PROSPECTIVE EVALUATION OF PRESCRIBING PRACTICES AND QUALITY OF LIFE OUTCOMES IN MIGRAINE PATIENTS

Dr Angel[1], Dr Neethu Mary[2], Dr Kailash Chander[1*], Dr Siddharth Arjun Atwal[3]

[1*]Associate professor, Anatomy, Jaipur National University Institute for Medical Sciences and Research Centre
[2]Drug Safety Physician, APCER Life Sciences, Delhi
[3]Medical officer, Civil Hospital, Malerkotla

*Corresponding author: Dr Kailash Chander
*Associate professor, Anatomy, Jaipur National University Institute for Medical Sciences and Research Centre

Abstract:

Background: Migraine is amongst the most common disorders of the central nervous system affecting people throughout the world. Migraine can be managed to some degree by a variety of non-pharmacological and pharmacological treatment includes both acute and preventive therapy. Migraine has also been associated with poor health related quality of life (HRQoL). Such a study is important in India as there is insufficient data on impact of migraine on HRQoL and also the pattern of intake of various drugs associated with migraine.

Material and methods: A total of 200 prescriptions of migraine patients were studied. Patient details were noted on case record form which included demographic information and details of disease. The demographic details and information on drug/drugs prescribed including dose, formulation and dosing frequency for acute as well as prophylactic treatment were noted.

Results: The average number of drugs prescribed per prescription is in line with the WHO core indicators. The use of drugs for migraine prophylaxis had a significant improvement on the quality of life for study participants, based on the HIT-6 scores. At baseline, the mean HIT-6 score was 58.44. At the end of 3 months, the mean score had reduced to 51. A reduction in HIT-6 score indicates a decrease in severity and disability associated with migraine. There was a statistically significant difference between HIT-6 score at baseline and at 3 months. (p value <0.0001). Out of 200 prescriptions, drugs were prescribed by generic names in 70% (140) of the prescriptions. Out of a total of 657 drugs, 209 drugs were prescribed by generic names. The drugs prescribed by generic name were 31.81%.

Conclusion: The prescribing pattern of drugs used for migraine was according to the guidelines. There is a potential for improving drug prescribing by generic name and drugs prescribed from essential drug list. The average number of drugs prescribed per prescription is in line with the WHO core indicators. The use of drugs for migraine prophylaxis had a significant improvement on the quality of life for study participants, based on the HIT-6 scores.

Keywords: Migraine, HRQol, HIT-6, prescription pattern, prophylaxis.

Introduction

Migraine is amongst the most common disorders of the central nervous system affecting people throughout the world.[1] The global burden of disease study 2016 (GBD 2016) found migraine among the most prevalent diseases in the world with a global occurrence of 1.04 billion.[2] In India, a urban community-based study conducted in 2017 on prevalence and risk factors for migraine reported the prevalence of migraine to be 14.12%.[3] Migraine can be managed to some degree by a variety of non-pharmacological approaches such as counselling, relaxation training, biofeedback and cognitive-behavioural treatments.[4] The pharmacological treatment includes both acute and preventive therapy aimed at reducing the duration, frequency and severity of attacks.[5] Despite the variety of treatment approaches available, patients report that they feel their treatment is insufficient or unsatisfactory.[4] A report by World Health Organization (WHO) stated that there is inappropriate prescribing of 50% of the medications worldwide. This led to formation of WHO core indicators which are being used to measure the pattern of drug use.[6] In addition to this, migraine patients also report poor health related quality of life (HRQoL). Although, there is availability of a variety of drugs for management of migraine, there is persistence of headache as quality of life was not evaluated.[7] Over the past few years, several HRQoL tools have been used to measure the disability associated with migraine by evaluating the quality of life before and after treatment for patients started on migraine prophylaxis.[8] Such a study is important in India as there is insufficient data on impact of migraine on HRQoL.[9] Since there are many treatment options available, this study aims to analyse the current prescribing pattern of drugs used as acute and prophylactic therapy for migraine and also to assess the change in quality of life in patients on prophylactic therapy

