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# Adult Acute Migraine Pain Protocol

#ListenToPain

PM-BH-NOBR-24-00013

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# ADULT ACUTE MIGRAINE PAIN PROTOCOL

## STEP 1: ASSESS MIGRAINE HEADACHE

### ASK THE PATIENT ABOUT MIGRAINE HEADACHE SYMPTOMS[1,2]

| Pulsatile quality of headache | Duration of headache (4 to 72 hours if untreated) | Unilateral headache | Nausea or vomiting | Disabling intensity of headache |
|---|---|---|---|---|

### IDENTIFY SYMPTOMS OR CIRCUMSTANCES REQUIRING REFERRAL[1,2]

- Change in established headache pattern or "the worst headache ever"
- New onset after 50 years of age
- Progressively increasing severity
- Symptoms of systemic disorders (e.g., fever, hypertension, myalgia, weight loss)

- "Thunderclap" headache (maximum severity at onset)
- Neurologic signs or seizures
- Neck stiffness
- Headache aggravated by postures

## STEP 2: IDENTIFY TREATMENT CONSIDERATIONS

### IDENTIFY ANY CONDITIONS OR MEDICATIONS LIMITING TREATMENT OPTIONS

| Medications limiting treatment[2-5] | Medical conditions limiting treatment[3,6-9] |
|---|---|
| • NSAIDs* – risk of bleeding, decreased antihypertensive efficacy, increased drug levels of medicines like methotrexate<br>• Paracetamol: Increased risk of paracetamol toxicity<br>• Triptans - Contraindicated in cardiovascular or cerebrovascular disease, uncontrolled hypertension and specific migraine syndromes. | • Chronic kidney disease<br>• Liver disease<br>• Peptic ulcer disease<br>• Cardiovascular disease<br>• Cerebrovascular Disease |

*NSAIDs, non-steroidal anti-inflammatory drugs; * With oral NSAIDs only*

### IDENTIFY WHAT THE PATIENT HAS USED IN THE PAST TO TREAT MIGRAINE HEADACHE

## STEP 3: RECOMMEND TREATMENT

### DOES THE PATIENT HAVE ANY PREFERENCE FOR TREATMENT BASED ON WHAT WAS USED IN THE PAST?

**IF YES**

Recommend non-pharmacological treatment[10]

- Using a diary for identifying important migraine triggers
- Good sleep hygiene practices
- Dietary lifestyle modifications
- Regular and moderate exercise
- Stress management
- Weight reduction to restore an ideal body weight
- Patient education

**IF NO**

Recommend non-pharmacological treatment[10]

- Using a diary for identifying important migraine triggers
- Good sleep hygiene practices
- Dietary lifestyle modifications
- Regular and moderate exercise
- Stress management
- Weight reduction to restore an ideal body weight
- Patient education

STEP 3: RECOMMEND TREATMENT CONT.

# ADULT MIGRAINE PROTOCOL

## STEP 3: RECOMMEND TREATMENT (CONT.)

**AND**

Recommend the PATIENT's preference if possible, taking into consideration step 2

**AND**

Recommend appropriate acute migraine treatment[1,2]

- **First-line medications:**
  - Aspirin 900–1000 mg
  - Ibuprofen 400 - 600 mg
  - Diclofenac 50 mg oral (soluble)
  - Paracetamol 1000 mg (for patients intolerant to NSAIDs)
- **Second-line medications:**
  - Triptans (Sumatriptan, Zolmitriptan)
- **Third-line medications:**
  - Ditans (Lasmiditan) or gepants (Ubrogepant)
- **Combination therapy:**
  - Paracetamol + aspirin + caffeine (in patients with contraindications to vasoconstrictors like Triptans))
- **Adjunct medications for patients who experience nausea and/or vomiting during migraine attacks:**
  - Domperidone (10 mg) and metoclopramide (10 mg)

# ADULT HEADACHE ALGORITHM

## STEP 1

### ASSESS SYMPTOMS

- Questions to ask (Table 1)
- Assess Migraine Type (Table 2)
- Symptoms or circumstances requiring referral (Table 3)

## STEP 2

### IDENTIFY TREATMENT CONSIDERATIONS

- Questions to ask to customize migraine treatment (Table 4)
- Conditions and medications (Tables 5 and 6)
- Assess previous treatment (Table 7)
- Questions to ask about previous treatment (Table 7)

