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Abstract Effective acute treatment of headache begins with making an accurate diagnosis and ruling out secondary causes of headache. Once a primary headache is diagnosed, it is important to choose the right combination of behavioural therapy and acute care (abortive and symptomatic) therapy for each patient. Some patients may need preventive medication on a daily basis. If patients overuse acute medications and develop medication overuse headache (previously called analgesic rebound headache), they often seek medical attention due to the chronicity and/or intensity of their pain and resultant disability. For acute care

of migraine, physicians should choose a triptan they know and expect to work. They should prescribe the dose and route of administration that will provide the most rapid and complete response to all the associated symptoms of migraine, in addition to the pain. The effectiveness of the 7 available triptans in early, double-blind, controlled trials is more similar than different. How and when to give them will be discussed. Treatment of cluster headache will be presented briefly.

Keywords Headache • Treatment • Acute care

Introduction

Effective treatment of headache begins with a proper evaluation of the patient to rule out secondary causes of headache. This is done by taking a careful history, doing a complete physical and neurological examination, and performing blood tests and scans when appropriate [1]. Then accurate diagnosis of primary headache disorders and choice of the right combination of behavioural therapy, acute care (abortive and symptomatic) therapy and preventive pharmacotherapy can proceed.

Establishing a close therapeutic partnership with the patient and then educating them about probable patho-

physiology and the various treatment strategies and trigger avoidance is essential. The physician must be aware of the specific headache characteristics he/she is treating, the degree of disability the patient is experiencing and the patient's preferences for treatment. It is also important to know why the patients have come to see you. Some patients visit the specialist to obtain a diagnosis or to be certain they do not have a brain tumour, and others want effective treatment. Some prefer treatments that work quickly, others treatments that work completely or consistently and still others treatments that do not cause any adverse effects. Goals should be discussed and therapeutic strategies planned. Expectations should be put in proper perspective.

Mild headaches are often treated with over-the-counter (OTC) medication by patients who never come to the doctor. When headaches become more severe and frequent or if patients overuse these non-specific medications and develop medication overuse headache (MOH) (previously called analgesic rebound headache), they often seek medical attention due to the chronicity and/or intensity of their pain and resultant disability. Doctors sometimes inadvertently cause the patient to develop MOH. Some patients are put on large amounts of prescription NSAIDs, butalbital-containing medication (in certain countries like the USA) and various simple and combination analgesics by their primary care physicians or nurse practitioners, often with limited effectiveness, or actual worsening and adverse effects.

Headache specialists shun *step care therapies* and usually opt for *stratified care*, treating with the correct medication (usually a triptan) the first time. Although there are some patients with frequent headaches that can take acute care analgesics and NSAIDs up to 2 days/week, and triptans for their more severe migraine attacks, this type of regimen often prevents significant improvement as the patient medicates too frequently. Physicians first need to assess and treat for overuse of analgesics or triptans, and then institute effective triptan and possibly preventive therapy.

Physicians should choose a triptan they know the best and expect to work in a given headache situation and should prescribe the dose and route of administration that will provide the most rapid and complete response to all the associated symptoms of migraine, in addition to the pain. If the original triptan chosen is not effective, the dose or route of administration can be changed, the patient can be encouraged to treat attacks earlier, another triptan can be tried or other medications, such as NSAIDs, steroids and anti-emetics can be added to the triptan.

There are 7 triptans tablets available in the USA as well as 2 nasal sprays, 2 oral disintegrating tablets (ODTs) and an injection. Their effectiveness in the early published controlled trials is well documented. The most common endpoint used for many years has been 2-h headache relief; although today we also like to look at 2-h pain freedom, especially if the patient is instructed to take their triptan early in the course of the migraine attack, when the headache is often milder. Clinically, the triptans are more similar than they are different. Dihydroergotamine is often effective as an injection or nasal spray when available. Other acute care treatments will be mentioned.

Cluster headache treatment will be discussed briefly.

The knowledgeable headache physician should be able to find effective treatment for most acute headache attacks.

General principles of acute care

- Proper treatment begins with accurate diagnosis of all headache types.
- A therapeutic partnership between you and the patient is important.
- Patient education and behavioural management techniques are vital.
 - Teach strategies for identifying triggers of headache.
 - Urge the patient to avoid their triggers when possible.
 - Strive for regular and adequate sleep, eating and exercise routines.
 - Arrange for behavioural medicine techniques (stress management, relaxation techniques and biofeedback).
 - Prescribe psychological evaluation and therapy when appropriate.
- Patients should be taught to participate in their own care.
- Those looking for a magic bullet often do not do that well.
- Patients with an inner locus of control that take over and try to help themselves will have a better outcome.