Material and methods

This prospective, observational study included participants enrolled from the Department of Medicine from 1st January 2023 to 31st Dec 2024. Patients with a diagnosis of migraine based on the diagnostic criteria defined by International Headache Society were enrolled in the study. The patients with a diagnosis of migraine who visited the Medicine OPD during the study period were invited to participate in the study. Patients willing to participate in the study were explained about the study. They were enrolled after signing the informed consent form. A total of 200 prescriptions of migraine patients were studied. Patient details were noted on case record form which included demographic information and details of disease. The demographic details and information on drug/drugs prescribed including dose, formulation and dosing frequency for acute as well as prophylactic treatment were noted. Any dose escalations and rescue medication use were also noted. The information obtained was used to determine the pattern of drug use for acute therapy as well as for prophylaxis of migraine. A photocopy/photograph of the patient's prescription was taken to analyse the prescribing pattern of drugs. If any patient required admission during the study period, the details of drugs prescribed for patient management were noted. The prescription was analysed using WHO core indicators. The WHO core indicators include the average number of drugs per prescription, percentage of drugs prescribed by generic name, percentage of injectables used and the percentage of drugs prescribed from essential drugs list.

All patients who were started on prophylactic therapy during the study period were administered Headache Impact Test (HIT-6) at baseline and 3 months after start of therapy to assess the change in quality of life, if any, with the therapy. The HIT-6 items measure the adverse impact of headache on social functioning, role functioning, vitality, cognitive functioning, psychological distress and severity of headache pain. It consists of six questions with score for each question varying from 6 points to 13 points each. The total score varies from 36-78. The four headache impact severity categories are little or no impact (49 or less), some impact (50–55), substantial impact (56–59), and severe impact (60–78). HIT-6 tool is simple and easy to use.

Inclusion Criteria

1. Patients of both genders aged 18 years and above diagnosed to have migraine.

2. Patient already undergoing treatment and newly diagnosed with migraine as per criteria were enrolled.

Exclusion Criteria
1. Those with chronic daily headache (undiagnosed or mixed type).

Study procedure
Patients first underwent a clinical work up including a detailed history and general physical examination. Patients fulfilling the inclusion criteria were enrolled into the study after obtaining a written informed consent. The details of all the patients were recorded as per the protocol. Patient information sheet was provided to the patients enrolled in the study. A photocopy/photo of the patient's prescription was collected.

WHO had designed core indicators for drug utilization on the basis of which these prescriptions were analyzed. The formula adapted from World Health Organization's manual is as follows.[10]

1. Average number of drugs per encounter = Total number of drugs prescribed/Total number of encounters sampled.

2. Percentage of drugs prescribed by generic name = (Number of drugs prescribed by generic name/Total number of drugs prescribed) × 100.

3. Percentage of encounters with an injection prescribed =
(Number of patient encounters with an injection prescribed/Total number of encounters sampled) × 100.

4. Percentage of drugs prescribed from essential drugs list =
(Number of drugs prescribed from essential drugs list/Total number of prescribed drugs) × 100

All patients who were started on prophylactic therapy during the study period were administered Headache Impact Test (HIT-6) at baseline and 3 months after start of therapy to assess the change in quality of life with the therapy.

Statistical Analysis
The results were analyzed using descriptive statistics and presented as percentage and proportions. A p value < 0.05 was regarded as statistically significant. SPSS version 23.0 was used for analysis. Mean HIT-6 score differences were analysed by Wilcoxon rank-sum test.

Results
1. Demographic profile
In this study, a large number of participants (82 out of a total of 200, i.e. 41%) were in the age group of 18-30 years. In the age group of 31-40 years, there were 53 study participants (26.5%), in 41-50 years age group, there were 34 study participants (17%), in the 51-60 years age group, there were 24 study participants (12%) and in age group above 60 years, there were 7 participants (3.5%). The mean age of the study participants was 35.64±12.83 years.
1.2 Gender distribution
Out of a total of 200 participants, 62 were males and 138 were females. So there was a female preponderance with 69% female participants in this study.

