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## Effectiveness of migraine prophylaxis on psychiatric changes and quality of sleep

**Tarunika Reddy P, Sri Lalitha YNS, Sreekanth Vemula, Narender Boggula and Vasudha Bakshi**

### Abstract

**Background:** Migraine is a 6<sup>th</sup> leading causes of disability worldwide. It is classified into two major types, migraine with aura and migraine without aura. Migraine is often associated with comorbid Psychiatric changes and poor quality of sleep. Migraine prophylactic therapy is used to reduce the frequency, severity and disability of migraine attacks. Along with headache, an appropriate prophylactic drug can show effect in treating comorbid conditions associated with migraine and improve sleep.

**Objectives:** The aim of the study is to show the effect of migraine prophylaxis on Psychiatric changes and Quality of sleep. Besides, the objective of our study is to determine frequency, severity and duration of migraine, severity of depression and anxiety and their minimization.

**Methods:** About 150 patients above 10 years were included in the study. The required data was collected from the patients through direct interview using standard questionnaires. The acquired data was evaluated based on the standard questionnaire scales i.e. Migraine Disability Assessment Scale, Zung Self Rating Depression scale, Zung Self-Rating Anxiety scale and Pittsburgh Sleep Quality Index were used to diagnose the severity of migraine, anxiety and depression along with impaired quality of sleep in migraine patients.

**Results:** We found a higher significant prevalence and risk of incident migraine is in females than in males. Age groups of 25-45 years are at a higher risk of migraine incidence. Prevalence of mild to severe depression (according to Zung Self-Rating Depression Scale) 29.3% and moderate to severe anxiety (according to Zung Self-Rating Anxiety Scale) is 27.3%. The study shows prevalence of migraine without aura (83%) is higher than migraine with aura (6%). In our study Propranolol (46.67%), Topiramate (39%), Amitriptyline (32%) were the most prescribed drugs. All the three drugs has shown an effect on frequency, severity, duration of headache with the significance of  $P < 0.01$  similarly these drugs has shown a significant difference in scores of migraine disability assessment index, Zung self rating depression scale, Zung self-rating anxiety scale and Pittsburgh sleep quality index ( $P < 0.01$ ).

**Conclusion:** Propranolol was the most prescribed drug among all the prophylactic drugs prescribed. Out of all the prophylactic drugs propranolol, amitriptyline, topiramate when used individually or in combination form it was observed that there is decrease in factors such as migraine frequency, severity, duration, MIDAS scores, depression and anxiety, whereas quality of sleep improved. In our study we also observed that not only amitriptyline (anti-depressant) but also propranolol and topiramate showed effect on Psychiatric symptoms and quality of sleep.

**Keywords:** Migraine, quality of sleep, prophylaxis, psychiatric changes, aura, propranolol

### Introduction

Migraine is a condition marked by recurring moderate to severe headache with throbbing pain that usually lasts from hours to three days, typically begins on one side of the head but may spread to both sides, is often accompanied by nausea, vomiting, and sensitivity to light or sound, and is sometimes preceded by an aura and is often followed by fatigue.

### Aim

The aim of the present research work is to study the effectiveness of migraine prophylaxis on psychiatric changes and quality of sleep.

### Objectives

- To estimate the prevalence of psychiatric changes (depression and anxiety) and quality of sleep associated with migraine.
- To assess the severity of the conditions.
- To determine the prescription pattern of migraine with complications.

- To assess the responsiveness of prophylactic therapy on migraine.
- To assess the responsiveness of migraine prophylaxis on depression, anxiety and quality of sleep.

## Methodology

### Study protocol

A prospective observation study being conducted for a period of 6 months. Patients who meet the study criteria will be included in the study. The required data will be collected through the patient's interview and their prescriptions.

### Study design

It is a prospective observational study.

### Study site

The study was conducted at Magna Neurology Clinic, Banjara hills, Hyderabad, Telangana, India.

### Study period

The study was conducted for a period of 6 months.

### Follow up period

One month.

### Study population

A total of 150 out patients were included in the study.

### Study criteria

#### Inclusion criteria

- Both male and female patients shall be included.
- Adults, pediatrics, Geriatric patients shall be included.

#### Exclusion criteria

- Patients with headache due to functional neurological disorder.
- In-patients are excluded.
- Patients who did not respond for the follow up.

### Statistical tools

The analysis was done using SPSS software (version-8). Paired-T test was used to analyze the difference in score from visit to follow-up 2 in frequency, severity, duration, MIDAS, Zung Self-Rating depression scale, Zung Self-Rating Anxiety scale and PSQI scale. Pearson's Chi-Square test was used to find the association between frequency, severity, Migraine Disability with depression, anxiety and Quality of Sleep. Pearson's Correlation was used to find the dependency/relation of the medications on frequency, severity, duration, MIDAS, Zung Self-Rating depression scores, Zung Self-Rating Anxiety scores, PSQI scores.

### Outcome measurements

Patients who meet the study criteria will be included.

### Migraine

Disability due to Migraine was assessed using standard questionnaire.

### Migraine Disability Assessment Scale (MIDAS)

The MIDAS questionnaire is a short test that can accurately and reliably determine how headaches impact daily life.

MIDAS questionnaire is a short, self-administered questionnaire designed to quantify headache-related disability over a 3-month period.

### Psychometric parameters

The psychiatric changes associated with migraine were assessed by using two standard questionnaires.

- Zung Self Rating Depression Scale
- Zung Self Rating Anxiety Scale

### Zung Self Rating Depression Scale

The Zung Self-Rating Depression Scale was designed by W.W. Zung to assess the level of depression for patients diagnosed with depressive disorder. The Zung Self-Rating Depression Scale is a short self-administered survey to quantify the depressed status of a patient. There are 20 items on the scale that rate the four common characteristics of depression. There are ten positively worded and ten negatively worded questions. Each question is scored on a scale of 1-4 (a little of the time, some of the time, good part of the time, most of the time). In scoring the SDS, a value of 1, 2, 3 and 4 is assigned to a response depending upon whether the item is worded positively or negatively.

### For items 1, 3, 4, 7, 8, 9, 10, 13, 15, 19 the scoring is

- A little of the time = 1
- Some of the time = 2
- Good part of the time = 3
- Most of the time = 4

### Items 2, 5, 6, 11, 12, 14, 16, 17, 18, 20 are reverse scored as follows

- Most of the time = 1
- Good part of the time = 2
- Some of the time = 3
- A little of the time = 4

The SDS index is derived by dividing the sum of the values (raw scores) obtained on the 20 items by the maximum possible score of 80, and expressed as a decimal point.

### Zung Self Rating Anxiety Scale

The Zung Self-Rating Anxiety Scale (SAS) was designed by William WK Zung. The self-administered test has 20 questions. Each question is scored on a scale of 1-4 (none or a little of the time, some of the time, good part of the time, most of the time).

### Clinical utility

It is used to quantify the level of anxiety for patients experiencing anxiety related symptoms.

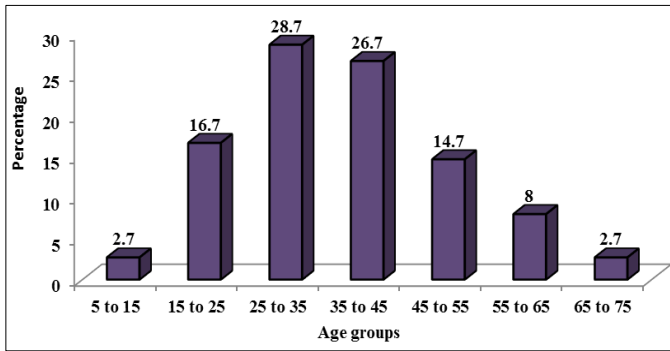
### Quality of sleep assessment

A standard scale is used to assess the quality of sleep in Migraine patients.

