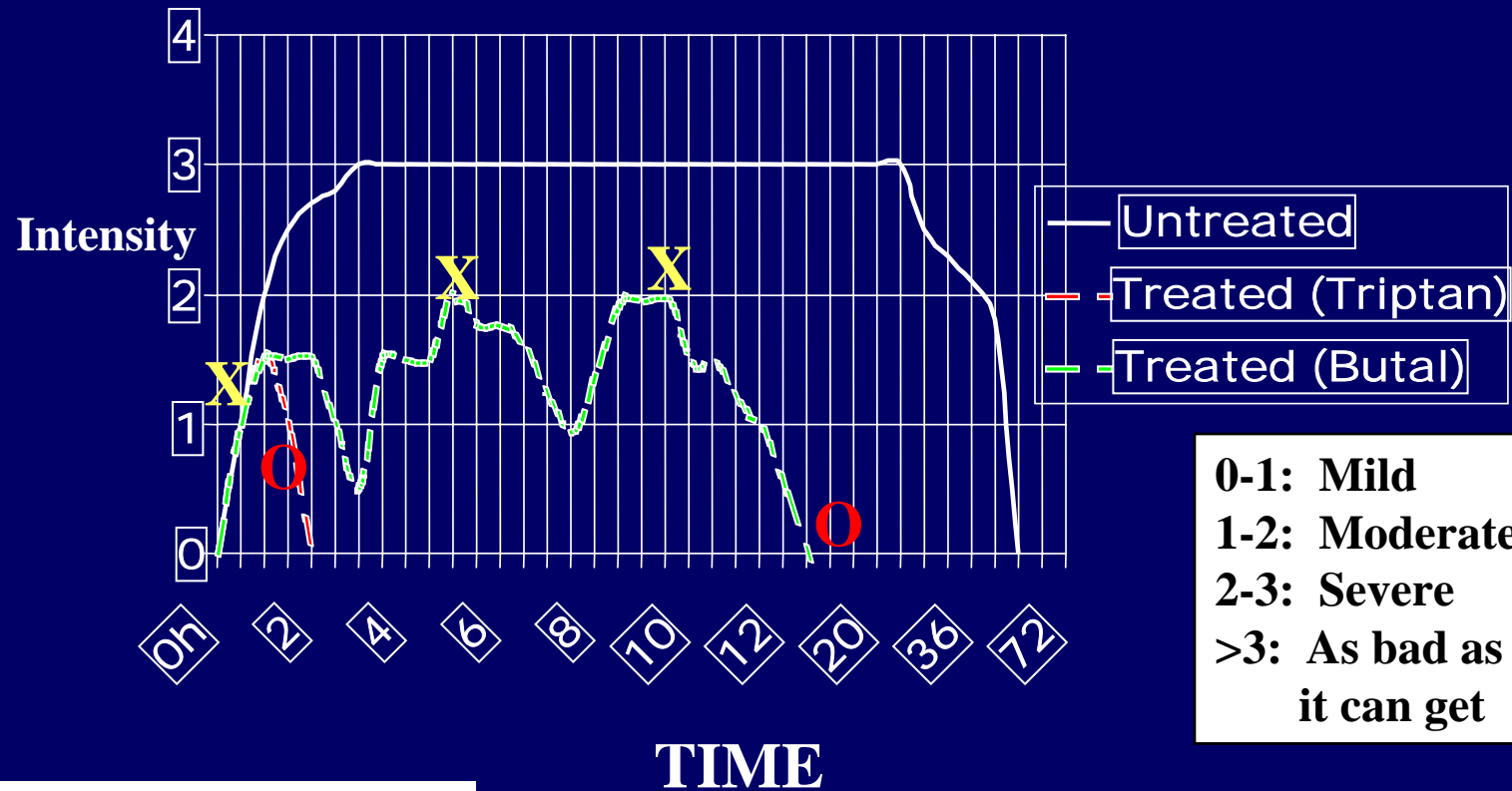
- OTC simple analgesics
- OTC NSAIDs
- OTC Combination analgesics
- Prescription NSAIDs
- Butalbital containing medications, isometheptene mucate combination medications
- Opiates and tramadol
- Antiemetics
- Steroids
- Ergots (ergotamine tartrate and DHE)
- 5-HT agonists (Triptans)

What is the Syndrome of “*Rebound Headache*” now called *Medication Overuse Headache*?



