A review study on recent advance of headache and facial pain disorders
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Headache and facial pain disorders are prevalent, disabling, and largely treatable, but are under-recognized, underdiagnosed, and undertreated, and a burden, both to the individual and to the society. Headache and facial pain cuts across a diverse group of physicians, including neurologists, neurosurgeons, headache specialists, otolaryngologists, dental specialists, anesthesiologists, and pain specialists. This review discusses the relevant neuroanatomy, the updates in pathophysiology, and classification of headache and facial pain disorders. We will also introduce the art of history-taking in headache patients, as well as physical examination, investigation, and treatment of the most common disorders.

Keywords: classification, cluster headache, diagnostic criteria, facial pain, headache, migraine, neuroanatomy, pathophysiology, rhinogenic headache, trigeminal neuralgia

Introduction
Headache and facial pains are very common. Approximately half to three-quarters of adults aged 18–65 years have had headaches in the past year in studies from all regions except Africa, where the estimated 1-year prevalence is lower at 22% [1]. Headache and facial pain is classified into 18 major types of headaches: four types of primary headache, 12 types of secondary headache, and cranial neuropathies and other facial pains and headaches.

Primary headaches are those without any identifiable cause on examination or investigation and in which diagnosis is made by recognizing a pattern. Primary headache types include migraine, tension, trigeminal autonomic cephalalgias, and other disorders [2]. Clinch et al. [3] noted that 90% of all headaches are primary headaches. Edelmayer et al. [4] proposed that activation of transient receptor potential ankyrin-1 (TRPA1) on meningeal nerve endings contributes to environmental irritant-induced headache but this channel may also contribute to other forms of headache, such as migraine. Treatment of primary headaches is classified into nonpharmacological and pharmacological and can be prophylactic or administered during attacks [5].

Secondary headaches are those with a definite underlying cause identifiable on examination or investigation [6]. Secondary headache types include those arising from trauma, vascular disorders, nonvascular disorders, infection, temporomandibular joints, dental factors, mucosal contact point, rhinosinusitis, and from eye, ear, and other infections.

Blood vessel spasms, dilated blood vessels, inflammation, infection of meninges, muscular tension, temporomandibular and dental disorders, head trauma, and tumor stimulate nociceptors and cause pain [7]. Presence of red flag symptoms means that a headache warrants further investigation with neuroimaging, laboratory tests, and lumbar puncture [3]. Treatment of secondary headaches involves treating the underlying cause [5]—for example, rhinogenic headache managed endoscopically in selective cases [8].

Facial pain syndromes include trigeminal neuralgia, glossopharyngeal neuralgia, nervous intermedius (facial nerve) neuralgia, occipital neuralgia, and others [2].

Discussion
Relevant neuroanatomy
The trigeminal nerve, or the fifth cranial nerve as the largest of the cranial nerves, is a mixed, predominantly sensory cranial nerve. Embryologically it is the first nerve of the branchial arch. After the differentiation...
of the branchial arch into mandibular and mastication muscles, it supplies as the fifth cranial nerve with its bigger sensorial part being facial skin, the conjunctiva, as well as the mucosa of the face, partially of the mouth, teeth, and most of the scalp. A smaller motoric part innervates the muscles of mastication [9].

Because a long course from the brainstem nuclei to the peripheral branches is seen, it is useful to subdivide the nerve into several segments and then tailor the imaging modality and the imaging study to that specific segment. This is particularly true in cases where topographic diagnosis can be used to locate a lesion in the course of these nerves [10].

**Pathophysiological considerations**

Headache can occur as a result of activation of pain-sensitive cranial structures, such as the dura mater, vasculature, the cranial, cervical muscles, and ligaments, which are innervated by primary afferent neurons originating from the trigeminal and dorsal root ganglia of the upper cervical spinal nerves. In relation to nociception in cases of headache, two types of nerve fibers are considered important: the small-caliber, unmyelinated, slow-conducting fibers called C fibers, and the small-diameter, lightly myelinated, more rapid-conducting fibers called A-delta fibers. Findings from nerve stimulation studies indicate that C fibers transmit aching, throbbing, or burning pain that builds up slowly, whereas the A-delta fibers conduct sharper initial pain sensation [11].

**Pain pathway**

There is neither a direct nor a simple ‘pain-specific’ conduit within the nervous system. Instead, the experience of pain is the final product of a complex information-processing network. Following delivery of a noxious stimulus, a series of electrical and chemical events occur. The first stage is transduction, where external noxious energy is converted into electrophysiological activity. In the second stage, transmission, this coded information is relayed through the spinal cord to the brainstem and thalamus. Finally, connections between the thalamus and higher cortical centers control perception and integrate the affective response to pain [12].

