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Management of Migraine Headaches in Different Systems of Medicine – A Comparative Study

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ABSTRACT

Migraine headache has been reported as a major problem and complication among various races worldwide affecting around 15% of the populations with a higher rate in women than men. In the present study, a survey has been done to collect data with regard to its management in three different system of medicine, which include: Greco–Arabic or Unani System, Herbal System and present day Modern (Allopathic) System of medicine. In the survey, major emphasis has been given on the treatment pattern and drugs available in the Greco-Arabic or Unani System of medicine and was compared with present day Herbal System and Modern system of medicine. The Greco-Arabic system is quite popular in South Asian countries, including Pakistan. It has a definite Philosophy and its practitioner are called – "Hakeems" while the clinics are called – "Dawa Khana or Matab" The methodology of the present survey includes collection of various drugs available in Dawa Khanas, for Unani Drugs and various Pharmacies for Herbal and Allopathic Drugs used in the management of migraine. In total, six different drugs from Unani System were collected and their constituents were analyzed with respect to their phytochemistry and pharmacology and reported in this paper to ascertain their role in the management of Migraine Headaches and compared with some of the well known herbal and allopathic drugs.

Keywords: Migraine Headaches, herbal and allopathic drugs

INTRODUCTION

In medicine, a headache or cephalalgia may be defined as different conditions of the head which is usually disturbance in the pain sensitive areas of the head or neck region. Head is one of the most common sites of pain in the body [1]. Is the most common medical disorder and a person has suffered from it at least once in his life. Its history is as old as the history of mankind himself. But the first description was given in the third millennium of BCE [2]. It was given medical importance in Babylonian civilization when vast research was done in this area. Historians such as Napoleon, Julius Ceaser and John Franklin Kennedy were known to have terrible headaches not properly defined at that time, now known as Migraine headaches [2].

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Migraine headaches, in medical literature is described as a sum of symptoms like nausea, visual disturbances (aura), vomiting, and severe pain on either side of the head. A huge population mostly women suffer from these kind of headaches [1]. The release of specific chemicals in brain leads to the events described above.

In our country, most of the people suffer from terrible cluster and migraine headaches but the cause remains unknown. Normally, a specific trend of avoidance in our society keeps a patient away from neurologists, due to which sooner or later in their lives, the pain extravagates. A huge population in our society turns towards Cumulative and Alternative system of medicine due to poverty and non-availability of proper medical resources in their respective areas. In view of the high importance of alternative medicine in our country, some important drugs known for the treatment of cephalalgias especially migraine will be discussed here. Alternatively, allopathic drugs will also be discussed so as to provide a good concept to both patients and practitioners. Furthermore, it is important to report the cause and management of such disorders to create awareness amongst researchers who further want to elaborate research in this field.

DEFINITION AND DESCRIPTION

Headache is defined simply as pain in head or neck. Lifestyle changes and medications can make a person feel much better. Most commonly headaches caused by tight, contracted muscles in shoulders, neck, scalp and jaws. They are attributed mainly to physical and emotional stress, depression, anxiety, insomnia. They may also be triggered by missed meals, alcohol, cheese, monosodium glutamate found most commonly in Asian type of foods, and excessive caffeine. Headaches may be dull, pounding, or aching. Headaches are thought to be due to chemical changes in nerves or blood vessels in specific areas of brain that lead to contraction of muscles. Headaches are often hereditary and the kids often get the same pattern of a typical headache as that of their parent or even worse. Headaches may be caused due to secondary reasons such as a trauma or injury to the head or neck, due to meningitis, or following an infection.

Headaches are mostly divided into three categories: Primary headaches, secondary headaches and cranial neuralgias. Primary headaches like cluster headaches, migraines and tension type headaches have a specific trigger whereas secondary headaches are mostly attributed to injuries and infections. Special preference to migraine headaches will be given regarding causes, symptoms and treatment.

MIGRAINE HEADACHES

Migraine headaches are usually considered as vascular headaches with severity ranging from severe to very severe [3]. They are often accompanied by visual disturbances (aura), nausea and vomiting. These headaches usually occur on one side of the head although the pain is so severe that it is felt on the other side of the head as well [4]. The severity causes the patient to refrain from daily work activities since physical activity worsens the pain. Migraine headaches are usually throbbing pounding headaches that usually occur in a specific pattern that varies from one individual to another [5]. They are due to changes in brain and surrounding blood vessels. A migraine headache usually lasts from 4-72 hours. It generally affects 15% of the population with a higher rate in women than men. More than 80% of people get it from their family.

Usually migraine is of two types:

- With aura (very severe)
- Without aura (severe)

Aura may be defined as visual disturbances for example flashes and bands of sharp colors in front of eyes that cause loss of half or complete vision. An individual with aura usually has very severe pain but the time interval is short of about 4-24 hours or even less [4] [5]. Whereas those without aura have intense pain of severe range but the time interval increases (from 8-72 hours).

SYMPTOMS AND PHASES OF MIGRAINE

Five phases can usually be identified in a migraine headache:

- *PRODROME:* these are the warnings accompanied with the start of migraine headaches. These may be a feeling of intense energy or elation, irritability, depression. Fatigue, muscle tension and insomnia may also occur.

- *AURA:* This is defined as visual disturbance that precedes 30-40 minutes before a migraine headache. It usually lasts for 20 minutes or more. Some people develop blind spots (called scotomas); see geometric patterns or flashing, colorful lights; or lose vision on one side (hemianopsia). Some physicians suggest any medication to be given in this phase only because once the headache starts, medicines usually do not help in lowering pain.

