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Review

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General approach to headache diagnosis and treatment management

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ABSTRACT

Headache is common worldwide and is one of the leading causes of disability. Given its high prevalence and high burden in terms of disability, it is important for clinicians to have general knowledge about the approach to the patient presenting with headache. Headache disorders are classified according to their etiology. The most important step in the approach to headache is to investigate the presence of a secondary cause of pain with a detailed history and physical examination. The presence of symptoms and signs considered as red flags requires further investigation in terms of secondary causes. Treatment of pain is also directed towards the etiology. Treatment of secondary headache disorders is directed towards the cause of the pain. In primary causes, there are some pharmacologic and non-pharmacologic treatment approaches for the diagnosis.

Keywords: Headache, red flags, SNNOOP10

INTRODUCTION

Headache is a common symptom affecting the majority of the population and has a wide range of etiologies. In order to treat headache effectively and successfully, an accurate diagnosis is essential. A systematic and multidisciplinary approach is important for making the correct diagnosis. In this review, we aimed to discuss the importance of systematic approach to the management of headache and current knowledge in the light of the existing literature.

EPIDEMIOLOGY

Although studies on the prevalence of headache have yielded different results, it is noteworthy that it is a complaint affecting the majority of the population. When prevalence studies are analyzed together, it is estimated that almost half of the global population has active headache complaints. Primary headache is more common than secondary headache. In addition, the prevalence of headache is higher in women.[1] According to WHO (World Healt Organization) it is estimated that half to three quarters of adults worldwide experience headaches. It is also stated that the vast majority of these headache sufferers do not consult health professionals due to headache and are not diagnosed by health professionals.[2]

Global Burden of Disease Study 2016, estimated that almost three billion people suffer from migraine or tension headache, and migraine is considered one of the leading causes of disability.[3]

ETIOLOGY AND CLASSIFICATION

Headache classification was first made by the International Headache Society in 1988 in order to facilitate the diagnosis of headaches with different etiology, duration, severity, frequency and accompanying findings and to use a common language. The latest version of the classification, ICHD-3, was published in 2018. This classification is guiding in terms of a systematic approach to headache. The headings in this classification are given in Table 1.[4]

Primary headache disorders are those in which there is no underlying cause of the headache and the disease manifests itself directly as headache. In secondary headache disorders,

headache is a manifestation of the underlying disease. In these cases, headache may be secondary to systemic or central nervous system pathology.[5]

Table 1. Classification of headache disorders

Primary Headaches
Migraine
Tension headache
Trigeminal autonomiccephalalgias
Other causes of primary headache
Secondary Headaches
Headache secondary to head or neck trauma/injury
Headaches due to cranial or cervical vascular disorders
Intracranial non-vascular headaches
Headache associated with substance (use) or withdrawal
Headache due to infection
Headache attributed to homeostasis disorder
Headache or facial pain associated with disorders of the cranium, neck, eyes, ears, sinuses, teeth, mouth or other facial or cranial structures
Headache associated with psychiatric disorders
Neuropathies, facial pain and other headaches
Painful lesions of the cranial nerves and other facial pains
Other headache disorders

Migraine, tension-type, trigeminal autonomic cephalalgias and other headaches that cannot be categorized constitute primary headaches. Cluster headache, paroxysmal hemicrania, unilateral neuralgiform short-term pain with conjunctival redness and lacrimation (SUNCT) and hemicrania continua are classified under trigeminal autonomic cephalalgias. Other primary causes of headache that have not yet been categorized include primary cough, exercise, cold stimuli, sexual activity, thunder and hypnic headache.[4]

Migraine is a common primary headache disorder that causes disability. Migraine is divided into two main types: with and without aura. Migraine without aura is a clinical syndrome defined by some specific features and associated symptoms. Migraine with aura usually progresses with transient focal neurological symptoms that precede or accompany the headache. Like migraine, tension-type headache is also common in the community. The mechanism of action of this type of headache is not yet fully known. This pain manifests itself as bilateral, compressive headache episodes6. Classification of primary headaches according to some common features is summarized in Table 2.

DIAGNOSIS

While laboratory and imaging tests help in the diagnosis of secondary headache disorders, the diagnosis of headache disorders is largely based on history.[7] It can be said that the patient's history is a more guiding step in the stages leading to the diagnosis of headache compared to many other neurological diseases.