Recent findings have underscored the possibility that transient receptor potential channels expressed in the nerve terminals of peptidergic nociceptors contribute to the migraine mechanism. Among this channel subset, TRPA1, a sensor of oxidative, nitrate, and electrophilic stress, is activated by an unprecedented series of irritant and pain-provoking exogenous and endogenous agents, which release the promigraine peptide, calcitonin gene-related peptide, through this neuronal pathway. Some of the recently identified TRPA1 activators have long been known as migraine triggers [13].

**Headache and facial pain classification**

Headaches are most thoroughly classified by the International Headache Society’s International Classification of Headache Disorders (ICHD). The ICHD is an in-depth hierarchical classification of headaches published by the International Headache Society. It contains explicit (operational) diagnostic criteria for headache disorders. The first version of the classification, ICHD-1, was published in 1988 [14].

The classification uses numeric codes. The top, one-digit diagnostic level includes 14 headache groups. The first four of these are classified as primary headaches, groups 5–12 as secondary headaches, and the last two groups comprise painful cranial neuropathies and other facial pains and headaches [2].

According to the ICHD-3 beta that was published in 2013 headache and facial pain is classified as follows:

**Part 1: Primary headaches**

1. Migraine.
2. Tension-type headache (TTH).
3. Trigeminal autonomic cephalalgias.
4. Other primary headaches.

**Part 2: Secondary headaches**

1. Headache attributed to trauma or injury to the head and/or neck.
2. Headache attributed to cranial or cervical vascular disorder.
3. Headache attributed to nonvascular intracranial disorder.
4. Headache attributed to a substance use or its withdrawal.
5. Headache attributed to infection.
6. Headache attributed to disorder of homoeostasis.
7. Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cervical structures.
8. Headache attributed to psychiatric disorders.
Part 3: Painful cranial neuropathies, other facial pains, and headaches

(1) Cranial neuralgias and central causes of facial pain.
(2) Other headache, cranial neuralgia, central or primary facial pain.

Clinical approach for management of patients presenting with headache and facial pain

The diagnosis of headache and facial pain is based on a careful history taking as well as physical and neurologic examination.

History taking

Routine history taking begins with a set of standard questions that will elicit basic information; further, depending on the acuity of onset, the age of the patient and whether he/she presents in the office/consulting room or emergency department/casualty, additional history is recorded. In every patient with a headache, the physician’s and patient’s primary concern is that no serious life-threatening cause is overlooked.

It is therefore important to be alert to the ‘red flags’:

(1) First or worst headache ever.
(2) New headache after age 50.
(3) Very sudden-onset headache.
(4) Headaches increasing in frequency and severity.
(5) New-onset headache in a person with possible HIV or cancer.
(6) Headache with signs of total body illness (fever, stiff neck, rash).
(7) Change in personality, consciousness, or mental status.
(8) Headache triggered by cough, exertion, or while engaged in sexual intercourse [15].

Physical examination

Vital signs, including temperature, are measured. General appearance (whether restless or calm in a dark room) is noted. A general examination, with a focus on the head and neck, and a full neurologic examination are performed. The scalp is examined for areas of swelling and tenderness. The ipsilateral temporal artery is palpated, and both temporomandibular joints are palpated for tenderness and crepitance while the patient opens and closes the jaw [16].

The eyes and periorbital area are inspected for lacrimation, flushing, and conjunctival injection. Pupillary size and light responses, extraocular movements, and visual fields are assessed. The fundi are checked for spontaneous venous pulsations and papilledema. If patients have vision-related symptoms or eye abnormalities, visual acuity is measured. If the conjunctiva is red, the anterior chamber and cornea are examined with a slit lamp if possible, and intraocular pressure is measured. The nares are inspected for purulence, congestion, septal deviation, spurs, turbinate hypertrophy, discharge, polypi, and adhesions [16].

Investigations

The vast majority of primary headaches do not require neuroimaging. An abnormal neurological examination in patients suffering from headaches is significantly more likely to reveal an underlying cause [17]. The European Federation of Neurological Societies guidelines suggest that MRI is the imaging modality of choice because of its greater sensitivity [18]. Lumbar puncture with cerebrospinal fluid analysis is appropriate for patients with thunderclap headache and normal neuroimaging to exclude a diagnosis of subarachnoid hemorrhage [19]. Increased erythrocyte sedimentation rate may be useful in predicting the presence or absence of giant cell arteritis in patients with suggestive symptoms [20].

