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Migraine-A Complete Review

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Migraine is a mysterious disorder characterized by pulsating headache, usually restricted to one side, appearing in the form of attacks lasting from 4-48 hrs which is characterized by altered bodily perceptions, severe headache, nausea, vomiting and sensitivity to light. Pulsate dilation of large cranial vessels is the immediate cause of pain. Impulses from the cortex, thalamus and hypothalamus activate the migraine centre responsible for generation of migraine attacks, putatively located in the brain stem. Two types of migraines are seen generally-classical migraine (a migraine with an aura or warning) and common migraine (migraine without an aura). Less common migraines are abdominal migraine, basilar migraine, cyclic migraine, hemiplegic migraine, nocturnal migraine, ophthalmic and pregnancy migraine. These can be diagnosed by the symptoms like intense headache, relentless throbbing pain, inability to carry out daily activities etc. Patients suffering with worst headaches associated with nervous system symptoms like visual, sensory or hearing losses require additional tests like blood test, brain scan (CT scan), spinal tap etc. One can get relief by allopathic and ayurvedic medications. Home remedies are also known to retard mild migraines. The frequency, severity of attacks and response of individuals and their sensitivity to drugs determine the choice of drug therapy.

Keyword: Aura, Brain Scan, Pulsating Headache, Spinal Tap, Throbbing Pain

1. Introduction^[1-4]

Migraine is a neurological syndrome characterized by altered bodily perceptions, photophobia (sensitivity to light), phonophobia (sensitivity to sound). It can be caused by abnormal brain activity which is triggered by many factors. It is believed that the attacks begin in brain and hence involve nerve pathways and chemicals. Thus the blood flow in brain and surrounding tissues is affected. Migraine headache is physiologically a neurological

condition found 3 times more common in women than in men. A typical migraine headache is unilateral i.e. affecting only one half of the head and is pulsating. Nearly one-third of the people suffering from migraine attack perceive an aura-unusual vision, olfactory and other sensory experiences warning that a bad headache soon will occur.

2. Signs and Symptoms^[5]

- Other types of headaches are differentiated from migraine headaches with specific symptoms. These symptoms differ from person to person individually in the intensity, frequency, character and duration. Migraine attacks may appear every day or infrequently as a couple of times a year. The symptoms of migraine are more commonly associated with:
 - An intense headache starting on one side of head and it spreads downwards to the eye, face and even neck. Less commonly, it affects both sides at once.
 - Vomiting, nausea.
 - A relentless throbbing pain or pounding in the head is felt.
 - Patients try to avoid light and sound as strong, painful reactions to light and sound are seen.
 - Cannot carry out the day to day activities.
 - Feels like resting down during the period of attacks.
 - In most of the cases all these symptoms are not seen. Hence they are not essential in migraine attacks. If not treated properly or badly treated, the attacks may long from 4hrs to 3 days.
 - Migraines typically start between the ages of 10-46 and most generally occur in women. They are not easy to diagnose. Patients don't get good treatment without appropriate diagnosis. So, it is advised to visit a physician frequently and describe the symptoms in a clear way.

2. Causes

- Many people who suffer from migraine can clearly identify triggers or factors that cause headaches, but many cannot. The most potential migraine triggers include:
 - Loud noises, bright lights, certain odors and perfumes
 - Allergic reactions and allergies
 - Physical or emotional stress
 - Irregular sleep or changes in sleep pattern
 - Skipping meals or fasting

- Alcohol consumption
- Birth control pills, menstrual cycle fluctuations, hormone fluctuation during menopause onset
- Foods containing tyramine (red wine, aged cheese, smoked fish, chicken liver, figs and some beans), monosodium glutamate and nitrates (bacon, hot dogs and salami)
- Other foods like chocolate, nuts, peanut butter, avocado, banana, citrus, onions, dairy products, fermented or pickled foods.
- Original migraine headache arises from brain tumor or other medical problems. Only an experienced physician can determine whether the symptoms are due to migraine or other conditions.