- *HEADACHE:* Normally it starts after 30 minutes of aura and ranges from severe to very severe. Mostly migraine is on one side of the head but 30-40% migrainuers get it on both sides of the head. 80% feel nausea and vomiting. People normally become photophobic and phonophobic. Throbbing pulsating pain is felt on one or both side of the head due to aggravated blood pressure and inflammation of nerves.

- *HEADACHE TERMINATION:* In some, usually the pain goes away with rest, sleep and treatment.

- *POSTDROME:* Nausea, vomiting, irritability, pain in eyes, loss of concentration, inability to eat, fatigue, dizziness, and weakness usually occurs when the episode ends [5].

TRIGGER FACTORS OF MIGRAINE HEADACHES

The history of migraine suggests a number of different triggers due to which the migraine starts. Triggering factors may not be common to everybody. Certain type of foods may cause migraine in some and may be completely unharmful for the rest. Some very common migraine triggers include cheese, monosodium glutamate (MSG which is common in Asian foods), aspartame, onions, tomatoes, chocolate, carbonated beverages, coffee, dairy products, nuts, citrus fruits etc [1]. Other than food triggers, hormonal and sudden seasonal changes, head trauma, physical and mental exertion, stress, fatigue, changes in sleep pattern, socialism may also trigger migraine. Stress is considered one of the most important in causing migraine headaches. Certain medicines like oral contraceptives, hormonal therapies, nitroglycerin, resperine, hydralazine, ranitidine may also be the trigger factors [1].

PATHOPHYSIOLOGY OF MIGRAINE

Migraine headaches are caused mainly due to exertion, dilation of blood vessels in the brain region of the head. Mostly headaches occur without a warning but some people get a visual warning or aura. Before the onset of pain which may also include blurred vision, loss of motor activity, disturbed thinking, tingling or numbness in one side of the body [6]. Migraine pain occurs when the blood vessels in the lining of the brain or scalp become stressed or tensed. Instability of vessels in brain and a reduction in blood flow occurs during the attack. Research also indicates that blood vessels constriction and dilation is impaired in some patients [6]. In addition, platelets in migraine sufferers are different, both during and after the attack. They clump together and release a chemical known as serotonin. A migraine begins when for some reasons the blood vessels in the brain constrict and the blood and the oxygen flow to the brain stops. Due to which other vessels also dilate and this results in inflammation, probing and pounding pain. Due to the involvement of vessels migraine is also known as vascular headache. Two theories have been presented to describe migraine headaches.

VASCULAR THEORY

Migraine occurs when the blood vessels in the brain constrict and expand inappropriately. This may start in occipital lobe as arteries spasm. The visual cortex in the occipital area in which there is a decrease in the blood flow, causes the well known symptom "aura" [1-2, 6]. When the constriction stops they expand too much causing leaking of the cell chemical. This is recognized by the pain sensitive receptors in the surrounding tissues causing pain. With each heart beat as the blood passes through the vessels a probing pain sensation is felt.

NEURAL THEORY

When certain areas in the brain stem become irritated, a migraine begins. As a response of this irritation the body releases certain chemicals that cause inflammation of the blood vessels. They further cause irritation of the nerves and causes pain. Substance-P is released as soon as the first signals of pain are received and further pain signals are sent to brain thus further increasing pain [7].

TYPES OF MIGRAINE

Two common types of migraines have been recognized that include migraine with aura and migraine without aura [8]. Migraine is classified according to the symptoms they produce.

- Migraine with aura: It is characterized by a neurological phenomenon that is known as aura. Aura starts 10 to 30 minutes prior to the headache. They are visual disturbances, described by migraine patients as flashes or bands of sharp lights and shimmering lights around objects or at the field of vision (scintillating scotomas) or zigzag lines, castles (teichopsia), wavy images and sometimes even hallucinations [8]. Some may experience temporary loss of half vision. Non visual auras may be loss of consciousness, vertigo, speech and thinking disturbances, motor weakness, dizziness, parasthesia of face tongue and extremities.

- Migraine without aura: It is most prevalent type and may be bilateral (occurring on both sides). Mood swings, tiredness may be the prodromes of the headache while nausea, vomiting, photophobia, phonophobia accompanies migraine headaches without aura.

- Abdominal migraine: It is most common in children with a family history of migraine. Symptoms include abdominal pain without a gastrointestinal cause, nausea, vomiting, and pallor (paleness). Children often develop typical migraine in later stages of their lives.

- Basilar artery Migraine: It involves disturbance of the basilar artery in the brainstem. Severe headache, vertigo, loss of speech may occur during the course of the headache.

- Carotidynia: Also called lower-half headache or facial headache. Produces deep and dull aches in the jaw or neck.

- Headache-free migraine: It is characterized by the presence of aura without any headache. It is common in patients with a migraine with aura history.

- Ophthalmologic migraine: It is headache of the eye and it is accompanied by nausea and vomiting. As the headache starts the eyelids droops and the nerves responsible for eye movements become paralyzed.

- Status migrainosus: It is of rare type with pain usually lasting for more than 72 hours. May cause stroke and seizures, and patient require hospitalization [8].

- Some women develop migraine headaches prior to or during menstruation, known as menstrual migraines. It is due to hormonal changes. It usually reduces or lessens during pregnancy [8].

MANAGEMENT OF MIGRAINE HEADACHES IN THE MODERN SYSTEM OF MEDICINE PHARMACOLOGICAL MANAGEMENT

There are two types of treatment that is acute abortive and preventive treatment.