2. CHARACTERISTICS OF MIGRAINE
There were 135 participants (67.5%) who presented with a unilateral headache. Twenty seven participants (13.5%) reported to have a unilateral headache which changed sides, while 38 participants (19%) presented with a bilateral headache. In this study, a majority of the participants i.e. 172 (86%), out of 200 participants, had a pulsatile headache while 28 participants (14%) had a constricting headache. A majority of the participants, 184 (92%) had migraine without aura in this study. Migraine with aura was reported by 16 participants (8%).

2.1 Associated features of migraine

Migraine was associated with a variety of features. The most common presenting feature was photophobia which was reported by 130 participants (65%). The associated features of migraine have been described in figure 1.

### FIG 1- PRESENTATION OF ASSOCIATED FEATURES OF MIGRAINE IN STUDY PARTICIPANTS
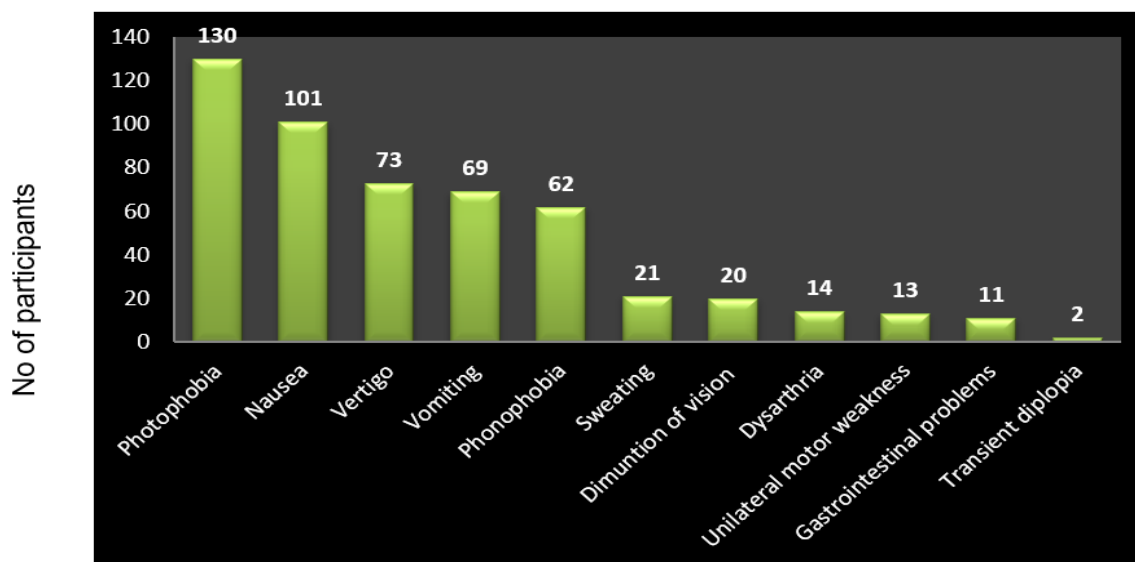
Associated features of migraine

2.2 Triggering factors for migraine

An array of triggering factors was reported for precipitation of migraine by the participants. This included stress which was reported by 106 participants (53%), history of travel by 105 participants (52.5%), increased physical activity in 60 participants (30%) and lack of sleep in 51 patients (25.5%). The triggering factors of migraine have been described in figure 2.