3. Types of Migraine^[6]

Two types of migraines are seen:

1. Classical migraine (migraine with aura)
Less number of migraine patients experiences the aura, which is the term of sign of occurrence of the pain. These can be described as the spots or the zigzag lines before the eyes associated with blurred vision. These symptoms go away usually within one hour and are replaced by a headache.
2. Common migraine (migraine without aura or no warning)
In the common migraine, headache begins without warnings which are experienced mostly by children.

3.1 Migraines without Aura

Many people who suffer from migraine do not experience auras during the attack. Migraines usually occur on one side of the head and are distinguished by a throbbing pain. Pain usually increases with activity and is often accompanied by nausea and vomiting. Patients feel comfortable and ease after vomiting. They tend to feel better when they lie down in a calm and quiet place.

3.2 Migraines with Aura

An aura is a neurological condition that generally occurs before the attack. They can be diagnosed by impaired vision, numbness (loss of sensation) of hands and feet.

3.3 Less Common Type Migraines

There are several types of migraines. These are less common than migraines with auras. Less than 2% of migraine sufferers experience these types of headaches. They are described below:

- a) Abdominal Migraine: It is also known as periodic syndrome. This variant most typically occurs in children. The attacks are characterized by periodic bouts of moderate to severe midline abdominal pain lasting for 1-72hrs along with nausea, vomiting, flushing or pallor. Medications used to treat migraine also help to control these attacks in most cases.
- b) Basilar Migraine: It is a rare form of migraine with aura symptoms from brain stem. Whether the basilar artery to back to brain is involved is uncertain. Aura symptoms are dizziness, double vision, tingling on both sides of the body.
- c) Cyclic Migraine Headache: Patients with cyclic migraines usually experience 10 or more attacks per month. These are long lasting. Patients do have typical migraine symptoms during these headaches. Lithium carbonate is some of the help in these cases. Careful monitoring of blood level and thyroid functioning is needed in this medication.
- d) Hemiplegic Migraine: It is a rare form of migraine and also the most severe type of migraines. Sufferer may develop temporary motor paralysis or sensory disturbances on one side of the body followed by headache.
- e) Nocturnal Migraine: Many people who have migraine will experience their

attacks during the middle of the night or early in the morning. This headache often awakens the patient from sleep. It is recommended that the patients treat the headache when the attack begins, elevate their upper torso (back, shoulders and head) and rest or try to get back to sleep.

- f) Ophthalmoplegic Migraine: Ophthalmoplegic migraine is a rare condition which is considered to be an unusual form of migraine. The pain usually surrounds eyeball and lasts from a few days to few months. It is caused by the weakness of the muscles surrounding the eye. It is important to confirm the diagnosis of ophthalmologic migraine as similar symptoms can be caused by the pressure on nerves behind the eye.
- g) Pregnancy Related Migraine: Approximately 80% of women who have migraine stop having migraine attacks from the end of 3rd month of pregnancy till delivery. This is believed to be hormonal stability. During pregnancy medicine use is discouraged unless absolutely necessary. Before using any medication for headache, a physician must be consulted. Non-medical treatment plan can be efficient in pregnancy.

4. Pathophysiology of Migraine^[7-9]

The cumulative effect of disturbances such as cerebral hypomagnesaemia, elevated concentrations of excitatory amino acids, and increased reactivity of cranial blood vessels is heightened sensitivity to nociceptive stimuli (migraine pain threshold). Impulses from the thalamus, hypothalamus and cortex activate the migraine centre responsible for the generation of migraine attacks located in brain stem. The migraine center triggers cortical spreading depression accompanied by oligemia, resulting in an aura. Trigeminovascular input from meningeal vessels is relayed to the brain stem, via projecting fibers to the thalamus, parasympathetic efferent pathway and back to meningeal vessels.