- Occurs only in patients with pre-existing chronic headache
- A self-sustaining rhythm of predictable and escalating medication use
- Headaches increase in frequency and intensity and become refractory to acute care and preventive treatments
- Medication withdrawal results in escalation of headache followed by improvement

Unique Migraine Profile of an Actual Patient at the New England Center for Headache



X = Medicates
 O=Meaningful Relief
 -Fred Sheftell, MD

Sheftell, F and Weeks, R

TRIPTANS: Routes of Delivery



Tablets

- Sumatriptan
- Zolmitriptan
- Naratriptan
- Rizatriptan
- Almotriptan
- Frovatriptan
- Eletriptan

Orally Disinteg Tabs

- Rizatriptan-**MLT**
- Zolmitriptan-**ZMT**

Suppository

- Sumatriptan (Europe)

Subcutaneous

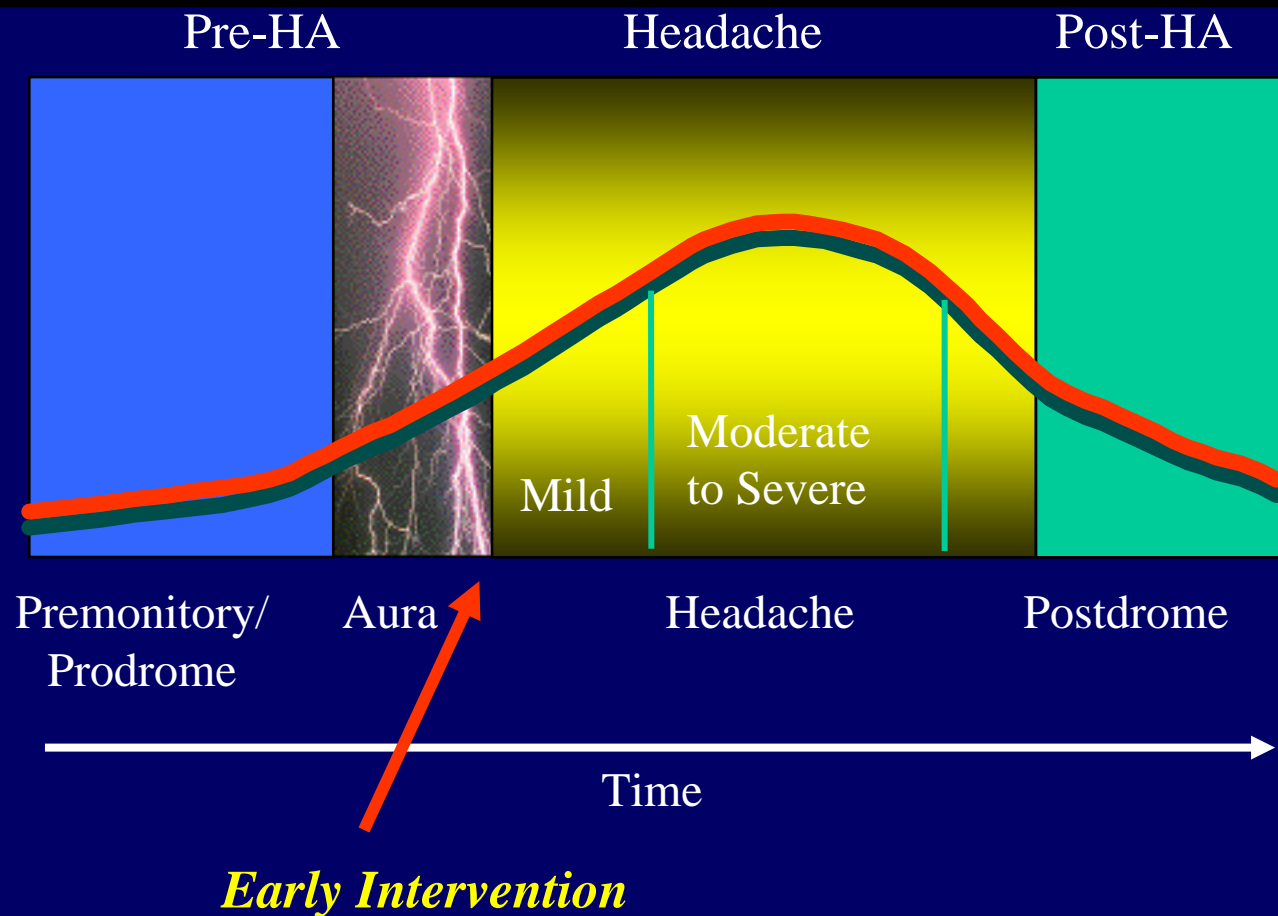
- Sumatriptan

Nasal Spray

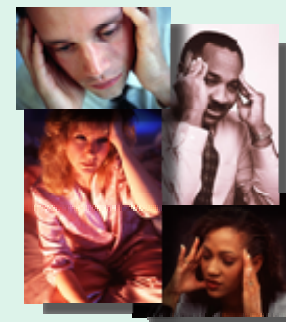
- Sumatriptan
- Zolmitriptan

Combinations

Phases of a Migraine Attack



Triptan Drug Interactions



Almotriptan Sumatriptan Rizatriptan Naratriptan Zolmitriptan Eletriptan Frovatriptan
 (AXERT®) (IMITREX®) (MAXALT®) (AMERGE®) (ZOMIG®) (RELPAX®) (FROVA®)

	Almotriptan (AXERT®)	Sumatriptan (IMITREX®)	Rizatriptan (MAXALT®)	Naratriptan (AMERGE®)	Zolmitriptan (ZOMIG®)	Eletriptan (RELPAX®)	Frovatriptan (FROVA®)
MAOI	No	Yes*	Yes*	No	Yes*	No	No
SSRI	No	Yes	No	No	No	No	No
Propranolol	No	No	Yes [†]	No	No	No	No
CYP 3A4 inhibitors	No	No	No	No	No	Yes*	No

Dahlöf CG et al. *Headache*. 2002;42:99-113.

MAOI = monoamine oxidase inhibitors., SRI = selective serotonin reuptake inhibitors.

*Contraindicated. [†]Modification to use required or may be required.

AXERT® (almotriptan malate) Tablets Prescribing Information. Imitrex (sumatriptan) Prescribing Information. Zomig (zolmitriptan) Prescribing Information. Amerge (naratriptan) Prescribing Information. Maxalt (rizatriptan) Prescribing Information. Frova (frovatriptan) Prescribing Information. Relpax (eletriptan) Prescribing Information. Association of the British Pharmaceutical Industry Medicines Compendium.

MIGRAINE MANAGEMENT



Issues at first visit

Initial Therapy

_n Recurrence

Based on attack profile,
associated symptoms
and level of disability

Back-up Therapy

If Fail