Investigation for rhinogenic headache

(1) Axial and coronal computed tomography (CT) of the nose and paranasal sinuses.
(2) Nasal endoscopy.

These tests are carried out to especially report on the following:

(1) Middle turbinate hypertrophy and abnormal shape.
(2) Uncinate process, its size, and any abnormalities.
(3) Large bulla ethmoidalis.
(4) Hiatus semilunaris and presence of pus in their vicinity.
(5) Nasopharynx, nasopharyngeal lymphoid tissue, and eustachian tube [8].

The adverse effects of investigation of headaches

The investigations to which patients are subjected are not without risk. A single head CT may slightly increase the lifetime risk for death from cancer because of exposure to radiation [21]. In susceptible individuals, there is a risk for anaphylaxis and renal insufficiency when iodinated contrast material is administered [22].
A procedure as ‘benign’ as a lumbar puncture may be complicated by postlumbar puncture headaches, a persistent cerebrospinal fluid leak, bleeding, low back pain, and, occasionally, infection [23].

**Treatment of common headaches and facial pain disorders**

The treatment of patients with headaches requires a great deal of understanding of the causative factors and understanding of the lifestyle attributes of the patient. Depending on the headache type, one would be prescribed medicines to terminate the headache episode (abortive treatment) or prevent the occurrence of headache (prophylactic treatment). Not all patients require prophylactic treatment. The decision is largely based on frequency of the headache and the perceived disability. Prevention of triggers is an important factor in the treatment protocol [16].

### Migraine headache

**Pharmacological treatment**

The physician should strongly consider avoiding abortive treatments in any patient with a prior history of drug misuse or abuse. Many drugs, including simple analgesics, ergot alkaloids, triptans, and NSAIDs, can produce serious consequences if they are abused [24].

A systematic review of eight randomized trials found that parenteral ketorolac (30 mg intravenous or 60 mg intramuscular) was effective for acute migraine in comparison with other agents, including intranasal sumatriptan, intravenous prochlorperazine, intravenous chlorpromazine, and intravenous dihydroergotamine combined with metoclopramide [25].

**Nonpharmacological treatment**

The portable transcutaneous magnetic stimulation device is available in the UK and selected centers in the USA, but more data are needed to confirm the benefit of this treatment for episodic migraine. The transcutaneous magnetic stimulation device may prove to be useful as a second-line intervention for those who have episodic migraine with aura that does not respond to first-line therapy with triptans or other agents discussed above or who are unable to take these agents because of contraindications or intolerance. Transcutaneous magnetic stimulation should not be used to treat migraine in patients who have epilepsy, as there is theoretical concern that transcutaneous magnetic stimulation could trigger seizures [26].

### Tension type headache

**Pharmacological treatment**

Attack treatment includes ibuprofen 200–800 mg, ketoprofen 25 mg, acetylsalicylic acid 500–1000 mg, naproxen 250–500 mg, diclofenac 12.5–100 mg, and paracetamol 1000 mg. Consequently, the choice of analgesics should be made on the basis of effect and side effects in the patient in question [27].

Antidepressant compounds are the drugs of choice for the prophylaxis of TTH. Antidepressants have been shown to not only decrease the frequency and intensity of headaches but also correct the pathologic sleep abnormalities and depression frequently seen in TTH sufferers [28].

**Long-term prophylaxis:** Verapamil is the first-choice drug for the prophylaxis of both episodic and
chronic cluster headache. Daily doses of 240–480 mg/day are frequently effective, and the short-acting preparation is usually preferred. Higher doses may be required (maximum dose: 960 mg/day), depending on drug tolerance and symptom evaluation. Doses greater than 240 mg/day require monitoring by electrocardiography. Adverse effects of verapamil include constipation, edema, bradycardia, gastrointestinal discomfort, gingival hyperplasia, and headache [36].

**Short-lasting unilateral neuralgiform headache attacks**

**Oral treatments**

Current guidelines for the preventative treatment of short-lasting unilateral neuralgiform headache attacks advise first-line treatment with lamotrigine. Other oral therapies, including topiramate, gabapentin, oxcarbazepine, carbamazepine, and mexiletine, have case reports to support their use as alternative agents [37].

**Injectable treatments and nerve blocks**

Intravenous lidocaine is a useful agent in the treatment of severe attacks or for short-lasting unilateral neuralgiform headaches. Lidocaine and mexiletine are both antiarrhythmic drugs acting on sodium channels [38].

