



Danish Knowledge Center
on Headache Disorders

Headache 1.2.3

Diagnosis, treatment & prevention



Headache 1·2·3

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About Headache 1·2·3

Headache 1·2·3 is developed by the Danish Knowledge Center on Headache Disorders in collaboration with clinical experts. The material is based on treatment guidelines from the Danish Headache Center, the Danish Headache Society, and the Danish Neurological Society.

Headache 1·2·3 provides practical guidance on the diagnosis and management of common headache disorders and highlights less common conditions relevant to the differential diagnosis. Each section summarises key clinical features, diagnostic considerations, and current treatment options.

This booklet is designed as a practical aid for diagnosis and treatment and does not constitute a comprehensive review. The recommendations should be considered in the context of each patient's individual circumstances, and responsibility for clinical decision-making remains with the treating physician.

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Introduction

Headache is the most common neurological condition. Nearly one in five people in Denmark is affected by frequent recurrent headache, most commonly tension-type headache or migraine.

Accurate diagnosis and differentiation between headache disorders are essential for appropriate management, as individual disorders differ in their clinical characteristics, underlying pathophysiology, diagnostic evaluation, and treatment.

Headache disorders commonly present with recurrent attacks of pain accompanied by characteristic associated symptoms. In chronic headache disorders, attacks may occur with such frequency that patients have few or no pain-free periods, or experience a continuous background headache with superimposed exacerbations.

Treatment generally comprises two main approaches:

- Acute treatment, aimed at relieving symptoms and reducing the duration and impact of individual headache attacks.
- Preventive treatment, administered regularly to reduce headache frequency and the overall burden of the disorder.

Although most headache disorders cannot be cured, appropriate diagnosis and treatment can substantially reduce their frequency, severity, and impact, thereby improving functioning and quality of life.



1. Diagnosis

The diagnosis of headache disorders is primarily based on a detailed clinical history. The physical and neurological examinations are usually normal in primary headache disorders. Additional investigations, including neuroimaging, lumbar puncture, or laboratory tests, should be performed when clinically indicated, particularly when a secondary cause of headache is suspected.

Patients may have more than one headache disorder. Distinct headache patterns should therefore be identified and characterised separately. The clinical history should include the following:

- Age at headache onset
- Duration of headache attacks (without treatment)
- Frequency of headache attacks
- Pain characteristics (e.g. location, quality, intensity, aggravating factors, relieving factors)
- Associated symptoms (e.g. photophobia, phonophobia, nausea, vomiting, restlessness, lacrimation, rhinorrhoea, ptosis)
- Neurological symptoms or deficits (e.g. transient and migrating visual disturbances)
- Impact of physical activity on symptoms
- Family history (if applicable)

A diagnostic headache diary facilitates the application of the diagnostic criteria defined in the International Classification of Headache Disorders (ICHD-3).

A headache calendar is used to monitor treatment response and to screen for medication-overuse headache (MOH).



2. Acute Treatment

When acute treatment is initiated, the response should be systematically assessed and documented. This should include pain freedom within 2 hours, resolution of associated symptoms, recurrence of headache, and the need for additional acute medication.

The frequency of acute medication use should be monitored, particularly in patients with frequent headache. Patients should be informed that frequent use of acute medication may lead to medication-overuse headache (MOH).

3. Preventive Treatment

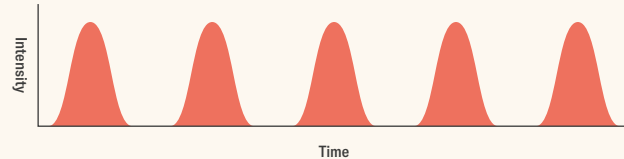
Preventive treatment should be considered in patients with a substantial headache burden or impaired quality of life despite optimised acute treatment. The choice of preventive treatment should consider efficacy, tolerability, comorbidities, and patient preferences.

Preventive treatment should be evaluated after an adequate trial at an appropriate dose and for an appropriate duration. Treatment response, adverse effects, and use of acute medication should be monitored regularly. A headache calendar should be used to document headache frequency and assess treatment response.