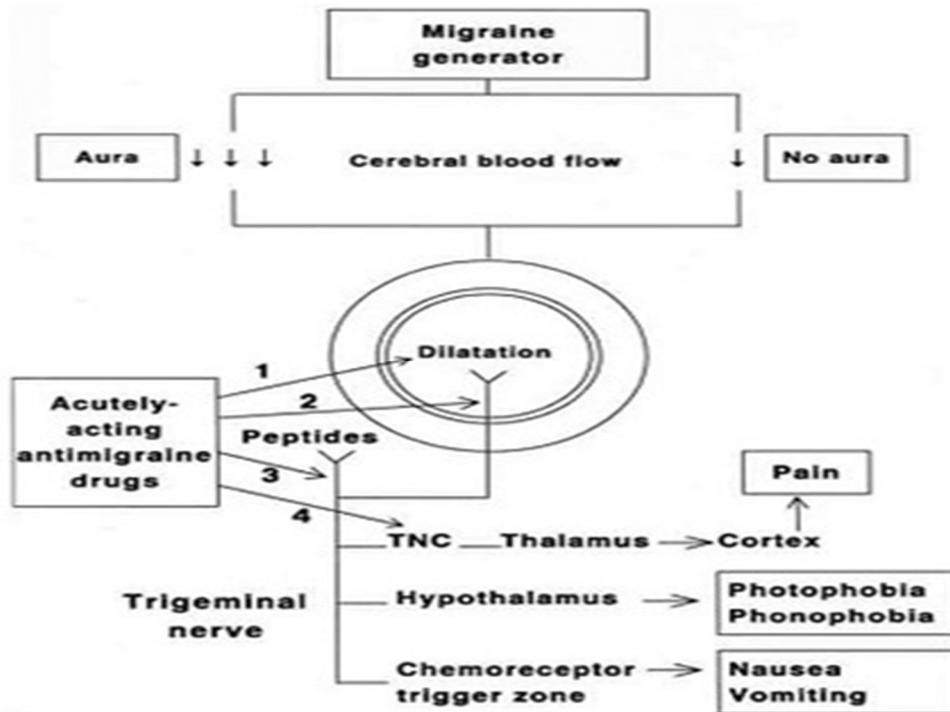


Fig.1: Pathophysiology of Migraine

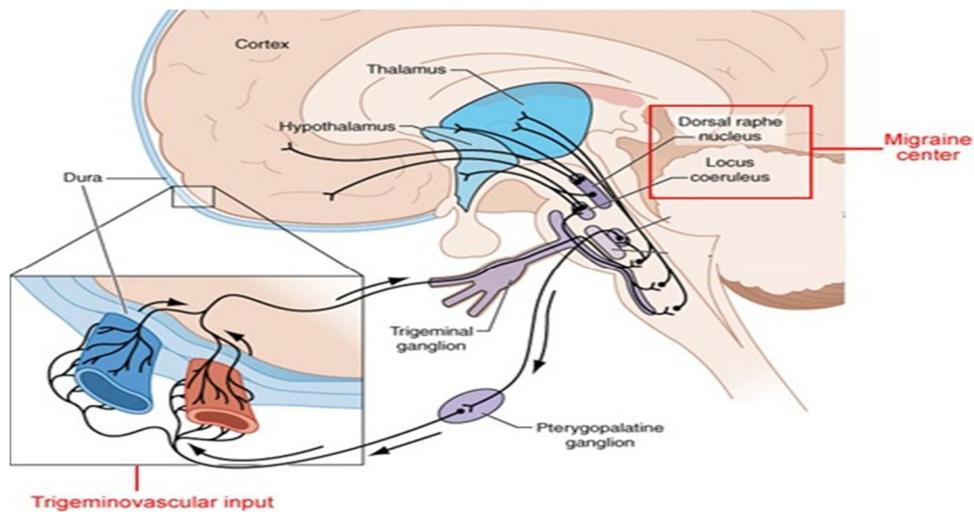


Fig.2: Perivascular trigeminal C-fiber endings are stimulated to release vasoactive neuropeptides like substance P, neurokinin A and calcitonin gene-regulated polypeptide (CGRP) leading to a sterile inflammation.