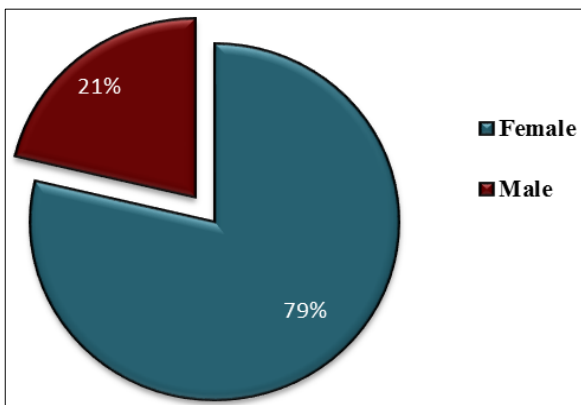
### Pittsburgh sleep quality index

The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep. The PSQI contains 19 self-rated questions. The 19 self-rated items are combined to form seven domains which differentiate "poor" from "good" sleep.

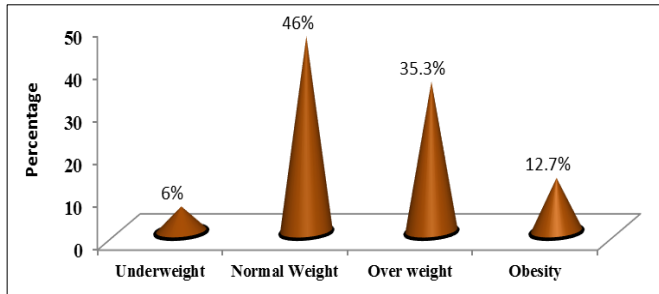
**Results**  
**Demographic details**



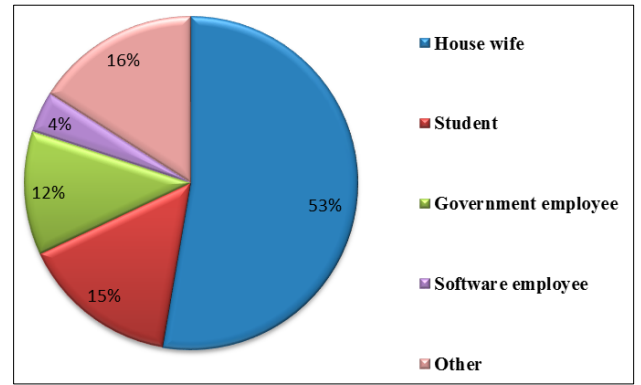
**Fig 1:** Age groups distribution chart



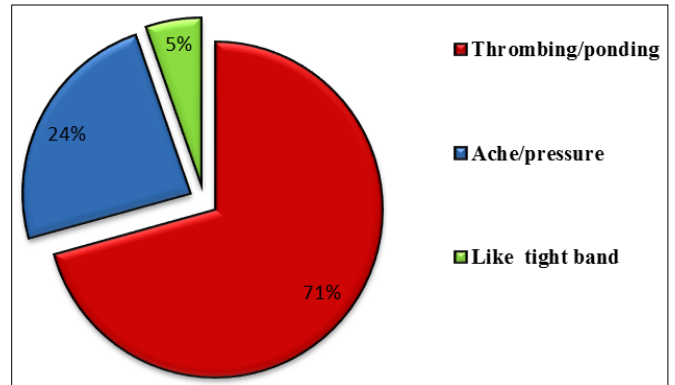
**Fig 2:** Gender variation



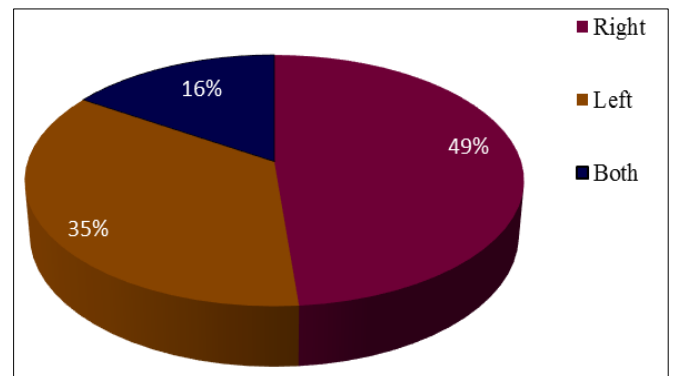
**Fig 3:** Distribution of population based on Body Mass Index



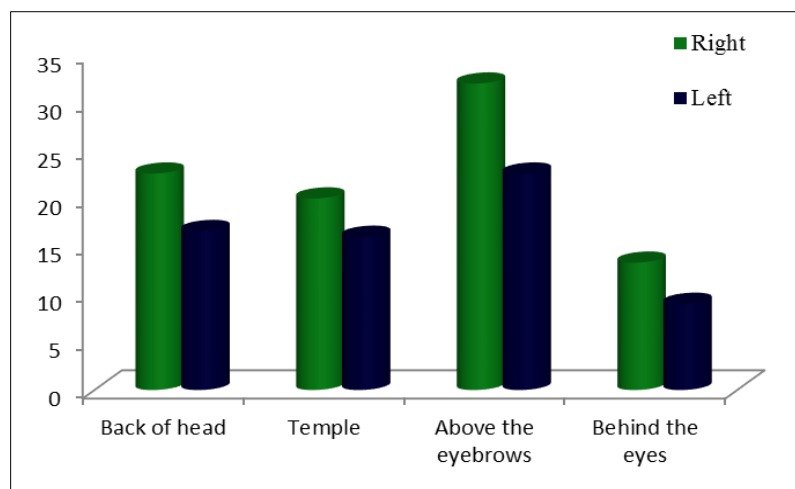
**Fig 4:** Occupation of study population Headache assessment



