Centre for Sustainable Delivery

NHS SCOTLAND

Modernising Patient Pathways Programme:

Acute treatment of Migraine in Primary Care

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Background

- Acute management of migraine in primary care should be based on SIGN guideline 155.
- Acute treatment of migraine is most effective when instituted early in an attack.
- Acute treatment should be limited to 8-10 days per month to prevent the development of Medication Overuse Headache
- Acute treatment can be stepped or stratified. In a stepped strategy, patients try an initial treatment, e.g. Aspirin 900mg, for 3 headaches before moving to a triptan if ineffective. In a stratified strategy patients chose the correct treatment for each individual attack, e.g. Aspirin 900mg for mild to moderate headache and a triptan for moderate to severe headache.
- Combinations of acute treatments can be helpful if individual treatments are not adequately effective e.g. Aspirin or NSAID + Triptan, Aspirin or NSAID + antiemetic, Aspirin or NSAID + anti-emetic + triptan.

Pathway recommendations

Limit acute treatment to less than 10 days per month (on average 2 days per week) to prevent development of Medication Overuse Headache

Mild to Moderate Attacks

- Consider NSAID such as
    - Aspirin 900mg or
    - Ibuprofen 400mg to 600mg
    - Alternatives include naproxen 500mg or diclofenac 75mg
- If NSAIDs are contra-indicated, or not tolerated, consider paracetamol 1000mg orally (doses may need to be adjusted in patients weighing <50kg). Paracetamol can also be taken alongside aspirin or an NSAID as a combination treatment.
- For patients with an inadequate response and /or nausea / vomiting consider
    - addition of an anti-emetic e.g metoclopramide 10mg orally, or prochlorperazine 10mg orally (independent effect on headache in addition to effect on nausea / vomiting)
- Opioids should not be used, as their use poses a risk of medication overuse headache

Moderate to Severe Attacks

- Consider a triptan if no contra-indication. We recommend sumatriptan 50-100mg orally, as the first line therapy (see attached notes on triptans)
    - A triptan is considered effective if it reduces migraine in 3 out of 4 attacks.

- If a particular triptan is ineffective, consider EITHER
    - an alternative triptan for future attacks (response to triptans is variable and people who fail to respond to one can try another), OR
    - the combination of a triptan and antiementic e.g. metoclopramide 10mg orally, or prochlorperazine 10mg orally (independent effect on headache in addition to effect on nausea / vomiting) AND / OR
    - the combination of a triptan and NSAID. The best evidence for combined therapy is for naproxen 500mg with oral sumatriptan, but any NSAID / triptan combination, including aspirin / triptan, can be considered
- For patients with nausea and / or vomiting consider
    - addition of an anti-emetic e.g. metoclopramide 10mg orally, or prochlorperazine 10mg orally AND / OR
    - use of an alternative triptan that is non-oral, such as nasal zolmitriptan 5mg or subcutaneous sumatriptan 6mg
    - use of an alternative NSAID that is non-oral such as diclofenac 75mg given once by intramusclular injection, can be considered as an alternative to either an oral NSAID or aspirin
- Triptan non-responders / contraindications
    - Consider rimegepant in patients who have had inadequate relief to trials of at least 2 triptans and timing (take triptan early in headache), correct route of administration and combination treatment has been considered
    - Consider rimegepant where triptans are contraindicated (see triptan contraindications below)
- Opioids should <u>not</u> be used, as their use poses a risk of medication overuse headache

Triptans

Please consider a prescription of a triptan, as per BNF. As a first option we recommend sumatriptan 50mg-100mg orally, as per SIGN 155.

Types of triptan: There are seven different triptans – almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan. Response to different triptans is variable, and people who fail to respond to one triptan may respond to another. Therefore, if the patient does not respond to one triptan after use in three separate attacks, consider an alternative triptan. It can be worth trying triptans in sequence to find the most suitable of any individual patient. Note that naratriptan and frovatriptan have a slower onset but a longer half-life (approximately 5-6h for naratriptan; 25h for frovatriptan) and are therefore useful if patients describe recurrence of headache with a shorter acting triptan. All preparations come in tablet form. Sumatriptan also comes as a subcutaneous injection, sumatriptan and zolmitriptan come in nasal spray preparations (useful if prominent nausea) and rizatriptan and zolmitriptan also come in an orodispersible (melt) preparation.

Adverse effects: Patients should be warned that triptan sensations and / or sedation may occur. Symptoms may include tightness in the jaw, throat, or chest, or pins and needles in the face.

Cautions and contraindications: Triptans are contraindicated in coronary heart disease, peripheral vascular disease, or those with a history of stroke, and are cautioned in those with Raynaud's phenomenon. They should not be used in patients with a history or moderate or severe hypertension. Do not prescribe if blood pressure measurements are consistently above 140/90mmHg. While triptans are not licensed for adults greater than 65 years, there is no reason they can't be used. Vascular risk factors are more common and should be actively looked for in this age group.