5. Clinical features of Migraine

Migraine can be subdivided into two types:

- Migraine with aura (classic migraine)
- Migraine without an aura (common migraine)

A classic migraine attack has four phases: prodromal, aura, headache and resolution.

Prodromal phase: Migraine can be preceded by a period of variable prodromal phenomena lasting a

few hours to few days. Many patients complain of sensitivity to smell, noise, irritability, restlessness, and drowsiness, and fatigue, lack of concentration, depression and polyuria. The chief complaints in children are abdominal pain and dizziness.

Aura: Aura develops over 5-20 minutes and lasts less than one hour but persists for one week. Auras typically involve visual disturbances ranging from undulating lines, circles, sparks or flashing lights. Emotional changes of variable intensity are common.

Headache phase: 60% of patients complain of pulsating, throbbing or continuous pain on one side of head. Others have pain in the entire head, particularly behind the eyes. Migraine is often accompanied by anorexia, malaise, and nausea and vomiting.

Resolution phase: This phase is characterized by lack of concentration, listlessness and increased pain and sensitivity in the head.

6. Diagnosis ^[10-12]

The recognition of the migraine has been enhanced by the introduction of diagnostic criteria for both the migraine with and without aura (formerly known as "classic" and "common" migraine, respectively) by the International Headache Society (IHS).

6.1 International Headache Society Criteria for Migraine without Aura

- A. At least 5 attacks that fulfill criteria in B, C, and D
- B. Headache attacks that last 4 to 72 hrs (untreated or unsuccessfully treated)
- C. Headache has at least 2 of the following characteristics:
 - Unilateral site
 - Pulsating quality
 - Moderate to severe intensity
- D. Aggravation by walking during headache, at least 1 of the following symptoms:
 - Nausea or vomiting , photophobia and phonophobia.

6.2 International Headache Society Criteria for Migraine with Aura

- A. At least 2 attacks that fulfill criteria in B and C
- B. At least 3 of the following 4 characteristics:
 - One or more completely reversible aura symptoms that indicate focal cerebral cortical or brain-stem dysfunction (or both)
 - At least one aura symptom develops gradually over >4 min or two or more symptoms occur in succession
 - No aura symptom lasts >60 min
 - Headache follows aura in <1 hr

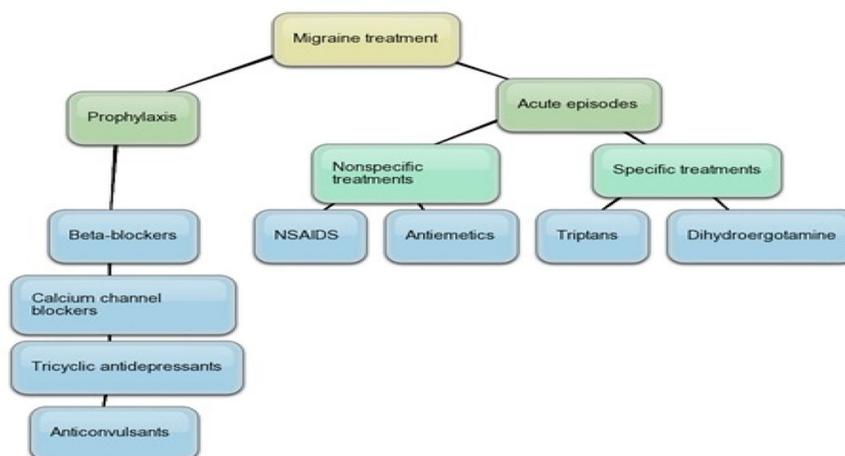


Fig.3: Treatment strategy for Migraine

7. Treatment ^[13-22]

Variety of drugs has been specifically designed to treat migraines. Medications used to combat migraines fall into broad categories:

A. Pain-relieving medications

They are also known as acute or abortive treatment; these types of drugs are taken during migraine attacks and are designed to stop symptoms that have already begun.