Abortive Treatment

Acute abortive treatment is used for relieving the symptoms immediately as soon as the headache starts. Medicines are used to either stop the pain or relieve it to some extent. Patients with acute migraine episodes are given the first line treatment with triptans and ergots[1].

Preventive Treatment

Preventive treatment is used to reduce the frequency and chances of getting a headache. It also increases the time interval between two headaches and decreases the severity of the pain. It usually involves taking the medicines for 3-6 months or more depending on the type of migraine and the severity associated with it. Choice of a particular drug also depends on this. These drugs are normally associated with specific side effects, limiting the use of a particular drug in a particular class of patient. For example, triptans and dihydroergotamine are associated with the vascular constriction and hence cannot be given to patients with a history of angina or coronary artery disease [8].

CLASSES OF DRUGS USED AS A PREVENTIVE TREATMENT OF MIGRAINE HEADACHES

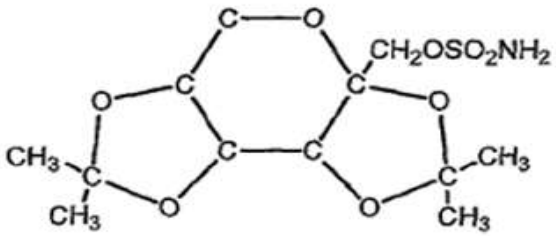
Four main classes of drugs are recognized as preventive treatment for migraine headaches:

- Anti-convulsants (divalproex, topiramate)
- Beta blockers (atenolol, propanolol, metaprolol, timolol)
- Calcium channel blockers (verapamil)
- Tricyclic anti-depressants (amitriptaline)
- Anti-serotonins

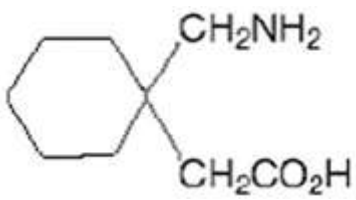
ANTI-CONVULSANTS

Anti-epileptics or anti-convulsants are a diverse group of drugs used for the treatment of seizures associated with epilepsy, a neurological dysfunction in which excessive surges of electirical energy are emitted in the brain. These agents work by preventing the spread of abnormal electric discharges in the brain, although the exact mechanism of action is unknown. Anti-seizure drugs are used singly or in combinations depending on the type and degree of seizure activity [9]. Anticonvulsants include a variety of agents, all capable of depressing abnormal neuronal discharges in the CNS that may result in seizures. They may work by preventing the spread of seizure activity, depressing the motor cortex, raising seizure threshold, or altering levels of neurotransmitters, depending on the group. Anticonvulsant drugs seem to be useful for the prophylaxis of migraine. This might be explained by a variety of actions of these drugs in the central nervous system that are probably relevant to the pathophysiology of migraine. Anticonvulsants that have demonstrated their efficacy in clinical trials are divalproex sodium, topiramate, sodium valproate, gabapentin, carbamazepine. Topiramate is the only anticonvulsant approved by the FDA for migraine prophylaxis [9]. Some common side effects are fatigue, loss of coordination, loss of apetite, loss of ability to speak or think clearly etc. [10-12].

Topiramate



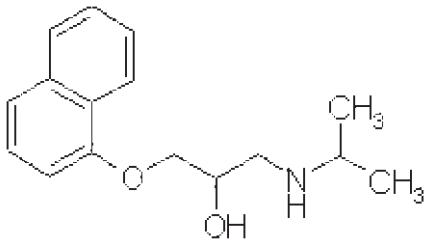
Gabapentin



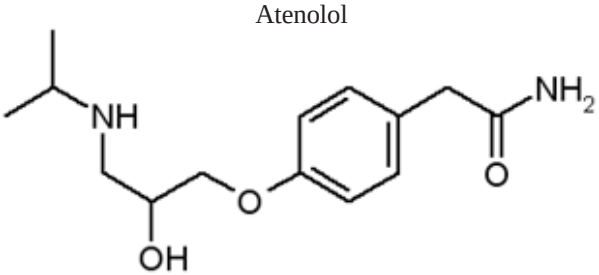
BETA-BLOCKERS

Beta-blockers are used in the treatment of high blood pressure, to relieve angina, and in heart attack patients. They are also used to treat tremors and to prevent migraine. Beta-blockers work by blocking the effect of beta-adrenergic chemicals produced by the nerves and adrenal glands. Beta-blockers have been used for many years for the prevention of migraine headaches. The exact mechanism of these drugs for migraine prevention is unknown but they may work by decreasing prostaglandin production, or may have a direct effect on serotonin or arteries. Beta-blockers used for this purpose are propanolol, atenolol, metoprolol, nadolol and timolol. Side effects include breathing difficulties in asthma patients, drowsiness, diarrhea, constipation, nausea and memory loss [3-4].

Propanolol



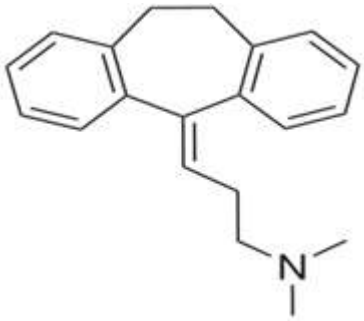
Atenolol



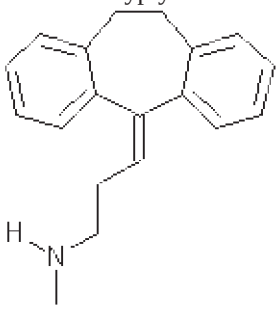
TRICYCLIC ANTI-DEPRESSANTS

Tricyclic antidepressants (TCAs) are used for the treatment of migraine headaches by altering norepinephrine and serotonin, which is used by the nerves for communication with each other. Drugs used for migraine prevention include amitriptyline, nortriptyline, doxepin, imipramine and protryptyline. Side effects include fast heart rate, low blood pressure when standing, dry mouth, constipation, and weight gain or loss [11-12].

