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TREATMENT PROTOCOLS FOR THE MANAGEMENT OF MIGRAINE

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ABSTRACT

Migraine is an episodic headache which affects almost more than 10% of population and three times more frequently in women than men. One of the main problems in the success of new therapeutic approaches is our limited knowledge of migraine neurobiology. However apart from this, there are also two main causes which are not understood. One of the primary causes of migraine leading towards the activation of trigeminovascular system and second one is the mechanism of pain generation after activation. The primary aim is to control the symptoms of migraine to prevent its affects on patient's lifestyle. Complete cure of patient is unrealistic; it is just controlled by following certain precautions and proper medication. Despite of many advances and progress in migraine, drug therapy for treating and preventing migraine still remains unsatisfactory for many patients. As migraine typically varies from patient to patient, different diagnosis and therapeutics should be reviewed properly.

INTRODUCTION

One of the most important disabling character is migraine characterized by severe headache and visual • disturbances. [1] Migraine is extremely painful sometimes • associated with symptoms like aura and nausea etc. It is a common in-capsicating neurological disorder characterized by severe attacks of headache, autonomic dysfunctions and sometimes aura involving neurological symptoms. [2]

Migraine is a very complex collection of diseases in which genetic, environmental and behavioral factors have great contribution. It is episodic pain syndrome. [3] Migraine is a syndrome with a wide variety of neurologic and non neurologic disorder. In a study in USA, it was concluded that it affects women 18% and men less than 6.5 %. [4] The International Headache Society has well developed criteria for migraine with and without aura. It affects typically half of the head causing pulsating pain lasting for 2-72 hrs. Genetic factor is one of the main factors for migraine and it runs in family. Hormonal imbalance especially in females causes migraine 2 to 3 times more in women than men. Exact pathophysiology of migraine is not known yet, some hypothesis explains that it occurred due to loss of control on pain neurons and hyperactivity of cerebral cortex. During pregnancy migraine risk decreases. [5]

Types of Migraine

There are two types of migraine:

- Migraine with aura commonly known as simple or common migraine.
 - Migraine without aura known as classical migraine
 - If you have migraine with aura, you may see things such as stars or zigzag lines before the pain starts. In case you don't have aura other warning signs like craving for sweets, thurst, sleepiness and depression may occur. There is no definite treatment for migraine, you can only prevent the condition from worsening or you may have only symptomatic relief therapy, reducing reoccurrence of attacks and pain. ^[6]

Signs and symptoms

Migraine is presented with severe headache with reoccurrence of blurring and neurologic symptoms. Duration of headache, pain severeness and relapse of attack is variable. Migraine may last for 72 hrs and includes four phases given below.^[7]

Prodrome Phase

Prodrome occurs before the headache starts. It may last from 2 hr to 2 days causing mood alterations, depression, irritability, fatigue, euphoria, stiff muscles, constipation, craving for food, diarrhea, and sensitivity to noise and smell. These symptoms occur in both types either migraine with aura or migraine without aura. [8]

Aura Phase

It is the second phase of migraine causing neurological disturbances. It starts gradually and last almost for one hour. Symptoms may be visually, sensory or of both

types. Visual disturbances occur in almost 99% of migraine patients and sensory disturbances are associated with the 50% of individuals. Visual disturbance includes change in vision field causing complexity in reading or driving. In sensory aura numbness occurred. Other symptoms include delusions, speech disturbance, weakness, motor problems etc. [9]

Pain Phase

Pain phase also known as headache phase. Usually this is half head pain throbbing and severe in nature. It starts gradually and aggravates slowly. It occurs in almost 40% of cases. Mostly top of the head and back are severely affected. Pain lasts for 4 hrs to 72 hrs in adults while in children it lasts for almost 1 hr. Symptoms accompanied includes nausea, vomiting, hallucination, smell and sound sensitivity, neurological symptoms, sensitivity to light, light headedness, confusion and neck stiffness. [10]

Postdrome Phase

The effects of migraine may lasts for a few days after the main headache this is called as postdrome stage. It includes hangover, head pain, GIT problems, mood elevation, cognitive difficulties and weakness,melase and depression are most common^[11]