Non-pharmacological interventions may be considered as adjuncts to preventive pharmacological treatment. Although the evidence for individual interventions is limited, manual joint mobilisation and pain and stress management may be considered in patients with migraine or tension-type headache.

Migraine (with or without aura)

CHARACTERISTIC PAIN PATTERN



1. Diagnosis

- A. At least 5 attacks fulfilling criteria B-D
- B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated).
- C. 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 (e.g. walking or climbing stairs)
- D. During headache at least one of the following:
 - Nausea and/or vomiting
 - Photophobia and phonophobia

Migraine headache is not necessarily unilateral; it may be bilateral or alternate between sides.

Approximately one-third of patients with migraine experience aura in association with some attacks. Visual symptoms are the most common manifestation of migraine aura. Sensory and speech and/or language symptoms occur less frequently.

Chronic migraine is characterised by headache on ≥ 15 days per month for > 3 months, with migraine features on ≥ 8 days per month. Episodic migraine is characterised by < 15 headache days per month.

2. Acute Treatment

PHARMACOLOGICAL TREATMENT

- First-line treatment: Ibuprofen, paracetamol or a combination analgesic (e.g. acetylsalicylic acid plus caffeine)
- Second-line treatment: Triptan (e.g. sumatriptan, eletriptan, rizatriptan, zolmitriptan)
- Third-line treatment: Gepants (atogepant and rimegepant).

Acute treatment should be administered early in the migraine attack, while headache intensity is still mild. In migraine with aura, triptans should be taken after headache onset rather than during the aura phase.

Acute treatment should be evaluated after three consecutive attacks before a final assessment of efficacy is made.

At least three different triptans should be adequately trialled before proceeding to third-line treatment.

In patients with nausea and/or vomiting, a prokinetic antiemetic such as domperidone or metoclopramide may be used.

Opioids should not be used for the treatment of migraine.

3. Preventive Treatment

PHARMACOLOGICAL TREATMENT

Preventive treatment should be considered in patients with ≥ 4 migraine days per month, insufficient response to acute treatment, or a significant impact on quality of life.

- First-line treatment: Candesartan and/or metoprolol or propranolol.
- Second-line treatment: Topiramate, which is often not a suitable treatment option. It is contraindicated in women of childbearing potential who are not using highly effective contraception.
- Third-line treatment: **For episodic migraine:** Gepants: rimegepant or atogepant.
For chronic migraine: Atogepant, a CGRP monoclonal antibody, or botulinum toxin type A.
- Fourth-line treatment: Amitriptyline, especially in patients with coexisting frequent tension-type headache.

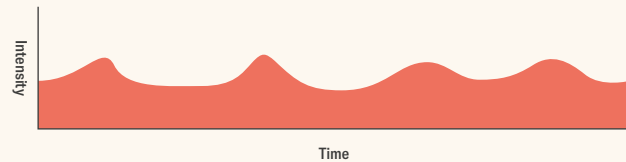
Preventive treatment should generally be continued at an adequate dose for at least 2–3 months before efficacy is assessed. Treatment response should be monitored using a headache diary.

NON-PHARMACOLOGIC TREATMENT

A range of non-pharmacological interventions may be used either as adjunctive therapy or when pharmacological treatment is contraindicated, although the evidence supporting their efficacy is limited.

Tension-type Headache

CHARACTERISTIC PAIN PATTERN



1. Diagnosis

- A. Headache lasting from 30 minutes to 7 days
- B. Headache has at least two of the following four characteristics:
 - Bilateral location
 - Pressing or tightening (non-pulsating) quality
 - Mild or moderate intensity
 - Not aggravated by routine physical activity such as walking or climbing stairs
- C. Both of the following:
 - No nausea or vomiting
 - No more than one of photophobia or phonophobia

Episodic tension-type headache (infrequent or frequent) is characterised by:

- 1–14 headache days per month

For chronic tension-type headache:

- Headache occurring on ≥ 15 days per month or continuous headache
- No more than one of the following: photophobia, phonophobia, or mild nausea
- Neither moderate or severe nausea nor vomiting during headache episodes

Tension-type headache is the most common headache disorder, and almost everyone will experience at least one episode during their lifetime.