B. Preventive medications

These types of drugs are taken regularly, often daily basis to decrease the frequency or severity of attacks.

7.1 Pain relieving medication

For best results, take pain-relieving drugs as soon as you experience signs or symptoms of a migraine. It may help if you sleep or rest in a dark room after taking them.

1. Pain-relievers

Medications like ibuprofen; acetaminophen may help relieve mild migraines. Drugs marketed specifically for migraines like combination of acetaminophen, aspirin and caffeine may ease moderate pain but are not effective for severe migraines. If taken for long periods, these can lead to ulcers, gastro intestinal bleeding and rebound headaches.

2. Triptans

Triptans are the drug of choice with people of migraine attacks. They are effective in relieving the pain, nausea, sensitivity to light and sound associated with migraines. Medication includes drugs like sumatriptan, rizatriptan, almotriptan, zolmitriptan, frovatriptan and eletriptan. Side effects are nausea, dizziness and muscle weakness. They are not suitable for people at risk for strokes and heart attacks. Combination of sumatriptan and naproxen sodium (treximet) has proved effective in relieving migraine symptoms than individual medications.

3. Ergot

Combination of ergotamine and caffeine (migrergot, cafergot) are less expensive and also less effective than Triptans. They are most effective where pain lasts for more than 48hrs. Dihydroergotamine is more effective and has fewer side effects than ergotamine. It is also available as nasal spray and in injection form.

4. Anti-nausea

Migraine attacks are often accompanied by nausea with or without vomiting. Medication for nausea is appropriate and usually combined with other drugs. Frequently prescribed medications are metoclopramide or prochlorperazine.

5. Opiates

Medications containing narcotics, particularly codeine are sometimes used to treat migraine headache pain when people can't take ergots or Triptans. They are usually habit forming and are used only as a last resort.

6. Butalbital combinations

Medications that combine the sedative Butalbital with aspirin/acetaminophen are sometimes used to treat migraine attacks. Some combinations also include caffeine or codeine. These drugs have a high risk of rebound headaches and so withdrawal symptoms should be frequently used.

7.2 Preventive medications

Nearly half of those who get the migraines could benefit from preventive medication. Only one in ten people take it. The patient can approach this therapy if he has two or more deliberative attacks a month. This therapy can reduce the frequency, severity and length of migraines. Doctor may recommend taking the preventive medications daily or only during a predictable trigger such as when menstruation is approaching. Some of the drugs used in preventive treatment are:

1. Cardiovascular drugs

Beta-blockers commonly used to treat high blood pressure and coronary artery disease can decrease the frequency and severity of

migraines. These are considered as the first line treatment drugs. Calcium channel blockers like verapamil are also helpful in preventing migraines and relieves from aura. Anti-hypertensive medications like lisinopril, candesartan are useful in decreasing the frequency and severity of migraines. The side effects include dizziness, drowsiness or lightheadedness.

2. Anti depressants

Tricyclic antidepressants like amitriptyline, nortriptyline and protriptyline are most effective in preventing certain headaches including migraines. They act by affecting the level of serotonin and other brain chemicals.

3. Anti-seizure drugs

Some anti-seizure drugs such as divalproex and topiramate and gabapentin reduce the frequency of migraines. These drugs may cause side effects like nausea, vomiting, diarrhea, cramps, hair loss and dizziness at high doses.

4. Cyproheptadine

These anti histamines specifically affect the serotonin activity. Physicians sometimes give it to children as a preventive measure.

5. Botulinum (toxin type A)-Botox

Sometimes it is used as treatment for chronic migraines. Injections are made in the muscles of forehead and the neck. When this is shown to be effective, the treatment typically needs to be repeated every 3 months.

