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"This is a description of an individual expert practitioner's approach, presented to give the learner some practical ideas. These treatment recommendations have not been endorsed by the American Headache Society® (AHS). For some of the statements and recommendations there is little formal evidence."

How Do I Do It Reference for the Acute Treatment of Migraine

Introduction

Migraine produces severe impact in the average patient complaining to their primary care provider about episodic headaches [Tepper SJ et al, 2004]. The goals of acute treatment should be consistent, rapid, and complete relief with resultant reduced disability, without headache recurrence, with little or no use of backup or rescue medications, all delivered in a cost effective manner. The key to acute treatment is stratified care, the matching of migraine-specific therapy such as triptans to patients with moderate to severe disability.

Strategies for Selecting Acute Treatment

Many practitioners continue to try stepping acute treatment for migraine, prescribing lower level treatment to all comers, and stepping up to migraine-specific treatment when non-specific therapy has failed. This strategy of step care across attacks or of stepping up intensity of treatment within attacks after initial non-specific therapy has failed and the migraine has progressed, has been shown to be inferior to stratifying acute treatment by disability [Lipton et al, 2000A]. Matching specificity of treatment to degree of disability is a superior way to select acute treatment, resulting in better patient outcomes, reduced time loss, and lower costs [Lipton et al, 2000A; Meddis et al, 2002].

A strategy for finding the right acute treatment from the beginning with a patient would involve 1) establishing a diagnosis of migraine, 2) establishing level of disability, and 3) establishing vascular suitability of the patient for a triptan or ergot as a migraine-specific treatment if disability is at least moderate to severe. Two paper tools used to evaluate level of disability are the Migraine Disability Assessment Scale (MIDAS) and the Headache Impact Test (HIT-6).

MIDAS is a 5-item questionnaire which can be summarized in a single sentence: How many days in the last 3 months were you at least 50% disabled from your migraines at work, home, school, or recreational activities? Moderate to severe disability is linked to a score >10, and in the absence of vascular contraindications, these patients would be given a triptan for their acute treatment at the first visit [Lipton et al, 2000A, 2000B]:

MIDAS QUESTIONNAIRE

INSTRUCTIONS: Please answer the following questions about ALL your headaches you have had over the last 3 months.

Write your answer in the box next to each question. Write zero if you did not do the activity in the last 3 months.

- | | DAYS |
|--|---|
| 1 On how many days in the last 3 months did you miss work or school because of your headaches? | <input style="width: 30px; height: 20px;" type="text"/> |
| 2 How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school.) | <input style="width: 30px; height: 20px;" type="text"/> |
| 3 On how many days in the last 3 months did you not do household work because of your headaches? | <input style="width: 30px; height: 20px;" type="text"/> |
| 4 How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (Do not include days you counted in question 3 where you did not do household work.) | <input style="width: 30px; height: 20px;" type="text"/> |
| 5 On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches? | <input style="width: 30px; height: 20px;" type="text"/> |
| <hr style="width: 50%; margin: 10px auto;"/> | |
| Total | <input style="width: 30px; height: 20px;" type="text"/> |
| A. On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day.) | <input style="width: 30px; height: 20px;" type="text"/> |
| B. On a scale of 0–10, on average how painful were these headaches? (Where 0 = no pain at all, and 10 = pain as bad as it can be) | <input style="width: 30px; height: 20px;" type="text"/> |

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Once you have filled in the questionnaire, add up the total number of days from questions 1–5 (ignore A and B).

Score range	Description	Grade
0 to 5	Little or infrequent disability	Grade I
6 to 10	Mild or infrequent disability	Grade II
11 to 20	Moderate disability	Grade III
>21	Severe disability	Grade IV

The HIT-6 is another paper tool with 6 domains and 6 questions to evaluate headache impact and a score of >60 suggests severe impact from migraine, suggesting a need for triptans [Kosinski et al, 2003]:

HIT-6™
(VERSION 1.0)

This questionnaire was designed to help you describe and communicate the way you feel and what you cannot do because of headaches.
To complete, please circle one answer for each question.