**Fig 5:** Types of pain



**Fig 6:** Location of headache



**Fig 7:** Site of pain during the migraine attack

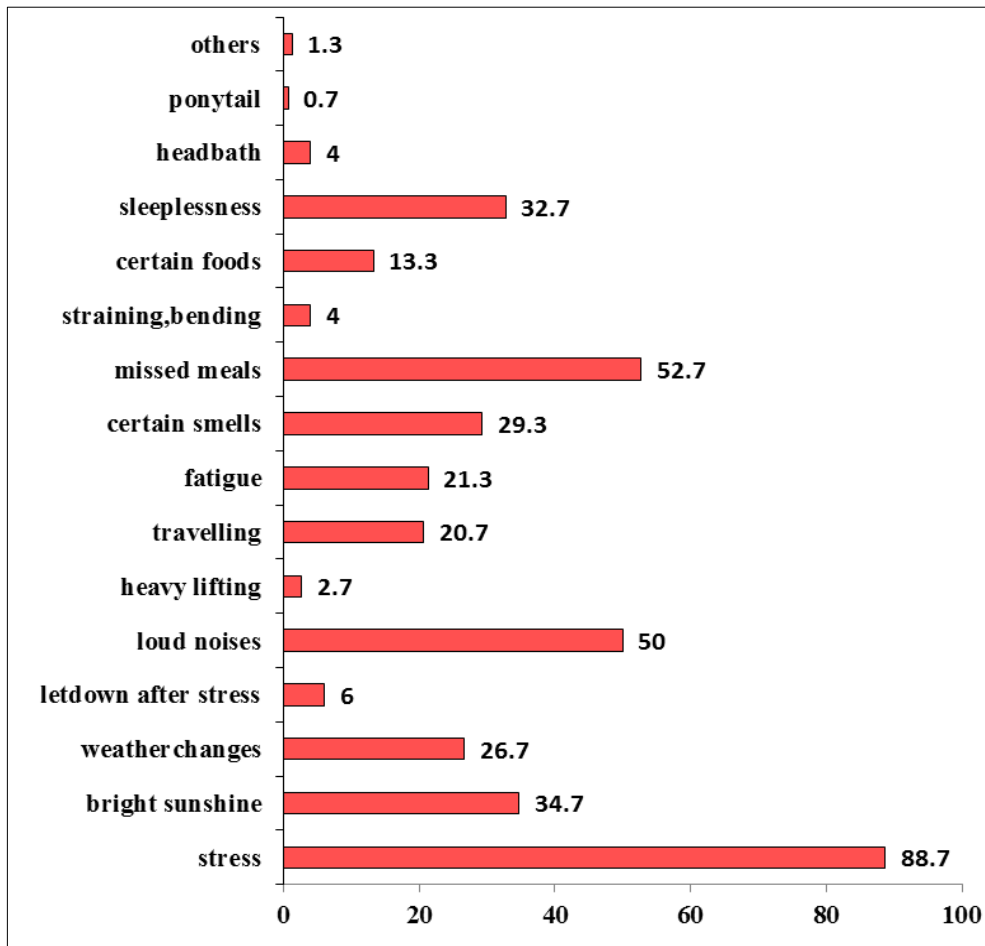


Fig 8: Triggering factors of migraine

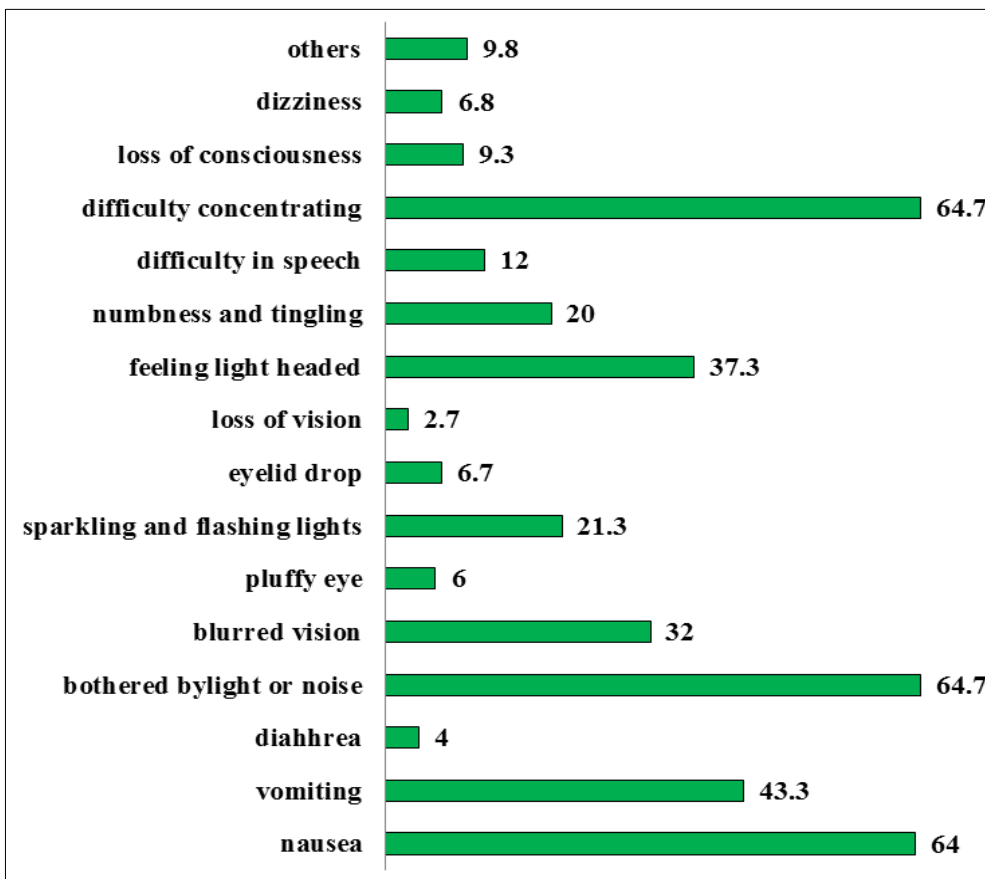


Fig 9: Symptoms of migraine

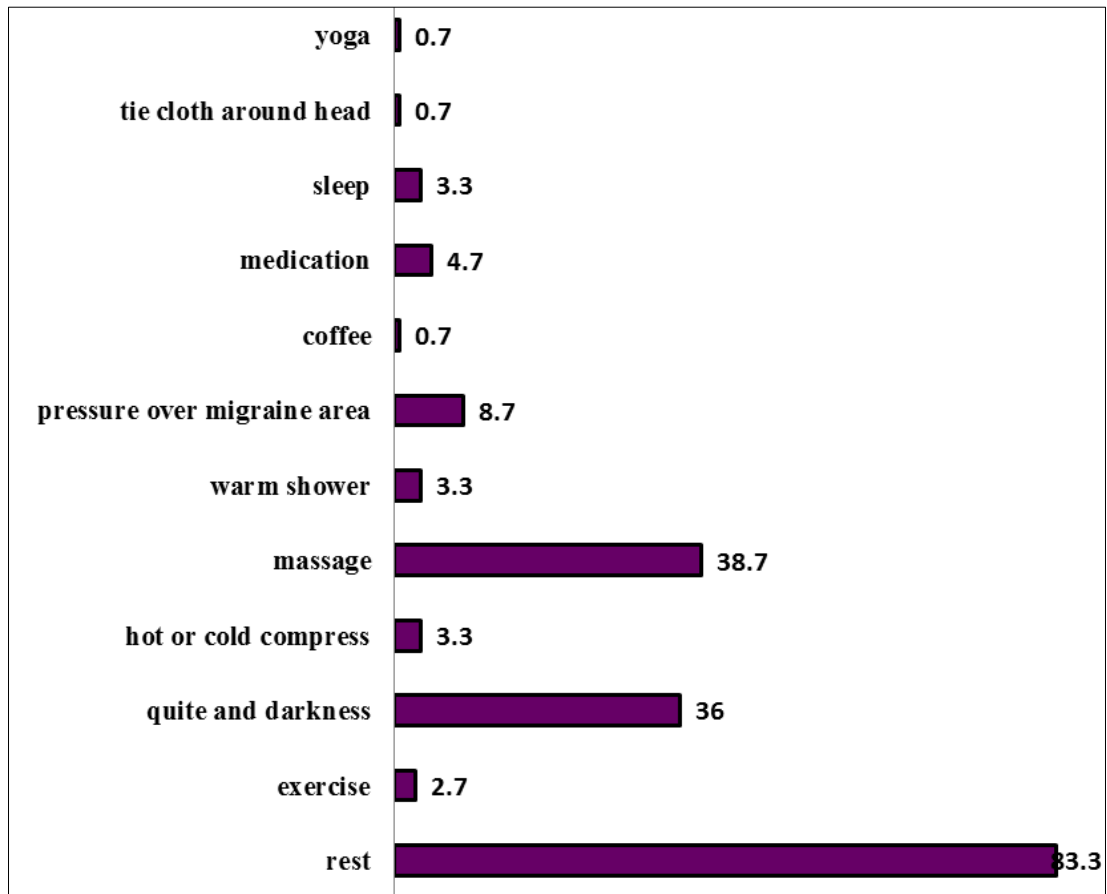


Fig 10: Relaxing factors of migraine

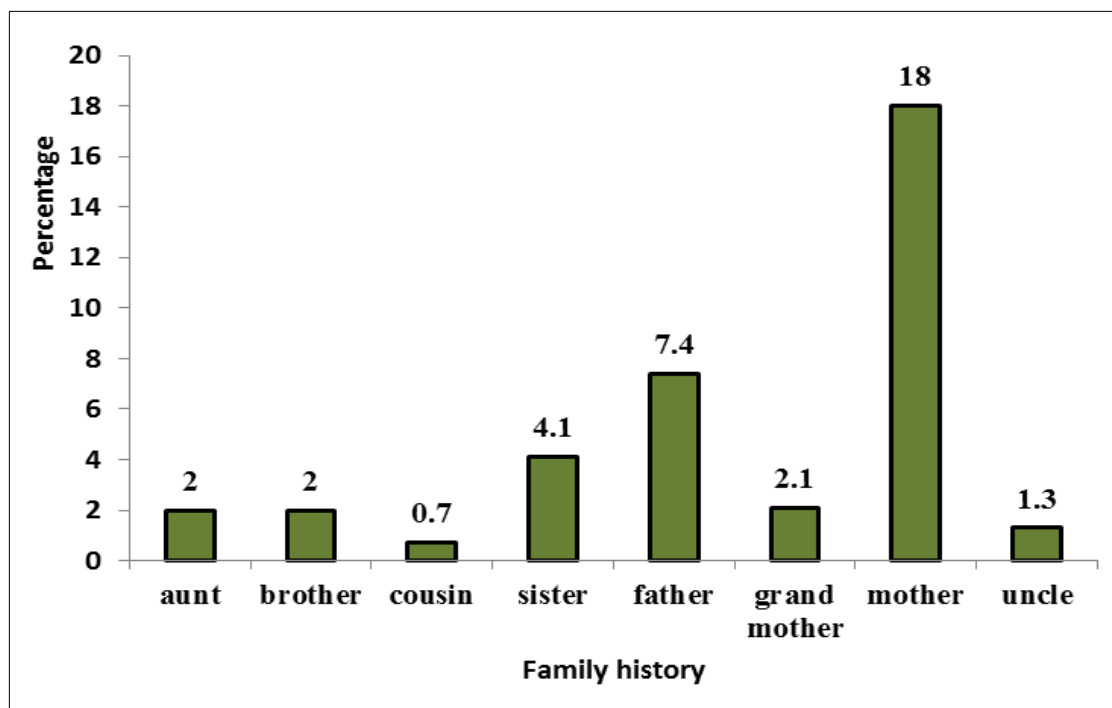


Fig 11: Family history of migraine

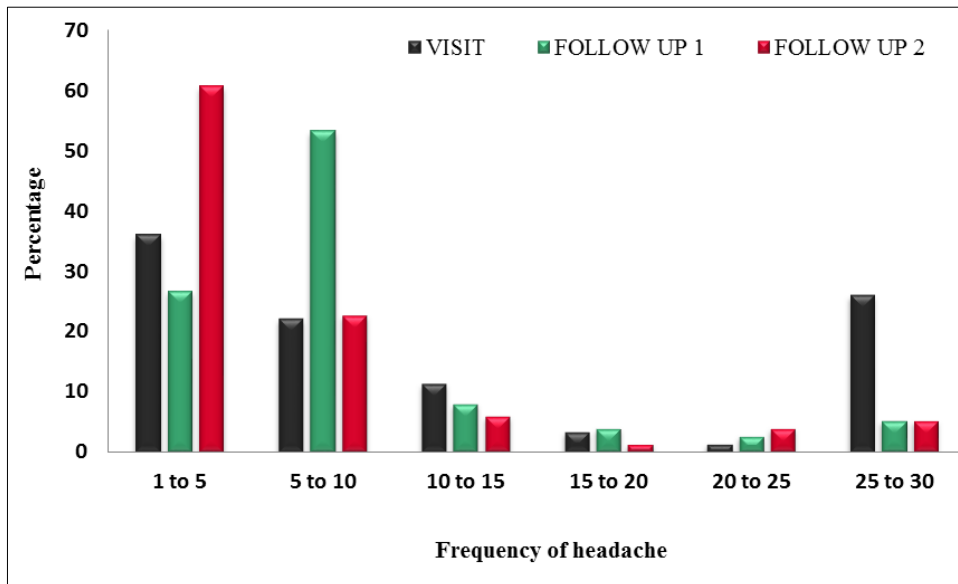


Fig 12: Frequency of Headache

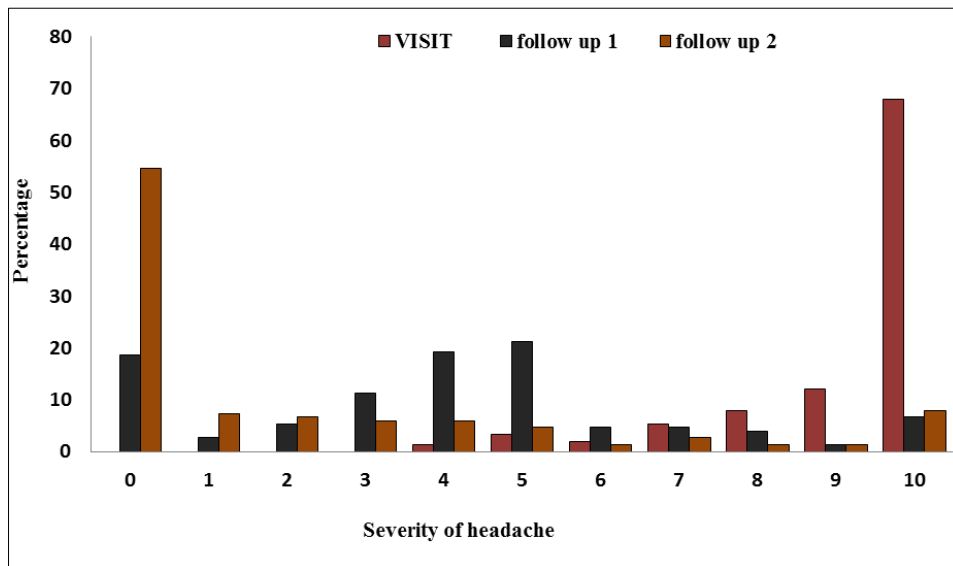


Fig 13: Severity of headache

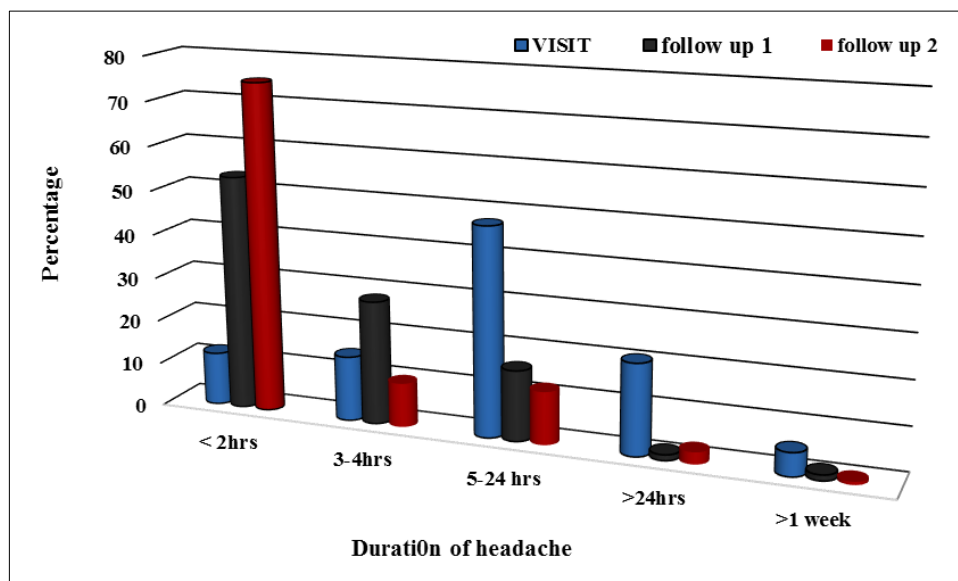


Fig 14: Duration of headache

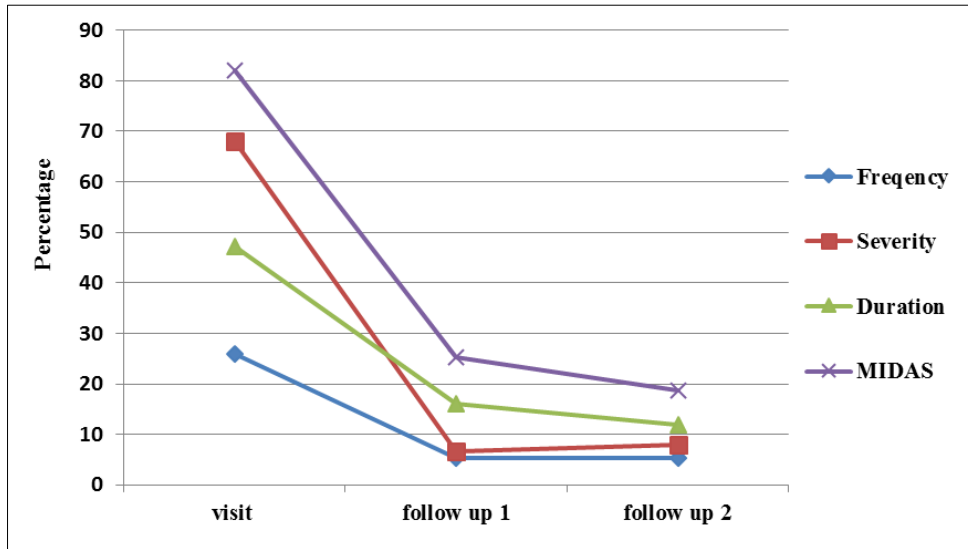


Fig 15: Headache assessment index

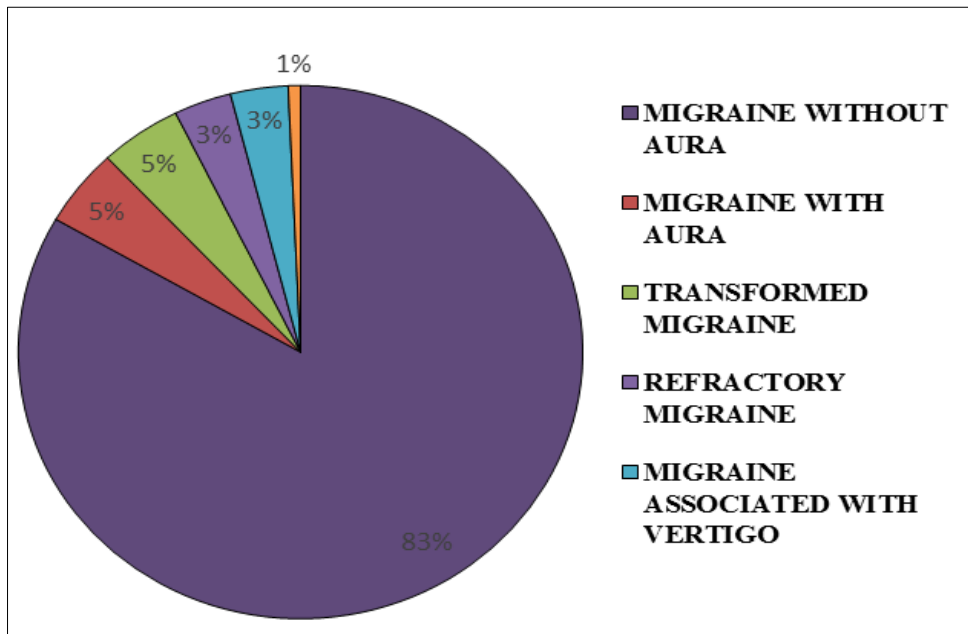


Fig 16: Diagnosis of migraine

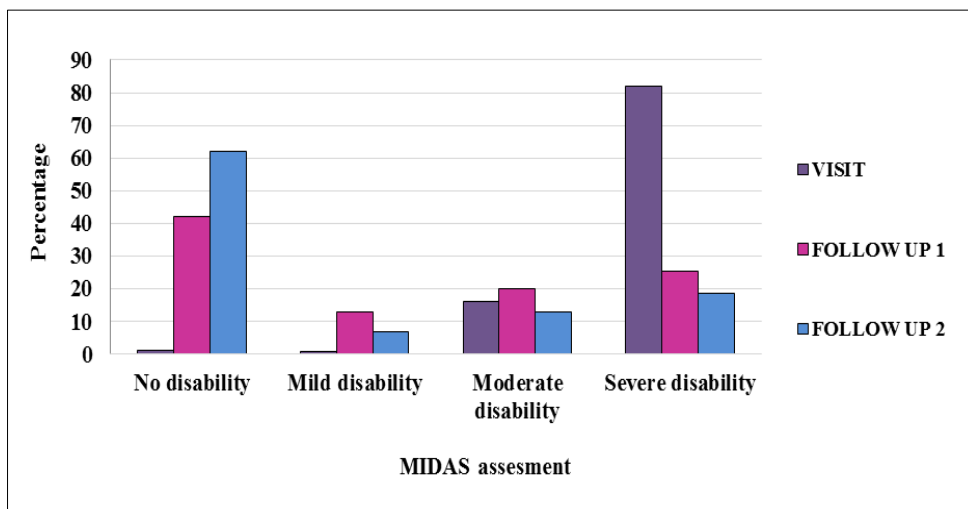


Fig 17: Distribution of population according to Migraine Disability Index scores

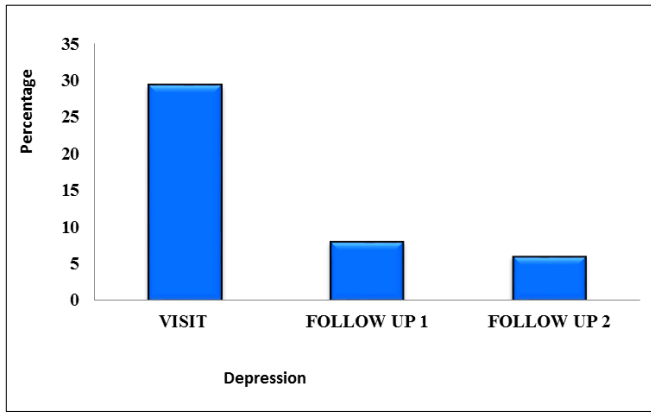


Fig 18: Zung self-rating depression scale scores

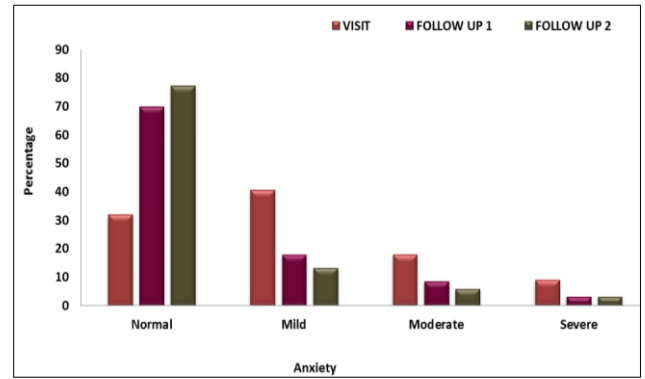


Fig 19: Distribution of population according to Zung self-rating anxiety scale

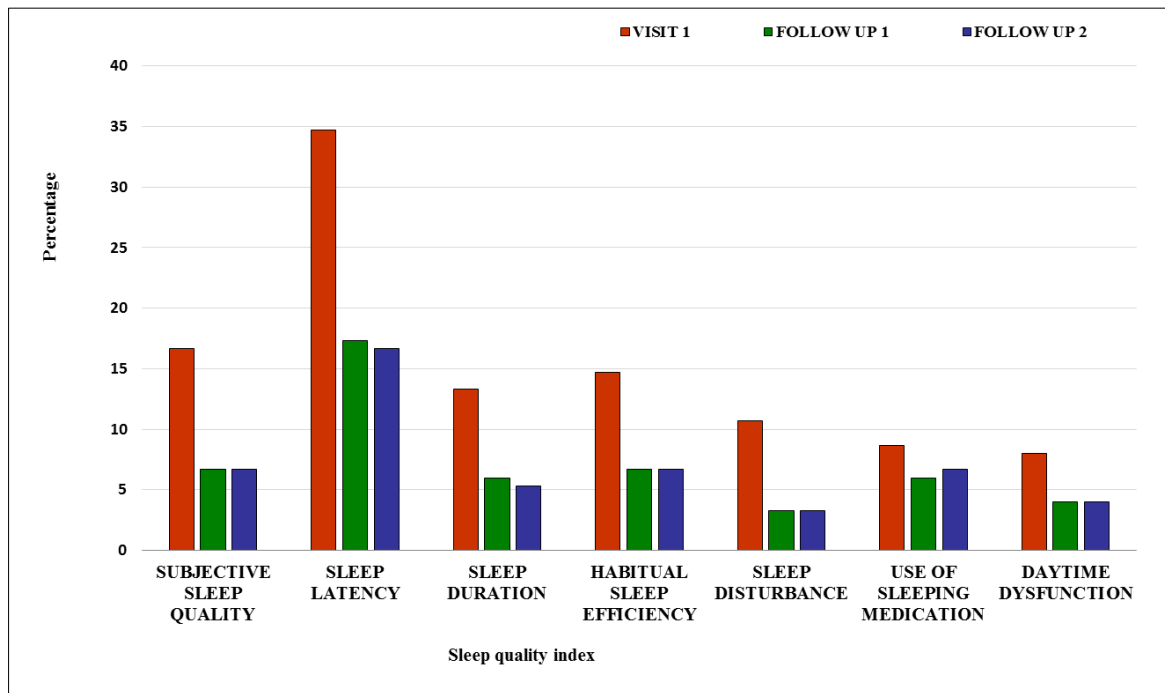


Fig 20: Pittsburgh sleep quality index

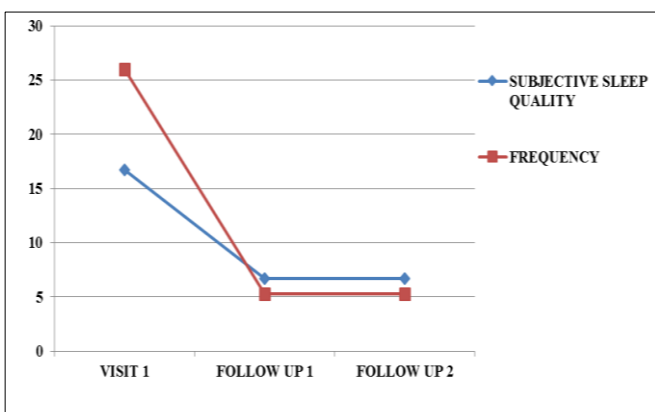


Fig 21: Influence of headache frequency on subjective sleep quality

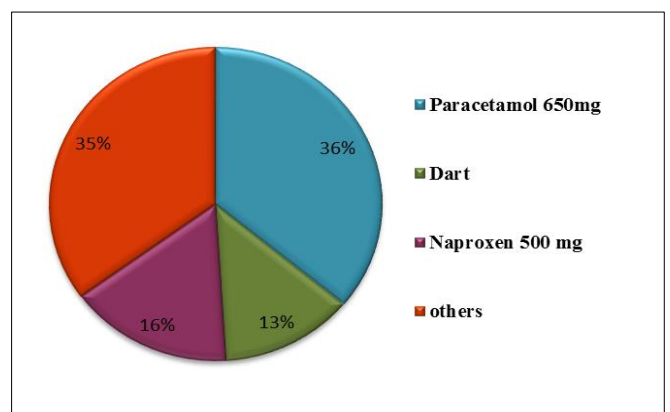


Fig 22: Use of over the counter drugs



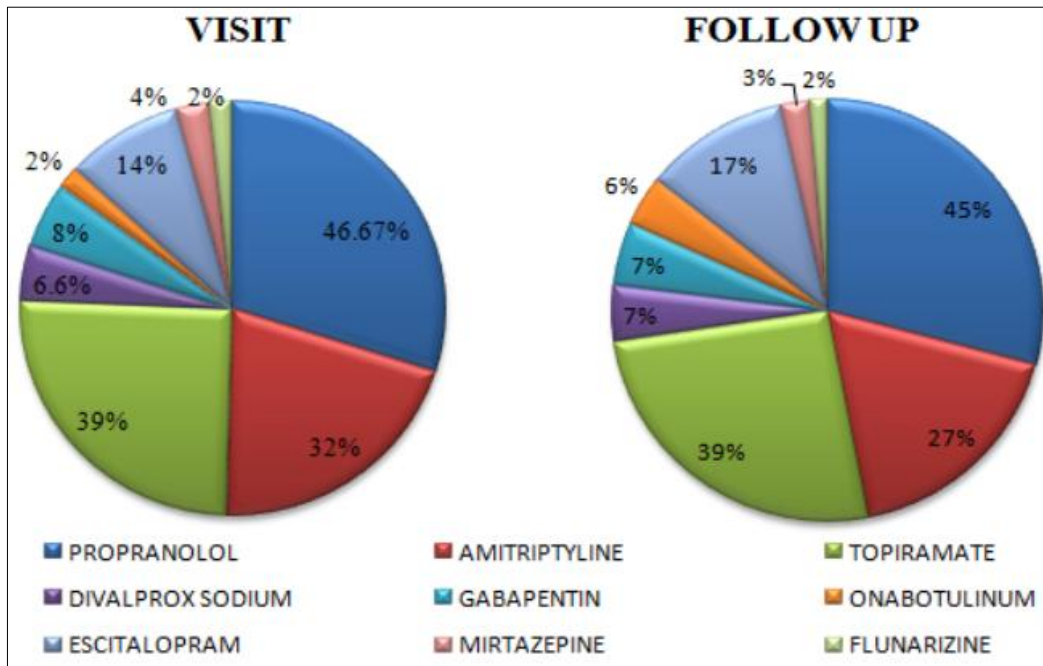