7.3 Home remedies

Migraine can be relieved by adapting self care measures as given under;

- Muscle relaxation exercises: Meditation, yoga and muscle relaxation for at least half an hour a day helps to relieve from headache. Something that you find relaxing like listening music, gardening, taking a hot water bath or reading may help.

- Sleep enough but do not oversleep:

An average adult needs 6-8hrs of sleep a day. It is best to go to bed and wake up at regular intervals.

- Relax and take rest:

Take rest in a dark quiet room if possible when you feel like pain. Make an ice pack by wrapping in a cloth and place it on the back of the neck and gently apply to painful areas on your scalp.

- Headache diary:

Maintain a headache diary and continue to keep it even after visiting your physician. It helps you to learn more what triggers your headache and which treatment is effective.

7.4 Ayurvedic treatment

Besides the availability of a wide variety of painkillers off-the-shelf for migraine, they may not always work because the remedy lies in the cause of migraine. Pain relievers help only to suppress the pain but the problem still persists in the body. Side effects like depression, anorexia, high blood pressure, giddiness and ulcer may be seen.

a. Excess Vata Migraines

Reasons: They may arise due to increase in cold, dry and rainy season, intensity increases due to exertion, stress, over fasting, late nights, insufficient sleep, sadness, worries, hunger, fear and trauma.

Symptoms: Unstoppable throbbing pain, difficulty in moving the head without feeling the unbearable pain.

Remedies: Take nutritious diet and vata reducing foods like rice, wheat, sesame, warm milk, butter, ghee, onion, sweet fruits, and garlic, jaggery, saffron and green gram. Hot oil massage is the best advised. Massaging your head with warm oil helps to reduce the pain. Take 1 tsp of castor oil with warm water at bed time. Have shirodhara and enema treatments from panchakarma (detoxifying sessions).

- Avoid cold and dry weather and motions that increase vata.

b. Excess Pitta Migraines

Reasons: Exposing to sun and heat, working near heat and fire, hot sunny weather, too spicy and fermented foods that increases pitta, hypertensives and too many antibiotics.

Symptoms: Heat increases with acidity, migraine increases in afternoon and head feels hot and burns.

Remedies: Eat healthy herbs like guduchi, shatavari, yasti madhu, black resins. Take 2 spoons of cow ghee in morning with milk eat more sweet fruits and cooling spices like cumin, crinda, fennel. Grains like rice, mung bean and millet are advisable.

7.5 Home remedies for migraine

- a) **Caffeine:** Caffeine hinders headache as it is a double edged sword. Caffeine restricts blood vessels, reduces pain. It is a constituent of pain over-the-counter pair medicines but has to be taken limitedly, because if taken excessively, it leads to rebound headache, thus making existing headaches worse.
- b) **Water:** Dehydration is a big cause for headaches. Hence drink water as much as possible.
- c) **Tie A Head Band Around Head:** It is a practice that has been done since ancient times.
- d) **Peppermint Oil:** Take some peppermint oil and rub it on the part of head that hurts.

8. References

1. Etymology of migraine, Online Etymological Dictionary. Available from: URL: <http://www.etymonline.com/index.php?term=migraine>. Retrieved 27 may 2009.
2. Headache Clasification Subcommittee of the International Headache Society (2004). The International Subcommittee O the International Headache Disorders : 2nd Edition". Cephalalgia 24 suppl: 9-160. Doi:10.1111/j.1468-2982.2004.00653.x.PMID 14979299.
3. NINDS Migraine Information Page. National Institute of Neurological Disorders and stroke, national Institutes of Health. Available from: URL: <http://www.ninds.nih.gov/disorders/migraine/migraine.htm>. Retrieved:2007-06-25.

