



A PROSPECTIVE STUDY TO ANALYZE THE DRUG - UTILIZATION PATTERN IN PATIENTS WITH PRIMARY HEADACHE SYNDROME

Prof. Dr. Mathew George, Prof. Dr. Lincy Joseph, Prof Dr. Robert Mathew and Jisha Susan Joji*

Pushpagiri College of Pharmacy, Medicity, Thiruvalla.

***Corresponding Author: Jisha Susan Joji**

Pushpagiri College of Pharmacy, Medicity, Thiruvalla.

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ABSTRACT

Headache is a pain anywhere in the orbiteomeatal line. It can be a symptom of different disease. It is being classified as primary and secondary headache based on source of pain. Primary headaches are benign, recurrent headache not caused by underlying disease or structural problems. About 47% of population is suffering from headache. 90% of all headaches are primary headache. A prospective study was designed & carried out after obtaining consent from the ethical committee as well as patient consent .100 patients were enrolled in the study. Out of that Migraine, tension type & cluster headache were the frequently observed primary headache. The prevalence of headache was more in female patients. Migraine is most frequently observed in female within the age group of 30-49 yrs certain cardiovascular drugs tend to increase the risk of headache. Acute medicational therapy as well as prophylactic therapy was followed, triptans, ergot derivatives. NSAIDS were prescribed as acute treatment. Beta blockers, Tricyclic antidepressants, calcium channel blockers, antiepileptic are prescribed as prophylactic medication for primary headache. Gastrointestinal problems, dizziness, drowsiness, dry mouth, blurred vision are most commonly observed adverse effects of drugs used for headache treatment.

KEYWORDS: Age, Drug utilization pattern, Headache, prospective study, medication, reoccurrence.

INTRODUCTION

Headache is a pain located above the orbit meatal line.^[1] It may be a symptom of number of disease. Headache is quite common health problem affecting people of all age group, income level, race and geographical areas. Headaches are divided into two classes based on the source of the pain. They are primary headache and secondary headache. Primary headaches are not dangerous whereas secondary headaches can be dangerous. Primary headache are benign recurrent headache not caused by any underlying disease or structural problems. 90% of all headaches are primary headache.^[2] Migraine, Tension type headache, cluster headache are the most commonly observed primary headache.^[3] Primary headache also includes primary stabbing headache, (ice-pricking), Hypnic headache, primary cough headache^[4] etc.

The first recorded classification system of headache was published by Thomas Willis, in the journal of De Cephalalgia in 1672. Christian Baurin 1787 divided headaches into idiopathic (primary headaches) and symptomatic (secondary ones), and further defined into 84 categories.^[5]

Secondary headaches may be the result of serious underlying diseases or other conditions like brain tumours, aneurysms, inflammatory diseases,

abnormalities of the spinal fluid etc. Although they are rare, it is important to recognize these types of headaches because the underlying disease causing the headaches may require urgent diagnosis and treatment. Even if the underlying disease is not particularly threatening, secondary headaches generally will not resolve until the specific cause is diagnosed and addressed. 77% of people have a headache at some point in their lives.^[6] Approximately 46-53% of people presented with headache in every year^[7] Most of headache observed in adults are benign.

Migraine stands at the 19th position of top disabling global health problem.^[7] In the Global Burden of Disease Study, updated in 2004, migraine on its own was found to account for 1.3% of years lost due to disability.^[8] Headache disorders are a public-health concern given the large amount of associated disability and financial costs to society. As headache disorders are most troublesome in the productive years (from teenage to up to 50 yrs), estimates of their financial cost to society – principally from lost working hours and reduced productivity – are massive. Drug utilization study as per W.H.O guidelines is defined as the marketing, distribution, prescription and use of drugs in the society.^[9] These studies play a vital role healthcare system. These studies help to assess whether the patient had encountered any health problem due to drug use. This may help to improve the

prescriber's awareness about the medicine and thus guiding them to practice towards appropriate prescribing. It also helps to ensure a coordinated health care system. Drug utilization studies not only provide information of drugs, but they also helps to choose a cost effective treatment so that health and wealth are reserved.

Medication adherence is defined as the rate and extent to which patient's medication taking behaviour coincides with the intention of the health advice he or she has been given.^[10] Non adherence to medication is one of critical issue in health care system. Non adherence may increase the disease morbidity. It may create economic burden to the society. This is in all age group. Reasons for non adherence may vary from individual to individual. Cost of the treatment, polypharmacy, lack of knowledge are some of reasons for which people may drop out from the therapy. Pharmacist may play a vital role in the medication adherence of the patients. By effective counselling pharmacist can sort out the reasons of their noncompliance, provide them proper guidance on how to improve their medication adherence and importance of practicing it. Importance of these studies in primary headache syndrome is necessary to know the rational prescribing of drugs as well as the patient's satisfaction to the therapy.

Headache is a major problem in India than elsewhere in the world.^[11,12] India being located in the north to equator, heat and humidity are high. Moreover it is a developing country with its large population accounting for 16% of total population. Landscape distribution, climatic variation, urbanization can possibly increase the frequency of headache. Even though headache is a major health care issue, proper management and care received are very low.

➤ **Types of Primary Headache**

The international headache society set up golden guideline known as ICHD guideline international classification of headache and disorders. Based on these guidelines primary headaches are again subdivided into migraine, cluster headache tension type headache.^[13]

Migraine Headache

Migraine is a common disabling primary headache disorder. Migraine ranks 19th position among the global disabling health care problems, by the survey of world health organization. The prevalence is 3times common in women when compared to men.^[13,14&15]

Causes of Migraine

There are many theories that discuss the causes of migraine. The cortical spreading depression (CSD) theory suggests that migraine is a disease of the brain such as anginas a disease of the heart. Disruption of normal brain functioning is believed to be the underlying cause of the migraine pain and aura .Another theory is the vascular theory which suggests that migraines result from the widening of blood vessels surrounding the

brain. The chemical serotonin is also thought to play an important role in migraine development.^[14]

Triggering factors of headache

Migraines can be triggered by^[16,17]

- Diet (foods such as cheese, coffee, tea, alcoholic beverages or nuts)
- Strong odours such as perfumes
- Bright lights: exposure to bright light can trigger migraine
- Loud noises: Sound pollution can also the migraine condition
- Changes in the weather: extreme cold or hot climate can also affect migraine conditions
- Stress: stress may increase migraine condition
- Disturbed sleep: migraine conditions may increase due to lack of sleep
- Certain medications: some of the medication tend to increase migraine condition.

Pathophysiology of Migraine

The exact mechanism of migraine is unclear. Some of the theories regarding the Pathophysiology of migraine are described below.

Depolarization theory

This theory suggests that a wave of electrical depolarization spreads across the cortex of the brain, depressing the function of certain brain areas as it moves over them. This leads to the release of inflammatory mediators that irritate the cranial nerve roots, particularly the trigeminal nerve. This nerve conducts the impulses that lead to sensation in most of the head and face. The depolarization theory is supported by positron emission tomography showing the spread of depolarization beginning around 24 hours before an attack. As the attack ensues, a large part of the brain becomes involved, which often includes the hypothalamus.

Vascular theory

This theory was suggested by Harold wolf. In his theory he explained that migraines typically occur when blood vessels in the head begin to contract and expand in an abnormal manner. The arteries in the back of the head have been shown to go into spasm, causing a reduced blood flow to the back part of the brain or the occipital lobe. This is thought to trigger aura that are followed by migraine.

Serotonin theory

Serotonin is a neurotransmitter found in the brain. It acts as a pain regulator and mood stabilizer and also plays a role in the dilation and constriction of blood vessels. In migraine conditions serotonin level are found to be low, which is thought to dilate and swell the blood vessels and cause pain in the side of the head.

Hypothyroidism

Hypothyroidism or low functioning thyroid glands are also considered to be one of the causes of migraine

attacks. It has been suggested that the slowed metabolism and circulation seen in hypothyroidism may lead to the retention of water and mucin which can cause blood vessels and tissues in the brain to swell and cause pain.

Types of Migraine and Its Signs & Symptoms

Migraine without aura

At least 5 attacks meeting the following criteria: Untreated or unsuccessfully treated attack lasting 4 to 72 hours The attack has at least 2 of the following characteristics: n Isolation of pain to one side of the head n Pain of a pulsating quality, Moderate to severe pain intensity n Severity of pain inhibiting or prohibiting daily activities During at least 1 attack the following symptoms should be present: n Nausea and/or vomiting, Sensitivity to light, noise or odour.

Migraine with aura

At least 2 attacks of aura symptoms May include visual disturbances such as seeing spots or unusual colours Lasting a minimum of 5 to 20 minutes and a maximum of 60 minutes. A headache with characteristics associated with a migraine without aura beginning during the aura or within 60 minutes following the aura.

Risk Factors of Migraine

The major risk factors which make a person prone to migraine include:18

□ Family history

Up to 90 percent of people with migraines show family history of migraine attacks. If any of the parents have migraines, then there is a good chance of having migraines.

□ Age

Migraine begins at any age, but most people experience their first migraine during adolescence. By age 40, most people who have migraines have had their first attack.

□ Sex

Women are more likely to have migraines by a factor of three. During childhood boys are more likely affected by headaches than girls, but by the time of puberty and beyond, more girls are affected.

□ Hormonal changes

Women with migraine may find headaches to begin just before or shortly after onset of menstruation.

□ Alcohol

Consumption of alcohol triggers migraine condition.

□ Smoking

Smoking also increase migraine condition.

Complications of Migraine

□ Chronic migraine

If migraine lasts for 15 or more days in a month extending for more than three months, it is a chronic migraine.

□ Status migrainosus

People diagnosed with this complication have migraine attacks lasting for more than three days.