FIG 2- PRESENTATION OF TRIGGERING FACTORS FOR MIGRAINE IN STUDY PARTICIPANTS
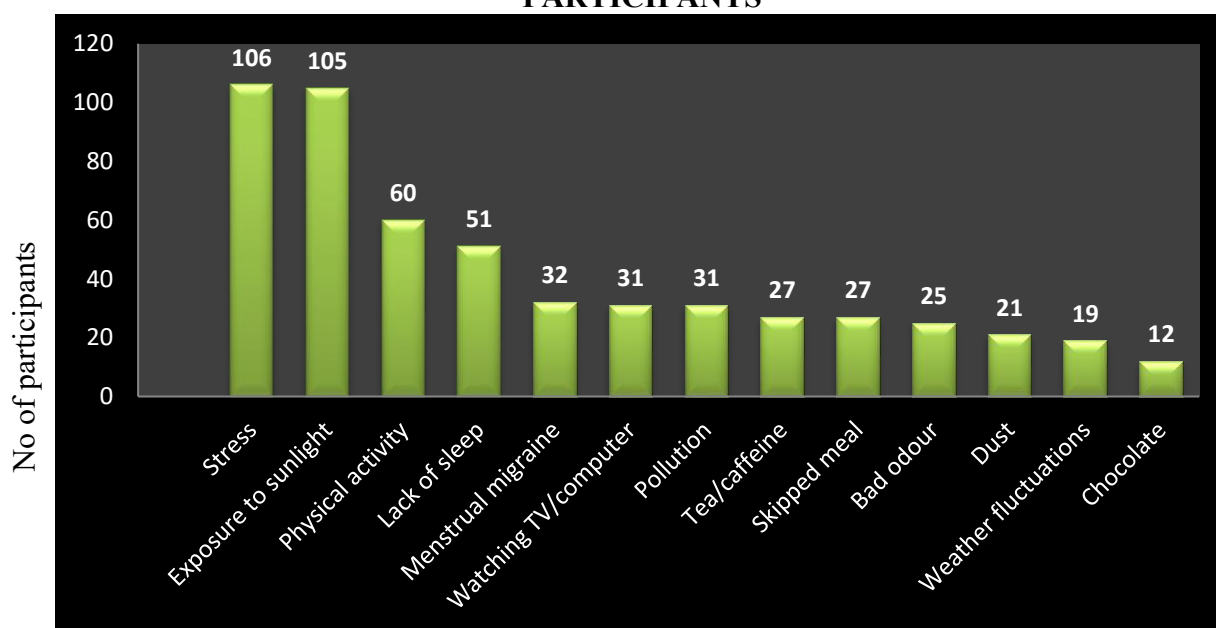
Triggering factors for migraine

3. PRESCRIPTION PATTERN

3.1 Drugs prescribed for acute and prophylactic therapy of migraine

In this study, out of 200 patients, 48 patients (24%) received therapy for acute migraine while 152 patients (76%) were started on prophylactic therapy for migraine.

3.2 Drugs for acute therapy of migraine

Forty-eight participants were prescribed therapy for acute migraine. A total of 79 drugs were prescribed and the average number of drugs prescribed per prescription in acute therapy was 1.65. The most common drug prescribed was a combination of naproxen and domperidone for 30 participants (62.5%). The details of drugs for acute therapy of migraine are mentioned in figure 3.

FIG 3 - DRUGS PRESCRIBED FOR ACUTE THERAPY OF MIGRAINE IN STUDY PARTICIPANTS (n=48)