Recommendations and Guidelines

Migraine has been ranked at 19th most common cause of disability through the world by WHO.^[12]

Level A

This medication therapy is found most effective for the management of migraine. Antiepileptics for e.g sodium valproate, divalproex sodium. Beta blockers for e.g. metoprolol, timolol and propranolol and Triptans for e.g frovatriptan.^[13]

Level A Negative

Lamotrigine medication is found ineffective and should not be used to cure migraine. [12]

Level B

This medication therapy is found most effective for migraine. Antidepressants for e.g amitriptyline and venlafaxine. Beta blockers for e.g nadolol and Triptans for e.g naratriptan, zolmitriptan.

Level B Negative

Clomipramine medication is found ineffective and should not be given in migraine.

Level C

These medications are found effective in migraine. ACE inhibitors for e.g lisinopril, angiotensin receptor blocker for e.g candesartan, alpha adrenoreceptor agonist for e.g clonidine and guanfacine, anti epileptic drugs for e.g carbamazepine and Beta blockers for e.g pindolol and nebivolol. [14]

Level C Negative

These medications are found ineffective and should not be considered for migraine. Acebutolol, clonazepam, nabumetone, oxcarbazepine and telmisartan (Headache Classification Committee of the International Headache Society).

Level U

Evidences for these drugs are in adequate to allow their use in migraine management. AEDs for e.g, gabapentin, Antidepressant, Selective serotonin reuptake inhibitor for e.g fluvoxamine, fluoxetine. Tricyclics for e.g protriptyline, antithrombotic for e.g picotamide, acenocoumarol and Coumadin, Beta blockers for e.g bisoprolol, Calcium channel blocker for e.g verapamil, nimodipine, nicardipine and nifedipine. Acetazolamide, and Cyclandelate. [12]

Causes of migraine

Migraine has many different potential causes. Mostly caused by primary headache disorder includes tension type headache, cluster and migraine. Secondary headache with pathologic causes is less common. Migraine is a severe condition with relapsing attack which varies from patient to patient. Some people suffering from migraine can easily identified the cause of headache but many cannot. Some potential migraine trigger are as under; allergies or allergic reactions, certain odours and perfumes, loud noises, bright lights, emotional stress, physical stress, irregular sleep pattern , smoking active or passive both, excessive fasting, alcoholism, hormonal imbalance during adolescence, tyramine containing food for e.g. red wine, smoke fish, chicken liver, chease, figs and hot dogs and other food such as chocolates, nuts, banana, onion, citrus foods, peanut butter, fermented or pickled foods. [15]

Risk factors

Women are three times more prone to migraine than men. Having other family members with migraine, taking contraceptives if your migraines are altered by change in estrogen level, being under 40 yrs of age and migraine goes better as you grow older. [15]

Prevalence and incidence

Migraine is common relapsing disorder effecting 11% of adults population in world wide. Prevalence is highest during productive years that is between 25 to 55 years of age. Females are at more risks than males.

African and Asian populations are at low risk than Americans and Europeans. Among women Caucasians are more prone to migraine than Africans, Asians and Americans. A similar pattern was seen among males. Among children it is more frequent headache disorder characterized by episodic headache, vomiting, nausea and abdominal pain. Boys experience migraine attacks more earlier than girls. [16]

Diagnosis

A detailed medical history is required by the physician so he/she may conclude that what type of headache is that. • Physician also required genetic history to know about the • genetic frequency of migraine among the families. It is • important to have a diary explaining your headache • schedule. Doctor may suggest following tests depending • upon signs and symptoms. [17]

- I. Computerized tomography (CT) SCAN for looking the other problems that are causing headache
- II. Magnetic resonance imaging (MRI) for checking brain abnormalities
- III. Lumbar puncture (spinal tap) in case doctor suspects that you are having meningitis

Treatment approaches

The treatment for migraine includes preventing the migraine and reducing pain once the attack starts. The migraine can be controlled by combination of medication, modification of life styles and other complementary therapies. Relaxation may reduce both intensity and frequency of attack. [16]