Fig 23: Comparison of drugs prescribed from visit to follow up

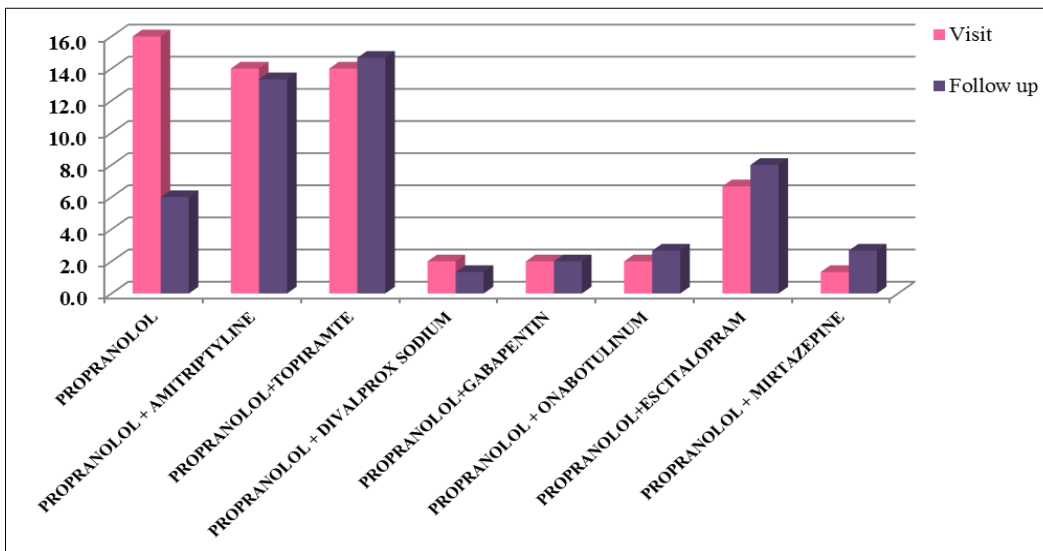


Fig 24: Comparison of Propranolol and its combinations from visit to follow up

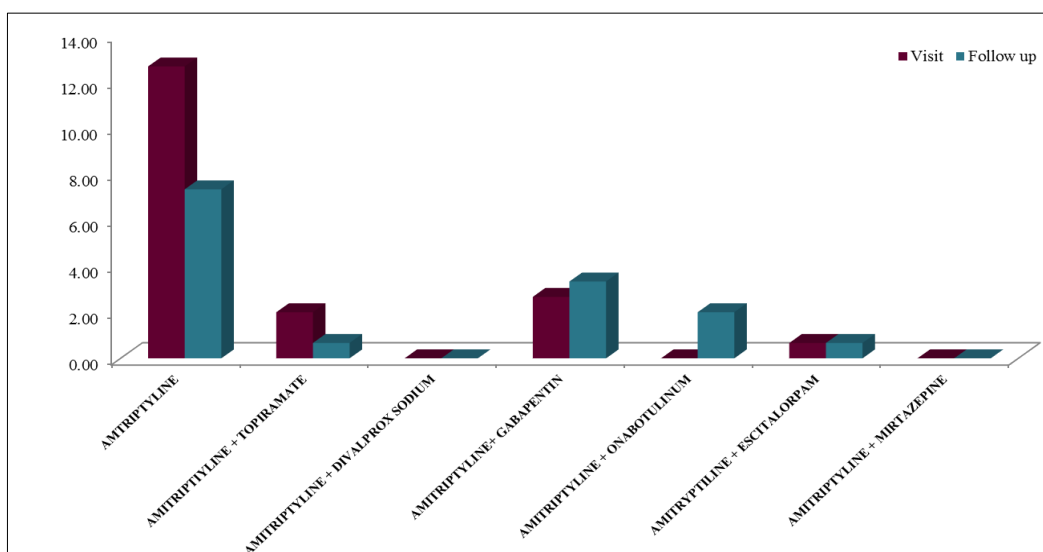


Fig 25: Comparison of Amitriptyline and its combinations from visit to follow up

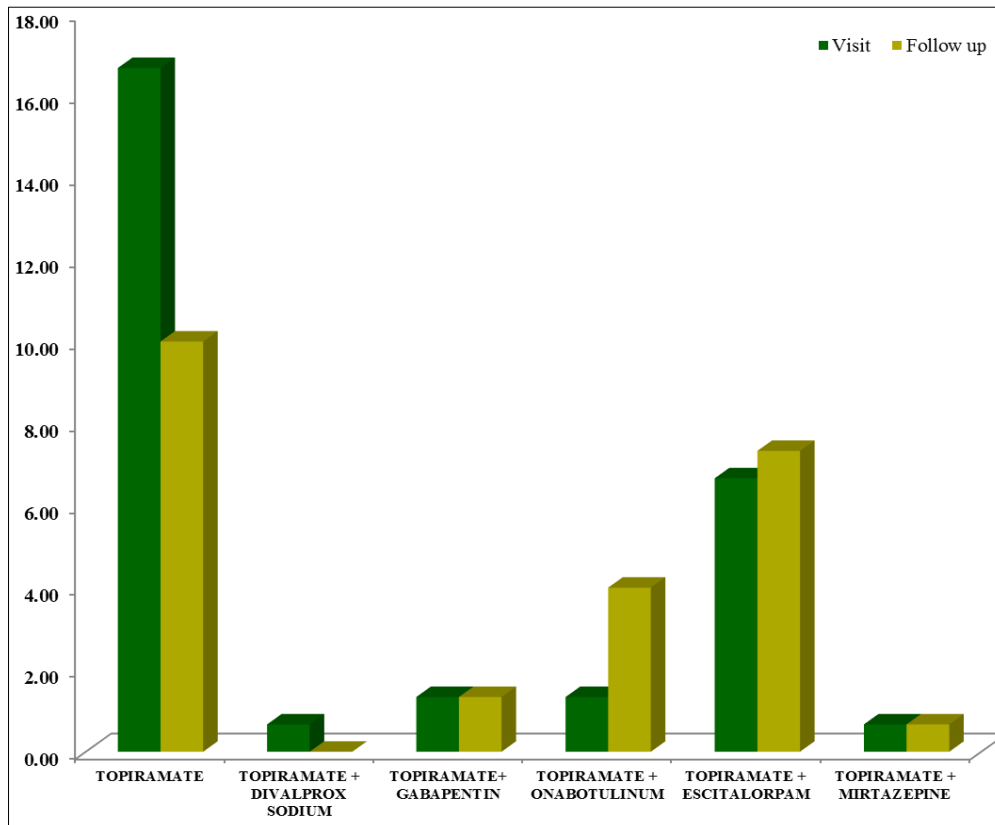


Fig 26: Comparison of topiramate and its combinations from visit to follow up

## Discussion

The study population included 150 patients with migraine were screened for depression, anxiety and quality of sleep. About 3/4<sup>th</sup> of population were females and 1/4<sup>th</sup> were males. Previous epidemiological studies also give evidence that females are more prone to migraine than males due to hormonal fluctuations in women during menstrual period or menopause. In our study, about 22% of females reported worsening of headaches during menstrual period. It was observed that 40 female patients had comorbid conditions out of which 37.5% had hypothyroidism. This may be suggested as one of the factors that influence the migraine headaches in female patients. Females (32.2%) are observed to be more prone to depression compared to males (18.75%). The results in the present study show that on an average 38 out of 118 females and 6 out of 32 males have observed to have mild to severe depression. Likewise depression, Females (72%) are observed to be effected with anxiety