2. Acute Treatment

PHARMACOLOGIC TREATMENT

First-line treatment: Ibuprofen, naproxen or paracetamol

Second-line treatment: Combination analgesics (acetylsalicylic acid with caffeine)

For chronic tension-type headache, acute analgesic treatment is rarely effective, and preventive therapy should therefore be considered.

Opioids should not be used for the treatment of tension-type headache.

3. Preventive Treatment

Preventive treatment should be considered in patients with frequent episodic or chronic tension-type headache.

PHARMACOLOGIC TREATMENT

First-line treatment: Amitriptyline

Second-line treatment: Mirtazapine

Third-line treatment: Venlafaxine

The efficacy of these agents is independent of comorbid depression.

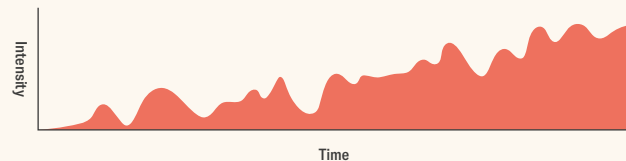
Preventive treatment should generally be continued at an adequate dose for at least 2–3 months before efficacy is assessed, unless adverse effects preclude continued treatment.

NON- PHARMACOLOGIC TREATMENT

Patient education should be an integral part of management. Potential aggravating factors, such as stress, muscle tension, posture, and insufficient sleep, should be identified and addressed where relevant. Manual therapy, behavioural interventions, and pain and stress management may be considered as adjunctive treatment, although the evidence supporting these interventions is limited.

Medication-overuse Headache

CHARACTERISTIC PAIN PATTERN



1. Diagnosis

- A. Headache occurring on ≥ 15 days per month in a patient with a pre-existing headache disorder.
- B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache:
 - Simple analgesics on ≥ 15 days per month
 - Triptans, ergotamines, opioids, or combination-analgesic medications on ≥ 10 days per month
 - Any combination of these medications on ≥ 10 days per month

Any use of acute pain-relieving medication, regardless of the indication for which it is taken, counts towards the total.

Medication-overuse headache (MOH) is defined as headache occurring on ≥ 15 days per month in a patient with a pre-existing headache disorder and regular overuse of acute or symptomatic headache medication for >3 months. The number of medication-use days constituting overuse depends on the type of medication.

MOH develops in patients with a pre-existing headache disorder, most commonly migraine or tension-type headache, and is associated with an increase in headache frequency and use of acute medication.

Medication overuse may contribute to headache chronification and should be assessed in patients with frequent or chronic headache.

2. Acute Treatment

MEDICATION WITHDRAWAL

Withdrawal of the overused acute medication is a key component of the management of medication-overuse headache (MOH).

Abrupt withdrawal is generally recommended for triptans and non-opioid analgesics. Opioids should be gradually tapered, and specialist or inpatient management may be required.

Patients should be informed that headache may temporarily worsen following medication withdrawal. Withdrawal symptoms are usually most pronounced during the first days after discontinuation and may include worsening headache, nausea, restlessness, and sleep disturbance. Headache frequency and intensity generally improve over the subsequent weeks to months.

The need for temporary sick leave during the initial withdrawal period should be considered on an individual basis.

Medication withdrawal should be supported by patient education, a clear management plan, and structured follow-up. The Brief Intervention approach may be used to support withdrawal and subsequent management (videnomhovedpine.dk/brief-intervention).

TRANSITIONAL TREATMENT

Supportive medication may be required during the first 1 to 3 weeks after medication withdrawal. Sedative medication and/or antiemetics can be used to help patients cope with the temporary worsening of headache, improve sleep, and reduce nausea.

Sedative medication:

- Promethazine or chlorprothixene

Antiemetic medication:

- Metoclopramide or domperidone

3. Preventive Treatment

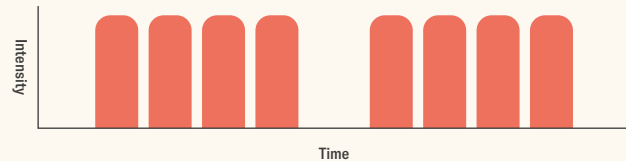
Following medication withdrawal, acute medication use should be monitored regularly to ensure that it remains within recommended limits and to reduce the risk of relapse. A headache diary should be used to document headache frequency, acute medication use, and treatment response.