Amitryptyline



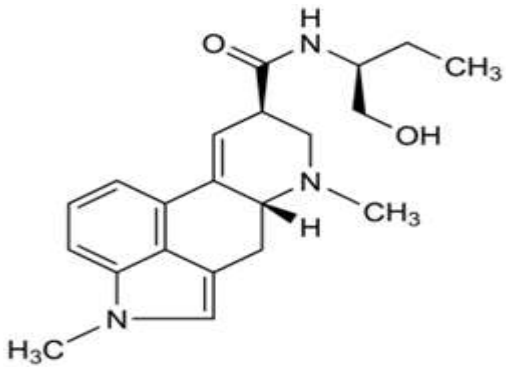
Nortryptyline



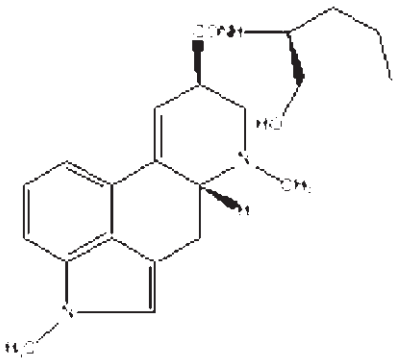
ANTI-SEROTONIN MEDICATIONS

Anti-serotonin prevents migraine headaches by constricting blood vessels and reducing inflammation of the blood vessels. Methysergide and methylergonovine belong to this class but their use is restricted due to the side effects associated with them. The most serious side effects include scarring of tissues around the ureters, scarring of tissues around the lung, scarring of heart valves as well as shortness of breath [11-12].

Methysergide



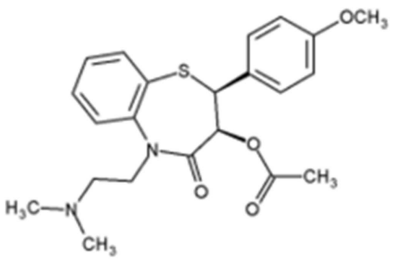
Methylergonovine



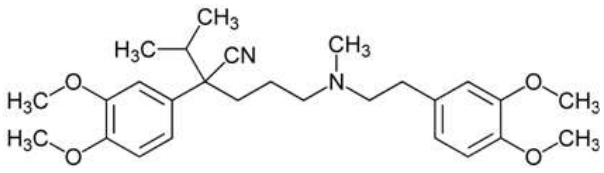
CALCIUM CHANNEL BLOCKERS

Calcium channel blockers block the entry of calcium in the muscular cells of the heart and the arteries. By doing so, they reduce heart contraction, decrease heart rate and thus lower blood pressure. They also block the effects of serotonin within the nerves and have been used occasionally to prevent migraine headaches. Drugs used are diltiazem, verapamil and nimodipine. Side effects associated include nausea, constipation, rash, edema, drowsiness and dizziness [11-12].

Diltiazem



Verapamil



CLASSES OF DRUGS USED AS AN ABORTIVE TREATMENT FOR MIGRAINE HEADACHES

Whenever an attack is progressed, these drugs alone or in a combination may be helpful in the treatment. The choice of drugs depends on the severity of the pain.

For very severe attacks, these are the drugs of choice:

- Anti-emetics (domperidone, pheriramine maleate)
- Triptans (sumatriptan, zolmitriptan)
- Ergot derivatives (dihydroergotamine)
- Opiods

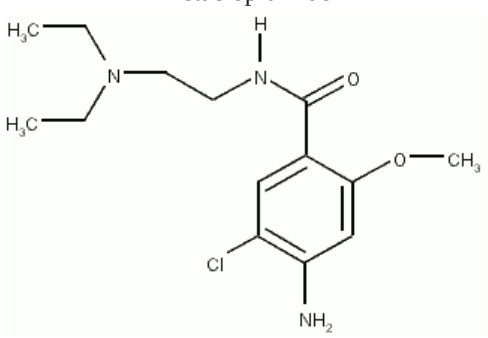
For less severe pain, mostly these drugs are prescribed:

- NSAIDs (aspirin)
- Analgesics (paracetamol, ibuprofen)

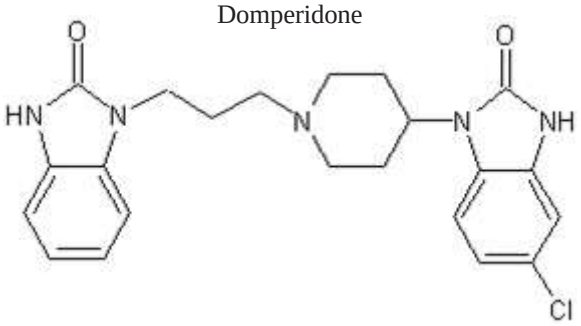
ANTI-EMETICS

For mild or moderate symptoms, phenothiazines or antihistamines may suffice and are widely available without prescription. Dopamine and 5-HT3 antagonists such as metoclopramide and domperidone have the added advantage of promoting absorption of oral analgesics, which can enhance efficacy. Domperidone alone may be effective if taken during the prodrome of migraine. If nausea or vomiting precludes oral medication, rectal anti-emetics should be used. Intramuscular chlorpromazine can be considered for emergency acute treatment. Empirical data suggest that combining these agents with triptans may also offer additional benefit but formal clinical trials are necessary to confirm this. Drugs such as metaclopramide, domperidone and other anti-nausea and anti-vomitting drugs are used in combination with other migraine drugs to prevent the nausea and vomiting that occurs with migraine attacks. They also allow a better absorption of migraine drugs [12].