Drugs for acute therapy of migraine
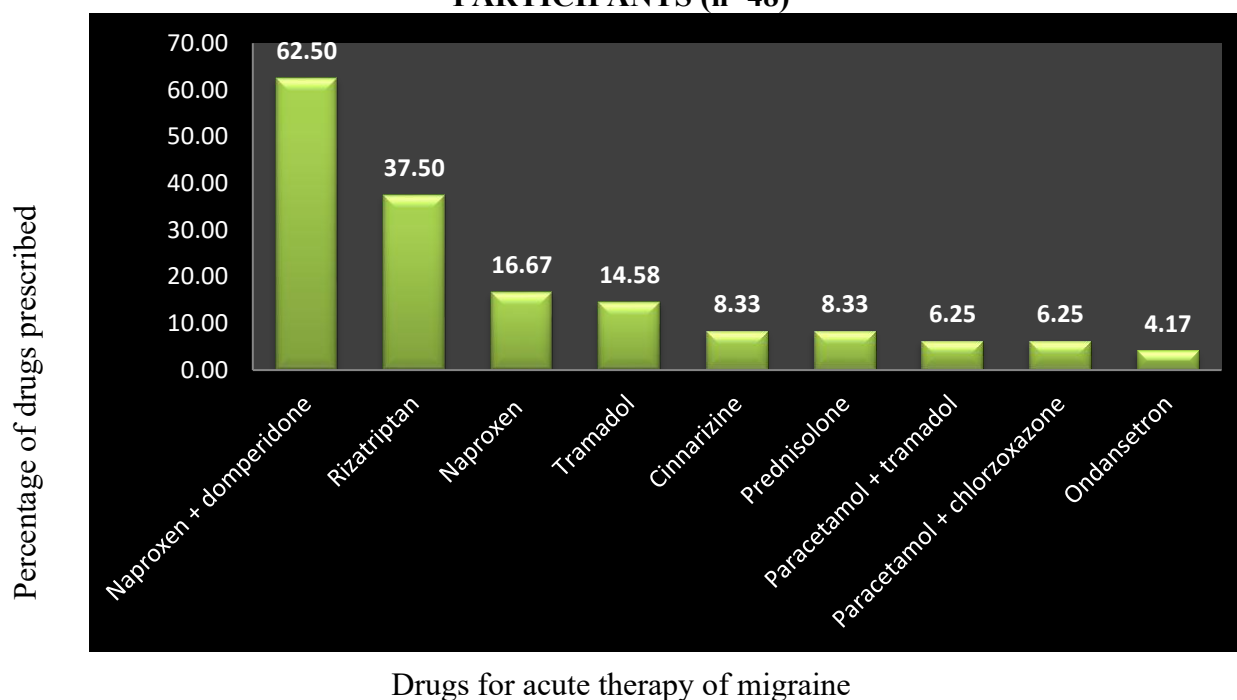
3.3 Drugs used for prophylaxis of migraine

A total of 152 participants were started on prophylaxis for migraine. A total of 220 drugs were prescribed in 152 prescriptions for prophylaxis of migraine.

The average number of drugs prescribed per prescription was 1.44. Out of these 152 prescriptions, 95 prescriptions (62.5%) contained a single drug, 46 prescriptions (30.26%) contained two drugs, 9 prescriptions (7.24%) contained three drugs and 2 prescriptions (1.31%) had four drugs.

In participants who received two drugs, a combination of propranolol and amitriptyline was most common, prescribed to 23 participants (50%). A combination of amitriptyline and topiramate was prescribed to 10 participants (21.7%), a combination of clonazepam and amitriptyline to 6 participants (13%), a combination of propranolol and topiramate to 5 participants (10.8%) and a combination of propranolol and etizolam to 2 participants (4.34%). The drugs used for prophylaxis of migraine are shown in figure 4.