□ Persistent aura without infarction

Usually the aura goes away after the migraine attack. However, some people have an aura that lasts for more than a week after the migraine attack. A prolonged aura may have similar symptoms to bleeding in the brain (stroke). In this condition, it may be a prolonged aura without signs of bleeding in the brain or other problems.

□ Migrainous infarction

People who have migraine with aura may have aura symptoms that last longer than a hour. This can be a sign of bleeding in the brain (stroke). If a migraine with aura occurs, and your aura symptoms last longer than an hour, you should have it diagnosed. Doctors can conduct neuro imaging tests to determine if you have bleeding in the brain.

□ Co morbidities of migraine

Co morbidity is the presence of one or more additional disorders (or diseases) co-occurring with a primary disease or disorder; or the effect of such additional disorders or diseases.

Vascular disease such as hypertension, diabetes, dyslipidemia, coronary artery disease, obesity can also increase the risk of migraine and other conditions. Some psychological problems like anxiety, depression are also found in migraine patients. Sensory imbalancing disorders can also increase the risk of migraine. Vertigo being a vestibular disease may increase risk of sensory problems in migraine patients.

➤ Tension Type Headache

A tension headache is generally a mild to moderate pain in your head that is often described as feeling like a tight band around the head.

Signs and Symptoms of Tension Headache

The signs and symptoms of tension headache include

□ Dull aching head pain

□ Sensation of tightness or pressure across the forehead or on the sides and back of head

□ Tenderness on the scalp, neck and shoulder muscles

Tension headaches are divided into two main categories — episodic and chronic.

Episodic tension headaches

Episodic tension headaches last from 30 minutes to a week. Frequent episodic tension headaches occur for less than 15 days a month lasting for at least three months.

Frequent episodic tension headaches can become chronic.

Chronic tension headaches

This type of tension headache lasts for hours and may be continuous. The headaches occur for 15 or more days a month for at least three months. They're considered as chronic.

Cause of Tension Headache

The cause of tension headache is not known. Experts used to think tension headaches stemmed from muscle contractions in the face, neck and scalp, perhaps as a result of heightened emotions, tension or stress. But research suggests that muscle contractions aren't the cause. The most common theories support a heightened sensitivity to pain in people who have tension headaches and possibly a heightened sensitivity to stress. Increased muscle tenderness, a common symptom of tension headache, may result from a sensitized pain system.

Triggering Factors of Tension Headache

Stress is the most commonly reported trigger for tension headaches.

Risk Factors of Tension Headache

Gender

Women are more prone this headache rather than men.

Age

Onset begins at the age of 40 onwards.

Cluster Headache

Cluster headache is a rare type of headache that affects about 1 to 2 people in every 1,000. Cluster headache usually starts at early age of 20. Unlike migraine, it is more common in men than women (by five to six times). It is also more common in heavy smokers.

Signs and Symptoms of Cluster Headache

The characteristic presentation is with periodic, severe, unilateral periorbital pain accompanied by unilateral lacrimation, nasal congestion and conjunctival injection, often with the other features of Horner's syndrome. The pain, whilst being very severe, is characteristically brief (30-90 minutes). Typically, the patient develops these symptoms at a particular time of day (often in the early hours of the morning). The syndrome may occur repeatedly for a number of weeks, followed by a respite for a number of months before another cluster occurs.

Other Types of Primary Headache

Primary Stabbing Headache

Recurrent episodes of stabbing ice pick pain or jabs and jolts for 1 second to several minutes without autonomic symptoms (tearing, red eye, nasal congestion).

Primary Cough Headache

Starts suddenly and lasts for several minutes after coughing, sneezing or straining (anything that may

increase pressure in the head). Serious etiologies (see secondary headaches red flag section) must be ruled out before a diagnosis of "benign" primary cough headache can be made.

Primary Exertional Headache

It is the throbbing, pulsative pain which starts during or after exercising, lasting for 5 minutes to 24 hours. The mechanism behind these headaches is unclear, possibly due to straining causing veins in the head to dilate, causing pain. These headaches can be prevented by not exercising too strenuously and can be treated with medications such as indomethacin.

Diagnosis of Primary Headache Syndrome

The international headache society is a worldwide organization set up to help the people suffering from headache. It was considered the official classification for headache by W.H.O. The ICHD was first published in 1988. The second edition was published in 2004.

Diagnostic Criteria of Migraine without Aura

A. It may occur with at least 5 attacks Headache attacks lasting 4-72 hours. Headache has at least two of the following characteristics: unilateral location; pulsating quality; moderate or severe pain intensity; aggravation by or causing avoidance of routine physical activity (eg: walking or climbing stairs).

B. During headache at least one of the following occur

1. Nausea and/or vomiting
2. Photophobia and phonophobia

Diagnostic Criteria for Migraine with Aura

Aura consisting of at least one of the following, but no motor weakness: fully reversible visual symptoms including positive features (flickering lights, spots or lines) and/or negative features (loss of vision) fully reversible sensory symptoms including positive features (pins and needles) and/or negative features (numbness) fully reversible dysphasic speech disturbance. It may also present with at least two of the following: homonymous visual symptoms or unilateral sensory symptoms at least one aura symptom develops gradually over ≥ 5 minutes and/or different aura symptoms occur in succession over ≥ 5 minutes each symptom lasts ≥ 5 and ≤ 60 minute.

Diagnostic criteria for cluster headache

Headache occurs more than >3 months -All of the following characteristics: unilateral pain without side-shift daily and continuous, without pain-free periods moderate intensity, but with exacerbations of severe pain At least one of the following autonomic features occurs during exacerbations and ipsilateral to the side of pain, conjunctival injection and/or lacrimation nasal congestion and/or rhinorrhoea ptosis and miosis.

□ Diagnostic criteria for tension headache

Infrequent episodes of headache lasting minutes to days act as diagnostic criteria for tension headache. The pain is typically bilateral, pressing or tightening in quality and of mild to moderate intensity, and it does not worsen with routine physical activity. There is no nausea but photophobia or phonophobia may be present. The diagnostic criteria includes.

A. At least 10 episodes occurring on <1 day per month on average (<12 days per year) and fulfilling criteria B-D

B. Headache lasting from 30 minutes to 7 days

C. Headache having at least two of the following characteristics:

1. Bilateral location
2. Pressing/tightening (non-pulsating) quality mild or moderate intensity

□ Diagnostic criteria of frequent tension type headache

They have frequent episodes of headache lasting for minutes to days. The pain is typically bilateral, pressing or tightening in quality and of mild to moderate intensity, and it does not worsen with routine physical activity. There is no nausea but photophobia or phonophobia may be present.

At least 10 episodes occurring on ≥ 1 but <15 days per month for at least 3 months (≥ 12 and <180 days per year) Headache lasting from 30 minutes to 7 days Headache has at least two of the following characteristics bilateral location pressing/tightening (non-pulsating) quality mild or moderate intensity not aggravated by routine physical activity such as walking or climbing stair Both of the following: no nausea or vomiting (anorexia may occur) no more than one of photophobia or phonophobia.

➤ Treatment of Primary Headache Syndrome

The treatment of primary headache is based on the patient's headache severity, concurrent symptoms, co morbid conditions efficacy and adverse effect and also based on the cost of the treatment .currently there are two types of treatment available for primary headache syndrome: Acute treatment and prophylactic treatment. Beside of these certain behavioural therapy and patient education is needed to maintain a good healthy life. Patients must be encouraged to keep headache diary.

Acute Treatment

The aim of acute treatment is to relieve headache pain and associated symptoms. It use should be limited to two or three times in a week. However the route of administration depends upon the patient preference, prior response to that route of administration, and the presence disease symptoms. The most commonly prescribed acute medication is analgesics, with or without caffeine, opioids, triptans, and dihydroergotamine.

• Triptans

The FDA approved triptans include sumatriptan, rizatriptan.

It is a potent selective, 5HT_{1D} receptor agonist.

Usually indicated for acute migraine with or without aura.

Dose: 50-100mg.

Adverse effects: nausea, vomiting, chest tightness, fatigue, dizziness, drowsiness

• Rizatriptan

Dose: 10mg

Adverse effects: drowsiness, palpitation, headache, insomnia, syncope, hypertension.

• Ergotamine

It is potent vasoconstrictor drug which shows antagonist effect on alpha adrenergic receptors

Dose: 1-2mg.

Adverse effects: muscle cramps, stiffness, tiredness, peripheral vasoconstriction, bradycardia.

NSAIDS

Analgesics are considered nonspecific migraine medications as they work on pain systems. Aspirin, indomethacin, diclofenac sodium, acetaminophen, mefenamic acid, naproxen sodium are some of common analgesics used in the acute treatment of migraine.

NAPROXEN SODIUM

It exerts its action by inhibiting prostaglandin synthesis. Drowsiness, dizziness, vertigo, constipation are the common side effects. It is usually indicated for the acute attacks of migraine. The daily dose varies from 250-500mg.

DICLOFENAC SODIUM

It is usually indicated in acute migraine, cluster headache and tension headache. It exerts its action by inhibiting prostaglandin synthesis. It is given 50mg daily. Skin rash, gastric pain, dizziness, fatigue are common side effects.

ANTIEMETICS

Migraines are often accompanied by nausea, with or without vomiting. In order to avoid nausea and vomiting antiemetic drugs are used. Some of commonly prescribed antiemetic includes domperidone, metoclopramideprochlorperazine. Gynaecomastia, diarrhoea, drowsiness are common adverse effects observed.

PROPHYLACTIC MEDICATION

They can reduce the frequency, severity and length of migraines and may increase the effectiveness of symptom-relieving medicines used during migraine attack. Tricyclic antidepressants, antiepileptic cardiovascular drugs such as beta blockers and calcium

channel blockers are used as prophylactic medications.^[25]

Tricyclic antidepressants

Certain antidepressants help to prevent some types of headaches, including migraines. Tricyclic antidepressants may be effective in preventing migraines. Tricyclic antidepressants may reduce the frequency of migraine headaches by affecting the level of serotonin and other brain chemicals. Amitriptyline is the only tricyclic antidepressant proved to effectively prevent migraine headaches. Dryness of mouth, constipation and weight gain are the common side effects observed. It is prescribed in the daily dose of 10-25mg at bed time.