HEADACHE
IMPACT TEST™

1 When you have headaches, how often is the pain severe?

Never Rarely Sometimes Very Often Always

2 How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?

Never Rarely Sometimes Very Often Always

3 When you have a headache, how often do you wish you could lie down?

Never Rarely Sometimes Very Often Always

4 In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?

Never Rarely Sometimes Very Often Always

5 In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?

Never Rarely Sometimes Very Often Always

6 In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

Never Rarely Sometimes Very Often Always

▼ + ▼ + ▼ + ▼ + ▼

COLUMN 1 (6 points each) COLUMN 2 (8 points each) COLUMN 3 (10 points each) COLUMN 4 (11 points each) COLUMN 5 (13 points each)

To score, add points for answers in each column. **Total Score**

Please share your HIT-6 results with your doctor. Higher scores indicate greater impact on your life.

Score range is 36-78.

Thus, migraine disability is a surrogate marker for disease severity, and when impact is moderate to high, triptans should be used for acute treatment of migraine in the absence of vascular contraindications. Use of non-specific treatment in the face of disabling headache leads to overuse and transformation into daily headache, medication overuse headache, or rebound. This is especially true of butalbital containing compounds and opioids, so these should be avoided as acute treatment in migraine patients.

Selecting the Right Triptan

Triptans can be chosen via the 3 F's, Fast versus Slow, Formulation, and Formulary tier and availability [Kaniecki R, personal communication]. Only two triptans are available in multiple formulations: zolmitriptan as a nasal spray and

tablet; sumatriptan as a nasal spray, subcutaneous injection, tablet, and tablet with naproxen sodium. The other triptans are all available as tablets. Oral triptans can be divided into two groups, fast onset with higher efficacy at 2 hours, and slower onset with lower response rates at 2 hours.

Triptans

Group 1	Fast Onset
Triptans	
Generic Name	Brand Name, US, (global)
Sumatriptan 25, 50, 100* mg tabs 20 mg nasal spray 6 mg subcu 4mg subcu	Imitrex, (Imigran)
Zolmitriptan 2.5, 5 mg tablet 2.5,5 mg orally dissolvable tablet 5 mg nasal spray	Zomig, (AscoTop, Zomigon)
Rizatriptan 5, 10* mg tablet, orally dissolvable tablet	Maxalt
Almotriptan 6.25, 12.5* mg tablet	Axert, (Almogran)
Eletriptan 20, 40* mg tablet	Relpax
Group 2	Slower Onset
Triptans	
Naratriptan 1.25, 2.5* mg tablet	Amerge, (Naramig)
Frovatriptan 2.5 mg tablet	Frova

*Optimal dose

Adapted from Tepper, 2006

The pace of the migraine clinical course determines the choice of triptan. If a patient suffers from a fast onset, use a Group I triptan. If the patient vomits, select a non-oral formulation (nasal or subcutaneous) for use in at least those attacks. After deciding on the triptan group and formulation, find out the formulary tier status and choose the lowest tier co-pay for that patient's insurance.

Another alternative to a triptan is the use of dihydroergotamine (DHE), available parenterally and by nasal spray (brand name Migranal). DHE has a slower onset, similar to the Group 2 triptans, but a low recurrence rate, similar to naratriptan.

Instructing the Patient

Triptans work best early in an attack, when the pain is mild. The likelihood of a pain free response, without recurrence is linked to early intervention with treatment.

In patients with a frequency of headache days < 10 days/month, patients should be instructed to take their triptans earlier than early, when the pain is mild, preferably in the first 30 minutes of the attack, to reduce likelihood of recurrence in the next 24 hours.

For those patients who are taking the triptan early but still suffering frequent recurrence, the addition of an NSAID to the triptan can increase the likelihood of a pain free response, and reduce the likelihood of recurrence. This can be accomplished with a fixed dose triptan/NSAID such as sumatriptan/naproxen sodium (Brand name Treximet) or by prescribing both a triptan and an NSAID for that patient. Another alternative to reduce recurrence is a switch from triptan to DHE.

Non-specific Acute Migraine Treatment

Evidence for effectiveness of non-specific medications for migraine is varied. These medications include: non-steroidal anti-inflammatories (NSAIDs) or their derivatives, aspirin (ASA), acetaminophen (APAP), or combinations of them with or without caffeine, opioids, butalbital, or isometheptene, and classes such as antihistamines, anti-nauseants, anti-epilepsy drugs (AEDs), or muscle relaxants.