FIG 4 – DRUG GROUPS USED FOR PROPHYLAXIS OF MIGRAINE IN STUDY PARTICIPANTS (n=152)
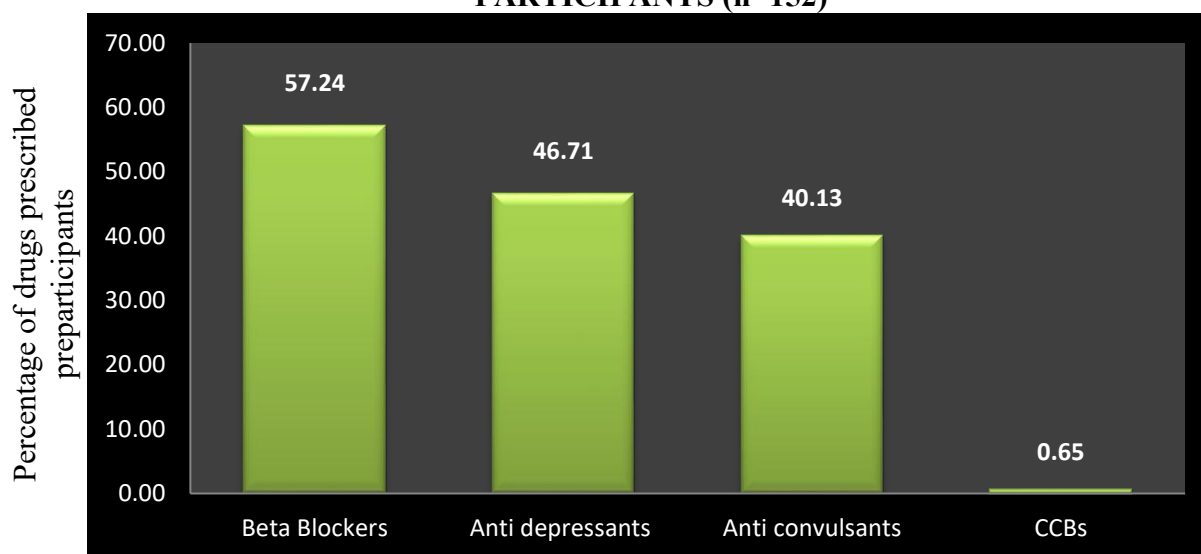
Drug groups used for prophylaxis of migraine

3.4 Drugs used as rescue medication for migraine

A total of 159 participants used rescue medication as a therapy for migraine. A total of 180 drugs were prescribed. The average number of drugs for rescue medication per prescription was 1.13. In this study, there were 21 participants who were prescribed two drugs as rescue medication. .

4. WHO CORE INDICATORS

4.1 Average number of drugs per prescription

The total number of drugs prescribed in 200 prescriptions was 657. The average number of drugs prescribed per prescription was 3.28. The details of drugs prescribed by generic name, percentage of injectable drugs and drugs from Essential Medicines List are shown in table 4.

Table 4: Drug Prescription Patterns Among Study Participants (N = 657)

Parameter	Value
Average number of drugs prescribed	3.28 ± 1.23
Maximum number of drugs prescribed	8
Minimum number of drugs prescribed	1
Total number of drugs prescribed	657
Drugs prescribed by generic name	209 (31.81%)
Injectable drugs prescribed	61 (9.28%)
Drugs from Essential Medicines List	418 (63.62%)

5. Comparison of HIT-6 Scores at baseline and at 3 months

Out of a total of 200 participants, 152 were started on prophylaxis for migraine. HIT-6 score was used to assess the health related quality of life in migraine patients. At baseline, the mean HIT-6 score was 58.44. At the end of 3 months, the mean score had reduced to 51. A reduction in HIT-6 score indicates a decrease in severity and disability associated with migraine. There was a statistically significant difference between HIT-6 score at baseline and at 3 months. (p value <0.0001). This is shown in figure 5.