Antiepileptic

Some anti-epileptic drugs, such as valproate sodium and topiramate are to reduce the frequency of migraine headaches. Nausea, tremor, weight gain, hair loss and dizziness are commonly observed side effects. Topiramate is prescribed in dose of 25-50mg, divalproex sodium is prescribed in dose of 250-500mg.

Beta blockers

The drugs such as propranolol metoprolol tartrate and timolol have proved effective for preventing migraines. It exerts action by antagonizing the effects of beta adrenergic receptors hypotension, insomnia, dizziness are commonly observed side effects. Propranolol is prescribed in the daily dose of 40 -160mg.

Calcium channel blockers

They inhibit the movement of calcium ions across the cell membranes. Thereby prevents mechanical contraction of the muscle wall of the artery. Flunarizine, verapamil diltizem are commonly prescribed drugs. Headache, drowsiness, weight gain, depression are commonly observed side effects. Flunarizine is prescribed at the dose of 5-10mg at bed time.

Drug Utilization Studies

Drug utilization studies as per WHO guideline are defined as marketing, distribution, prescription and use of drugs in the society with special emphasis on the resulting medical, social and economic consequences. Drug utilization study was started in early 1960.^[26] These have become more important after thalidomide disaster.

Importance and Uses of Drug Utilization Studies

The principle aim of drug utilization research is to facilitate the rational use of drugs in population. This study plays a vital role in the health care system. They provide a wide variety of information on drugs, disease management, patient information, prescribers pattern, it also help to choose best safe drug of affordable price.^[27]

Types of Drug Information

Prescribers Information

Drug utilization data provides feedback information to prescribers. These studies may help them to assess

number of drug problem such as adverse effects, drug interaction, which has occurred due to the use of drug by the patients. It is possible to detect that the reaction is more common in a certain age group or in certain conditions or at a given dose level.

Drug use information

They may provide wide information about various therapeutic uses of drugs. They give wide knowledge on indications, contraindication, appropriate dosages and its available formulation in the market.

Patient information

It can be used to estimate the numbers of patients exposed to specified drugs within a given time period. Such estimates may either refer to all drug users, regardless of when they started to use the drug (prevalence), or focus on patients who started to use the drug within the selected period (incidence).

Pattern of drug use

Researchers can estimate (e.g. on the basis of epidemiological data on a disease) to what extent drugs are properly used, overused or underused. It can determine the pattern or profile of drug use and the extent to which alternative drugs are being used to treat particular conditions. It can be used to compare the observed patterns of drug use for the treatment of a certain disease with current recommendations or guidelines.

Pharmacoeconomics

They help to assess the economic impact of clinical care and medical technology.

Types of Drug Utilization Studies

The drug utilization studies are of two types: quantitative drug utilization study and qualitative drug utilization studies.^[27]

Qualitative drug utilization studies involve collecting, organizing, analyzing and providing information on actual drug use. These studies provide information on appropriateness on drug use such as various indication of the drug its specific doses and also give an idea about length of therapy of the specific drug.

Quantitative drug utilization studies involve the collection, organization and display of estimates and measurements of drug use. They are often used for making purchase decision and other financial activities such as preparation of drug budgets.

Sources of Drug Utilization Studies

The success of drug utilization study depends on the type and quality of resources and tools used to design and evaluate the study. The main resource for drug utilization study is humans. Professional literatures, national and international guidelines are some of resources available for development of drug utilization studies. Some

computer database and specially designed drug utilization software are also act as resources for documentation, management evaluation and reporting of data.^[28]

Role of Pharmacist In Drug Utilization Study

Pharmacist plays a crucial role in the overall development of drug utilization studies. They can act as link between clinicians and patients. As their experience on pharmaceutical care they may have idea on different disease condition and therapeutic management however the pharmacist have knowledge on current trends of drug use, safe and cost effective drugs available in the market. Pharmacist along with other health care team members may help to improve quality of life of patients, avoid unnecessary or inappropriate drug therapy, prevent adverse drug reactions and improve overall drug effectiveness.

Need of Drug Utilization Studies In Primary Headache Syndrome

Primary headache syndrome is a common neurological global health care problem. Even though specific drug treatment are available patients are unaware of this, drug utilization study in primary headache syndrome may provide information on different drug therapy used in the treatment of primary headache. These studies may give an idea of safe, cost effective drugs prescribed. These studies help to assess drug related problems occurred during the drug therapy. Drug utilization studies in primary headache may reduce disabling feature of headache and its economic burden.

Medication Adherence in Primary Headache Syndrome

Adherence to therapies is a primary determinant of treatment success. Failure to adherence is a serious problem which not only affects the patient but also the health care system. Medication non adherence in patients leads to substantial worsening of disease, death and increased health care costs. Medication adherence is defined by the World Health Organization as "the degree to which the person's behaviour corresponds with the agreed recommendations from a health care provider."^[28]

"There are several types of non-adherence but most often the categorization is indisputable, and there is a degree of overlap. The first is known as primary non adherence, in which providers write prescription but the medication is never filled or initiated. This type is commonly called non fulfilment adherence. A second type of non-adherence is called non persistence in which patients decide to stop taking a medication after starting it, without being advised by a health professional to do so. A third type of non-adherence is known as non-conforming, this type includes a variety of ways in which medication are not taken as prescribed, this behaviour can range from skipping doses, to taking medications at incorrect times or at incorrect doses, to even taking more than prescribed. Rate of adherence is usually reported as

the percentage of the prescribed doses of the medication actually taken by the patient over a specified period.^[26]

Barriers of Non Adherence

Barriers to the effective use of medicines specifically include poor provider patient communication, inadequate knowledge about a drug and its use, not being convinced of the need for treatment, fear of adverse effects of the drug, long term drug regimens, complex regimens that require numerous medications with varying dosing schedules, cost and access barriers. It has also been observed that patient non adherence varies between and within individuals, as well as across time, recommended behaviours and diseases.^[32] Adherence to drug therapy varies with patient age group also.

Steps to Improve Medication Adherence

The effectiveness of a treatment depends on both the efficacy of a medication and patient adherence to the therapeutic regimen. Patients, healthcare providers, and health care systems, all have a role to improve medication adherence. A single method cannot improve medication adherence, instead a combination of various adherence techniques should be implemented to improve patient's adherence to their prescribed treatment.

A systematic approach that could be instituted in improving medication adherence is as follows:

Introduce a collaborative approach with the patient at the level of prescribing

Whenever possible, involve patients in decision making regarding their medications so that they have a sense of ownership and they are partners in the treatment plan.

Simplify medication taking

Use the most possible simplified regimen based on patient characteristics at the first level of drug use.

Communicating with the patient

Explain key information when prescribing/dispensing a medicine. Address the key information about the drugs (what, why, when, how, and how long).

Use medication adherence improving aids

Provide medication calendars or schedules that specify the time to take medications, drug cards, medication charts or medicine related information sheets or specific packaging's such as pillboxes, 'unit-of-use' packaging, and special containers indicating the time of dose

Provide behavioural support

Collaborate with patient to incorporate the medication regimen in to his/her daily regimen (essential in those on complex drug regimens, those having unintentional difficulties in adherence e.g. elderly).

During follow ups

• Schedule appropriate follow up

Monitoring the medication adherence should also be criteria while scheduling patient follow-up.

- **Follow Assess adherence during consequent ups**

Measure adherence by various methods may be dependent on patient as well as drug characteristics. Check the effectiveness of medication adherence aids used, if any. This should be done by physicians as well as pharmacists.

Methods to Measure Adherence

Various methods have been reported and are in use to measure adherence. The methods available for measuring adherence can be broken down into direct and indirect methods of measurement. Direct methods include direct observed therapy, measurement of the level of a drug or its metabolite in blood or urine and detection or measurement of a biological marker added to the drug formulation, in the blood. Direct approaches are one of the most accurate methods of measuring adherence but are expensive. Moreover, variations in metabolism and white coat adherence can give a false impression of adherence. Indirect methods include patient questionnaires, patient self-reports, pill counts, rates of prescription refills, assessment of patient's clinical response, electronic medication monitors, measurement of physiologic markers, as well as patient diaries. Each method has its own advantages and disadvantages and no method is considered as the gold standard.

MATERIALS AND METHOD

Study design: Prospective observational studies of one month follow up.

Study population

Patients diagnosed with primary headache syndrome (migraine, tension type).

Inclusion criteria

Both male and female patients diagnosed with primary headache disorder Patients of age group of 16-65 OP patients only

Exclusion criteria

Patients of age group < 16 yrs.

The patients diagnosed with complicated disorder such as brain tumor, stroke

Patients not willing to participate

Pregnant and breast feeding women

Study site

Neurology Department of Pushpagiri Medical College Hospital Thiruvalla.

DEMOGRAPHIC DETAILS OF THE PATIENTS

AGE WISE DISTRIBUTION

Table 1: Distribution of patients based on age

AGE	FREQUENCY (n=100)	PERCENTAGE (%)
16-26	27	27
27-36	30	30
37-46	23	23
47-56	10	10
57-66	10	10

Sample size of the study: 100

$$n = (4(p*100-p) / d^2)$$

where n= sample number, p= expected prevalence, d = allowed error, d = 45

Study period: 6 months, from February 2015 –August 2015

Source Of Data: Patient data collection form.

Medical record files.

Direct interview with patients.

Ethical Consideration

The institutional ethical committee clearance certificate was obtained prior to the commencement of the study. Informed consent was obtained from all patients / caregivers who met the inclusion criteria were enrolled for the study.