There are various strategies to keep in mind as you evaluate a patient for therapy. You need a lot of previous history on treatment that has already occurred.

- You must review past treatments.
 - What has been successful?
 - If a medication did not work, was the dose correct?
 - Was it given early in the attack?
 - Did it cause adverse events, and what were they?
- The attack frequency determines the treatment plan.
- Think about treating the “entire” migraine complex, not just the headache.
- Treatment needs to encompass pain relief *and* associated symptoms.
- Specifically ask the patient about their degree of *disability*.
- Consider co-morbid and co-occurring conditions and treat them.

In your history, obtain information about co-morbid illnesses that may affect headache, as these have to be treated as well. Some of the more common ones are:

- Raynaud’s disease,
- mitral valve prolapse,
- stroke at a young age,
- patent foramen ovale (PFO),
- epilepsy,
- depression,

- anxiety/panic disorder,
- bipolar disease,
- irritable bowel syndrome.

Each patient has different expectations of a migraine medication, and what one patient wants may be quite different from another. Ideally, patients would like to get completely better quickly and get back to their usual activities, without recurrence or adverse events. Here are the goals we should expect from any good acute care medication:

- Treat attacks rapidly and consistently without recurrence eventuating in a *pain-free state*.
- Restore the patient's ability to function.
- Prevent adverse events.
- Minimise the use of rescue and back-up medications.
- Optimise self-care and reduce resource utilisation.
- Be cost-effective.

How can we measure the effectiveness of our treatment? There are many scales and endpoints that we can utilise, such as:

- a new better goal: pain free at 2 h with 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; and
- level of patient satisfaction.

When someone comes to your office or clinic, what are the therapeutic options that you have? I like to consider five general categories of treatment:

- non-pharmacologic approaches (behavioural medicine techniques),
- acute therapy (abortive, symptomatic),
- preventive therapy, on a daily basis,
- adjunctive therapies (vitamins, minerals, supplements, herbs): vitamin B-2, magnesium, feverfew, petasites, melatonin and coenzyme Q 10,
- physical techniques (manipulation, acupuncture, physical therapy).

Some mild headaches will not be migraine and can be treated with non-triptans, as long as they respond. Even some mild migraine attacks can be treated with non-triptans, especially if there are frequent headaches. Here are the types of medication that have been found to be effective in certain patients:

- OTC simple analgesics (aspirin and paracetamol),
- combination analgesics (often containing caffeine),
- non-steroidal anti-inflammatory medications (NSAIDs),

- butalbital-containing medications in the USA and a few other countries,
- isometheptene containing combination products,
- other combination medications (usually sinus medications),
- anti-emetics,
- opiates,
- steroids,
- ergots (ergotamine tartrate and dihydroergotamine [DHE]), and
- 5-HT agonists (triptans).

When you first see a patient with migraine, you should choose a triptan and the best formulation for that patient. Your choice will depend on the characteristics of a typical attack, including intensity of pain, time to reach peak intensity, associated symptoms such as nausea and vomiting and degree of disability. You should provide a back-up medication in case the triptan you prescribe does not work. You should also prescribe a rescue medication in case the back-up plan does not work.

Even before you choose a triptan, you should determine if the patient has MOH, either from OTC medication or prescription drugs. The specific medications that are taken in excess have changed over the last 15 years [2]. Over 60% of patients at a US tertiary care headache centre overuse acute care medications. The most common today are triptans and a combination of acute analgesic medications. If MOH is present, the first step is detoxification. Not taking this into consideration may cause your acute care medication, and even preventive therapy from working optimally. Some facts about MOH (which we used to call analgesic rebound headache) are that it:

- Occurs only in patients with a pre-existing, chronic headache syndrome.
- Causes a self-sustaining rhythm of predictable and escalating medication use.
- Causes headaches to increase in frequency and intensity and become refractory to acute care and preventive treatments.
- Often results in escalation of headache followed by improvement when the patient is withdrawn from the offending medication.