FIG 5- COMPARISON OF HIT-6 SCORE AT BASELINE AND AT 3 MONTHS FOR MIGRAINE PATIENTS ON PROPHYLACTIC THERAPY
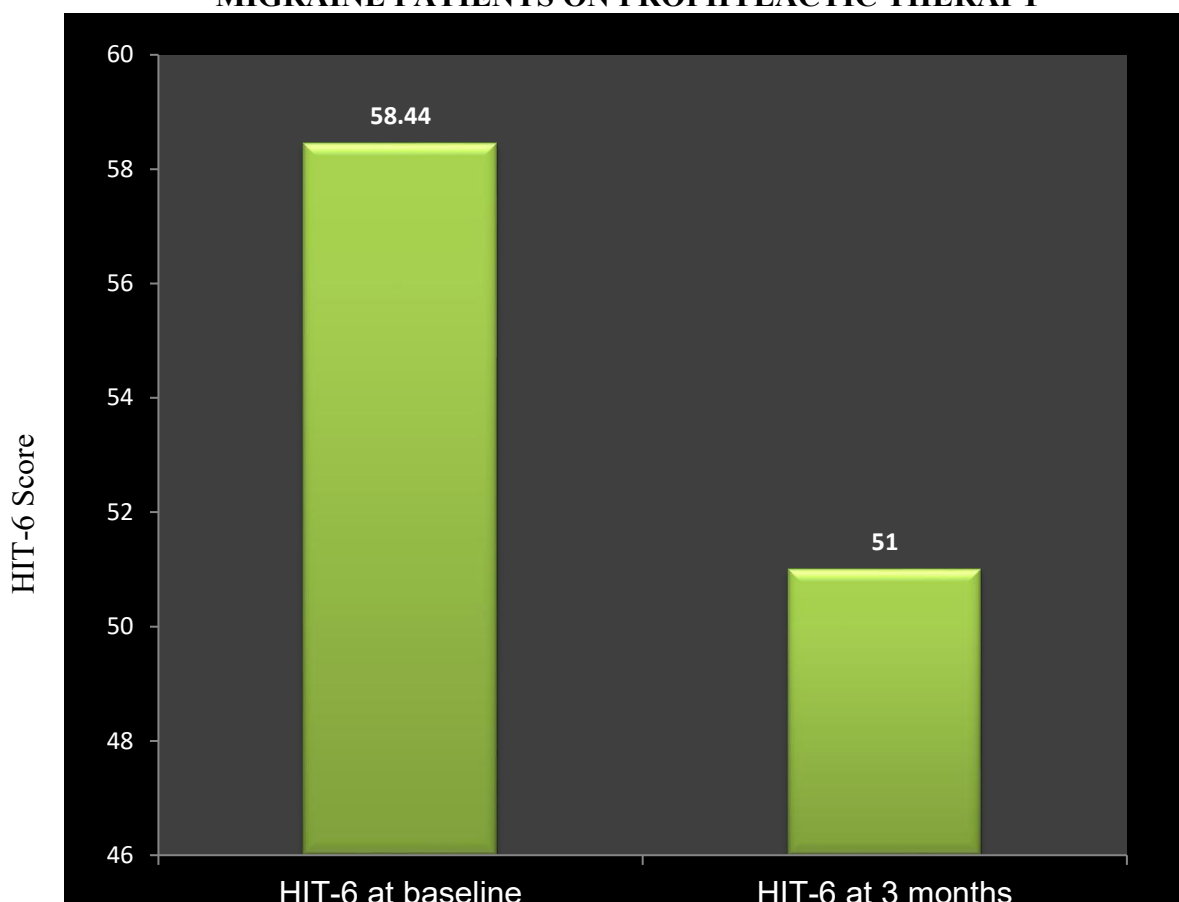
Discussion

This study was done to analyze the prescription pattern of drugs used for acute and prophylactic therapy for migraine and also to assess the change in quality of life in patients on prophylactic therapy. In this study, the mean age of the study participants was 35.6 years. There were a higher number of females (69%) as compared to males (31%). This study is in concordance with a large-scale UK real-world study, the mean age of participants was approximately 35 years, with a female predominance of nearly 70%, mirroring your study's demographics. It also reports on acute and prophylactic migraine medication patterns and includes patient-reported outcomes related to quality of life.[11] The current study group had a majority of the participants (67.5%) in the working age group of 18-40 years.

Out of 200 participants in this study, 135 participants (67.5%) presented with unilateral headache. A study conducted on comorbidity of Migraine and Psychiatric Disorders had a similar finding as it reported 59.8% of participants presented with unilateral headache, while 40.2% reported having bilateral headache.[12] In this study, the most common migraine subtype was migraine without aura, reported in 92% of the participants. An observational study on clinical pattern of migraine, reported migraine without aura as the most common presentation in 80% of the participants.[13] Migraine is accompanied with features such as photophobia, phonophobia, nausea, vertigo, vomiting and vertigo. In the present study, photophobia was the most common feature seen in 65% of the participants, followed by nausea seen in 50.5% participants. Similar findings were noted in a study conducted on pattern and prescription of migraine, which found photophobia (82%) to be the most common symptom, followed by nausea (76%).[14]

