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Adult Acute Migraine Pain Protocol

#ListenToPain

PM-PK-NOBR-24-00008

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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 • Paracetamol: Increased risk of paracetamol toxicity • Triptans - Contraindicated in cardiovascular or cerebrovascular disease, uncontrolled hypertension and specific migraine syndromes.	• Chronic kidney disease • Liver disease • Peptic ulcer disease • Cardiovascular disease • 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)

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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] • Do you have recurrent headache of moderate to severe intensity? • Is the pain unilateral and/or pulsating? • What is the duration of the headache episode? (Is it 4 to 72 hours if untreated or unsuccessfully treated) • Do you have a disabling intensity of headache? • Was the onset of symptoms at or around puberty?
Do you have any other symptoms?[2] • Do you have sensitivity to light and/or sound? • Is the headache accompanied with nausea and/or vomiting? • Do you have visual disturbances with the headache? • 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 2. Headache attacks that last 4–72 h when untreated or unsuccessfully treated 3. Headache has at least two of the following four characteristics: • unilateral location • pulsating quality • moderate or severe pain intensity • aggravation by, or causing avoidance of, routine physical activity (for example, walking or climbing stairs) 4. At least one of the following during the headache: • nausea and/or vomiting • photophobia and phonophobia 5. Not better accounted for by another ICHD-3 diagnosis	1. At least two attacks that fulfil criteria 2 & 3 2. One or more of the following fully reversible aura symptoms: • visual • sensory • speech and/or language • motor • brainstem • retinal 3. At least three of the following six characteristics: • at least one aura symptom spreads gradually over ≥5 min • two or more aura symptoms occur in succession • each individual aura symptom lasts 5–60 min • at least one aura symptom is unilateral • at least one aura symptom is positive • the aura is accompanied with or followed by headache within 60 min 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 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 3. On ≥8 days/month for >3 months, any of the following criteria are met: • criteria 3 and 4 for migraine without aura • criteria 2 and 3 for migraine with aura • believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative 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 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) 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 • Atypical aura • Head trauma • Progressive headache • Headache aggravated by postures or manoeuvres that raise intracranial pressure • Headache brought on by sneezing, coughing or exercise • Headache associated with weight loss and/or change in memory or personality • Headache onset at >50 years of age
Physical examination	• Unexplained fever • Neck stiffness • Focal neurological symptoms • Weight loss • Impaired memory and/or altered consciousness or personality

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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? • Do you have any medical conditions? • What have you used before for your headache? • What are the triggers for your headache? • What are the aggravating or relieving factors? • 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) • Some tricyclic antidepressants • Acetylsalicylic acid (ASA) • Corticosteroids • Warfarin • Ginkgo biloba
Decreased antihypertensive efficacy with oral NSAIDs	• Angiotensin converting enzyme (ACE) inhibitors • Angiotensin II receptor blockers (ARB) • Diuretics • Beta-blockers
Increased drug levels with oral NSAIDs	• Lithium • Methotrexate
Increased risk of paracetamol toxicity	• Epilepsy medications (e.g. carbamazepine) • Other P450 enzyme inducers (e.g. isoniazid, rifampin) • 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)

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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 • 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. • 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. • 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. • NSAIDs are contraindicated in patients who have undergone coronary artery bypass graft surgery • 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 • Environmental triggers: Weather and its changes, including decreased atmospheric pressure, low temperature, and high humidity. • Sensitivity to odors (perfumes, cigarette smoke, and cleaning products) • Noise triggers (neighborhood noise from roads, railways etc.)
Good sleep hygiene practices • Convenient bedrooms with fewer stimulations such as television, cell phone, light, and noise • Waking at a specific time range in the mornings, even on weekends
Dietary lifestyle modifications • Preventing hunger and fasting, having regular meals • Sticking to frequent meals (e.g. five or six small meals per day) • Consuming foods that provide a stable level of blood glucose (slow-digesting foods) • Cooking food rather than eating processed or fast foods • Remembering proper fluid intake and hydration • Having a low-fat diet • 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 (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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