more than males (53%). It was observed that the overweight and obese category in females was 51.4% and that of males was 34.37%, which illustrates that females are more prone to migraine than males. Considering the age groups as a part of our study, the mean age group of females was 38.32years and males were 32.18years. Among 150 patients maximum number patients belong to age group of 25-45 (mean=37.322) in which housewives are more in number.

The other part of the study includes various factors such as triggering factors, relaxing factors and symptoms, the other major triggering factors include missed meals, loud noises, fatigue, bright sunshine, weather changes, sleeplessness and travelling, whereas few patients reported certain smells (perfumes) has provoking factors for migraine. Foods on the other hand also act as triggering factors as such. Cold items, sweets, and citrus fruits were the most commonly reported foods that trigger migraine. The sucrose and fructose contents

present in sweets and citrus fruits increase 5-HT levels which may trigger migraine. Very few patients reported that ponytail, head bath as the triggers for migraine. As family history of migraine is one of the risk factors for migraine.

On investigation for symptoms, it was observed that they exhibited various symptoms. Majority of patients were presented with nausea (64%), sensitivity to light or noise and difficulty in concentration. Vomiting, blurred vision, feeling light headed, numbness and tingling, sparkling and flashing of lights were some other migraine symptoms accounted. Loss of vision, loss of consciousness, speech difficulty, dizziness and eyelid drooping are rarely recorded symptoms. As a part of the treatment, majority of patients opted for various relaxing methods and use of over the counter medications. It was observed that rest (83.3%) is the major relaxing factor followed by Massage (38.7%) and Quite and Darkness (36%). Adding on pressure over migraine area, hot or cold compression, warm shower and yoga are some other methods which helped in relieving migraine. About 4.7% of patients chose used analgesics as relaxing method for relieving headache contributing as a risk factor to the incidence of "Analgesic Abuse Headache". The screenings was done three times throughout the study i.e. at visit, first follow up (after 1 month) and second follow up (after two months from the time of visit to hospital). The time interval between each screening session was 1 month. The Frequency of headache per month was recorded. At the time of visit maximum members have reported frequency of headache 25-30 times per month, during the course of treatment frequency got decreased to 5-10 times per month, while in some patients there is no much improvement due to discontinuation of medications.