A migraine attack can be triggered by a variety of factors. In the present study, stress was the most common triggering factor which was noted in 53% of the patients. A study conducted by Rothrock D et.al on analysis of migraine triggers, reported stress as a triggering factor in 59% participants.[15]

In the current study, 48 participants (24%), out of a total of 200 participants received therapy for acute migraine. The most common drug prescribed for acute migraine was a combination of naproxen and domperidone in 62.5% of the participants. A study done in United Kingdom reported the use of a combination of naproxen and domperidone in 29.2% of the participants, which was significantly lower from our study.[11] This much higher figure could be because 50.5% participants had presented with nausea and 34.5% participants presented with vomiting in the current study, and both the drugs were indicated. Rizatriptan was prescribed to 37.5% of the participants in this study. Triptans are considered effective for the acute therapy of migraine according to the American Headache Society guidelines.[16] There were 152 participants (76%) in our study who received prophylactic therapy. In this study, propranolol was the most commonly prescribed (57.2%) drug for prophylaxis of migraine. According to the American Headache Society guidelines propranolol is a first-line drug for migraine prophylaxis.[17] In the present study, 71 participants (46.7%) were prescribed anti-depressants, a large proportion of which was amitriptyline and 61 participants (40.1%) were prescribed anti-convulsants. According to the American Academy of Neurology (AAN) guidelines anti-depressants and anti-convulsants are regarded as effective for prophylaxis of migraine and should be considered for prophylaxis of migraine.[5]

In the present study the average number of drugs prescribed for acute management of migraine was 1.65, while average number of drugs prescribed for prophylaxis of migraine was 1.44. This study is comparable to another study where an average of 1.5 drugs were used for prophylaxis of migraine.[14] WHO core prescribing indicators has developed a reference value such as percentage of injectables used which should be between 13.4-24.1%, which is higher as compared to in this study (9.2%).[18] The percentage of injectables is also low which could be due to the fact that migraine is not an emergency condition and consequently lesser number of admissions were required as injectables were used for in-patients only.

WHO core indicators also recommended that maximum possible drugs should be prescribed by generic name and drugs from the essential drug list.[18] The current study reported the number of prescriptions having drugs by generic name were 140 (70%) and the number of drugs prescribed by generic name were 209 (31.8%). The prescription of a low percentage of generic medicines is usually associated with preference of branded products.[7] However, generic prescribing rates are likely to increase with the regulatory guidelines which mandate their use. In this study, prescriptions containing a drug belonging to EDL were 97.5% and total number of drugs prescribed from EDL were 418 (63.1%). A study conducted to assess prescribing practices using WHO core prescribing pattern, reported that 100% of the prescriptions contained a drug belonging to essential drug list, which is comparable to our study.[18]

In the present study, for patients who were started on prophylaxis, the mean HIT-6 score at baseline was 58.4 and after 3 months of prophylaxis, it was 51. A decrease in HIT-6 is a measure of improvement in headache disability.[19] Our results are similar to a study conducted by Rendas-Baum et.al who used HIT-6 among chronic migraine patients using a botulinum toxin A as a prophylaxis in two clinical trials. In the study conducted, the mean HIT-6 score at baseline were 65.6 and 65.3. After twenty four weeks, the mean HIT-6 score was 58.7 and 58.4, respectively, in the two studies: the difference was statistically significantly different from the baseline score.[20] A study conducted to review the evidence for use of preventive migraine treatment reported that prophylaxis plays an important role in management of migraine. When a migraine patient is started on prophylaxis, the frequency of headache decreases and thus it improves the quality of life.[5]

Conclusion

The prescribing pattern of drugs used for migraine was according to the guidelines. There is a potential for improving drug prescribing by generic name and drugs prescribed from essential drug list. The average number of drugs prescribed per prescription is in line with the WHO core indicators. The use of drugs for migraine prophylaxis had a significant improvement on the quality of life for study participants, based on the HIT-6 scores.

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