Patients presenting to the outpatient clinic or emergency department with headache complaints usually have a primary headache disorder, most commonly migraine.[7,8] Nevertheless, in every patient presenting with headache, the priority should be to exclude secondary causes and a detailed and systematic approach should be adopted. This approach is important to avoid overlooking serious underlying causes that can be treated.[9,10]

In 2003, some symptoms, findings and features that are seen as red flags in headache were listed in order to suggest secondary causes that require further examination in patients presenting with headache, and the initials of these features were used to make an abbreviation called SNOOP. Some features were added to the list in 2019 and the name was updated as SNNOOP10 The red flags in the list are defined as findings or features that require further examination of the patient, while orange flags are defined as information that is of concern only when it occurs in combination with other orange or red flags.[11] The criteria in this abbreviation are listed in Table 3. Although there is no clear recommendation in the literature for the use of this list yet, SNNOOP10 has gained

Table 2. Classification according to common features in primary headaches

Headache	Character	Duration	Side	Location of pain	Concomitant finding	Frequency
Migraine	Throbbing	4-72 hours	Unilateral	Neck and forehead	Nausea, vomiting	Variable
Tension	Compactor	Half an hour - 7 days	Bilateral	Nape	Loss of appetite, nausea	Variable
Cluster	Reamer/driller	15-180 minutes	Unilateral	Orbital circumference	Autonomic symptoms	1-8/day
Cough	Stabbing, throbbing	1 second - 30 minutes	Bilateral	Back of the head	No	Associated with cough
Exercise	Blunt	5 minutes - 48 hours	Bilateral	Back of the head	No	Exercise-related
Hipnik	Compressive, throbbing	15-180 minutes	Bilateral	Widespread	No	More than 15 per month
Thunder	Explosive	1 hour-10 days	Bilateral	Nape or widespread	Nausea, vomiting	Does not recur regularly
SUNCT	Throbbing	5-240 seconds	Unilateral	Orbital circumference	Eye tearing	3-200/day
CPH	Burning, piercing	2-30 minutes	Unilateral	Orbital circumference	Autonomic symptoms	5>/day

Table 3. SNNOOP 10 Criteria	
Sign or symptom	Related Secondary Headaches
Systemic symptoms including fever	Headache attributed to infection or nonvascular intracranial disorders, carcinoid or pheochromocytoma
Neoplasm in history	Neoplasms of the brain; metastasis
Neurologic deficit or dysfunction (including decreased consciousness)	Headaches attributed to vascular, nonvascular intracranial disorders; brain abscess and other infections
Onset of headache is sudden or abrupt	Subarachnoid hemorrhage and other headaches attributed to cranial or cervical vascular disorders
Older age (after 50 years)	Giant cell arteritis and other headache attributed to cranial or cervical vascular disorders; neoplasms and other nonvascular intracranial disorders
Pattern change or recent onset of headache	Neoplasms, headaches attributed to vascular, nonvascular intracranial disorders
Positional headache	Intracranial hypertension or hypotension
Precipitated by sneezing, coughing, or exercise	Posterior fossa malformations; Chiari malformation
Papilledema	Neoplasms and other nonvascular intracranial disorders; intracranial hypertension
Progressive headache and atypical presentations	Neoplasms and other nonvascular intracranial disorders
Pregnancy or puerperium	Headaches attributed to cranial or cervical vascular disorders; postdural puncture headache; hypertension-related disorders (eg, preeclampsia); cerebral sinus thrombosis; hypothyroidism; anemia; diabetes
Painful eye with autonomic features	Pathology in posterior fossa, pituitary region, or cavernous sinus; Tolosa-Hunt syndrome; ophthalmic causes
Posttraumatic onset of headache	Acute and chronic posttraumatic headache; subdural hematoma and other headache attributed to vascular disorders
Pathology of the immune system such as HIV	Opportunistic infections
Painkiller overuse or new drug at onset of headache	Medication overuse headache; drug incompatibility

a widespread place in studies on headache and provides guidance in clinical practice. In some studies evaluating the efficacy and sensitivity of SNNOOP10, it has been concluded that its sensitivity is high in the detection of risky headaches requiring further investigation.[12,13]