Brief Procedure of the Study

A written informed consent was taken from patient, in a prescribed format. Patients who met the inclusion criteria were enrolled in the study. The study was executed by direct interview with the patient. The drug utilization pattern in primary headache syndrome was analyzed through patient prescription records and using patient data collection form Performa Medication adherence scale (MARS) developed by Katherine Thompson⁴⁰ was used in the study. Scoring was based on the answers given by the patients enrolled in the study. This questionnaire consists of 10 questions. It was assessed to know patient's attitude and behavior towards treatment. A Score Of <6 Showed non adherence and a score of 6 and >6 Showed Adherence. Medication adherence during the first visit and follow-up were assessed and compared. Patients were advised to keep a headache diary. It was assessed as patients came for the follow-up. Statistical data was analyzed through data was entered in SPSS software version 16. Significance was measured through wilcoxon signed rank test (at significance level of 0.001).

RESULTS

In the six month study, about 100 patients were enrolled as per inclusion and exclusion criteria. The results obtained are as follows.

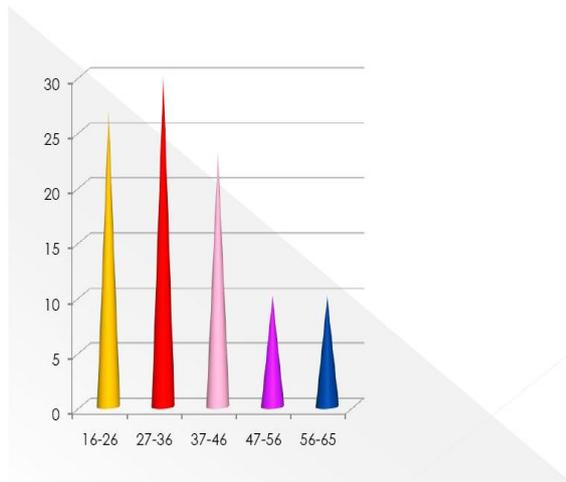


Figure 1: Distribution of patients based on age

From the table and figure (1) it was found that people of age groups ranging from 27-36 showed higher percentage of disease occurrences.

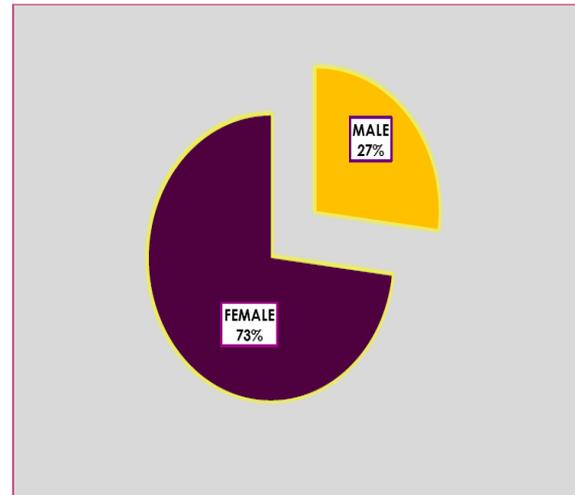


Figure 1: Distribution of patients based on age

In this study of the given sample size, females dominated over the male population who came for the headache treatment.

GENDERWISE DISTRIBUTION

Table 2: Distribution of patients based on gender

GENDER	FREQUENCY (n=100)	PERCENTAGE (%)
MALE	27	27
FEMALE	73	73

MARITAL STATUS

Table 3: Distribution of Patients Based On Marital Status

MARITAL STATUS	FREQUENCY (n=100)	PERCENTAGE (%)
MARRIED	80	80
UNMARRIED	20	20

■ Married ■ Unmarried

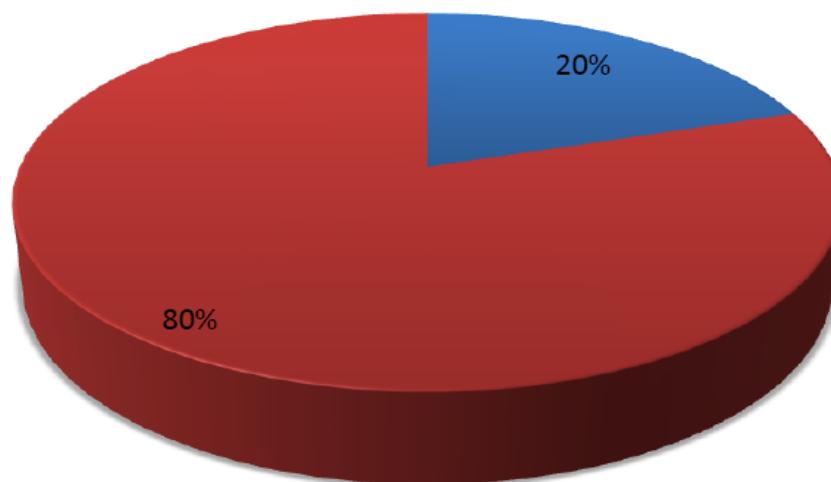


Figure 3: Distribution Based On Marital Status

Table and figure (3) shows that majority of the patients were married.

EDUCATIONAL STATUS

Table 4: Distribution based on educational status

EDUCATIONAL STATUS	FREQUENCY (n=100)	PERCENTAGE (%)
GRADUATES	52	52
POST GRADUATES	28	28
HIGH SCHOOL	20	20

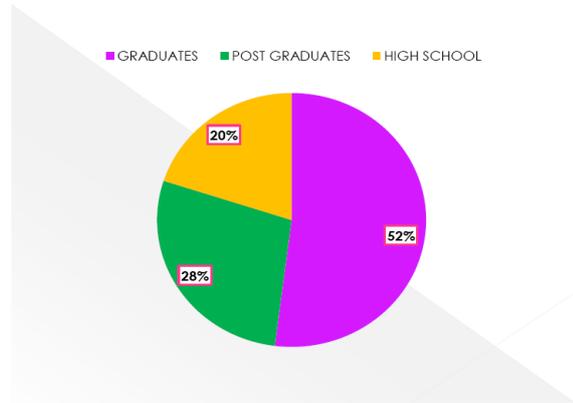


Figure 4: Distribution of patients based on educational status

From the table & graph (4): it is understood that headache was more commonly seen in graduates, followed by postgraduates and high school level patients.

■ Nurses ■ Buisness ■ Teaching ■ engineers ■ painters ■ none

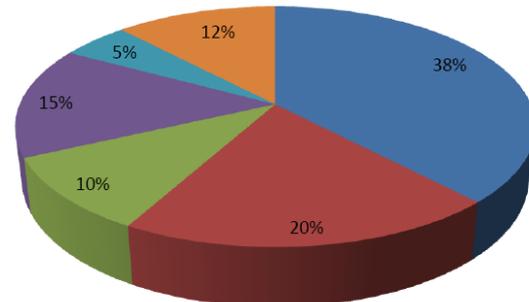


Figure 5: Distribution of patients based on occupation

From the table & graph (5), it was found that nurses had increased chances for headache.

OCCUPATION

Table 4: Distribution based on occupation

OCCUPATION	FREQUENCY (n=100)	PERCENTAGE (%)
NURSING	38	38
BUSINESS	20	20
TEACHING	10	10
ENGINEERING	15	15
PAINTERS	5	5
NONE	12	12

TYPES OF PRIMARY HEADACHE

Table 6: Distribution of patients based on the type of primary headache

TYPE OF HEADACHE	FREQUENCY (n=100)	PERCENTAGE (%)
MIGRAINE	79	79
TENSION TYPE	21	21
ICE PRICKING	1	1

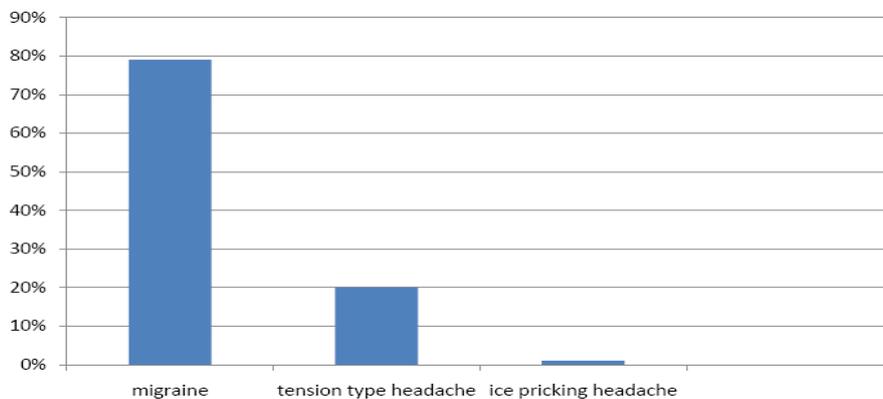


Figure 6: Distribution of patients based on type of headache

The table &figure (6) depicts; People diagnosed with migraine shows headache more frequently.

TYPES OF MIGRAINE BASED ON AURA

Table 7: Distribution of migraine among headache patients based on presence of aura

TYPE OF MIGRAINE	FREQUENCY (n=100)	PERCENTAGE (%)
MIGRAINE WITH AURA	79	79
MIGRAINE WITHOUT AURA	21	21

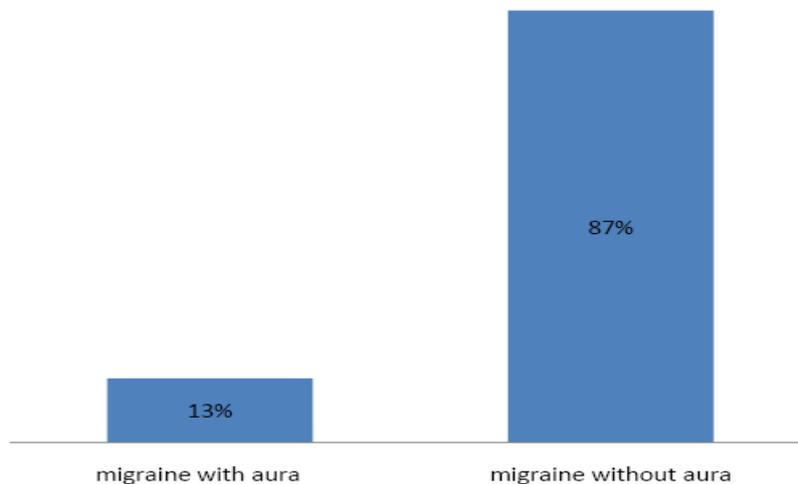


Fig 7: Distribution of Migraine among Headache Patients Based On Presence of Aura

The graph & table (7) revealed that most of the patients presented migraine without aura.