Preventive treatment of the underlying headache disorder should be initiated when clinically indicated and should not be unnecessarily delayed because of medication withdrawal. Treatment should be tailored to the underlying headache disorder, most commonly migraine or tension-type headache.

Cluster Headache

(Also formerly referred to as Horton's headache)

CHARACTERISTIC PAIN PATTERN



1. Diagnosis

- A. At least 5 attacks fulfilling criteria B-D
- B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes (when untreated).
- C. At least one of the following:
 - 1. The headache is accompanied by at least one of the following ipsilateral symptoms or signs:
 - Lacrimation and/or conjunctival injection
 - Nasal congestion and/or rhinorrhoea
 - Eyelid oedema
 - Forehead and facial sweating
 - Miosis and/or ptosis
 - 2. A sense of restlessness or agitation
- D. Occurring with a frequency of between one every other day and eight per day.

Cluster headache attacks occur in cluster periods (bouts), which typically last from 2 weeks to 3 months. In episodic cluster headache, cluster periods are separated by pain-free remission periods lasting ≥ 3 months. Remission periods may last for months or years.

Cluster headache is classified as episodic or chronic according to the presence and duration of remission periods. Chronic cluster headache is characterised by attacks occurring for ≥ 1 year without remission or with remission periods lasting < 3 months.

Cluster headache is more common in men than in women.

2. Acute Treatment

PHARMACOLOGIC TREATMENT

First-line treatment: Oxygen inhalation therapy

Second-line treatment: Triptans (preferably administered by injection or nasal spray)

Acute cluster headache attacks should be treated with 100% oxygen (at a flow rate of at least 12 L/min for approximately 15 minutes), administered via a non-rebreather mask. Home oxygen therapy may be arranged through an oxygen provider following prescription by a neurologist.

Subcutaneous sumatriptan is recommended for the acute treatment of cluster headache and provides rapid relief. Intranasal triptans may be used as an alternative but generally have a slower onset of action. When a nasal spray is used, administration into the nostril contralateral to the headache side may be preferable. Oral triptans are generally not recommended for acute cluster headache because of their slower onset of action.

The frequency of triptan use should be monitored, particularly in patients with frequent attacks or coexisting migraine.

3. Preventive Treatment

Preventive treatment should be initiated as early as possible at the beginning of each cluster bout.

PHARMACOLOGIC TREATMENT

First-line treatment: Verapamil

Corticosteroids may be used as short-term transitional treatment to suppress cluster headache attacks until preventive treatment becomes effective. The duration and tapering regimen should be individualised.

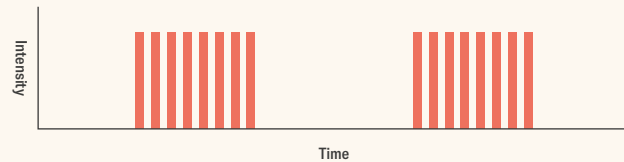
A greater occipital nerve (GON) block with a corticosteroid, with or without local anaesthetic, may be considered as transitional treatment and is generally performed in a specialist setting.

NON-PHARMACOLOGIC TREATMENT

Evidence for non-pharmacological treatment of cluster headache is limited.

Trigeminal Neuralgia

CHARACTERISTIC PAIN PATTERN



1. Diagnosis

- A. Recurrent paroxysms of unilateral facial pain in one or more divisions of the trigeminal nerve, fulfilling criteria B and C.
- B. Recurrent pain paroxysms lasting from a fraction of a second to 2 minutes. The pain is of severe intensity and has an electric shock-like, shooting, stabbing, or sharp quality.
- C. Attacks are triggered by non-painful sensory stimuli in the affected area (e.g. chewing, wind on the face, toothbrushing, or light touch).

The pain is most commonly distributed within the maxillary (V2) and/or mandibular (V3) divisions of the trigeminal nerve.

Trigeminal neuralgia requires specialist management. Preventive treatment should be started, and referral to a specialist is recommended.

2. Acute Treatment

The brief duration of individual trigeminal neuralgia attacks generally precludes effective acute treatment. In severe cases, hospital admission may be required, and intravenous phenytoin or fosphenytoin may be considered as rescue treatment.