Rescue Therapy

_n Follow-up visit

If Fail

Rochelle is a banker who often awakens with headaches



Case History

- 27 year-old, married, female banker, mother of 2
- Headaches since childhood, age 13. History of asthma.
- HA frequency is 2 times/mo
- Unilateral, moderately severe, throbbing – some nausea and photophobia. Worse with bending. Often awakens at 5 am with HA.
- Pain lasts 1 – 2 days, untreated.
- Four times per year, 20 minute visual aura of colored flashing dots in either homonymous field

Rochelle is a banker who often awakens with headaches



Case History (continued)

- **Triggers: exercise, red wine, over work, menses (day #1-2)**
- **Rx: ASA/APAP/Caffeine (250/250/65) {Excedrin Migraine} (6/day), 4 d/month - mild relief**
- **Some disability, missing work 1-2 days/mo**
- **Physical, neurological and MRI examinations – nl**
- *Diagnosis ?*
- *Treatment ?*

Rochelle is a banker who often awakens with headaches



Diagnosis:

1. Migraine without aura + migraine with aura

Treatment:

1. Vitamin B2 200 mg bid.
2. Rizatriptan 10 mg taken shortly after the migraine starts. If not markedly improved in 2 hours repeat the dose.
3. If not better 1 hour later, take dexamethasone 4 mg po. May repeat in 3 hours. Use only 1-2 times per month.
4. Rescue with promethazine (Phenergan) 50 mg suppository or capsule. May also be used for nausea.
5. Could rescue with an opiate, up to 2 times per month.
6. Other options: any of the other 6 triptans, or a triptan or DHE nasal spray or a triptan + NSAID.

Techniques for Achieving Sustained Pain Free Response: *One and Done*



- **Optimal Dose of a Triptan**
- **Optimal Formulation**
- **Early Intervention, during mild pain, <30 minutes into attack**
- **Add an NSAID to the triptan to increase efficacy and decrease recurrence**

After Tepper

Optimal Migraine Treatment



Choose your favorite one of the 5 fast acting triptans (sumatriptan, zolmitriptan, rizatriptan, almotriptan or eletriptan), at maximal dose for your desired route of administration. Then instruct the patient to take the full dose within 30 minutes of the start of migraine symptoms. If there is not almost complete relief at 2 hours that dose should be taken once more.