Severity of headache was taken on a scale of 0 to 10. Greater than 60% of patients had severe headache during the visit, later severity got decreased to less than 10% by 1<sup>st</sup> follow up. While in few patients there was no change in severity due to

medication in adherence. After counselling, 20% of patients reported mild severity and 54.7% had no headache. Duration of migraine attacks in patients were recorded based on five categories (i.e. < 2hrs, 3-4hrs, 5-24hrs, >24hrs and >1week). Likewise severity and frequency, duration also decreased by second follow up gradually as explained in Figure 14). In our study, the prevalence of migraine without aura (83%) is higher than migraine with aura. Along with migraine with aura and without aura other types of migraine headaches were also observed (Figure 16). The disability due to migraine was analysed based on Migraine Disability Assessment Scale (MIDAS). MIDAS is used to measure the impact of headaches on patient's life and also helped to determine the level of disability based on scores 0-5 (little or no disability), 6-10(mild disability), 11-20 (moderate disability), >21 (severe disability). In our study, MIDAS scores decreased gradually from the time of visit to second follow up after treatment. Number of patients with severe migraine disability from time to visit dropped from 123 to 28 by 2<sup>nd</sup> follow up (after 2 months). There exists an association between frequency, severity, duration of headache and MIDAS scores which is explained in Figure 15.