Metaclopramide



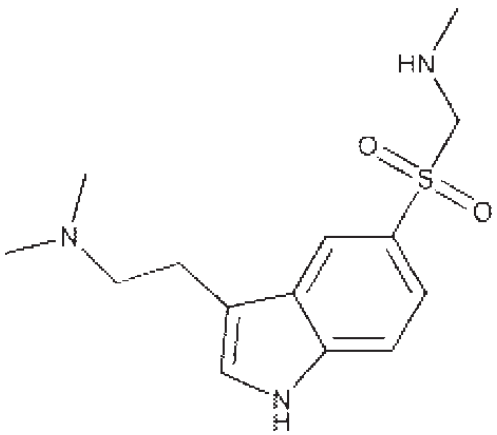
Domperidone



TRIPTANS

Triptans that are also known as serotonin agonists were the first drugs that were developed against use as migraine agents. Triptans narrow (constrict) blood vessels in the brain and relieve swelling. They are clinically the most important drugs available. They target serotonin specifically, by keeping the level down. They are recommended as the first-line of therapy for migraine patients when NSAIDs are not effective. These drugs are used to effectively and quickly relieve headache pain, sensitivity to light and noise, and nausea and vomiting associated with migraines. They are especially helpful if you have moderate to severe headaches that interfere with your ability to perform daily tasks. They are effective for patients with both tension-type and migraine headaches and it does not have sedative effects. Drugs used include sumatriptan, zolmitriptan, almotriptan, naratriptan, rizatriptan, frovatriptan and eletriptan. Side effects include tingling and numbness of extremities, nausea, dizziness, and drowsiness [10].

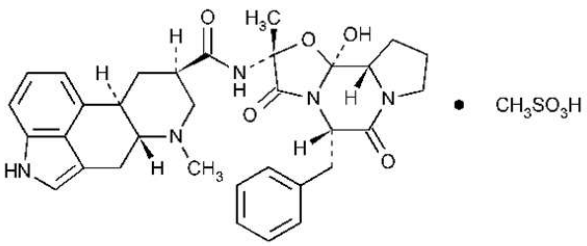
Metaclopramide



ERGOTS

Ergotamines narrow (constrict) blood vessels in the brain. Drugs containing ergotamine, that are commonly known as ergots, cause constriction of smooth muscles of the blood vessels and are thus used for migraine prevention. Dihydroergotamine is available which can be used as a nasal spray and also by injections. Ergotamine is available as sublingual tablets, and rectal suppositories. The role of ergotamines has become less certain after the introduction of triptans for migraine use. But it is still helpful for patients with status migrainosus or those with frequent recurring headaches. Side effects include nausea, vomiting, tingling sensations and muscle cramps. Ergots should be avoided during pregnancy. They cause blood vessel contraction due to which it may pose danger for patients with cardiac problems [13-14].

Metaclopramide

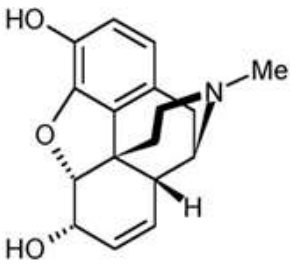


OPIOIDS

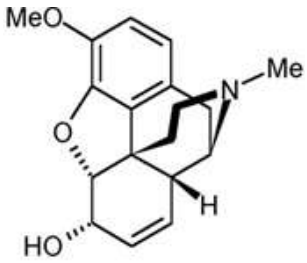
Opioids are drugs that are known for their potential pain relieving characteristic. If the migraine pain does not respond to any other drugs then doctors may prescribe drugs with opioids. Drugs include morphine, codeine, thebaine, meperidine, oxycodone, and butorphanol. Opioids are not approved for migraine treatment and should not be used as first-line therapy. Nevertheless, many opioid products are prescribed to patients with migraine, sometimes with dangerous results. In 2007, following reports of several drug-related deaths, the Food and Drug Administration warned that the cancer pain pill fentanyl (Fentora) should not be used to treat patients with migraine or others conditions for which the drug is not specifically approved.

Side effects include drowsiness, impaired judgement, nausea, and vomiting. Opioids also have a risk for severe addiction thus further limiting its use especially in patients with personality and psychiatric disorders [4].

Morphine



codeine

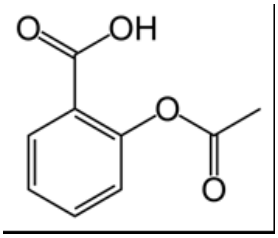


PAIN RELIEVERS (NSAIDs AND ANALGESICS): Mild migraine responds very well to commonly available over-the-counter pain relieving medications particularly taken in prodrome. OTC pain relievers, (also called analgesics), include

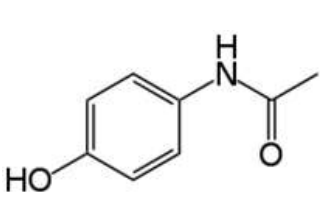
- Nonsteroidal anti-inflammatory drugs such as ibuprofen (Advil, Motrin), naproxen (Aleve), and aspirin. The FDA-approved migraine products Advil Migraine and Motrin Migraine Pain both contain ibuprofen.

