In The Name Of God

Islamic Azad University

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Comparative efficacy of topamax and sodium valproate in management of migraine headache among patients attending to Amiralmomenin hospital during 2006-7

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LIST

Comparative efficacy of topamax and sodium valproate in management of migraine headache among patients attending to Amiralmomenin hospital during 2006-7

Current study was performed as an experimental and interventional survey to evaluate the comparative efficacy of topamax and sodium valproate in management of migraine headache among patients attending to Amiralmomenin hospital during 2006-7. Two-hundred and eighty-five patients (50.1%) received sodium valproate and 284 subjects (49.9%) received topamax for the treatment of migraine headache. In sodium valproate group, 262 patients (91.9%) and in topamax group 266 subjects (93.7%), were cured (P=0.424). In sodium valproate group, 40 patients (14%) and in topamax group 41 subjects (14.4%), experienced drug adverse effects (P=0.891). Accordingly, both treatments may be indicated upon with patient's conditions.

Keywords: Migraine, Sodium Valproate, Topamax

Introduction

Migraine headache is a neurologic disorder associated with significant disability and impaired quality of life, adversely affecting daily activity and work-related productivity for many persons. Approximately 11% of the US population experiences migraine, and a similar prevalence is evident in other industrialized countries. Many migraineurs patients do not consult a physician for treatment, and even among patients who are treated, less than one third report consistently effective results with their current pharmacologic regimens, most of which include over-the-counter analgesics. Furthermore, most migraine patients require bed rest in addition to medication, indicating that migraine continues to significantly affect their lives.

The goals of managing migraine are to reduce migraine frequency, severity, and disability; reduce reliance on poorly tolerated, ineffective, or unwanted acute pharmacotherapies; improve quality of life; reduce headache-related distress and psychologic symptoms; educate patients and enable them to manage their disease; and avoid dose escalation of acute medications. Recent studies suggest that habitual overuse of acute medications, including triptans, ergots, and other analgesics, can lead to the development of chronic daily headaches. Preventive medications can serve an important role in the treatment of migraine by reducing migraine frequency and by ameliorating dose escalation and the potential for

overuse of acute pharmacotherapies. So, comparative surveys on therapeutic efficacy of different drugs in Iran are scarce, current study was conducted to evaluate the comparative efficacy of topamax and sodium valproate in management of migraine headache among patients attending to Amiralmomenin hospital during 2006-7.

Review of Literatures

Pathophysiology

The mechanisms of migraine remain not completely understood. However, the advent of new technologies has allowed formulation of current concepts that may explain parts of the migraine syndrome.

Vascular theory

For many years, headache pain during a migraine attack was thought to be a reactive hyperemia in response to vasoconstriction-induced ischemia during aura. This explained the throbbing quality of the headache, its varied localization, and the relief obtained from ergots; however, it did not explain the prodrome and associated features, the efficacy of some drugs used to treat migraines that have no effect on blood vessels, and the fact that most patients do not have an aura.

Also, intracarotid and single-photon emission computed tomography (SPECT) studies revealed that the headache is dissociated from hyperperfusion at its onset and termination in patients suffering from migraine headache with aura. They also revealed that regional cerebral blood flow (rCBF) decreases in the posterior area of the relevant cerebral hemisphere even before the aura is noted and that headache occurred while rCBF remained decreased; rCBF gradually increased throughout the remainder of the headache phase. No consistent flow changes have been identified in patients suffering from migraine headache without

aura, but rCBF remains normal in the majority. However, bilateral decrease in rCBF beginning at the occipital cortex and spreading anteriorly has been reported.

Cortical spreading depression

The spread of hypoperfusion propagates at a speed similar to that of cortical spreading depression (CSD) and migraine aura. This suggests not only that CSD is the disturbance resulting in the clinical manifestation of migraine aura but also that this spreading oligemia can be clinically silent (ie, migraine without aura). Perhaps a certain threshold is required to produce symptoms in patients having aura but not in those without aura. CSD with or without clinical manifestation (aura) may be a key trigger for the headache of migraine. Although this question is unsettled, CSD has been postulated to directly excite trigeminovascular afferents by promoting release of nociceptive substances from neocortex into the interstitial space, causing direct firing of the nociceptive stimulus.