ASA-APAP-caffeine (AAC) mixtures are FDA-approved for migraine based on a randomized controlled trial (RCT) in AAC was superior to placebo for pain relief and associated symptoms up to 6 hours post-dose for a pre-selected, less disabled group of migraine [Lipton et al, 1998; Goldstein et al, 1999]. NSAIDs (naproxen, diclofenac, and solubilized ibuprofen) have also been superior to placebo in RCTs, with ibuprofen also tested in less severe migraine subjects. [Kellstein et al, 2000; Limmroth et al, 2000; Krymchantowski and Tepper, 2005]. The US Headache Consortium states the NSAIDs and AAC can be effective for

moderate migraine [Silberstein et al, 2000; Matchar et al, 2000], but the evidence for these non-specific medications is not as powerful as that for triptans, since the latter were tested on all migraine patients, including the most severely afflicted

Evidence for opioid use in acute migraine is generally poor or negative [Silberstein and McCrory, 2000]. The US Headache Consortium states: "Oral opioid combinations may be considered when sedation will not put the patient at risk and/or the risk for abuse has been addressed." [Silberstein et al, 2000; Matchar et al, 2000].

There is no positive evidence via RCTs for butalbital mixtures in the acute treatment of migraine. Because of lack of evidence for efficacy and excessive risk of habituation and dependence, butalbital mixtures are not available in most countries of the world. Dr. Marcelo Bigal presented data published in abstract form in 2008 from the American Migraine Prevalence and Prevention population-based study suggesting that episodic use of butalbital as infrequently as 5 days/month was linked to transformation into chronic daily headache and medication overuse headache or rebound [Bigal et al, 2008].

The best advice clinically is not to prescribe opioids or butalbital for acute treatment of migraine, and not to use non-specific treatment in patients with disabling migraine.

Rescue medications

Opioids prevent migraine-specific medications from reversing central sensitization, and therefore should not be used for acute treatment of migraine, for rescue in outpatients, or in the ER for treatment [Jakubowski et al, 2005]. When simpler measures have failed and a patient is in status migrainosus, three outpatient approaches that we use are subcutaneous sumatriptan, repetitive DHE nasal spray, or a brief several-day course of steroids, such as dexamethasone until the patient is 24 hours headache-free. Some specialists also use repetitive triptans or repetitive methylergonovine (brand name Methergine), a long-acting ergot, to break migraine as an outpatient.

In the clinic or emergency department, a variety of IM or IV treatments can be used together or separately, as one treatment, or in repetitive infusions. Remember to check for pregnancy, and not to mix triptans and ergots the same day. We mix and match parenteral rescues from a list including DHE, sumatriptan, neuroleptics (metoclopramide, promethazine, prochlorperazine), ketorolac, dexamethasone, valproate, and other anti-nauseants (hydroxyzine, ondansetron, granisetron, dolasetron).

Following the Outcomes

All patients should be given a headache diary to fill out to document when they treated, response, recurrence, and frequency of use. An outcome paper tool, Migraine-ACT, can evaluate whether or not to switch acute treatment and consists of 4 yes/no questions in 4 domains:

- Consistency of response: *Does your migraine medication work consistently, in the majority of your attacks?*
- Global assessment of relief: *Does the headache pain disappear within 2 hours?*
- Impact: *Are you able to function normally within 2 hours?*
- Emotional response: *Are you comfortable enough with your medication to be able to plan your daily activities?*

One or more 'no' answers may indicate the need to change treatment. An increasing number of 'no' answers indicates increasing treatment needs, and each "yes" counts as "1". A Migraine-ACT score of ≤ 2 suggests a need to consider changing the patient's acute medication [Dowson et al, 2004; Kilminster et al, 2006]. The diary allows the clinician to evaluate outcomes, and to count the number of acute treatment days per month. Acute treatment days should be kept to < 10 days/month to avoid transformation into medication overuse headache and chronic daily headache. When acute treatment days reach 10 days/month, daily preventive medication should be added to reduce frequency of attacks.

Conclusions

- Establish a clear diagnosis of episodic migraine, and establish the level of disability or impact.
- Evaluate vascular risk factors.
- Use triptans or DHE as first line acute medications in patients with disabling migraine in the absence of vascular contraindications.
- Advise patients with episodic migraine to take the triptan early in the attack, when pain is mild, in the first 30 minutes of the attack.
- Add an NSAIDs (in the absence of contraindications) to the triptan if recurrence or inadequate pain-free response occurs.
- Avoid non-specific medications in patients with disabling migraine to avoid transformation into daily headache. Do not use opioids or butalbital in migraine patients.
- Follow with a diary and Migraine-ACT, and keep acute treatment days to < 10 days/month. Add prevention if acute days exceed 10 days per month.

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