## STEP 3

### RECOMMEND TREATMENT

- Non-pharmacological recommendations (Table 8)
- Pharmacological recommendation (Table 9)

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# STEP 1: ASSESS SYMPTOMS

## TABLE 1

| QUESTIONS TO ASK |
|---|
| **Can you tell me about your headache symptoms?[2]**<br>• Do you have recurrent headache of moderate to severe intensity?<br>• Is the pain unilateral and/or pulsating?<br>• What is the duration of the headache episode? (Is it 4 to 72 hours if untreated or unsuccessfully treated)<br>• Do you have a disabling intensity of headache?<br>• Was the onset of symptoms at or around puberty? |
| **Do you have any other symptoms?[2]**<br>• Do you have sensitivity to light and/or sound?<br>• Is the headache accompanied with nausea and/or vomiting?<br>• Do you have visual disturbances with the headache?<br>• Look for symptoms that require referral to a doctor (red flag symptoms) |
| **Do you have a family history of migraine?[2]** |

## TABLE 2

**ICHD-3* DIAGNOSTIC CRITERIA FOR DIFFERENT TYPES OF MIGRAINE HEADACHES[2,13]**

| Migraine without aura | Migraine with aura |
|---|---|
| 1. At least five attacks that fulfil criteria 2–5<br>2. Headache attacks that last 4–72 h when untreated or unsuccessfully treated<br>3. Headache has at least two of the following four characteristics:<br>• unilateral location<br>• pulsating quality<br>• moderate or severe pain intensity<br>• aggravation by, or causing avoidance of, routine physical activity (for example, walking or climbing stairs)<br>4. At least one of the following during the headache:<br>• nausea and/or vomiting<br>• photophobia and phonophobia<br>5. Not better accounted for by another ICHD-3 diagnosis | 1. At least two attacks that fulfil criteria 2 & 3<br>2. One or more of the following fully reversible aura symptoms:<br>• visual<br>• sensory<br>• speech and/or language<br>• motor<br>• brainstem<br>• retinal<br>3. At least three of the following six characteristics:<br>• at least one aura symptom spreads gradually over ≥5 min<br>• two or more aura symptoms occur in succession<br>• each individual aura symptom lasts 5–60 min<br>• at least one aura symptom is unilateral<br>• at least one aura symptom is positive<br>• the aura is accompanied with or followed by headache within 60 min<br>4. Not better accounted for by another ICHD-3 diagnosis |

**TABLE 2 CONT.**

# STEP 1: ASSESS SYMPTOMS

## TABLE 2 CONT.

| Chronic Migraine |
|---|
| 1. Headache (migraine- like or tension- type- like) on ≥15 days/month for >3 months that fulfil criteria 2 and 3<br>2. Attacks occur in an individual who has had at least five attacks that fulfil the criteria for migraine without aura and/or for migraine with aura<br>3. On ≥8 days/month for >3 months, any of the following criteria are met:<br>• criteria 3 and 4 for migraine without aura<br>• criteria 2 and 3 for migraine with aura<br>• believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative<br>4. Not better accounted for by another ICHD-3 diagnosis |
| **Medication overuse headache (MOH)** |
| 1. Headache on ≥15 days/month in an individual with a pre- existing headache disorder<br>2. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache (regular intake of one or more non- opioid analgesics on ≥15 days/month for ≥3 months or any other acute medication or combination of medications on ≥10 days/month for ≥3 months)<br>3. Not better accounted for by another ICHD-3 diagnosis- |
| **ICHD: International Classification of Headache Disorders* |

## TABLE 3

| SYMPTOMS OR CIRCUMSTANCES REQUIRING REFERRAL[2] | |
|---|---|
| **When to look** | **Physical examination** |
| **Patient history** | • Thunderclap headache<br>• Atypical aura<br>• Head trauma<br>• Progressive headache<br>• Headache aggravated by postures or manoeuvres that raise intracranial pressure<br>• Headache brought on by sneezing, coughing or exercise<br>• Headache associated with weight loss and/or change in memory or personality<br>• Headache onset at >50 years of age |
| **Physical examination** | • Unexplained fever<br>• Neck stiffness<br>• Focal neurological symptoms<br>• Weight loss<br>• Impaired memory and/or altered consciousness or personality |