RISK FACTORS OF PRIMARY HEADACHE DISORDER

Table 8: Distribution of headache in patients based on triggering factor

TRIGGERING FACTOR	FREQUENCY (n=100)	PERCENTAGE (%)
CHANGES IN CLIMATE	25	25
SKIPPING MEALS	20	20
ODOR	15	15
LIGHT	10	10
STRESS	20	20
TRAVEL	5	5

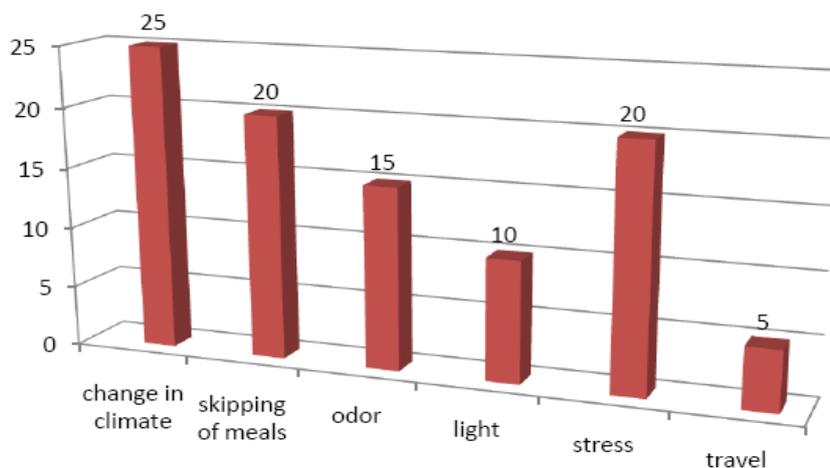


Figure 8: Distribution of triggering factor in primary headache

Climatic factor was a major role player in triggering headache.

SOCIAL HABITS

Table 9: Distribution of social habits in patients with primary headache syndrome

SOCIAL HABITS	FREQUENCY (n=100)	PERCENTAGE (%)
PRESENT	17	17
ABSENT	83	83

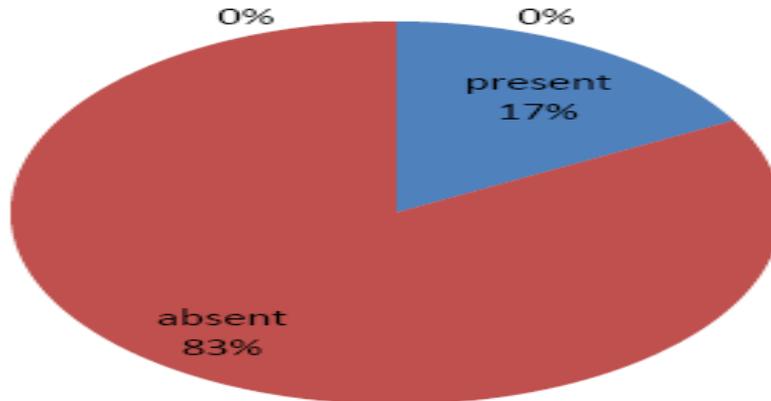


Figure 9: Distribution of social habits in patients with primary headache syndrome

In the study, the graph & table (9) pointed out social habits of total population. 17% of patients had social habits such as smoking and alcohol. The remaining 83%

patients include both male and female were free from social habits.

Table 10: Distribution based on Social Habits in Male Patients with Primary Headache Syndrome

SOCIAL HABITS	FREQUENCY (n=27)	PERCENTAGE (%)
SMOKING	10	37
DRINKING	5	19
SMOKING & DRINKING	2	7
NONE	10	37

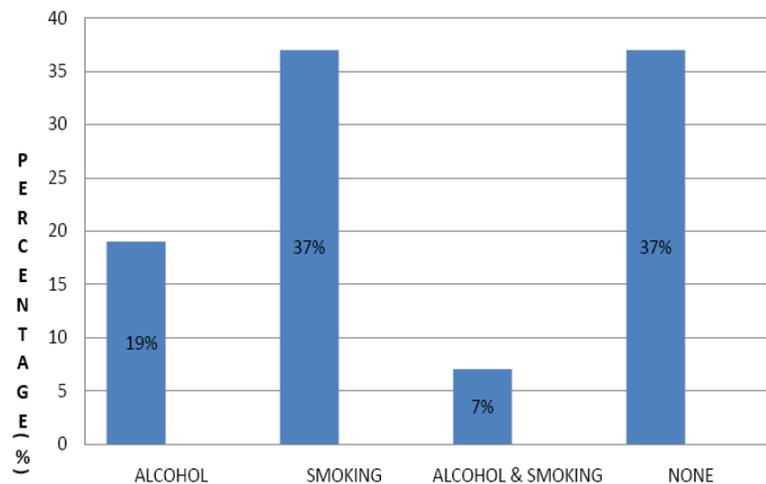


Figure 10: Distribution of Social Habits in male patients with Primary Headache Syndrome

From the study, it was found that 37% patients had smoking, 19% had alcohol & 7% had alcohol & smoking habits.

FAMILY HISTORY

Table 11: Distribution based on family history

FAMILY HISTORY	FREQUENCY (n=100)	PERCENTAGE (%)
PRESENT	40	40
ABSENT	60	60

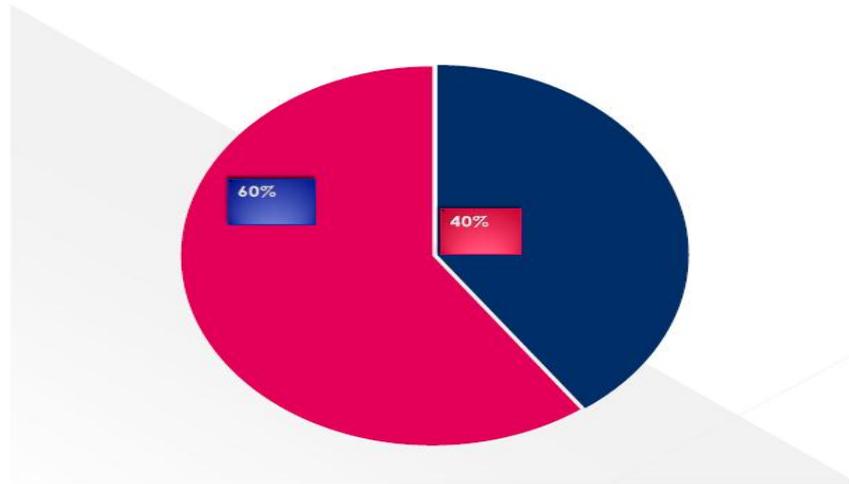


Figure 11: Distribution based on family history

From the table & the graph (10), it was found that patients with previous family history were more prone to the disease.

CO-MORBID CONDITIONS IN HEADACHE PATIENTS

Table 12: Distribution of patients based on co-morbid condition

CO-MORBIDITIES	NO. OF PATIENTS	PERCENTAGE (%)
HYPOTHYROIDISM	12	16.4
DIABETES MELLITUS	10	13.6
INSOMNIA	11	15.0
HYPERTENSION	20	27.3
VERTIGO	15	20.5
DEPRESSION	5	6.8

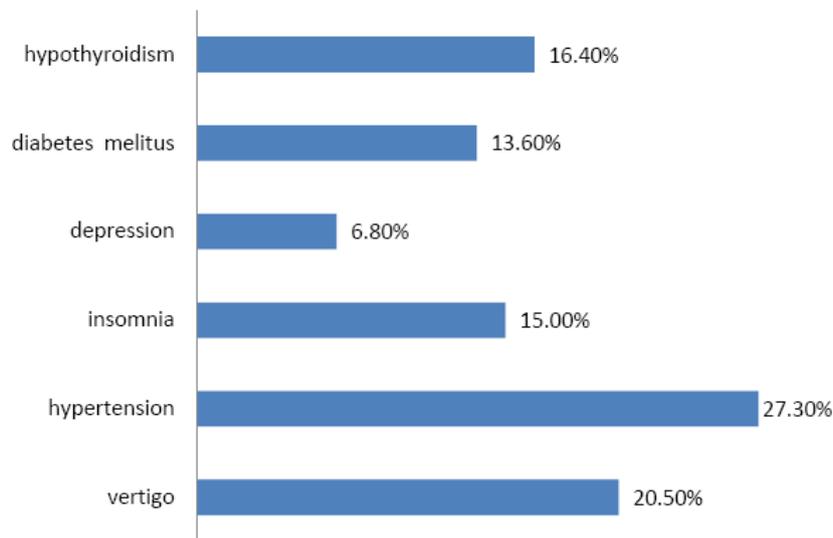


Figure 12: Distribution of patients based on co-morbid condition

In this study hypertension (27.30%) was the most frequently observed co-morbid condition among headache patients.