- Acetaminophen (Tylenol). The FDA-approved migraine product Excedrin Migraine contains acetaminophen, as well as aspirin and caffeine. Side effects may include the risk of heart attacks, stroke, kidney problems and stomach bleeding [2] [3] [6].

Aspirin



Acetaminophen



MANAGEMENT OF MIGRAINE HEADACHES IN COMPLEMENTARY AND ALTERNATIVE MEDICINE

ALTERNATE TREATMENT FOR MIGRAINE HEADACHES:

Herbal medicine refers to folk and traditional medical practice based on the use of plant parts and extracts from the plants for the treatment of a specific medical condition. The use of herbs as drugs is almost universal among native people [1]. The most commonly used herbs and enzymes for the relief of migraine in most of the combinations include the following:

FEVERFEW

The herb feverfew (Tanacetum parthenium), which literally means fever reducing, has been used in Europe most popularly from 1980s for pain like headache, arthritis, migraine and fever [15]. Fever few (fig.1[16]) works by inhibiting the release of blood dilating substances from platelets and thus inhibits the production of inflammatory chemicals [4]. Several studies have been done to determine the effectiveness of this drug for use in migraine headaches. In a study, the extract of feverfew was used or a placebo in 170 people with migraines. There was a significant decrease in migraine frequency, which decreased by 1.9 migraines per month compared to the placebo, which decreased to 1.3 migraines per month. Not all studies by far have shown effective and confirmed results, however. In a critical review of five studies on feverfew over migraines that involved 343 people, showed that the results were mixed and they did not convincingly showed migraine decrease or prevention by the use of feverfew. Some of the side effects with the use of feverfew are abdominal disturbances like gas, diarrhea, and vomiting. Others include nervousness and anxiety [1]. Drug interactions include interaction with blood thinning medicines like aspirin, warfarin and NSAIDs. Those taking blood thinning medications must consult a physician before using feverfew [17].

Figure 1

HYDROXYTRYPTOPHAN (5-HTP)

5-HTP (5-Hydroxytryptophan) is a compound produced in the body from the amino acid tryptophan. It is used in the body to make the neurotransmitter serotonin and the hormone melatonin.

5-HTP is also available in supplement form. It is extracted from the seeds of Griffonia simplicifolia. Since supplements affect the level of serotonin in brain therefore 5-HTP has been suggested and explored as an alternative treatment. Research has indicated that 5-HTP reduces as well as prevents migraine frequency and severity. In one study, 124 people were given 5-HTP (600 mg/day) or the drug methysergide. After six months, 5-HTP was found to be as effective as methysergide in reducing the severity and duration of migraines. Another study compared the drugs 5-HTP and propranolol for a period of four months. Both treatments suggested a statistically reduction in both the frequency and severity of migraines. However, the group using propranolol showed a better result with a reduction in the duration and reduction of migraine episodes [3]. Research shows that 5-HTP becomes more effective by the passage of time with results increasing positively after 30 days of use [18]. The role of 5-HTP in the body also increases the endorphin levels that are body endogenous pain relieving substances. Endorphins are low in migraine sufferers [19-20].

MAGNESIUM

Magnesium is a naturally occurring mineral in human body. It is found in green leafy vegetables, nuts, seeds, and whole grains. Magnesium is required in the body for more than 300 biochemical reactions. It also helps regulate blood sugar levels and is needed for normal muscle and nerve function, immune function, heart rhythm and for bones. Patients with migraine have been shown to have low blood concentrations of magnesium that needs supplementation since magnesium's key function is to regulate blood vessels tone.

Several studies have shown promising results in the use of magnesium for migraine headaches. In one study, evaluating 81 people, oral magnesium (600 mg/day) or a placebo was given. After nine weeks, the results showed that the frequency of migraine headaches was reduced by 41.6 percent in the group taking oral magnesium as compared to placebo that showed a decrease of 15.8 percent.

Side effects include diarrhea, nausea, loss of appetite, muscle weakness and confusion. Drug interactions include medicines used for osteoporosis, calcium channel blockers, some antibiotics and diuretics [21]. Migraine is also known to treat food-allergy induced migraines.

BUTTERBUR

Butterbur (Petasites hybridus) has been used for the treatment of migraines, stomach cramps, cough, allergies and asthma [15]. Several studies have been done regarding the efficacy of butterbur for migraine headaches. A study that involved 245 people who took butterbur extract (50-75 mgs/day) or placebo showed significant results in migraine headaches [22]. Side effects include digestive complaints mainly indigestion, burping, headache, fatigue, nausea, vomiting, diarrhea, or constipation. Butterbur (figure. 2) should not be used during pregnancy or lactation and in people with kidney or liver disorders [22]. The daily dosage should not exceed one

microgram per day due to the presence of pyrrolizidine alkaloids in the teas, extracts and even capsule form prepared from the raw herb.

Figure 2

VITAMIN B2 (RIBOFLAVIN)

It is a water-soluble vitamin. It is involved in energy production, red blood cell synthesis and body growth. Vitamin B2 is used in migraine prevention along with a beta-blocker (like metoprolol, atenolol, and propanolol) [1]. Vitamin B2 works by allowing cells to store energy without increasing the excitability of nerve cells. Dosage is 200 mg twice a day with meals. Side effects include nausea and vomiting [23].

CO-ENZYME Q10

This compound is centrally involved in the energy production within the cells and was first identified in 1957. It can be used to decrease migraine frequency. It works by boosting the brain's energy reserves. In a 2005 study, migraine attacks decreased by 48% in people who took the supplement three times daily [24]. Typical dosage is either one single daily dose or is divided into three doses per day. In rare cases, nausea or diarrhea is observed [24].