Life style

Keeping a migraine diary is very important as you can prevent the factors by which migraine occurred before. Note down the migraine schedule and the things you ate before 24 hrs, your sleep schedule, what you were doing just before headache started and any tension in your life and what you did to make headache stop. Other lifestyle modification include, cigarette cessation, avoiding alcohol and caffeine, regular exercise, good sleep schedule, minimizing stress, eating balanced meal, preventing dehydration especially when you vomited. [17]

Medication

Medication for migraine is divided into two major categories:

- To prevent attack
- · To relief pain

Drugs for prevention

Depending upon the condition physician may prescribe single or combination of following drugs.^[17]

- Beta blockers for e.g atenolol, metoprolol and propranolol
- Calcium channel blockers for e.g verapamil and diltiazam
- Anti depressants for e.g amitriptyline, nortriptyline and imipramine
- Anti convulsions and anti seizures for e.g divalproex sodium, gabapentin and topiramate

Drugs for treatment

These medicines should be taken as soon as it possible when you feel that migraine is coming.

Triptans – these medicines are firstly prescribed for relieving pain, nausea, and other symptoms. These

worked by constricting brain blood vessel.^[18] These include:

Almotriptan (Axert)

Eletriptan (Relpax)

Frovatriptan (Frova)

Naratriptan (Amerge)

Rizatriptan (Maxalt)

Sumatriptan (Imitrex)

Zolmitriptan (Zomig)

Ergot – these drugs works by constricting blood vessels but they are having more side effects. ^[19] These drugs include:

- Dihydroergotamine (Migranal)
- Ergotamine (Ergomar, Cafergot)
- Isometheptene ,dichloralphenazone
- Acetaminophen(Midrin)

Antinausea drugs- Acetaminophen, aspirin and caffeine (Excedrin Migraine) is an FDA- approved otc treatment for migraine.

Message and physical treatment

For treating migraine, reflexotherapy is also used for relaxing body by putting pressure on hands and feet. According to some studies it may relieve pain however some more evidence are needed to support this hypothesis. Some studies shows that reflexology help relaxing body in many aspects. [16]

Other considerations

Pregnancy

Many of the drugs used in migraine are directly contraindicated in pregnancy whether they are of allopathic origin or homeopathic origin. Physicians recommendations are very important for selecting the drug so that we could prevent some major loss in the future. Acetaminophen is prescribed in case of mild to severe migraine during pregnancy. [20]

Warnings and Precautions

Medications should be used only when they are directed. Using medicine on regular basis can cause relapses. Consult to your doctor if you experience a new headache or previously taking medicines have no longer effective. Donot stop medicines without consultation to your physician. Should not take migranal if having any disease which affects heart, circulation or arteries and also in case of uncontrolled high blood pressure. The safety and effectiveness should not be established in children and adults more than 65 yrs of age. Avoid to take alcohol while using migranal because its mixing lead towards severe reaction. [21]

Prognosis and Complications

Migraine doesn't lead to affect overall body although it is acute, chronic, relapsing and frustrating. Caffeine, over dose of medicines also leads to a new headache. A general guideline should be followed that don't use

medicines more than nine times within a month. Keep medication record and regularly follow up the prescription and consult to physician. Multiple use of drugs in migraine can cause the elevation of serotonine level including triptan and certain antidepressants. The symptoms of serotonin syndrome include diarrhea, rapid heart rate, sweating, confusion, agitation and muscle twitching. People suffering from migraine especially females are at high risk of stroke, depression, anxiety and panic disorders. [21]

CONCLUSION

A migraine is a very painful headache which occurs as aching or pulsing in any one area of the head. People suffering from migraine are sensitive to sound and light, and also become nauseated and vomited. Doctor believed that migraine occurred due to the narrowing and opening of blood vessels in head. Females are more affected then males. Peoples who experienced aura can tell about their migraine while in case of migraine without aura it is difficult. Researchers have some ideas of underlying causes and mechanisms of migraine. There is no treatment of migraine but proper management and life style adjustment can help in overcoming the migraine. In addition, treatment focused on preventing trigger attacks and reducing severity or pain of attack.

