L.G.Vijayaalakshmi /J. Pharm. Sci. & Res. Vol. 6(12), 2014, 420-422

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Genetics of Migraine-Review

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Abstract:
Migraine headache should be considered as a diagnosis in anyone who has recurrent episodes of transient symptoms, especially those that are visual or neurological or involve vertigo. Visual and neurological symptoms due to migraine are not unusual and most commonly occur in older persons with a history of migraine headaches. Migraine aura without headache should be diagnosed only when transient ischemic attack and seizure disorders have been excluded.

Key Words: Migraine, aura, genetic disorder, medication.

INTRODUCTION:

Migraine is a chronic neurological disorder characterized by recurrent moderate to severe headaches often in association with a number of autonomic nervous system symptoms. Migraines are believed to be due to a mixture of environmental and genetic factors. About two-thirds of cases run in families. The exact mechanisms of migraine are not known. It is, however, believed to be a neurovascular disorder. The primary theory is related to increased excitability of the cerebral cortex and abnormal control of pain neurons in the trigeminal nucleus of the brainstem [1]. Globally, approximately 15% of the population is affected by migraines at some point in life.

SIGNS AND SYMPTOMS:

Migraines typically present with self-limited, severe headache associated with autonomic symptoms. About 15-30% of people with migraines experience migraines with an aura and those who have migraines with aura also frequently have migraines without aura. The severity of the pain, duration of the headache, and frequency of attacks is variable. A migraine lasting longer than 72 hours is termed status migrainosus[2].There are four phases to a migraine, although not all the phases are experienced.

FOUR PHASES:

1. The prodrome, which occurs hours or days before the headache
2. The aura, which immediately precedes the headache
3. The pain phase, also known as headache phase
4. The postdrome, the effects experienced following the end of a migraine attack.

1. PRODROME PHASE:

Prodromal symptoms occur in about 60% of those with migraines, with an onset of two hours to two days before the start of pain. These symptoms may include a wide variety of phenomena including altered mood, irritability, depression, craving for certain food and sensitivity to smells or noise [3].This may occur in those with either migraine with aura or migraine without aura.

2. AURA PHASE:

An aura is a transient focal neurological phenomenon that occurs before or during the headache. Auras appear gradually over a number of minutes and generally last fewer than 60 minutes. Symptoms can be visual, sensory or motor in nature and many people experience more than one. Visual effects occur most frequently; they occur in up to 99% of cases and in more than 50% of cases are not accompanied by sensory or motor effects [4].

3. PAIN PHASE:

Classically the headache is unilateral, throbbing, and moderate to severe in intensity. It usually comes on gradually and is aggravated by physical activity. In more than 40% of cases however the pain may be bilateral, and neck pain is commonly associated. Bilateral pain is particularly common in those who have migraines without an aura. Less commonly pain may occur primarily in the back or top of the head. The pain usually lasts 4 to 72 hours in adults, however in young children frequently lasts less than 1 hour. The frequency of attacks is variable, from a few in a lifetime to several a week with the average being about one a month [5][6]

4.POSTDROME PHASE:

The effects of migraine may persist for some days after the main headache has ended and this is called the migraine postdrome. Many report a sore feeling in the area where the migraine was, and some report impaired thinking for a few days after the headache has passed. The patient may feel tired or "hung over" and have head pain, cognitive difficulties, gastrointestinal symptoms, mood changes, and weakness [7].

CAUSES:

The underlying causes of migraines are unknown. However, they are believed to be related to a mix of environmental and genetic factors. They run in families in about two-thirds of cases [8] and rarely occur due to a single gene defect [9]. Migraines were once believed to be more common in those of high intelligence, this does not appear to be true. A number of psychological conditions are associated, including depression, anxiety and bipolar disorder [10].

GENETICS:

Single gene disorders that result in migraines are rare. One of these is known as familial hemiplegic migraine, a type of migraine with aura, which is inherited in an autosomal dominant[11][12]. Four genes have been shown to be involved in familial hemiplegic migraine. Three of these genes are involved in ion transport[13].The fourth is an axonal protein associated with the exocytosis complex[14].Another genetic disorder associated with migraine is CADASIL syndrome or cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy.

PHYSIOLOGICAL ASPECT:

Common triggers quoted are stress, hunger, and fatigue. Migraines are more likely to occur around menstruation[15]. Other hormonal influences, such as menarche, oral contraceptive use, pregnancy, perimenopause, and menopause, also play a role[16]. These hormonal influences seem to play a greater role in migraine without aura[17]. Migraines typically do not occur during the second and third trimesters or following menopause[18].

CLASSIFICATION OF MIGRAINE:

Migraines are divided into seven classes:

- Migraine without aura, or "common migraine", involves migraine headaches that are not accompanied by an aura
- Migraine with aura, or "classic migraine", usually involves migraine headaches accompanied by an aura. Less commonly, an aura can occur without a headache, or with a nonmigraine headache. Two other varieties are familial hemiplegic migraine and sporadic hemiplegic migraine, in which a person has migraines with aura and with accompanying motor weakness.]
- Childhood periodic syndromes that are commonly precursors of migraine include cyclical vomiting (occasional intense periods of vomiting), abdominal migraine (abdominal pain, usually accompanied by nausea), and benign paroxysmal vertigo of childhood (occasional attacks of vertigo).
- Retinal migraine involves migraine headaches accompanied by visual disturbances or even temporary blindness in one eye.
- Complications of migraine describe migraine headaches and/or auras that are unusually long or unusually frequent, or associated with a seizure or brain lesion.
- Probable migraine describes conditions that have some characteristics of migraines, but where there is not enough evidence to diagnose it as a migraine with certainty (in the presence of concurrent medication overuse).
- Chronic migraine is a complication of migraines, and is a headache that fulfills diagnostic criteria for *migraine headache* and occurs for a greater time interval. Specifically, greater or equal to 15 days/month for longer than 3 months[19].

PREVENTION:

Preventive treatments of migraines include medications, nutritional supplements, lifestyle alterations, and surgery. Prevention is recommended in those who have headaches more than two days a week, cannot tolerate the medications used to treat acute attacks, or those with severe attacks that are not easily controlled. The goal is to reduce the frequency, painfulness, and/or duration of migraines, and to increase the effectiveness of abortive therapy[20]. Another reason for prevention is to avoid medication overuse headache. This is a common problem and can result in chronic daily headache [21][22].

CONCLUSION:

At present, the most important task is the discovery of drugs that can suppress migraine. These will have to be well tolerated (without side effects) if they are to be used to prevent migraine, because migraineurs will have to take them repeatedly over a long period, just as epileptic patients take drugs to prevent their seizures. In the brains of people with migraine, the aura occurs without such strong external stimuli. It is likely that several anomalies of the complex machinery associated with the brain cell membrane can promote the occurrence of CSD (cortical spreading depression), and this certainly includes several types of genetic anomalies. The discovery of these altered genes will dramatically improve our understanding of the genesis of migraine attacks. This scientific knowledge may allow us to tailor the treatment of migraine to the specific genetic predisposition of a given group of patients. The possibility for such a gene-directed therapy of migraine is certainly a worthwhile long-term objective.

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