# STEP 2:
# IDENTIFY TREATMENT CONSIDERATIONS

## TABLE 4

| QUESTIONS TO ASK TO CUSTOMIZE HEADACHE TREATMENT |
|---|
| • Are you taking any medication, both prescribed and over the counter? If yes, what are those and what is the dose?<br>• Do you have any medical conditions?<br>• What have you used before for your headache?<br>• What are the triggers for your headache?<br>• What are the aggravating or relieving factors?<br>• Is there a family history of migraine? |

## TABLE 5

**MEDICATIONS TO USE WITH CAUTION WITH PARACETAMOL/ORAL NSAIDS AND TRIPTANS[3-5,14]**

| Concern | Potential drug interaction |
|---|---|
| Increased risk of bleeding with oral NSAIDs | • Some Selective-Serotonin Reuptake Inhibitors (SSRI)<br>• Some tricyclic antidepressants<br>• Acetylsalicylic acid (ASA)<br>• Corticosteroids<br>• Warfarin<br>• Ginkgo biloba |
| Decreased antihypertensive efficacy with oral NSAIDs | • Angiotensin converting enzyme (ACE) inhibitors<br>• Angiotensin II receptor blockers (ARB)<br>• Diuretics<br>• Beta-blockers |
| Increased drug levels with oral NSAIDs | • Lithium<br>• Methotrexate |
| Increased risk of paracetamol toxicity | • Epilepsy medications (e.g. carbamazepine)<br>• Other P450 enzyme inducers (e.g. isoniazid, rifampin)<br>• Alcohol |
| Excessive blood vessel narrowing | • Triptans and Ergot Alkaloids |
| Excessive levels of serotonin | • Triptans and a serotonin reuptake inhibitor antidepressant (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI) |

# STEP 2:
# IDENTIFY TREATMENT CONSIDERATIONS

## TABLE 6

**CONSIDERATIONS WHEN SELECTING ANALGESICS IN PATIENTS WITH COMORBIDITIES[5-9]**

| Comorbidity | Notes |
|---|---|
| Chronic kidney disease[6] | • NSAIDs have proven nephrotoxic class effects and should be avoided where possible in patients with symptoms of renal impairment<br>• Paracetamol is the preferred first-line analgesic for episodic treatment of mild pain in patients with renal dysfunction, CKD, and/or requiring dialysis. However, dose minimization may sometimes be warranted (maximum of 3 g/day has been recommended for patients with advanced kidney failure) |
| Liver disease[6,7] | • NSAIDs- NSAIDs can cause acute liver injury with variable severity.<br>• Paracetamol: Not contraindicated in liver disease. Can cause liver toxicity if taken in large amounts. |
| Peptic-ulcer disease[6,8] | • Chronic NSAID drug use is associated with potentially serious upper gastrointestinal adverse drug reactions including peptic ulcer disease and gastrointestinal bleeding.<br>• Paracetamol – Lesser risk of adverse effects compared to NSAIDs |
| Cardiovascular disease[3,6,8] | • All non-aspirin NSAIDs may be associated with a potential increase in CV thrombotic risk.<br>• NSAIDs are contraindicated in patients who have undergone coronary artery bypass graft surgery<br>• Use of paracetamol at recommended doses is not associated with any additional risk of major CV events. |

## TABLE 7

**QUESTIONS TO ASK TO ABOUT PREVIOUS TREATMENT**

- What have you used before to treat your migraine headache?
  - What dose did you use?
  - Was it effective?
  - Did you have any side effects from it?
- Do you have any preference for any specific treatment?

# STEP 3: RECOMMEND TREATMENT

## TABLE 8

| NON-PHARMACOLOGICAL RECOMMENDATIONS FOR MIGRAINE HEADACHE[2] |
|---|
| **Using a diary for identifying important triggers, avoid the trigger factors if possible or cope with them**<br>• Environmental triggers: Weather and its changes, including decreased atmospheric pressure, low temperature, and high humidity.<br>• Sensitivity to odors (perfumes, cigarette smoke, and cleaning products)<br>• Noise triggers (neighborhood noise from roads, railways etc.) |
| **Good sleep hygiene practices**<br>• Convenient bedrooms with fewer stimulations such as television, cell phone, light, and noise<br>• Waking at a specific time range in the mornings, even on weekends |
| **Dietary lifestyle modifications**<br>• Preventing hunger and fasting, having regular meals<br>• Sticking to frequent meals (e.g. five or six small meals per day)<br>• Consuming foods that provide a stable level of blood glucose (slow-digesting foods)<br>• Cooking food rather than eating processed or fast foods<br>• Remembering proper fluid intake and hydration<br>• Having a low-fat diet<br>• Using a food diary to identify food triggers– common triggers include red wine and alcohol, chocolate, caffeine in products such as coffee, tea, cola, etc. |
| **Regular and moderate exercise** - especially aerobic exercises such as cycling and walking, after careful warm-up. Avoid exercise during their headache attacks |
| **Stress management** - learning to cope with stressors, problem-solving, social support, changes in living situations and lifestyle, exercise, and avoiding certain situations that cause severe stress and anxiety |
| **Weight reduction to restore an ideal body weight** might be a useful intervention, to control migraine attacks, especially in obese patients |
| **Patient education is an important part of the management of hormonal migraine attacks** |