COMPLICATIONS

Table 13: Complication associated with primary headache syndrome- epilepsy

SL. NO.	EPILEPSY	FREQUENCY (n=100)	PERCENTAGE (%)
1	PRESENT	10	10
2	ABSENT	90	90

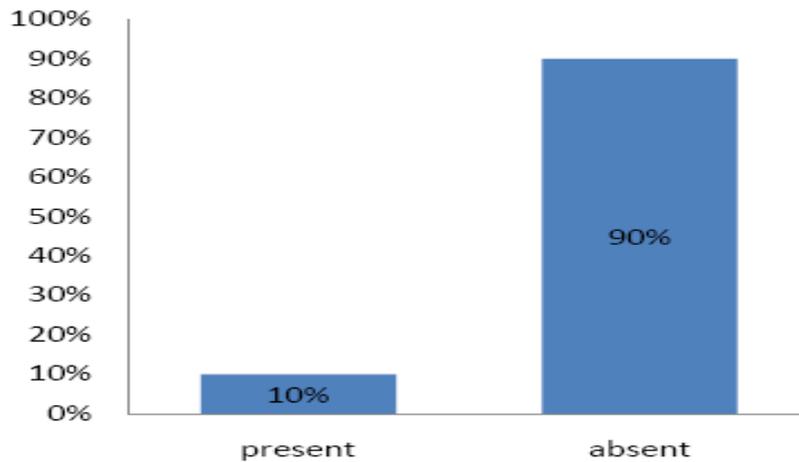


Figure 13: Complication associated with primary headache syndrome- epilepsy

The above table and graph (13) shows that 10% of patients had epilepsy which complicated their headache disorder.

DRUG UTILIZATION PATTERN IN PRIMARY HEADACHE SYNDROME

Table 14: Drug utilization pattern of acute medicines in primary headache syndrome

DRUGS	PRESCRIBED	PERCENTAGE (%)
NAPROXEN-DOMPERIDONE	86	86
ACECLOFENAC-PARACETAMOL	4	4
MEFENEMIC ACID	3	3
ETORICOXIB	7	7

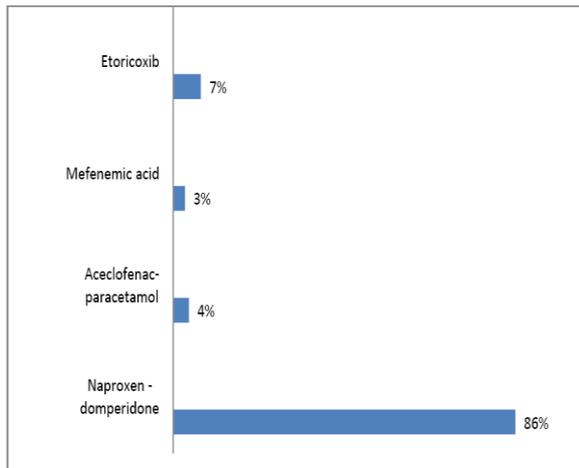
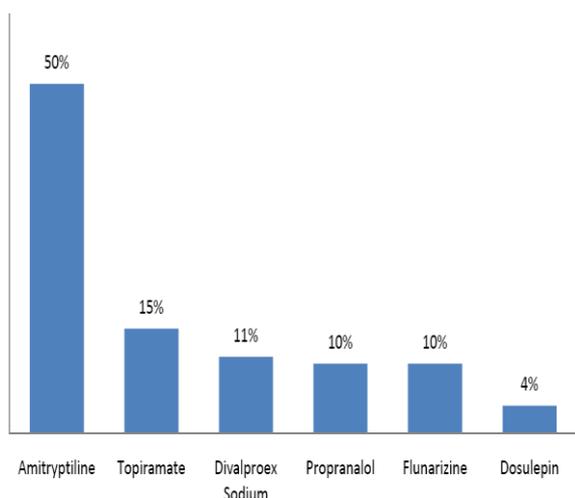


Figure 14: Drug utilization pattern of acute medicines

The above figure and table (14), showed the drug utilization of acute medication in primary headache syndrome. NSAIDS were prescribed as acute medication. Naproxen-domperidone combination was most commonly prescribed drug from NSAID class, followed by Etoricoxib, Aceclofenac-Paracetamol and Mefenamic Acid.

Table 15: Drug utilization of prophylactic medication in primary headache disorder

DRUGS	PRESCRIBED	PERCENTAGE (%)
AMITRIPTYLINE	50	50
PROPANOLOL	10	10
FLUARIZINE	10	10
TOPIRAMATE	15	15
DOSULEPIN	4	4
DIVALPROEXSODIUM	11	11



This figure depicts the drug utilization pattern of prophylactic medication in primary headache syndrome. Among the prophylactic medication, Amitriptyline was most often prescribed (50%) followed by topiramate (15%), Divalproexsodium (11%), Propranolol (10%), Flunarazine (10%), Dosulepin (4%).

Figure 15: Drug utilization of prophylactic medication in primary headache disorder

Table 16: Drug utilization pattern of antihypertensive drugs among primary headache patients

DRUGS	FREQUENCY (n=100)	PERCENTAGE (%)
AMLODIPINE	7	35
TELMISARTAN	3	15
OLMESARTAN	6	30
LOSARTAN	4	20

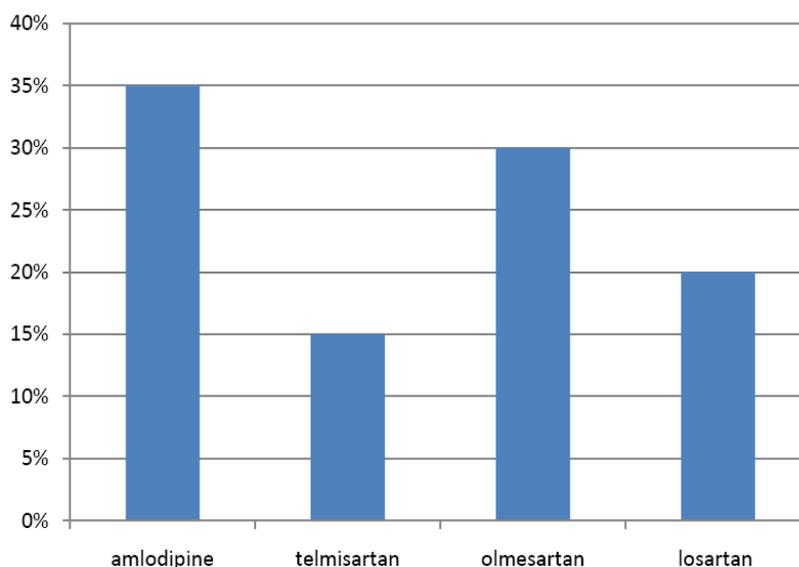
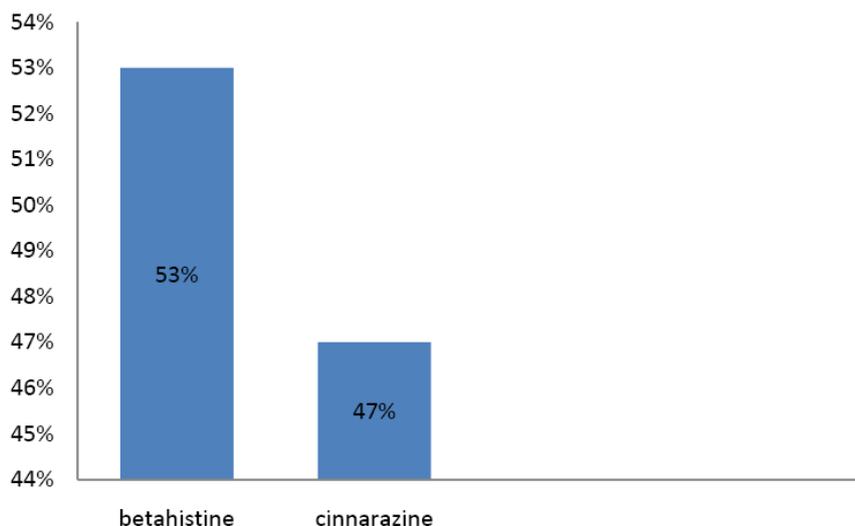


Figure 16: Drug utilization pattern of antihypertensive drugs among primary headache patients

In the study Amlodipine was the commonly prescribed medication for hypertension among headache patients.

Table 17: Drug utilization of antivertigo drugs among patients with primary headache

DRUGS	FREQUENCY (n=100)	PERCENTAGE (%)
BETAHISTINE	8	53
CINNARIZINE	7	47



■ drug utilization of antihistamines among patients with primary headache

Figure 17: Drug utilization of antiemetic for vertigo among patients with primary headache

In the present study betahistine (53%) and cinnarazine (47%) were prescribed for vertigo in headache patients.

Table 18: Drug utilization of hypothyroid drugs among patients with primary headache syndrome

DRUGS	FREQUENCY (n=100)	PERCENTAGE (%)
PRESCRIBED	12	12
NOT PRESCRIBED	88	88

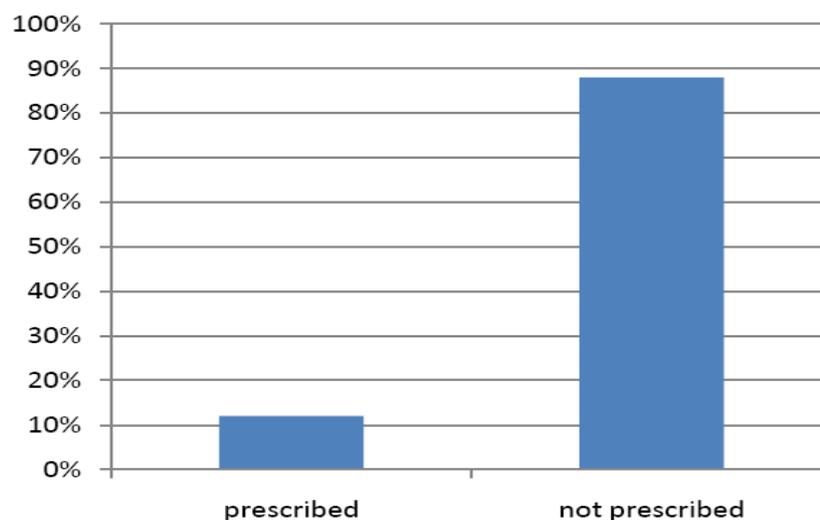


Fig18: Drug utilization of thyroid drugs among patients with primary headache syndrome

The above graph shows the drug utilization of levothyroxine among headache patients. Levothyroxine was prescribed in 12% of headache patients.