REFERENCES

- 1. Barrows, K.A. and B.P. Jacobs, *Mind-body medicine: an introduction and review of the literature*. Medical Clinics of North America, 2002;. 86(1): 11-31.
- 2. Evers, S., et al., *EFNS guideline on the drug treatment of migraine–revised report of an EFNS task force*. European Journal of Neurology, 2009; 16(9): 968-981.
- 3. Loder, E., R. Burch, and P. Rizzoli, *The 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines.* Headache: The Journal of Head and Face Pain, 2012; 52(6): 930-945.
- 4. Kutner, J.S. and M.C. Smith, *CAM in chronic pain and palliative care*, in *Handbook of pain and palliative care*2013, Springer. p. 649-696.
- 5. Cady, R. and C. Schreiber, Sinus headache or migraine? Considerations in making a differential diagnosis. Headache: The Journal of Head and Face Pain, 2003; 43(3): 305-305.
- 6. Haneline, M.T., *Chiropractic manipulation and acute neck pain: a review of the evidence.* Journal of manipulative and physiological therapeutics, 2005; 28(7): 520-525.
- 7. Vernon, H., The effectiveness of spinal manipulation for the treatment of headache disorders: a systematic review of randomized clinical trials. Cephalalgia, 2003;. 23(6): 479-480.

- 8. Contag, S.A., H.L. Mertz, and C.D. Bushnell, *Migraine during pregnancy: is it more than a headache?* Nature Reviews Neurology, 2009;. 5(8): 449-456.
- 9. Ghayee, H.K., et al., *Mediastinal paragangliomas:* association with mutations in the succinate dehydrogenase genes and aggressive behavior. Endocrine-related cancer, 2009; 16(1): 291-299.
- 10. Mauskop, A., *Alternative therapies in headache: is there a role?* Medical Clinics of North America, 2001; 85(4): p. 1077-1084.
- 11. Andersson, J., M. Gaviola Poblete, and C. Volioti, Migrän: En osynlig sjukdom: En litteraturstudie om icke-farmakologiska metoder vid migränanfall hos vuxna. 2014..
- 12. Goldstein, L.B., et al., Guidelines for the primary prevention of stroke a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke, 2011; 42(2): 517-584.
- 13. Weissman, A.M., G.J. Jogerst, and J.D. Dawson, *Community characteristics associated with child abuse in Iowa*. Child abuse & neglect, 2003; 27(10): 1145-1159.
- 14. Silberstein, S., et al., *Probable migraine in the United States: results of the American Migraine Prevalence and Prevention (AMPP) study.* Cephalalgia, 2007; 27(3): 220-229.
- 15. Diener, H., et al., *Placebo-controlled comparison of effervescent acetylsalicylic acid, sumatriptan and ibuprofen in the treatment of migraine attacks.* Cephalalgia, 2004; 24(11): 947-954.
- 16. Tfelt-Hansen, P., et al., *Ergotamine in the acute treatment of migraine*. Brain, 2000; 123(1): 9-18.
- 17. Ferrari, M.D., et al., *Oral triptans (serotonin 5-HT 1B/1D agonists) in acute migraine treatment: a meta-analysis of 53 trials.* The Lancet, 2001; 358(9294): 1668-1675.
- Macedo, A., M. Farré, and J.-E. Baños, A metaanalysis of the placebo response in acute migraine and how this response may be influenced by some of the characteristics of clinical trials. European journal of clinical pharmacology, 2006; 62(3): 161-172.
- 19. Mandema, J., E. Cox, and J. Alderman, *Therapeutic benefit of eletriptan compared to sumatriptan for the acute relief of migraine pain-results of a model-based meta-analysis that accounts for encapsulation.* Cephalalgia, 2005; 25(9): 715-725.
- 20. Pascual, J., et al., Marketed oral triptans in the acute treatment of migraine: a systematic review on efficacy and tolerability. Headache: The Journal of Head and Face Pain, 2007: 47(8): 1152-1168.
- 21. Geraud, G., et al., Comparison of the efficacy of zolmitriptan and sumatriptan: issues in migraine trial design. Cephalalgia, 2000; 20(1): 30-38.