# STEP 3: RECOMMEND TREATMENT

## TABLE 9

| MEDICATIONS FOR MANAGEMENT OF ACUTE MIGRAINE[1,2] | | | |
|---|---|---|---|
| **Drug Class** | **Drug** | **Dosage and Route** | **Contraindications** |
| **First line medications** | | | |
| **Non-steroidal anti-inflammatory drugs (NSAIDs)** | Aspirin | 900–1000 mg oral | Gastrointestinal bleeding, heart failure |
| | Ibuprofen | 400-600 mg oral | |
| | Diclofenac | 50 mg oral (soluble) | |
| **Other simple analgesics (If NSAIDs are contraindicated)** | Paracetamol (Good safety profile at therapeutic levels.) | 1000 mg oral | Hepatic disease, renal failure |
| **Combination therapy** | Paracetamol + Aspirin + Caffeine *(Preferred in patients with contraindications to vasoconstrictors like Triptans)* | Acetylsalicylic acid (250 or 265 mg) + paracetamol (200 or 265 mg) + caffeine (50 or 65 mg) oral (2 tablets of FDC) | Contraindications to individual drugs. |
| **Antiemetics (when necessary)** | Domperidone | 10 mg oral or suppository | Gastrointestinal bleeding, epilepsy, renal failure, cardiac arrhythmia |
| | Metoclopramide | 10 mg oral | Parkinson disease, epilepsy, mechanical ileus |
| **Second-line medications** | | | |
| **Triptans** | Sumatriptan | 50 or 100 mg oral or 6 mg subcutaneous or 10 or 20 mg intranasal | Cardiovascular or cerebrovascular disease, uncontrolled hypertension, hemiplegic migraine, migraine with brainstem aura<br><br>(Caution: Patients who use too frequently may develop medication overuse headache) |
| | Zolmitriptan | 2.5 or 5 mg oral or 5 mg intranasal | |
| | Almotriptan | 12.5 mg oral | |
| | Eletriptan | 20, 40 or 80 mg oral | |
| | Frovatriptan | 2.5 mg oral | |
| | Naratriptan | 2.5 mg oral | |
| | Rizatriptan | 10 mg oral tablet (5 mg if treated with propranolol) or 10 mg mouth- dispersible wafers | |

**TABLE 9 CONT.**

# STEP 3: RECOMMEND TREATMENT

## TABLE 9 CONT.

| Third line medications/newer therapies | | | |
|---|---|---|---|
| **Gepants** | Ubrogepant | 50, 100 mg oral | Co- administration with strong CYP3A4 Inhibitors |
| | Rimegepant | 75 mg oral | Hypersensitivity, hepatic impairment |
| **Ditans** | Lasmiditan | 50, 100 or 200 mg oral | Pregnancy, concomitant use with drugs that are P- glycoprotein substrates |

**Summary of pharmacological recommendations for management of acute attacks of migraine:[2]**

- Offer acute medication to everyone who experiences migraine attacks.
- Advise use of acute medications early in the headache phase of the attack, as effectiveness depends on timely use with the correct dose.
- Advise patients that frequent, repeated use of acute medication risks development of medication-overuse headache.
- Use NSAIDs (acetylsalicylic acid, ibuprofen or diclofenac potassium) as first- line medication.
- Use Paracetamol when NSAIDs are contraindicated.
- Use Paracetamol as first- line medication for acute treatment of migraine in pregnancy.
- Use triptans as second- line medication.
- Consider combining triptans with fast- acting NSAIDs to avert recurrent relapse.
- Consider ditans and gepants as third- line medications.
- Use prokinetic antiemetics (domperidone or metoclopramide) as adjunct oral medications for nausea and/or vomiting.
- Avoid oral ergot alkaloids, opioids and barbiturates.

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