Vasoactive substances and neurotransmitters

Perivascular nerve activity also results in release of substances such as substance P (SP), neurokinin A (NKA), calcitonin gene-related peptide (CGRP), and nitric oxide (NO), which interact with the blood vessel wall to produce dilatation, protein extravasation, and sterile inflammation, stimulating the trigeminocervical complex as shown by induction of c-fos antigen by positron emission tomography (PET) scan. Information then is

relayed to the thalamus and cortex for registering of pain. Involvement of other centers may explain the associated autonomic symptoms and affective aspects of this pain.

Is the neurologically mediated sterile plasma extravasation the cause of this pain? Neurogenic plasma extravasation is inhibited by 5-HT1 agonists, GABA agonists, neurosteroids, prostaglandin inhibitors, SP antagonists, and the endothelin antagonist bosentan; the latter 2 are ineffective as antimigraine drugs, showing that blockade of neurogenic plasma extravasation is not completely predictive of antimigraine efficacy in humans. Neurogenically induced plasma extravasation may play a role in expression of pain in migraine, but whether this in itself is sufficient to cause pain is not clear; the presence of other stimulators may be required. Also, the pain process needs not only the activation of nociceptors of pain-producing intracranial structures but also reduction in the normal functioning of endogenous pain control pathways that gate the pain.

Migraine center

What generates a migraine episode? A potential "migraine center" in the brain stem has been proposed based on findings on PET of persistently elevated rCBF in the brain stem (ie, periaqueductal gray, midbrain reticular formation, locus ceruleus) even after sumatriptan produced resolution of headache and related symptoms in 9 patients who had experienced spontaneous attack of migraine without aura. This increased

rCBF was not observed outside of the attack, suggesting that this activation is not due to pain perception or increased activity of the endogenous antinociceptive system.

That sumatriptan reversed the concomitant increased rCBF in the cerebral cortex but not the brainstem centers suggests dysfunction in the regulation involved in antinociception and vascular control of these centers. Thalamic processing of pain is known to be gated by ascending serotonergic fibers from the dorsal raphe nucleus and from aminergic nuclei in the pontine tegmentum as locus ceruleus and that the latter can alter brain flow and blood-brain barrier permeability. Perhaps when these modulatory controls are timed to dysfunction, the migrainous process ensues.

Frequency

United States

More than 23 million people in the United States suffer from migraine. This roughly corresponds to 17.6% of females and 6.0% of males.

Mortality/Morbidity

Headaches may serve as a warning: not all severe headaches are due to migraine; they can be a warning sign of more serious conditions. Headache characteristics that should raise concern include the following:

- Change in character of the headache over the time should raise a red flag. Headaches associated with other neurological signs or symptoms

(eg, diplopia, loss of sensation, weakness, ataxia) or those of unusually abrupt onset.

- Headaches that are persistent (especially beyond 72 hours), that first occur after the age of 55 years, or that develop after head injury or major trauma. Headaches that are persistent on one side of the head (persistent one sided throbbing headaches mimicking like migraines: arteriovenous malformation should be excluded with imaging).
- Headaches that are associated with stiff neck or fever
- Headaches without a clear family history of migraine headache

Race

The prevalence of migraine appears to be lower among African Americans and Asian Americans than among whites.

Sex

- Migraine headaches are reported to affect women more than men.
- Approximately 75% of all persons who experience migraines are women.

Age

- The prevalence of migraine appears to be similar for boys and girls in the prepubescent years.
- The prevalence of migraine is higher in adolescent girls than in boys of similar age.

- By early adulthood, migraine is 3 times as frequent in women as it is in men.

CLINICAL

History

The typical headache of migraine is throbbing or pulsatile. It is initially unilateral and localized in the frontotemporal and ocular area, then builds up over a period of 1-2 hours, progressing posteriorly and becoming diffuse. It typically lasts from several hours to a whole day. Pain intensity is moderate to severe, prompting the patient to remain still as it intensifies even with routine physical activity.