While red flags are common in the approach to headache, some recent studies have suggested that it may be useful to designate a few symptoms as green flags. Green flags are designed to indicate that the pain of patients with these symptoms often points to a primary etiology. The symptoms and findings identified as green flags are compiled in Table 4.[14] It has been emphasized that green flags often indicate primary headache, but the priority is to question red flags when evaluating patients and more studies are needed in this regard for the widespread use of green flags.[14,15]

Table 4. Green flags in headache
Existing pain has persisted since childhood
The patient has days without headache
Family members have a headache similar to the patient's headache
Headache has a temporal relationship with the menstrual cycle
The headache has appeared or stopped a week ago

It is important to remember that the presence of a pre-existing primary headache does not exclude a secondary cause that may have developed in the patient's current condition.[9] Therefore, changes in the characteristics of headache must be questioned during history taking and a detailed examination must be performed in terms of new clinical symptoms.[16] Family history, age at onset, frequency and intensity of pain, localization of pain, other complaints accompanying pain, comorbidities, and conditions that trigger or increase pain should be questioned during anamnesis.

There are some conditions that require further investigation in the follow-up of patients with existing primary headache disorder. For example, patients with tension-type headache will need further investigation at the slightest sign of progression, as brain tumors and some secondary headaches can sometimes present with tension-type headache-like. Another scenario in which a patient with a primary headache should be investigated is if there is a change in pattern. When a patient with a chronic migraine has an acute sinus infection, chronic meningitis or an intracranial lesion, the patient may not be investigated because the headache is thought to be due to migraine. Therefore, any additional features or changes in the headache pattern or incurability should always be investigated in a patient with chronic primary headache.[17]

Questioning the period of onset of headache is an important step in the diagnosis. Headaches that begin at older ages, during pregnancy and in the postpartum period require the exclusion of secondary causes. New onset headache in the elderly is more likely to have a serious underlying cause compared to young adults.18 In this age group, intracranial space-occupying lesions (tumor, bleeding), temporal arteritis and drug-related headaches should be excluded. If secondary causes are excluded and primary headache is considered in the etiology, hemicrania continua, hypnic headache, primary cough headache, trigeminal neuralgia should be considered. Migraine and tension headache should be kept in mind in the differential diagnosis, although they occur less frequently in the older age group.[19]

Table 5. Secondary headache causes, symptoms and signs

Condition, signs and symptoms	Secondary headache cause
Periorbital, facial pain, especially in diabetic patients	Mucormycosis and other opportunistic infections
New-onset pain in immunosuppressed patients	Meningitis, intracranial infections, brain abscess, intracranial space-occupying lesion
Pain in the temporal region, presence of systemic symptoms, elevated sedimentation in a patient over 50 years of age	Temporal arteritis
Pain during pregnancy	Eclampsia, prolactinoma, idiopathic intracranial hypertension
Pain in the immunosuppressed patient	Neoplasm, opportunistic infections
Pain defined as acute, severe and the most severe pain in a person's life	Subarachnoid hemorrhage
Pain associated with head and neck trauma	Dissection of neck vessels, intracranial, epidural, subdural hematomas
Pain that increases in frequency and intensity	Increased intracranial pressure, chronic subdural hematoma, headache due to drug overuse
Pain associated with coughing and straining	Increased intracranial pressure
Increased pain when standing up	Low intracranial pressure

In headache that occurs during pregnancy, it is important to exclude secondary causes in order not to overlook important conditions such as eclampsia.[17]

There may be some secondary conditions that should be considered in the foreground in the association of some conditions, findings and symptoms such as onset period, comorbidities. Some examples of these secondary headaches are given in Table 5.[20]

LABORATORY AND IMAGING

Laboratory and imaging tests should be aimed at the preliminary diagnosis. If the cause of the headache is primary, blood tests, electroencephalography (EEG) and other imaging tests have no diagnostic value. These tests are of diagnostic importance in cases suggestive of secondary headache.[17] Extensive diagnostic tests ordered without a preliminary diagnosis will have low diagnostic value and high costs.