FISH OIL

Fish oil is rich source of omega-3 fatty acids that are heart-healthy and provides other benefits as well. Omega-3 fatty acids can decrease frequency, severity and duration of migraine [25]. The exact mode of action of omega-3 fatty acids in migraine headaches is not known but it decreases inflammation and relax blood vessels. It also reduces platelet aggregation. Typical dosage is 2-6 g/day. Some people notice bad breath, burning and gas while taking fish oil. In a higher-quality pharmaceutical grade fish oil this problem can be minimized. Patients with high blood cholesterol and diabetes should ask their doctor before using fish oils [25].

MATERIALS AND METHODS

Materials and methods of the present study is based on the survey on herbal medicines used for the treatment and prophylaxis of headache/migraine, available in Pakistan was done through available herbal medical stores/ dawakhanas. The survey covers three most reputable dawakhanas and herbal laboratories situated in Karachi.

The following are the names of the manufacturers that produce products for headache/migraine:

1. Marhaba Laboratories
2. Hamdard dawakhana
3. Tayyebi dawakhana

Following polyherbal formulations were identified and collected from these dawakhanas:

1. Itrafeel Kishneezi (Hamdard Laboratories)
2. Itrafeel Ustukhudoos (Hamdard Laboratories)
3. Chinnkni (Tayyebi dawakhana)
4. Khamira Gaozaban Amberi Jawaharwala

(Tayyebi dawakhana)

5. Itrafeel Ustukhudoos (Tayyebi dawakhana)

6. Itrafeel zamani (Marhaba Laboratories)

STUDIES ON THE COMPOSITION OF THE POLYHERBAL FORMULATIONS

All six polyherbal formulation collected from different manufacturers/laboratories were studied with respect to their constituents are presents in Table 1 in Results and Discussions.

INDIVIDUAL ACTIVITY OF THE PLANTS COMMON IN THE POLYHERBAL FORMULATIONS

Individual pharmacological activity of the plants/herbs present/common in the polyherbal formulations were also studied and depicted in Table 2 in Results and Discussion.

RESULTS AND DISCUSSION

The migraine begins with a throbbing headache that is usually centered above or behind one eye; or, it can begin at the back of the head and spread to one entire side of the head. It is usually accompanied by nausea, vomiting, blurred vision, and tingling and numbness in the limbs that can last up to several hours. A classic migraine is preceded by an aura, which can consist of disturbances of vision, specach disorders, weakness, and sensory disturbances. An aura can also consist of brilliant stars, sparks, flashes, or simple geometric forms passing across the visual field. Allergies have been reported to be the most common cause of migraine. However, others, including liver malfunction, constipation, stress, lack of exercise should also be considered as possible underlying causes of migraine headache. Various studies and reports suggest that seventy percent of migraine sufferers are women, and migraine often run in families. The peak incidence is between 20 to 30 years of age, then gradually declining. Many patients have abnormal level of brain chemicals that cause excessive dilation and / or contraction of the brain's blood vessels.

Considerable evidence supports an association between migraine headache and vascular system instability, but the mechanisms are still not clear. Although most clinicians and researchers believe that the sequence of events is excessive intracranial arterial constriction (causing inadequate blood supply to the brain) followed by rebound dilation of the extracrainial vessels (the headache phase), sophisticated studies of brain blood flow before, during and after are inconsistent in their support of this hypothesis.

Migraine headache is perhaps the result of remarkably diverse range of causes. There is little doubt that food allergy / intolerance is the major cause of migraine headache. Foods such as chocolate and cheese have been reported to precipitate migraine attacks. Patients with dietary migraine have been found to have significantly lower levels of a platelet enzyme (phenolsulphotransferase, which normally breaks down these dietary amines) than either migraine patients without a history of dietary provocation or normal controls.

Herbal or botanical medicines have a long history of use as flok cures for migraine headache. Based on this, a detailed survey has been performed in the present study to observe local market with respect to various herbs and their combinations available for this particular disorder. It was observed that some polyherbal formulations are available in Pakistan market for headaches and migraine. Among the products identified and collected from various dawakhanas and herbal product manufacturers include:

1. Marhaba laboratories

2. Hamdard dawkhana

3. Marhaba laboratories

The following formulations were identified and collected from these dawakhanas:

7. Itrafeel Kishneezi (Hamdard Laboratories)
8. Itrafeel Ustukhudoos (Hamdard Laboratories)
9. Chinnkni (Tayyebi dawakhana)
10. Khamira Gaozaban Amberi Jawaharwala (Tayyebi dawakhana)
11. Itrafeel Ustukhudoos (Tayyebi dawakhana)
12. Itrafeel zamani (Marhaba Laboratories)

and their constituents are reported in Table 1.

It was also observed that a diversified group of plants and plant-based extracts have been used in the formulation of these products. The major plants/herbs used in the development of these polyherbal formulations capable of managing or curing various types of headaches including migraine are presented in Table 2.