Screening for depression was done using Zung Self-Rating Depression Scale (SDS). SDS is 20 item questionnaires that rate the four common characteristics of depression. There are 10 positively worded and 10 negatively worded questions which are used to diagnose the depression and rate the severity of depression. In accordance with depression scores, 29.3% of total population exhibit moderate to severe depression. During the time of visit conducted after one month. During the first follow up session, from visit there is significant difference in scores. By the second follow up only 6% of patients reported depression symptoms (as explained in Figure 18). Frequency, severity of headache and depression score is interdependent, with decrease in frequency and severity of headache depression decreases. This interdependency is due to serotonergic system. A total of 150 patients, were assessed for anxiety using Zung Self Rating anxiety scores (SAS) consisting of 20 questions of which 15 questions worded toward increasing anxiety levels and 5 questions worded towards decreasing anxiety levels. The Raw scores were converted to index scores to categorise the subjects according to level of anxiety based on anxiety scores. Based on the anxiety scores, it was observed that 27.3% of subjects had moderate to severe anxiety followed by 40.7% had mild anxiety. After treating migraine, the percentage got decreased to 3.3 (moderate to severe) and 8.7 (mild) respectively, showing no significant difference from follow up 1 and follow up 2. The association between Zung Self Rating Anxiety scores and MIDAS scores were observed. There is decrease in Anxiety scores with decline in MIDAS score during follow up 1 and follow up 2. Pittsburgh Sleep Quality Index (PSQI) was used to measure the Quality and patterns of sleep in patients. It is categorised into seven components based on nineteen questions.

Subjective Sleep Quality improved by 6.7% from visit to second follow-up. There is no significant difference in quality of sleep after treating migraine from 1<sup>st</sup> follow up to 2<sup>nd</sup> follow up. By measuring the sleep latency in patients 34.7% had severe difficulty falling asleep. This has decreased to 18% by 2<sup>nd</sup> follow up, after treatment the difficulty to fall asleep remained same during follow up 1 and follow up 2. The duration of sleep was recorded in patients and it was observed that duration of sleep increased by 11.4% from less than 5 hrs

to greater than 7 hrs by 2<sup>nd</sup> follow up after treating migraine. Out of 150 patients, 48% had greater than 85% habitual sleep efficiency, during second follow up session; it is increased by 13.3%. The sleep efficiency scores remained same during follow up 1 and follow up 2.5. Patients were screened for sleep disturbances. During the time of visit 10.7% had severe sleep disturbances after the treatment for migraine, by the end of 2<sup>nd</sup> follow up 23.3% patients used sleeping medication greater than 3 times a week during the time of visit to improve their quality of sleep, while 8% of patients had daytime dysfunction during the time of visit. The percentages of patients with daytime dysfunction decreased by follow up 2 after treating migraine.

Several studies have been conducted which mostly favour the evidence that quality of sleep and migraine show bi-directional pathway, which is also observed in our study. About 32.7% patients reported sleep deprivation as a trigger for migraine, similarly increase in headache frequency leads to poor quality of sleep (as explained in Figure 8 and 21). Preventive therapy or prophylactic therapy was prescribed to treat migraine among which propranolol (46.6%) was most prescribed followed by topiramate (39%) and amitriptyline. Other prophylactic drugs like gabapentin (8%), divalproex sodium (6.6%), mirtazepine (4%), flunarizine (2%), were also prescribed to treat migraine with aura and migraine without aura. Patients were categorized into three groups based on percentage of drugs prescribed to observe the effect of various prophylactic drugs on migraine, psychiatric changes and quality of sleep. As propranolol was the most prescribed drug among all the prophylactic drugs. We have considered patients taking propranolol as Group 1. It was observed that three patients discontinued the medication. During first follow-up propranolol was prescribed in various daily divided doses i.e. 10mg, 20mg, 30mg, 40mg and 80mg. Group 2 comprised of patients prescribed with topiramate. After propranolol, topiramate was the most prescribed drug. Topiramate was prescribed to 59 patients were prescribed with topiramate as such while Topiramate was prescribed in 25mg, 50mg, 75mg, 100mg and 150mg in daily divided doses. Group 3 is the patients who are prescribed with amitriptyline. Among 150 patients 48 patients were prescribed with amitriptyline. During first follow-up (after a month from visit) it was observed that seven patients discontinued the medication due to various reasons. Amitriptyline was prescribed in various daily divided doses i.e. 5mg, 10mg and 25mg.

During follow up sessions it was observed that the severity got decreased and only seven patients reported severe to unbearable headaches. In group 2, out of 59 patients, Topiramate was prescribed to 50 patients with severe to unbearable headaches. On the follow-up session the number of patients decreased to five with severe and unbearable headaches. A like group 1 and 2, in group 3 the number of patients decreased from 45 to 5 during follow-up 1. Out of 48 patients administered with amitriptyline due to discontinuation of medications the severity of headache increased in few patients by follow up 2. Identical to frequency and severity of headaches, the duration of migraine attacks decreased in patients of all three groups. Along with frequency, severity, duration of migraine, the MIDAS scale was used to assess the impact of headache on life. In the study, it was observed that number of patients with Grade IV decreased from visit to follow up 2. In group 1 patients, with the administration of propranolol the number of patients with

severe disability decreased about three times by the end of follow-up 2 i.e. from 57 to 13 patients. In respect with group 2 the severity decreased by 3 folds by follow-up 2. The psychiatric changes like depression and anxiety were screened in 150 patients.

Based on depression scores it was observed that the percentage of patients with mild to severe depression decreased from visit to follow-up 2. Propranolol was administered to 18 patients having mild to severe depression out of 70 patients. The number of patients decreased to 4 with mild to severe depression by the end of follow-up 2. In case of patients administered with topiramate the number of patients with mild to severe depression decreased from 24 to 8 i.e. almost three times. Only ten patients of mild to severe depression were prescribed with amitriptyline during visit. This count got decreased to 1 by 2<sup>nd</sup> follow-up. Anxiety was also observed to be decreased from visit to follow-up during treatment. Propranolol was prescribed to 17 patients with moderate to severe anxiety during visit. By the end of follow-up 2 the number got decreased to 4. Out of 59 patients prescribed with topiramate 18 had moderate to severe anxiety. On follow-up sessions, the number of patients decreased to 6, while amitriptyline was administered to 10 patients with moderate to severe anxiety. The number of patients decreased to 1 by follow-up 2. One of the notions of the study is to assess the effect of prophylactic drugs on quality of sleep. Irrespective of drugs, overall quality of sleep improved from visit to follow-up 1. There was no much change in scores from follow-up 1 to follow-up 2. The global score of PSQI decreased from visit (mean=7.16) to follow-up 1 (mean=5.32). There was no much change in quality of sleep from follow-up 1 (mean=5.32) to follow up 2 (mean= 5.30).

### Conclusion

We found a higher significant prevalence and risk of incident migraine is in females than in males. Age groups of 25-45 years are at a higher risk of migraine incidence. Prevalence of mild to severe depression (according to Zung Self-Rating Depression Scale) 29.3% and moderate to severe anxiety (according to Zung Self-Rating Anxiety Scale) is 27.3%. The study shows prevalence of migraine without aura (83%) is higher than migraine with aura (6%). Increase in frequency of headache was associated with poor quality of sleep and increased psychiatric symptoms in migraine patients. Stress is observed to be the most common triggering factor (as a part of non-pharmacological management patients can identify the triggering factors and avoid them to subside migraine) Propranolol was the most prescribed drug among all the prophylactic drugs prescribed. Out of all the prophylactic drugs propranolol, amitriptyline, topiramate when used individually or in combination form it was observed that there is decrease in factors such as migraine frequency, severity, duration, MIDAS scores, depression and anxiety, wherein quality of sleep improved. In our study we also observed that not only amitriptyline (anti-depressant) but also propranolol and topiramate showed effect on psychiatric symptoms and quality of sleep.

### Acknowledgement

The authors wish to thank the management of School of Pharmacy, Anurag Group of Institutions, Venkatapur, Ghatkesar, and Telangana, India for providing necessary equipment for research, constant encouragement, praiseworthy inspiration, facilities and support.

### Conflict of Interest

Author declares that there is no conflict of interest to disclose.

### Sponsorship

Nil.

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