How to Take Triptans: Triptans should be taken at the onset of the headache pain, as they are more effective when taken early in an attack. Treatment frequency should be limited to two days per week (up to 2 doses can still be taken in any one day if needed) – more frequent use can result in medication overuse headache. If the first dose is ineffective, a second dose should not be taken for the same attack. If there is response to the first dose, but symptoms recur, a second dose may be taken provided there is a minimum of 2 hours between doses of almotriptan, eletriptan, frovatriptan, rizatriptan, sumatriptan, zolmitriptan, and 4 hours between doses for naratriptan.

Drug Interactions (not exhaustive)

Triptans should not be combined with monoamine oxidase inhibitors.

Triptans are not contra-indicated with Selective Serotonin Reuptake Inhibitors (SSRIs).

In patients taking propranolol, limit rizatriptan to the 5mg dose, and ensure a minimum separation of 2h between taking propranolol and rizatriptan. No more than 2 doses of rizatriptan should be taken in a 24h period.

Please check BNF for drug interactions in those taking antibiotics, antifungal agents, cimetidine, antiretroviral agents, and verapamil – interactions vary between triptans.

Although all UK summary of product characteristics caution against the concomitant use of triptans and selective serotonin reuptake inhibitor (SSRI) / serotonin – norepinephrine reuptake inhibitor (SNRI) anti-depressants due to the risk of serotonin syndrome, in practice this combination can be taken safely in most patients. It is the opinion of the authors that this combination is not contra-indicated. Nonetheless, patients should be monitored for signs of serotonin syndrome if this combination is used.

Gepants (CGRP antagonists)

Rimegepant is an oral selective calcitonin gene-related peptide (CGRP) receptor antagonist. It is thought to relieve migraine by blocking CGRP-induced neurogenic vasodilation, returning dilated intracranial arteries to normal by halting the cascade of CGRP-induced neurogenic inflammation which leads to peripheral and central sensitisation and / or by inhibiting the central relay of pain signals from the trigeminal nerve to the caudal trigeminal nucleus.

For patients who have not responded to adequate trials of at least 2 triptans or triptans are contraindicated then Rimegepant 75mg can be considered.

The maximum dose is 75mg per day. If also on a CYP3A4 inhibitor (e.g., clarithromycin, itraconazole, ritonavir) then a second dose should be delayed for 48 hours. Rimegepant is generally well tolerated. Nausea is the main adverse effect. Hypersensitivity reactions have been reported but are uncommon occurring in <1%.

Before Rimegepant is considered patients should have had an adequate trial of at least 2 triptans unless contra-indicated

- Ensure triptan has been taken early in the headache phase
- Ensure mode of administration is correct, e.g. use nasal or subcutaneous in patients with early vomiting
- Consider combination treatment as detailed above

The European Headache Federation (EHF) consensus on the definition of effective treatment of a migraine attack by a triptan is adequate symptom relief in 3 out of 4 headaches. Triptan resistance as inadequate symptom relief after trials of at least two triptans, and triptan refractory is inadequate symptom relief after trials of at least three triptans.

Treatment of a prolonged migraine attack

Ensure adequate hydration

For patients in whom oral preparations have been ineffective, parenteral NSAIDs (such as intramuscular diclofenac 75mg) or subcutaneous sumatriptan 6mg should be considered.

Evidence also supports the use of parenteral antiemetics (intramuscular metoclopramide 10mg or prochlorperazine 10mg).

Opioids have not been shown to be significantly effective and should not be used.

Most patients should be able to be managed in the community. For patients, in whom standard treatment has not been effective and migraine is persisting, who attend the Emergency Department or are admitted to hospital, the following additional measures should be considered:

1. Ensure adequate hydration (consider iv saline)
2. Iv / im antiemetic with metoclopramide 10mg or prochlorperazine 10mg (both anti-emetic and analgesic) if not already administered in the community
3. 6mg sc Sumatriptan (if the patient has already had an oral triptan this should be delayed to at least 2 hours after the oral dose) if not already administered in the community
4. Consider 1g iv Aspirin or 1g iv Paracetamol if sc Sumatriptan ineffective or contraindicated (may require admission to a medical ward), 75 mg im Diclofenac is an alternative in ED if not already administered in the community.

References and further resources

SIGN 155 Pharmacological management of migraine – updated March 2023; includes clinician and patient guidelines

url: Pharmacological management of migraine (sign.ac.uk)

British Association for the Study of Headache (BASH) National Management System 2019; includes clinician and patient portals

url: Headache UK

Sacco et al. The European Headache Federation (EHF) consensus on the definition of effective treatment of a migraine attack and of triptan failure. The Journal of Headache and Pain (2022) 23:133)

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