Table 1: Studies on the composition of Polyherbal Formulations

Name of product	Ingredients
1.Itrafeel kishneezi (Hamdard laboratories)	Terminalia chebula Retz. [Black] Coriandrum sativum Linn. (Dried) Emblica officinalis Linn. (Dried) Terminalia belerica Roxb. (Peel) Terminalia chebula Retz. (Yellow)
2. Itrafeel Ustukhudoos (Hamdard Laboratories)	Cassia angustifolia Vahl. Cuscuta reflexa Roxb. Emblica officinalis Linn. Lavandula stoechas Linn. Polypodium vulgare Linn. Rosa damascena Miller Terminalia belerica Roxb. (Peel) Terminalia chebula Retz. (Yellow) Terminalia chebula Retz. [Black] (Peel) Vitis vinifera Linn.
3.Chinnkni (Tayyebi dawakhana)	Eucalyptus oil Elettaria cardamomum Cinnamomum camphor Pterocarpus santalinus Mentha piperata
4.Khamira Gaozaban Ajmeri Jawaharwala (Tayyebi dawakhana)	Abresham Physter macrocephalus Rosa damascene aqueous distillate Nepeta hindostana Centurea behen Onosma bracteatum Elettaria cardomomum Coriandrum Sativum Pearls Santalum album Phyllanthus maderaspatensis Silver foil
5.Itrafeel Ustukhudoos (Tayyebi dawakhana)	Cuscuta reflexa Embelica officinalis Terminillia chebula Terminillia belerica Polypodium vulgare Rosa damascene Vitis vinifera Lavandula stoechas
6.Itrafeel zamani (Marhaba Laboratories)	Bambusa arundinacaea Cassia angustifolia Citric acid Cochlospermum gossypium Convolvulus scammonia Cordial latifolia Coriandrum sativum Embelica officinalis Ipomoea terpetrum Nymphaelotus Ricinus communis oil Rosa damascene Santalum album Sugar Termenalia chebula Viola odorata Ziziphus vulgaris

Table 2: Individual activity of the plants common in the formulations

Plants/herbs with common names	Pharmacological activity and constituents reported
1. Termenelia chebula (Halaila)	Anti-diarrhoeal, carminative, astringent, brain tonic. Medicinal use: Effective in bloody piles, liver debility, constipation, cough, asthma, urinary complaints, flatulence. Researchers have isolated a number of glycosides from Haritaki, including the triterpenes arjunglucoside I, arjungenin, and the chebulosides I and II. Other constituents include a coumarin conjugated with gallic acids called chebulin, as well as other phenolic compounds including ellagic acid, 2,4-chebulyl-?-D-glucopyranose, chebulinic acid, gallic acid, ethyl gallate, punicalagin, terflavin A, terchebin, luteolin, and tannic acid.
2. Embelica officinalis (amla)	Carminative, diuretic and antiseptic, anti-oxidant. Medicinal use: Effective in palpitation, tachycardia, scurvy, cardiac and stomach debility, excessive body heat. [2] Amla is highly nutritious and is an important dietary source of Vitamin C, minerals and amino acids. Key components are Emblicanin A&B, Puniglucanin, Pedunculagin, 2-keto-gluconolactone (Vitamin-C equivalents). Ellagic acid, Hexahydroxy-diphenic acid and conjugates.
3.Rosa damascena (Gul surkh)	Refrigerant, mild laxative and mild astringent. Medicinal use: Effective in relieving body heat, perspiration, palpitation, headache, chronic fevers and inflammations. The chemical composition of rose oil is one of the most complex and contains more than 300 known compounds, yet the main chemical components of rose oil can be listed as -citronellol, phenyl ethanol, geraniol, nerol, farnesol and stearpoten with traces of nonanol, linalool, nonanal, phenyl acetaldehyde, citral, carvone, citronellyl acetate, 2-phenylmenthyl acetate, methyl eugenol, eugenol and rose oxide.
4.Coriandrum sativum (dhania)	Carminative, anti-flatulent, cardiac refrigerant. Medicinal use: Effective in gastro-intestinal complaints such as dyspepsia, flatulence and vomiting. Also used in rheumatism. [2]. In the ripe fruits, the con¬tent of essen¬tial oil is com-parably low (typic¬ally, less than 1%); the oil consists mainly of linalool (50 to 60%) and about 20% terpenes (pinenes, ?-ter¬pinene, myrcene, camphene, phell¬andrenes, a-ter¬pinene, limonene, cymene).
5.Onosma bracteatum (gaozaban)	Carminative, anti-flatulent, cardiac refrigerant. Medicinal use: Effective in gastro-intestinal complaints such as dyspepsia, flatulence and vomiting. Also used in rheumatism. [2]. In the ripe fruits, the con¬tent of essen¬tial oil is com-parably low (typic¬ally, less than 1%); the oil consists mainly of linalool (50 to 60%) and about 20% terpenes (pinenes, ?-ter¬pinene, myrcene, camphene, phell-andrenes, a-ter¬pinene, limonene, cymene).

Interestingly, however, the drugs/compounds that are studied here and that are available in international market for the management of this specific disease include:

1. Fever few,
2. 5-HTP,
3. Magnesium,
4. Butterbur,
5. Vitamin B2 ,
6. Co-enzyme Q10,
7. Fish oil,
8. Peppermint oil,
9. Passion flower,
10. Gingko

are quite different than the products which are manufactured in Pakistan with respect to ingredients and herbs used for this specific application.

CONCLUSION

The objective of this study was to create awareness in patients, practitioners and researchers. This study provides patient-oriented information regarding the phases and types of migraine. It also provides an insight of the commonly used medicines as a first line of therapy by the practitioners for the migraine patients and also other alternative treatments that could be recommended. In view of the importance of headaches in our society, it is worth to study and report the cause and management of migraine headaches. Though, enough research has been done on this particular disorder internationally but there is an urgent requirement for research on migraine headaches in Pakistan also. There are a lot of patients currently suffering from migraine headaches but only a few of them have an awareness of their condition. A wide population of migraine sufferers is misdiagnosed for sinusitis and tension headaches. Awareness should be created amongst practitioners who commonly misdiagnose this disease.

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