- The attack commonly occurs when the patient is already awake, although it may have already started upon awakening and less commonly may awaken the patient at night.
- Nausea and vomiting usually occur later in the attack in about 80% and 50% of patients, respectively, along with anorexia and food intolerance.
- Some patients have been noted to be pale and clammy, especially if nausea develops.
- Photophobia and/or phonophobia also commonly are associated with the headache.

- The headache usually subsides gradually within a day and after a period of sleep; a majority of patients report being tired and weak afterwards.
- About 60% of people who experience migraines report a prodrome, often occurring hours to days before headache onset. Patients describe a change in mood or behavior that may include psychological, neurological, constitutional, or autonomic features.
  - These symptoms may be difficult to diagnose as part of the migraine complex if they occur in isolation from the headache or if they are mild. The prodrome of migraine has yet to receive significant investigational attention.
  - Because of the set periodicity of migraine, linkage to the suprachiasmatic nucleus of the hypothalamus that governs circadian rhythm has been proposed. Discovering the central trigger for migraine would help identify better prophylactic agents.
- The migraine aura is a complex of neurological symptoms that may precede or accompany the headache phase or may occur in isolation.
  - It usually develops over 5-20 minutes and lasts less than 60 minutes.
  - The aura can be visual, sensory, motor, or any combination of these.
  - The most characteristic visual aura of migraine is a scintillating scotoma (occurring in about 64% of cases), beginning as a hazy spot from the center of a visual hemifield followed by shimmering light of different

patterns expanding peripherally to involve a greater part of the hemifield with scotoma.

- Paresthesias, occurring in 40% of cases, constitute the next most common aura; they are often cheiro-oral with numbness starting in the hand then migrating to the arm and then jumping to involve the face, lips, and tongue.
- As with visual auras, positive symptoms typically are followed by negative symptoms; paresthesias may be followed by numbness.

- Sensory aura rarely occurs in isolation and usually follows visual aura.
- The rate of spread of sensory aura is helpful in distinguishing it from transient ischemic attack (TIA) or a sensory seizure.
- Just as a visual aura spreads across the visual field slowly, the paresthesias may take 10-20 minutes to spread, which is slower than the spread of sensory symptoms of TIA.
- The migrainous aura generally resolves within a few minutes and then is followed by a latent period before the onset of headache, although merging of the 2 also is reported.

- Motor symptoms may occur in 18% of patients and usually are associated with sensory symptoms.
- Motor symptoms often are described as a sense of heaviness of the limbs before a headache but without any true weakness.

- Speech and language disturbances have been reported in 17-20% of patients, commonly associated with upper extremity heaviness or weakness.

- Whether migraine with and without aura (prevalences, 36% and 55%, respectively) represent 2 distinct processes remains debatable; however, the similarities of the prodrome, headache, and resolution phases of the attacks, similarity in therapeutic response, and the fact that 9% of patients experience both suggest that they are the same entity.

- When an aura is not followed by a headache, it is called a migraine equivalent or acephalic migraine. This is reported most commonly in patients older than 40 years who have a history of recurrent headache. Scintillating scotoma has been considered to be diagnostic of migraine even in the absence of a headache; however, paresthesias, weakness, and other transient neurological symptoms are not. In the absence of a prior history of recurrent headache and first occurrence after age 45 years, TIA should be considered and must be investigated fully.

- Although headache is a very common reason for physician visits, the majority of headache complaints are benign in origin. However, migraine with its protean manifestation may simulate or be simulated by primary and secondary headache disorders. Also, it can coexist with a secondary headache disorder. When headache is episodic, recurrent, and with a well-established pattern, a primary headache disorder is likely.

Differentiating between migraine, tension-type, and cluster headaches is important, as optimal treatment may differ.