Early intervention is critical in treatment with triptans. When triptans are given, the patient should be told to take them early in the course of the migraine attack, when the headache is mild to moderate in intensity [3]. This usually helps them to work better. If the patient waits till the headache progresses, and central sensitisation sets into the brainstem, triptans are often less effective in up to 80% of patients [4]. Early treatment means at the very start of a migraine attack. Some patients are not sure when a

headache starts if it will turn into a migraine attack. In that case, I tell them to take the triptan as soon as their headache begins to escalate. If they have only a few migraines per month, and no mild headache, then I tell them to medicate as soon as they develop any type of headache. Some doctors will let patients take a triptan tablet during a visual aura under certain conditions (the patients always has a headache following the aura and the aura only lasts for 20 min). In that situation, I tell patients to use their triptan tablets 5 min into the aura. As it takes about 30 min for the triptan to reach adequate concentrations in the brain, the headache will start just before the triptan starts to work. But do not give a nasal spray or injection of a triptan during an aura, as it may get to the brain too quickly, before the headache begins, and then it may not be effective.

There are 7 triptans in the USA and most of them are available in various countries. There are at least 3 countries that have generic sumatriptan (Brazil, Canada and the UK). These are the triptans and their modes of delivery:

Tablets

- sumatriptan
- zolmitriptan
- naratriptan
- rizatriptan
- almotriptan
- frovatriptan
- eletriptan

“Fast-melt” tablets or ODT

- rizatriptan-MLT
- zolmitriptan-ZMT

Suppository

- sumatriptan (Europe)

Subcutaneous injection

- sumatriptan

Nasal spray

- sumatriptan
- zolmitriptan

The pharmacokinetics of the triptans varies considerably from one to another. However it has never been adequately determined what PK characteristics produce the most beneficial clinical effects. A short T_{max} might produce a quicker start to efficacy or a long half-life might increase the length of effect of a triptan, but these facts have not been proven.

Some techniques for attaining optimal results with the best sustained pain-free effects are:

- Use the optimal dose of triptan in the optimal formulation for that patient.
- Use early intervention, and treat when the pain is mild, no more than 30 min into a migraine attack.
- Add an NSAID to the triptan to improve efficacy and decrease recurrence.
- Set limits on the number of days per week, on average, that your patients use triptans or any other acute care medication. My upper limit is an average of 2 days/week for acute care medications. That will not usually cause MOH or increase the frequency of attacks.

After choosing a triptan, have the patient treat at least two or three attacks before judging its effectiveness. Review outcome measures with the patient to see if the triptan is working properly. Having the patient keep a diary or calendar is essential to getting accurate reporting from the patient. You should assess efficacy, adverse events, speed of onset, completeness of response, recurrence and patient satisfaction with the current regimen, to determine if the triptan is working optimally or needs to be changed. Each patient may prefer their own goals for improvement, some wanting quick relief and others wanted long-lasting relief or no adverse events [5]. If the treatment is not working, consider:

- choice of drug,
- choice of dose or route of administration,
- need for adjunct therapy,
- presence of interfering medication or medication overuse, and
- incorrect diagnosis.

The range of efficacy of the triptans is wide. Although some consistently seem to work better than others in head to head studies, there is probably one triptan that is best for each patient. The only way to tell if the triptan a patient is using is optimal is to ask questions about how it works when the patient comes in to the office. Typical questions are: In how many minutes does the triptan start to work? When does it reach its maximum effect? What percentage of the headache goes away? Does the headache recur after it is gone? Are there any significant adverse events? If the answers do not indicate optimal efficacy with few adverse events, then another triptan should be tried.

Cluster headache often responds well to specific acute care medications such as:

- 100% oxygen inhalation at 7–10 l/min (up to 15 l/min if refractory);
- sumatriptan 6 mg sc at headache onset;
- zolmitriptan 10 mg tablet or 5 mg nasal spray;
- DHE 0.5–1.0 mg by injection or 2 mg by nasal spray;
- ergotamine tartrate orally or rectally;

- lidocaine 4–6% nasal drops at headache onset;
- intranasal capsaicin or the z isomer civamide.

In conclusion, the acute care of migraine and cluster headache can be very effective and patients are often able to control their headaches when they occur. Here are some concluding suggestions to help your patients achieve optimal therapy:

- Triptans should be your first acute care choice for disabling migraine attacks, in the absence of vascular and other contraindications.
- Treat MOH first, before using triptans.
- Use a stratified care approach, and give the right treatment the first time.
- Set limits on acute care medications. I suggest only 2 days/week.
- Administer triptans early in the attack, when pain is mild, in an optimal formulation to maximise likelihood of a sustained, pain-free response.
- Change triptan or route of administration if response is poor.
- The addition of an NSAID, such as naproxen sodium, to the triptan at initial presentation, both increases efficacy and reduces recurrence, making a sustained pain-free response even more likely.
- Triptans are more similar than different, but there may be one triptan or formulation of that triptan which is the best for each patient.

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