Radiologic examinations, lumbar puncture (LP) and CSF examination, laboratory tests, biopsy, EEG, ECG, fundoscopy, intraocular pressure measurement are among the examinations that can be considered specific to the preliminary diagnosis. Table 6 lists the tests that can be evaluated for some secondary causes.[20]

Table 6. Investigations to be requested for some specific reasons

Secondary Headache Cause	Audit to be Evaluated
Subarachnoid Hemorrhage	Computed tomography (CT), lumbar puncture (LP), cerebral angiography (DSA)
Intraparenchymal/Subdural/ Epidural Hemorrhage	CT, magnetic resonance imaging (MRI)
Ischemic cerebrovascular diseases	CT, MRI, MR venography
Temporal Arteritis	Sedimentation, CRP, doppler USG, temporal artery biopsy
Cervical Artery Dissection	MRI, magnetic resonance angiography, doppler ultrasound, CT angiography, DSA
Sinusitis	Waters radiograph, CT
Central nervous system infections	MRI, EEG, LP, blood and CSF microbiological examinations
Metabolic and Endocrine Causes	Prolactin levels, pituitary hormones, TSH, free T4

TREATMENT

In treatment, the etiology of the pain determines the approach route. In secondary headaches, treatment should be directed towards the cause. It should be noted that symptomatic treatment without excluding secondary causes may mask the underlying cause of the pain. In primary headache disorders, there are many different pharmacologic and non-pharmacologic treatment approaches to address the etiology.

Migraine Treatment

Migraine treatment is basically analyzed under two main headings: acute attack for the attack that has already started and prophylactic treatment to reduce the frequency of attacks. The main topics in migraine treatment are compiled and given in Table 7.

Table 7. Migraine treatment

Acute Attack Treatment
Non-steroidal anti-inflammatory drugs (NSAIDs) group
Triptan group drugs
Symptomatic treatments for nausea and vomiting
Prophylactic Treatment
Lifestyle changes
Antiepileptics, antidepressants, beta-blockers and calcium channel antagonists
Botulinum neurotoxin-A (BoNT-A)
Interventional methods
New Drug Therapies
Gepants and ditans

ACUTE ATTACK TREATMENT

The goal of acute treatment is to reduce the duration and severity of the onset of an attack and ideally to terminate it. The aim of treatment is not only to relieve the headache but also other accompanying symptoms. The International Headache society's recommendation for acute treatment clinical trials is that the headache should stop after 2 hours and that the headache and other accompanying symptoms should not recur for 24-48 hours.[21]

As a general principle, non-specific and easily accessible drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) may be preferred for mild to moderate attacks, and if these are not effective, more pathophysiology-specific drugs such as triptans may be preferred. Another symptom to keep in mind is nausea and vomiting, which can be more unpleasant than the headache itself .

In addition to NSAIDs or triptans, metoclopramide (10 mg) or domperidone (10 mg) are usually effective in symptomatic treatment of nausea. NSAIDs with proven efficacy in migraine

treatment are acetylsalicylic acid, ibuprofen, naproxen, ketorolac and diclofenac. Ergot alkaloids and triptans are migraine-specific drugs with agonistic effects on serotonergic 5-HT1B/1D receptors. In addition to symptomatic treatment of nausea and vomiting in migraine, they have been found to be effective against the primary migraine attack. Therefore, they are used as adjunctive therapy and intravenous metoclopramide is preferred in the treatment of acute attacks in emergency departments.[22]

While triptans are selective to 5-HT1B/1D receptors, ergot alkaloids bind to other serotonergic, dopaminergic and adrenergic receptors. For these reasons, ergot derivatives carry with them the potential for significant side effects. For example; since they also have a high affinity for vascular serotonergic receptors, systemic vasoconstriction and thus cardiovascular risks arise.[23]

PROPHYLACTIC TREATMENT

The goal of prophylactic treatment is to reduce the frequency of attacks by at least half. In general, the effect of prophylactic treatments appears 6-8 weeks after initiation and should be continued without interruption for at least 3-12 months for the effect to be permanent.[24]

Lifestyle Changes

In patients complaining of frequent and severe migraine attacks, in addition to pharmacological treatment approaches, regular nutrition, adequate sleep patterns and stress avoidance should be recommended.[25]

Antiepileptics, Antidepressants, Beta-Blockers and Calcium Channel Antagonists

Topiramate and valproic acid are antiepileptics approved by the United States Food and Drug Administration (FDA) for the prophylactic treatment of migraine. The effect of these drugs on migraine prophylaxis was discovered incidentally during their use in epilepsy and their mechanism of action in migraine is still unknown. When both topiramate and valproic acid are administered chronically to mice for several weeks, similar to migraine prophylaxis in patients, the threshold for triggering Cervicocephalic syndrome(CCS) increases and the propagation rate decreases.[24]