- e) **Fish Oil:** Fish oil works by restricting the blood vessels in brain and reduce inflammation.
- f) **Ginger:** Eating ginger or ginger capsules may help sometimes. It also reduces nausea clearly.
- g) **Magnesium:** Menstrual associated migraines and migraines associated with auras can be markedly reduced by the intake of Magnesium in dose of 400-600mg/day. Caution: when taken excess it results in diarrhea.
- h) **Riboflavin:** Vitamin B2 can also prevent migraine in dose of 400mg/day. Dose has to be adjusted because it causes frequent urination or might cause darker urine.
- i) **Coenzyme Q10:** It is effective in reducing headache when taken 300mg/day.
- j) **Butterbur:** Also known as petasites. Butterbur is the most effective natural medicine. It is grown extensively in Germany. It is very effective in treating asthma and migraine. When taken in pill form, it is also alleviates upset stomach.
- k) **Hot Or Cold Compress:** It acts like a placebo treatment. It may have distracting effect on patient. But a lot of patients swear by it.

4. Guidelines for all healthcare professionals in the diagnosis and management of migraine, tension-type, cluster and medication-overuse headache, January 2007, British Association for the study of Headache (PDF). Available from: URL: http://216.25.100.131/upload/NS_BASH_guidelines_2007.pdf. Retrieved 2007-06-25.
5. Bartleson JD, Curter FM (May 2010). Migraine updates diagnosis and treatment. Minn Med 93 (5): 36-41, PMID 20572569.
6. Available from: URL : <http://migrainesymptoms-guide.com/different-types-of-migraine-headaches/>
7. Fauci, Anthony S., Braunwald, Eugene., Kasper, Dennis L. Harrison's Principles of Internal Medicine, 17 edition .Mc Graw Hill:2008.

8. Rohkamm, R color atlas of Neurology, 1st edition. Thieme: 2004.
9. Villalon CM et al. Migraine: pathophysiology, Pharmacology, Treatment and Future Trends Curr Vasc Pharmacol. 2003 Mar; 1(1):71-84.
10. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders for headache disorders, cranial neuralgias and facial pain. Cephalalgia. 1988; 8 (suppl 7):71-84.
11. Grunfeld E, Gresty MA. Relationship between motion sickness, migraine and menstruation in crew members of a "round the world" yacht race. Brain Res Bull. 1998; 47(5):433-436.
12. Aromaa M, Sillanpaa ML, Rantava P. childhood headache at school entry: a controlled clinical study. Neurology. 1998; 50(6):1729-1736.
13. Bajwa ZH, et al. Pathophysiology, clinical manifestations, and diagnosis of migraine in adults. Available from: URL: <http://www.uptodate.com/home/index.html>. Accessed jan 9, 2009.
14. Headache hope through Research. National Institute of Neurological Disorders and Stroke. Available from : URL: http://www.ninds.nih.gov/disorders/headache/detail_headache.htm?css=print. Accessed jan. 11, 2009.
15. Pelak VS. Approach to the patient with visual hallucinations. Available from: URL: <http://www.uptodate.com/home/index.html>. Accessed jan 9, 2009.
16. Ramzan M, et al. Headache, migraine and stroke. Available from URL: <http://www.uptodate.com/home/index.html>. Accessed jan 9, 2009.
17. Bajwa ZH, et al. Acute treatment of migraine in adults. Available from: URL: <http://www.uptodate.com/home/index.html>. Accessed jan 9, 2009.
18. Migraine – What are the treatments? American Academy of Neurology. Available from: URL: <http://www.thebrainmatters.org/index.cfm?key=1.9.61/>. Accessed jan. 12, 2009.
19. Bajwa ZH, et al. Preventive treatment of migraine in adults. Available from: URL: <http://www.uptodate.com/home/index.html>. Accessed jan 9, 2009.
20. Swanson Jw (expert opinion) . Mayo Clinic, Rochester, Minn. Jan. 15, 2009.
21. Tinel D, et al. vertebrobasilar ischemia after cervical spine manipulation: A case report. Annales de readaptation et de medicine physique 208; 51:403.
22. Haldeman S, et al. Stroke, cerebral Artery Dissection, and Cervical Spine Manipulation therapy. Journal of Neurology. 2002; 249:1098.