If that does not work, the choices are usually a steroid (4 mg dexamethasone), an opiate of your choice, a sedative or sleeping pill or a visit to the ER, where parenteral medications including neuroleptics might be appropriate.

Some IV options are: prochlorperazine, metoclopramide, chlorpromazine, promethazine, diphenhydramine, valproate, magnesium sulfate, ketoralac, steroids as well as others.

Optimal Migraine Treatment



If the triptan does not work taken properly for 2 or 3 migraine attacks, or if it causes adverse events, switch to a second or even a third.

Consider adding a large dose of an NSAID to the triptan to increase effectiveness or decrease recurrence, or use a combination tablet

Do not give sumatriptan, zolmitriptan or rizatriptan to a patients on an MAO inhibitor. If the patient is on propranolol (not other beta blockers), cut the dose of rizatriptan in half. If the patient is on macrolide antibiotics, do not use DHE, ergotamine tartrate or eletriptan.

If the patient is on SSRIs you should use triptans with caution.

If the patient is a smoker or on birth control pills, avoid naratriptan. If the patient is on birth control pills or cimetidine, avoid zolmitriptan or reduce the dose. If a patient is on any of these potent CYP 3A4 inhibitors, they should not take eletriptan: ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir and nelfinavir.

Optimal Migraine Treatment



Using a **headache calendar regularly** to accurately record clinical and medicinal information will help both the patient and physician to properly track headaches, triggers, menstrual patterns, and medication usage.

The regular assessment of disability and the impact of migraine on daily life (with such disability tools as MIDAS or HIT-6), will help document the **severity of the disability** and track the response to the patient's treatment plan. Using a headache calendar over the long-term will also help identify improvement in illness severity parameters and regression of the patient's headaches.

SUMMARY OF ACUTE MIGRAINE MANAGEMENT



- ☐ Make a specific, credible diagnosis and communicate it
- ☐ Assess migraine severity and its impact on the patient
- ☐ Determine the patient's preferences and needs (e.g., fast or complete relief, no AEs)
- ☐ Identify coexistent conditions that influence therapy
- ☐ Develop a therapeutic partnership and communicate realistic expectations
- ☐ Create plan based on migraine type and severity, as well as patient's needs, preferences, and comorbidities
- ☐ Consider need for preventive treatment

Future Acute Treatments



- **Generic sumatriptan launched**
- **Suma 85 mg + Naprox Na 500 mg launched in 1 tablet**
- **CGRP Antagonists (MK-0974 {telcagepant}) + others**
- **Sumatriptan patch**
- **Sumatriptan needless injection**
- **Inhalers: prochlorperazine, loxapine and DHE**
- **AMPA/KA Antagonists (Glu Inhibitor)**
- **NOS Inhibitors**
- **Tonabersat (Gap junction blocker (preventive))**
- **Devices: DBS, ONS, PFO closure, TMS**

CGRP Antagonist

MK-0974 (telcagepant)



- **Phase III data released at the AHS in Boston on June 28, 2008**
- **Results: DB, Placebo and active controlled with zolmitriptan, multicenter trial of 1854 patients**
- **2 h headache relief: placebo 27.7%, zolmi 5 mg 56.4%, tel 150 mg 49.8%, tel 300 mg 55.0%**
- **Sustained pain free at 24 h: pl 5.0%, zolmi 5 mg 18.2%, tel 150 mg 10.7%, tel 300 mg 20.2%,**
- **AEs: zolmi > telcagepant**
- **Telcagepant is not a vasoconstrictor**

Conclusions



- **Triptans should be your first choice for patients with significant acute migraine attacks, in the absence of vascular contraindications. Consider DHE.**
- **Treat medication overuse headache first**
- **Use the Stratified Care Approach**
- **Set limits on acute care medications to 2 days per week**
- **Administer triptans early in the attack, when pain is mild, in optimal dose and formulation to maximize likelihood of a sustained pain free response**
- **Change triptan, or dose or route of administration if response is poor**
- **The addition of an NSAID, such as naproxen sodium, to a triptan at initial presentation, may increase efficacy and reduces recurrence, making a sustained pain free response even more likely**

Welcome to Philadelphia!



IHC 2009 *In Philadelphia, PA*

September 10-13, 2009

American Headache Society

Thanks for your attention!