As with antiepileptics, the migraine prophylaxis effects of some antidepressants have been found to be incidental. There is insufficient evidence for the prophylactic effect of selective serotonin reuptake inhibitors, which are frequently used in the clinic.[26]

Flunarizine is a nonselective calcium channel antagonist, but also shows dopamine and histamine receptor antagonism. Although its mechanism of action in migraine prophylaxis is still unknown, there is evidence for an inhibitory effect on neurogenic inflammation.[27]

Botulinum neurotoxin-A (BoNT-A) inactives SNAP-25, a known presynaptic protein and suppresses neurotransmitter release from cholinergic terminals. Following local injection, BoNT-A enters the trigeminal nerve endings innervating the skin and is retrogradely transported by axonal transport mechanisms. In this way, it first reaches the trigeminal ganglion and then reaches the trigeminocervical complex by transcytosis. It has been suggested that BoNT-A suppresses the release of neuropeptides such as CGRP and P-substance at the site where it reaches, which may constitute a prophylactic effect.[28]

METHODS

Interventional methods can be used for acute and preventive purposes. The interventional methods can be summarized as large and small occipital nerve, supraorbital, supratrochlear nerve, auriculotemporal nerve blocks, sphenopalatine ganglion blocks.[29]

Different GON blockade techniques have been described. The most widely used and recommended technique is to place the sensitive point 1/3 medial to the imaginary line drawn between the protuberant a occipitalis externa and the mastoid process, medial to the occipital artery palpation. Local anesthetic volumes between 0.5-10 mL were used in the studies. The majority of researchers used 1.5-2 ml of 0.5% bupivacaine as local anesthetic and its efficacy has been shown.[30]

Acupuncture treatment method may have an analgesic effect and can be used during the treatment of migraine attacks, but studies on its usefulness in prophylactic treatment are mostly not statistically significant.For acupuncture, needles are inserted into the trigger points detected as a result of the examination. Although the effectiveness of dry needling has been proven in many musculoskeletal diseases, it has not been shown to be beneficial in migraine. It should not be considered as a treatment option in migraine cases.[31]

Trigger points occur as a result of abnormal depolarization of motor endplates leading to excessive release of acetylcholine at the neuromuscular junction. Prolonged contracted muscles lead to muscle shortening, hypoxia and metabolite accumulation. Algesic proinflammatory molecules such as substance P, CGRP and bradykinin have been detected in active trigger points. Trapezius, splenius capitis, levator scapula, temporal, and sternocleidomastoid muscles are the most common muscles in which trigger points occur. The association of primary headaches and myofascial pain is common and injections to these trigger points significantly reduce pain. In migraine patients, various studies have shown that the presence of trigger points and injections applied to these points provide a decrease in pain frequency and intensity.[32]

New Drug Therapies

The high prevalence of migraine and its high burden in terms of disability has increased the search for new migraine-specific treatments. This has led to the discovery of new drugs such as 5HT1F receptor agonists-ditans (lasmiditan), small molecule calcitonin gene-related peptide (CGRP) monoclonal antibodies.

These drug therapies may not be suitable for all patients due to their higher cost and limited accessibility. Lasmiditan and gepants are a good choice in the treatment of patients with severe migraine attacks who cannot use triptans for various reasons such as cardiovascular or cerebrovascular disease.

The anti-CGRP monoclonal antibodies should be considered as a last-line treatment for patients for whom other drug therapies have not been effective or who have side effects associated with these drugs and should be saved for last.[33]

TREATMENT OF TENSION HEADACHE

Acute Attack Treatment

Acute attack treatment to stop the attack and reduce its severity includes the use of simple analgesics and nonsteroidal anti-inflammatory agents alone or in combination (Table 8).[34]

Table 8. Drugs used in the treatment of attacks, their doses, and side effects.[35]

Attack treatment	Dose	Side effects
İbuprofen	200-800 mg	Gastrointestinal side effects
Flurbiprofen		
Paracetamol	1000 mg	Gastrointestinal side effects, Liver toxicity
Ketoprofen	25 mg	Gastrointestinal side effects
Aspirin	500-1000 mg	Gastrointestinal side effects
Naproxen	375-1000 mg	Gastrointestinal side effects
Diclofenac	12.5-100 mg	Gastrointestinal side effects
Dexketoprofen	25-75 mg	Gastrointestinal side effects