Table 19: Drug utilization of antihyperglycaemics among patients with primary headache disorder

DRUGS	FREQUENCY (n=10)	PERCENTAGE (%)
GLIMEPERIDE	5	50
METFORMIN	2	20
INSULIN	3	30

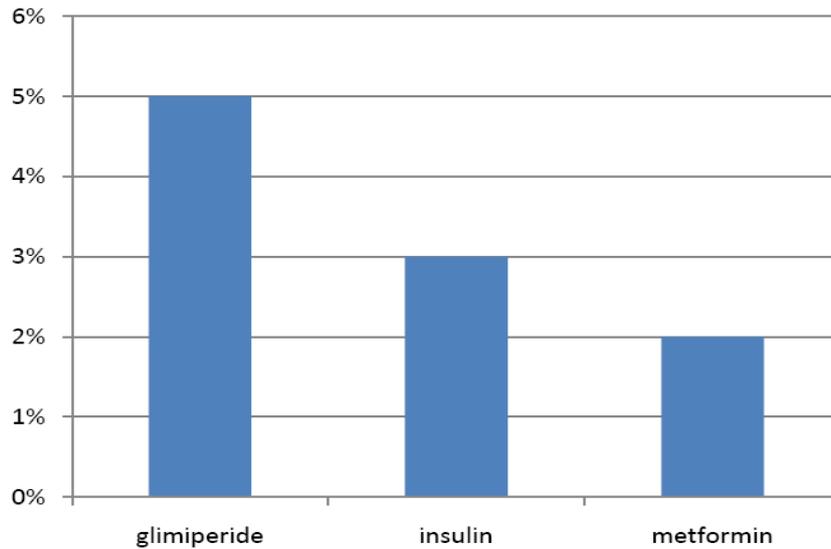


Figure 19: Drug utilization of antihyperglycaemics among patients with primary headache disorder

The table & graph showed the drug utilization pattern of antihyperglycaemic drugs among headache patients with diabetes co-morbid.

Table 20: Drug utilization of sedatives for insomnia among primary headache patients

DRUGS	FREQUENCY (n=11)	PERCENTAGE (%)
ZOLPIDEM	6	55
ALPRAZOLEM	5	45

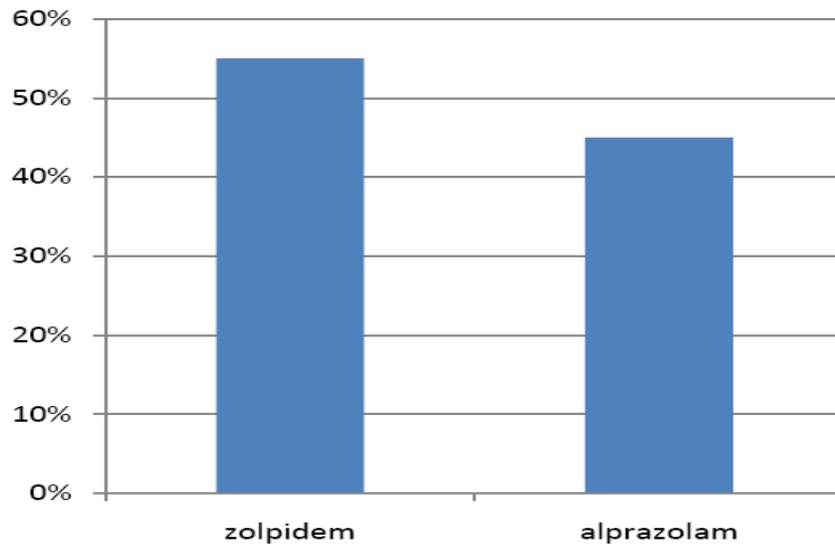


Figure 20: Drug utilization of sedatives for insomnia among primary headache patients

In the study, sedatives such as zolpidem(55%)& alprazolam (45%) were prescribed for insomnia condition in headache patients.

Table 21: Drug utilization of proton pump inhibitors among primary headache patients

DRUGS PRESCRIBED	FREQUENCY (n=70)	PERCENTAGE (%)
RABEPRAZOLE	40	57
PANTOPRAZOLE	30	43

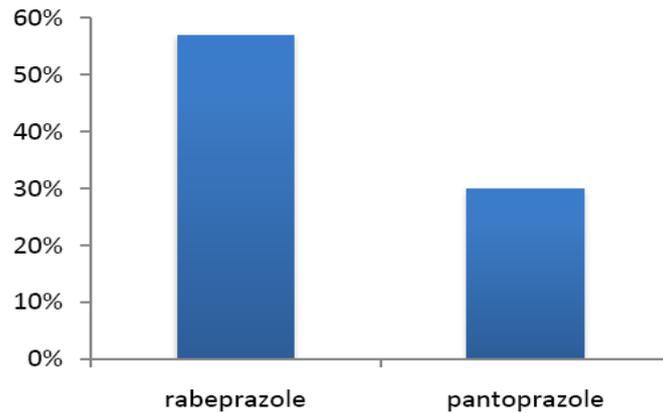


Figure 21: Drug utilization of proton pump inhibitors among primary headache patients

The results of the study reveal that, proton pump inhibitors were prescribed among headache patients. Rabeprazole was prescribed in 57% of patients & 43% were prescribed with Pantoprazole.

ADVERSE DRUG REACTION PATTERN

Table 22: Distribution of adverse events

ADVERSE EVENT	FREQUENCY (n=100)	PERCENTAGE (%)
DRY MOUTH	41	41
DROWSINESS	35	35
WEIGHT GAIN	12	12
ALOPECIA	12	12

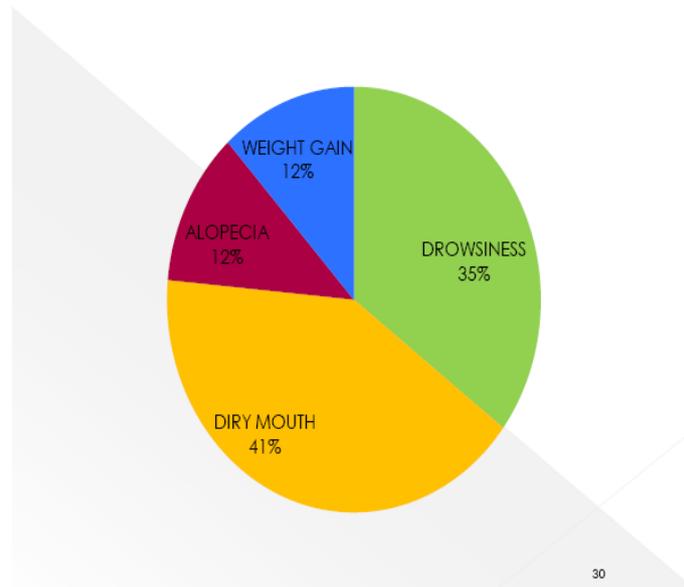


Figure 22: Distribution of adverse events

In this study, 17 cases of adverse effects were reported. Dry mouth was most frequently observed (41%) followed by drowsiness 35%, weight gain 12% and alopecia 12%.

MEDICATION ADHERENCE AMONG PATIENTS WITH PRIMARY HEADACHE DISORDER

Table 23: Distribution of adherence based on patient visit

ADHERENCE LEVEL	BEFORE	PERCENTAGE (%)	AFTER	PERCENTAGE (%)
ADHERENCE	46	46	81	81
NON-ADHERENCE	54	54	19	19

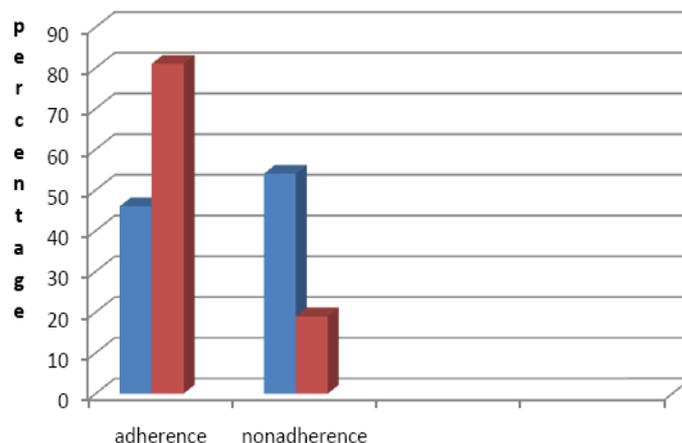


Figure 23: Distribution of adherence based on patient visit

From the graph & table (23), it was noted that patients showed good adherence during their follow-up. A significant change in adherence was found when compared to the patients' previous visits.