- Any of the following features suggest a secondary headache disorder and warrant further investigation:
  - Atypical history or unusual character that does not fulfill the criteria for migraine
  - Occurrence of a new, different, or truly "worst" headache
  - Change in frequency of episodes or major characteristics of the headache
  - Abnormal neurological examination
  - Inadequate response to optimal therapy
- When patients are seen shortly after the initial headache and their level of anxiety is such that more than reassurance is needed, further diagnostic studies may be necessary.
- Severe headache of sudden onset is a concern despite its occurrence in primary headache disorders. Typically, migraine is gradual in onset, peaking within 2 hours, although some have abrupt onset; these are termed "crash" migraine and are similar to a "thunderclap" headache.
  - Cluster headache also may be sudden and excruciating, but it lasts only 15-180 minutes and is recognized easily if the patient has had previous attacks. Exertional headache builds in intensity over minutes and occurs

with sustained physical exertion. Coital headache can develop at the height of orgasm or it may build up through intercourse.

- Despite these possibilities, a ruptured intracranial aneurysm is the primary consideration if the headache is severe with sudden onset and reaches maximum intensity in minutes. The classical presentation of an aneurysmal subarachnoid hemorrhage (SAH) is a severe headache with sudden, explosive onset, stiff neck, photophobia, nausea and vomiting, and possibly alteration of consciousness. An extensive evaluation is indicated in this case, including initial CT scan of the head without contrast. Lumbar puncture (LP) should be considered if CT scan is negative, as 25% of cases are missed by CT.
- The question persists of whether an angiogram should be performed after normal findings of neurological examination, cerebrospinal fluid (CSF) examination, and CT or MRI. In one study, acute severe thunderclap headache comparable to that of SAH without the nuchal rigidity occurred in 6.3% of patients with unruptured aneurysm. Other studies have revealed that in patients with severe thunderclap headache with normal CT and CSF findings, none developed SAH, leading to more confusion.

If the CT scan and LP are performed late after symptom onset, so that negative results are unreliable, and if clinical features such as family history or past medical history, classic SAH-like symptoms, or the

presence of neurological signs (in particular a third cranial nerve palsy affecting the pupil) suggest that the patient is at risk, such patients probably should undergo angiography if an experienced angiographer is available. In patients with unrevealing studies in whom the diagnosis of aneurysmal SAH is possible but very unlikely, MRI and magnetic resonance angiography (MRA) are screening tests, and close follow-up is appropriate if the findings of these tests are negative.

- Another concern is the possibility of a space-occupying lesion mimicking migraine. In a series of 111 patients with primary (34%) or metastatic (66%) brain tumor, headache was reported in 48%; the headache had characteristics similar to migraine in 9% and to tension-type headache in 77%, while the so-called classic brain tumor headache occurred in only 17%. Headache was intermittent in 62%, usually lasting a few hours, and was constant in 36%. It was bilateral in 72% and was moderate to severe in intensity in most patients. All patients with headaches similar to migraine had other neurological symptoms or abnormal signs. Of note is that 32% had history of headache; in 36% of those, the headache was of identical character to prior headaches but was more severe or frequent and was associated with other symptoms such as seizures, confusion, prolonged nausea, and hemiparesis.[1]

These data indicate that patients with a history of headache should have further diagnostic workup if the headache is accompanied by new

symptoms or abnormal signs or differs in any way from their usual headache. With new-onset headache, imaging should be obtained if headache is severe or occurs with nausea, vomiting, or abnormal signs.

- Other space-occupying lesions must be considered in the appropriate clinical setting. Large intraparenchymal hemorrhage presents dramatically with headache and neurological symptoms or signs shortly after onset. Of patients with chronic, subacute, or acute subdural hematoma, 81%, 53%, and 11%, respectively, have headaches. In brain abscesses, a progressive, severe, intractable headache is common, and headache is reported in 70-90% of patients.
- Cerebral venous thrombosis involves the sagittal sinus in about 70% of cases; these patients present with signs and symptoms of increased intracranial pressure (ICP), such as headache and papilledema. Should the thrombus extend to the superficial cortical veins, then focal findings may be noted. In the appropriate setting with known risk factors, cerebral venous thrombosis must be considered and evaluated with MRI, MRA, or magnetic resonance venography (MRV).
- Spontaneous internal carotid artery dissection is an uncommon cause of headache and acute neurological deficit, but it must be considered in the younger individuals who have unilateral, severe, persistent head pain of sudden onset preceding neurological signs, most