Conventional analgesics, including opioids, are generally ineffective and are not recommended.

3. Preventive Treatment

All patients diagnosed with trigeminal neuralgia should be offered preventive treatment with antiepileptic medication.

PHARMACOLOGIC TREATMENT

First-line treatment: Carbamazepine or oxcarbazepine

Second-line treatment: Gabapentin, pregabalin or lamotrigine

If first-line treatment provides insufficient pain control or is poorly tolerated, an alternative agent may be used as monotherapy or added to carbamazepine or oxcarbazepine. Treatment should be individualised according to efficacy and tolerability.

SURGICAL TREATMENT

Surgical treatment should be considered when pain is insufficiently controlled with pharmacological treatment or when treatment is poorly tolerated.

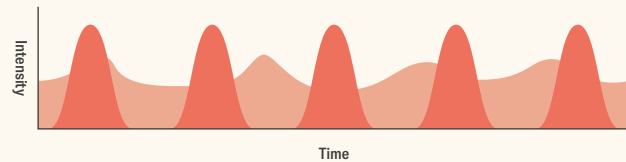
- Microvascular decompression (MVD) is the preferred surgical treatment in patients with classical trigeminal neuralgia and neurovascular compression identified on MRI.
- Neuroablative procedures may be considered in patients without neurovascular compression or in those who are not suitable for, or do not wish to undergo, microvascular decompression.

NON-PHARMACOLOGIC TREATMENT

Evidence for non-pharmacological interventions is limited.

Post-traumatic Headache (PTH)

CHARACTERISTIC PAIN PATTERN



1. Diagnosis

- A. Any new headache, or a significant worsening of a pre-existing headache, fulfilling the criteria below.
- B. A traumatic injury to the head has occurred prior to the onset of the headache, including mechanisms such as blunt trauma, falls, penetrating injuries, or blast exposure.
- C. The headache develops within 7 days after the injury.
- D. The headache may also develop within 7 days after regaining consciousness or within 7 days after discontinuation of medication that impaired the ability to perceive pain or report symptoms.

During the acute phase, the need for emergency neuroimaging, most commonly CT of the brain, should be evaluated.

Common associated symptoms include impaired concentration, memory difficulties, fatigue, photophobia, phonophobia, visual disturbances, dizziness, and irritability.

Treatment of post-traumatic headache is determined by the underlying headache phenotype. In most cases, the clinical presentation resembles migraine, tension-type headache, or a combination of the two.

2. Acute Treatment

Evidence to guide the treatment of post-traumatic headache (PTH) remains limited. Current management is based primarily on a phenotype-guided approach. As PTH frequently resembles migraine or tension-type headache, treatment should generally follow established management principles for the corresponding primary headache phenotype.

Treatment response and acute medication use should be monitored systematically. Medication-overuse headache (MOH) should be considered and prevented in patients with frequent use of acute headache medication. Preventive treatment should be considered in patients with frequent or disabling headache and individualised according to headache frequency, severity, functional impact, response to acute treatment, and comorbidities.

PHARMACOLOGIC TREATMENT

Migraine phenotype:

First-line treatment: Ibuprofen, paracetamol, or a combination analgesic (e.g. acetylsalicylic acid with caffeine)

Second-line treatment: Triptan (e.g. sumatriptan, rizatriptan, eletriptan, zolmitriptan)

Tension-type Headache phenotype:

First-line treatment: Ibuprofen, naproxen or paracetamol

Second-line treatment: Combination analgesics (acetylsalicylic acid or paracetamol combined with caffeine)

3. Preventive Treatment

PHARMACOLOGIC TREATMENT

Migraine phenotype:

First-line treatment: Candesartan

Second-line treatment: Metoprolol or propranolol

Tension-type Headache phenotype:

First-line treatment: Amitriptyline

Second-line treatment: Mirtazapine

NON- PHARMACOLOGIC TREATMENT

There is very limited evidence supporting non-pharmacological treatment of post-traumatic headache, and management should be tailored to the individual patient's symptom profile. Some patients may benefit from manual therapy targeting the cervical spine and vestibular symptoms, graded physical exercise, ergonomic advice, and psychological interventions focusing on pain and stress management.

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