Table 24: Distribution of medication adherence score based on patients visit

MEDICATION ADHERENCE	MEAN+/- SD	P- VALUE
BEFORE	5.3663 +/- 0.67413	0.001
AFTER	6.1485 +/- 0.81714	

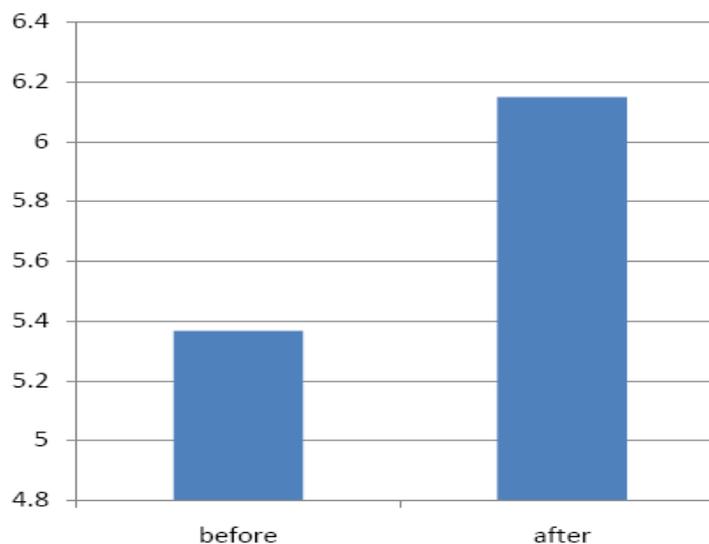


Figure 24: Distribution of adherence score based on patients visit

From the study it was noted that mean adherence score among headache patients during the first visit was 5.663 which was increased to 6.148 in the follow up session. Pvalue(0.001) is significant.

COST OF MEDICATION FOR PRIMARY HEADACHE DISORDER

Table 25: Per Month Cost of Acute Drug Therapy

SL. NO.	DRUGS	PER MONTH COST OF TABLET IN Rs.
1	NAPROXEN DOMPERIDONE	60
2	MEFENAMIC ACID	45
3	ETORICOXIB	120
4	ACECLOFENAC PARACETAMOL	75

From The Table 25: It was found that Mefenamic acid was cheapest NSAID prescribed for acute therapy for headache patients, followed by Naproxen-Domperidone combination.

Table 26: Per month cost of prophylactic drug therapy

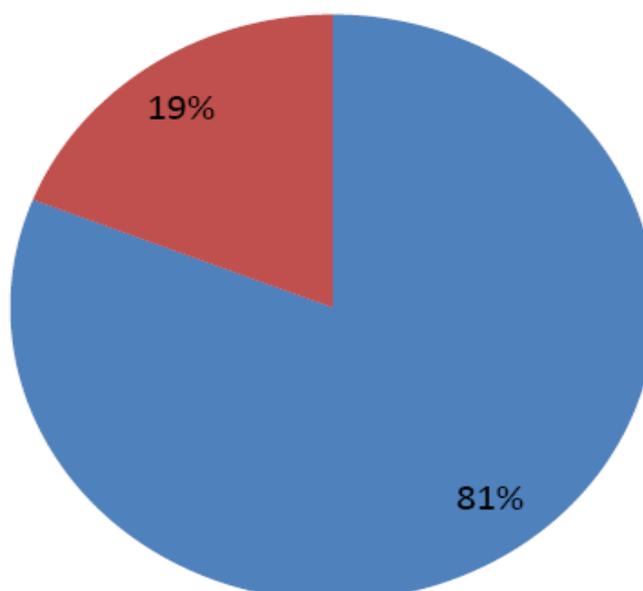
SL. NO.	DRUGS	PER MONTH COST OF TABLET IN Rs.
1	AMITRIPTYLINE	60
2	FLUNARIZINE	90
3	DIVALPROEXSODIUM	300
4	TOPIRAMATE	120
5	DOSULEPIN	180
6	PROPANOLOL	120

From table (26): Amitriptyline was the cheapest and most effective drug prescribed for prophylactic treatment of primary headache.

OUTCOME OF THE TREATMENT

Table.27: Distribution of headache based on the reoccurrence

HEADACHE REOCCURRENCE	FREQUENCY (n=100)	PERCENTAGE (%)
REDUCED	81	81
PERSISTED	19	19

**Figure 27: Distribution of Recurrence of headache among the patients**

The table & graph (27) depicts that headache recurrence had reduced in 81% patients. 19% patients had recurrence of headache. Recurrence had occurred due to skipping of prescribed doses. This was observed among students and nurses.

DISCUSSIONS

Headache is one of the common neurological problems which may affect both quality of life as well as economy. About 47% of total population is suffering from headache. Primary headaches are the most commonly seen ones. It includes migraine, tension type and cluster headache. Other primary headache include primary stabbing headache, (ice pricking), hypnic headache, primary cough headache. Migraine ranks 19th position of the world health problems. Epidemiological facts reveal that headache is high in India. The study entitled "A Prospective study to analyze drug utilization pattern in patients with primary headache syndrome." was

carried out at the neurology department of Pushpagiri Medical College Hospital, Thiruvalla. The study was started after getting the ethical clearance certificate. The study design was a prospective observational study. The patients were enrolled as per the inclusion criteria. Patients with complicated health problems, such as brain tumor, were excluded from the study. Patient consent was obtained before starting the study. A total of 100 patients participated in the study. Out of this 79% had migraine, 20% presented with tension type, and 1% presented with ice pricking headache.

Patient Demographic Details

Age

Majority of the patients in this study belongs to the age group of 26-36, followed by 16-25yrs.

Gender

Regarding the gender distribution, prevalence of

headache was quite greater in female patients when compared to males. This result correlates a previous study done by *SubranshuShekharetal.*

Socio-Economic Class

In the study majority of patients diagnosed with primary headache disorder belonged to middle class families.

Educational status

Majority of the patients in this study were graduates.

Employment status

In the study most of the patients were employed.

Type of primary headache

Migraine was the most frequently observed primary headache syndrome. Migraine without aura (common migraine) was the most common case of head ache found in this study. Similar trends were observed in a study conducted by *SubranshuShekharetal.* on migraine pattern of prescription and adverse drug profile in a tertiary care hospital.

Family history

In the study out of 100 patients, 40% patients presented with positive family history of migraine.

Social history

In the study, 17 % of patients had social habits. 7% had smoking with alcoholism and about 37% patients had smoking habits. 19% of patients were found be alcoholic.

Risk factors

Social habits and some life time disorders may tend to increase the risk of headache disorder some life time disorders such as hypertension, hypothyroidism, vertigo etc. may increase risk of headache. Family history can also increase the risk of the disease. Climatic variations, odor, food, travel also precipitated the headache disorder.

Co-morbidity

Most of the patients with primary headache were adults who presented with co-morbid conditions like vertigo, hypertension, diabetes, depression and hypothyroidism.

Complications

Only 10% of the study population had the complication. Epilepsy had complicated the primary headache disorders.

Drug utilization pattern

In the study, both the acute and prophylactic medications were prescribed for primary headache disorder. Most commonly prescribed acute medication was naproxen-domperidone combination (86%). It was prescribed in the brand name of Naxdom 250mg which was given as S.O.S (take whenever necessary). Other NSAIDS prescribed for headache included aceclofenac, mefenamic acid, and etoricoxib. Tricyclic antidepressants, beta blockers, calcium channel blockers and anti-epileptic

were prescribed as prophylactic medication. Amitriptyline (50%) was most oftenly prescribed from the prophylactic headache medicines. It was given in the daily doses of 10-25mg at bedtime. This result correlates the finding of a previous study done by Anna Dozzaetal. Divalproexsodium of the dose of 250-500mg OD were also prescribed (11%). Topiramate was prescribed from the dose range of 25mg initial dose which was subsequently increased to 50mg (15%). Propranolol was prescribed in a dose of 40mg daily. It was prescribed in the brand name of Beta cap 40mg (10%). Flunarizine a calcium channel blocker were also prescribed. 10% of prescription contained this drug. These were given as prophylactic medication. It was mostly prescribed in the trade name of Sibelium. It's dosing varied from 5-10mg. The other prescribed drugs among headache patients were antihypertensive, antihistamines, thyroid preparations, anti-hyperglycemics, anti-anxiety drugs for management of their co-morbid conditions. Amlodipine was the most commonly prescribed drugs among antihypertensive which was followed by telmisartan, olemisartan, and losartan hydrochloride. Thus overall drug utilization in primary headache was in accordance of neurophysicians prescription guideline.

Medication adherence

In the study medication adherence was assessed through prescription refill pattern. Medication adherence of the patient during the first and second visits were assessed and compared. In the first visit 46% patients adhered to the medication prescribed. After effective patient counseling patients attitude towards the therapy had changed. Medication adherence was high in the study. 81% adhered to the medication prescribed. The result correlates with a previous study done by *Anna dozzaetal.*

Cost of the medication

NSAIDS-antidepressants were found to be cheap and cost effective rather than NSAIDS with other class.

Headache reoccurrence

In this study, with effective patient counseling headache incidence was found to be reduced. Patients reported that they were satisfied with current treatment & counseling tips.

Distribution of adverse effects

In the study, 17 cases of adverse event were reported which were mild. Dry mouth was observed in 7%, drowsiness in 6% patients followed by alopecia & weight gain as the as the other adverse effects. In short, a drug utilization study was effectively done in neurology department of Pushpagiri Medical College Hospital. Patients were prescribed with safe & cost effective medication. Patients have been counseled about the disease, life style modifications to be taken in consideration for healthy life. 81% adhered to the current therapy. They reported that their headache incidence had reduced a lot than the earlier.

CONCLUSIONS

The study concluded that:

Drug utilization study plays a key role in the health care system. It is an on-going process.

- Pharmacist plays a pivot role in conductance of drug utilization study.
- Patients medication adherence had been improved after effective patient counselling
- Patient knowledge about the disease had been increased.
- From the study it was found that diary keeping had helped the patients to sort out the triggering factors of headache.

Physicians must discuss with the patients about their disease and treatment available for disease. They must communicate with patients before implementing a drug therapy. Patients must be educated on their disease. Drug utilization study in primary headache had provided information on various acute and prophylactic medication used for primary headache syndrome. It also reported drug related problems observed in the patients during the treatment. The study also provided an idea of cost of different medicines used for the primary headache disorder. More and more drug utilization studies must be carried out in the future for enlightening and updating the knowledge.

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