Metamizole

Metamizole has been shown to be effective in GTBA at doses of 0.5-1 g. However, its use is avoided because it causes agranulocytosis.[36]

Butalbital

Butalbital-containing drugs are recommended when first-line analgesics are ineffective or not used. Butalbital + acetaminophen + caffeine (esgic, floricet).[37]

Lumiracoxib

It is a new COX-2 receptor inhibitor and has been shown to be effective in tension headaches at doses of 200-400 mg.[38]

Flupirtine

Flupirtine is one of the non-narcotic analgesics and has effects on potassium channels and NMDA.[39]

Antiemetic Districts

Antiemetic drugs facilitate the absorption of analgesic drugs by providing rapid emptying of the stomach. Metoclopramide 10 mg (metpamide) and domperidone 10 mg (motilium) are among the drugs that are used and effective.[34]

Tension Headache Prophylaxis Treatment

The aims of prophylactic treatment are to decrease the frequency, severity, and duration of headache attacks and to ensure recovery in cases where acute attack treatments are unresponsive. In addition, prophylactic treatment may be started in advance during acute treatment due to lack of response to preventive treatment, side effects, overuse of the drug, and contraindications of the drug.(Table 9)[34]

Table 9. Dosage, side effects, and contraindications of antidepressant drugs.[40]

Primary treatment	Dose	Side effects	Contraindication
Amitriptyline	30-75 mg	Dry mouth, constipation, palpitations, blurred vision, weight gain, orthostatic hypotension	Hypersensitivity, arrhythmias, hypertension, mania, urinary retention and heart block, use with monoamine oxidase inhibitors
Secondary treatment			
Mirtazapine	30 mg	Weight gain, sedation, orthostatic hypotension, mania	Hypersensitivity
Venlafaxine	150 mg	GIS side effects, anorexia, irritability, insomnia, sexual dysfunction	Mania, use with monoamine oxidase inhibitors
Tertiary treatment			
Clomipramine	75-150 mg	Similar to amitriptyline side effects	Similar to amitriptyline
Maprotiline	75 mg	Headache, dizziness, seizures, ataxia, fatigue, sedation, similar to the side effects of amitriptyline	Use with monoamine oxidase inhibitors
Mianserin	30-60 mg	Seizures, hypomania, hypotension, arthralgia and edema	Use with monoamine oxidase inhibitors, DM, heart failure

In prophylaxis, amitriptyline is the first choice, venlafaxine and mirtazapine are the second choices.

Nonpharmacologic Therapies

Non-pharmacologic methods should also be considered in the treatment of primary headaches.[41]

Information about the disease

- Lifestyle change
- Regular sleep and nutrition
- Exercise
- Posture regulation
- Awareness and avoidance of triggers
- EMG- biofeedback
- Cognitive-behavioral therapies
- Psychological support
- Physical therapy
- Acupuncture
- Local injections
- TENS (Transcutaneous electrical nerve stimulation)

Cluster Type Headache Treatment

1- Acute attack treatment

- Oxygen inhalation: it has been shown that inhalation of 6-12 lt/min of 100% oxygen for 15-20 min with a mask during a headache attack was effective in approximately 2/3 of the patients.[42]
- Triptans:Subcutaneous sumatriptan (5-HT1B/D receptor agonist) was found to be superior to placebo at 6 mg and 4 mg doses. Response is obtained in 2/3 of patients within 15 minutes.[43]

2- Prophylactic treatment

- Verapamil: The first choice for prophylaxis for both episodic and chronic cluster headaches. It is started with 80 mg three times a day. If there is no response, 80 mg can be increased weekly up to 960 mg.[44]
- Lithium: It is used at a dose of 300-1200 mg/day. It has been found to be more effective in chronic cluster-type headaches.[45]

- Antiepileptic drugs: topiramate, sodium valproate, gabapentin are the main antiepileptic drugs used in cluster headache prophylaxis 46.

CONCLUSION

Headache is common in the community and is one of the most common causes of hospital admission. Although pain may have many etiologies, it is basically divided into primary and secondary headache disorders. The most important step in the evaluation of a patient presenting with headache is to differentiate between primary and secondary causes. The treatment approach should be directed towards the cause in secondary headache disorders. There are some traditional treatments for primary headache disorders and some newly developed drug therapies. Considering the prevalence and disability burden of primary headache disorders in the community, more studies are needed to develop effective drug therapies.

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Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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