Limited reports exist on the use of botulinum toxin and greater occipital nerve block for short-lasting unilateral neuralgiform headaches [39].

**Resectional and ablative surgery**

A number of procedures have been conducted over the years, often under the misdiagnosis of trigeminal neuralgia, including microvascular decompression, glycerol rhizotomy, trigeminal nerve radiofrequency ablation, balloon compression of the gasserian ganglion, and gamma knife therapy. Outcomes are mixed but, in general, the adverse effects outweigh any benefit. The one procedure that has appeared in recent reviews to be efficacious, even with long-term follow-up, is microvascular decompression of the trigeminal nerve [40].

**Neurostimulation**

The outcomes of deep brain stimulation for short-lasting unilateral neuralgiform headaches with conjunctival injection appear promising [40].

**Treatment for rhinogenic headache**

**Medical treatment**

(1) Nasal decongestant drops twice daily (oxymetazoline).

(2) Antihistamines: for example, loratadine and cetirizine.

(3) Antibiotics (doxycycline, amoxicillin clavulanic acid) if there is suspected infection.

(4) Occasionally, local corticosteroids such as beclomethasone, or fluticasone, or long-acting steroid injection. Betamethasone dipropionate was also given [8].

If the condition of the patient improves no further management is carried out; if not improved, we proceed to surgery if the patient agrees.

**Surgical treatment**

**Criteria for surgery**

(1) Presence of chronic headache (>2 months), or pain or pressure feeling over the nasal bridge, glabella, or forehead as the main chief complaint without any apparent sinus disease including sinusitis, tumors, polyp, or cyst in CT scanning of the nasal cavity and failure of standard medical therapy for headache.

(2) Normal ophthalmologic, neurologic, and systemic examinations, despite the presence of headaches.

(3) Existence of concha bullosa of the middle turbinate in paranasal sinus coronal CT and visible contact points between the mucosal surfaces of the middle concha and lateral wall in the osteomeatal complex region, or between the medial wall and septum in diagnostic endoscopy of the nasal cavity.

(4) Relieving of the headache by an application of local anesthetic (2% lidocaine) over the contact point.

(5) Absence of any other obvious cause of headaches after a complete evaluation by an ophthalmologist, neurologist, dentist, internist, or any other related specialist [41].

**Surgical procedures**

These were tailored according to endoscopic and CT scan findings, and includes the following:

(1) Concha bullosa was treated by lateral, subtotal, or submucous resection to allow the lateralization of the medial remnant of the turbinate away from the nasal septum.

(2) An uncinate process was resected if pneumatized or medially or laterally bent.

(3) In the presence of an over-pneumatized bulla, it was opened removing only the bulge of the cell following uncinectomy. Agger nasi cells, if narrowing the frontal recess, were also removed carefully without traumatizing the mucosa of the frontal recess area.

(4) A paradoxically bent middle turbinate was treated by segmental resection with turbinate scissors.
throughout its bulbous part leaving the lamellar or superior part of the turbinate intact.

(5) In cases with nasal septal deviation or septal spurs, nasal septoplasties or spur resections were carried out [42].

In a study 36 patients reported a postoperative absence of headaches or a decrease in their intensity. Nineteen (52.7%) patients reported complete relief from pain following surgery and 17 (47.3%) reported occasionally having minimal pain that they no longer considered significant. None of the patients reported an increase in the frequency or intensity of their headaches postoperatively [42].

Conclusion
Headache is one of the most common symptoms in the general population. It causes a significant burden, both to the individual and to society. Understanding the anatomy and pathophysiology of headache helps to establish the right diagnosis and treatment. The International Headache Society has published a system of classification and operational diagnostic criteria for headache based on clinical consensus.

Classifying headaches as primary, secondary, and cranial neuropathy can facilitate evaluation and management. A detailed headache history helps to distinguish among the different headache disorders.

The vast majority of primary headaches do not require neuroimaging.

Brain CT should be performed in patients with headache who have unexplained abnormal neurological signs, unless the clinical history suggests MRI is indicated.

The management of headache and facial pain can be challenging. Many patients require coordination of care among multiple providers, including neurology, otolaryngology, ophthalmology, oral surgery, pain management, psychology, and neurosurgery. Headache disorders are common in Egypt. Still headache is under-estimated and under-recognized in Egypt and this problem should be targeted by health care providers. There is abundance of epidemiological studies of headache in developed and western countries; however, data in developing countries and in Egypt are still lacking. Further multicenter studies are needed to evaluate headache epidemiology and prevalence in the whole country.

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Conflicts of interest
There are no conflicts of interest.

References


