RESEARCH ARTICLE

DRUG UTILIZATION AND QUALITY OF LIFE IN PATIENTS OF MIGRAINE AT A TERTIARY CARE HOSPITAL IN INDIA

[1]Medha Rawat, [2]Pranav Joshi, [3,*]Harsh Joshi, [4]Kartik Shah and [5]Supriya Malhotra

[1]Third MBBS student, NHL Municipal Medical College, Ahmedabad, Gujarat
[2]Assistant Professor, Department of Neurology, VS hospital, Ahmedabad, Gujarat
[3]Junior lecturer, Department of Pharmacology, NHL Municipal Medical College, Ahmedabad, Gujarat
[4]Associate Professor, Department of Pharmacology, NHL Municipal Medical College, Ahmedabad, Gujarat
[5]Professor and Head, Department of Pharmacology, NHL Municipal Medical College, Ahmedabad, Gujarat

ABSTRACT

Background: Migraine is a common neurological disorder associated with a significant disease burden. It is characterized by unilateral/bilateral severe pulsating headache. Insufficient data are available regarding the utilization pattern of available drugs for the prevention and management of migraine. Migraines can be severe enough to limit sufferers' causing significant lost productivity and decrements in health-related quality of life. **Objectives**: To study drug utilization pattern in patient of migraine in the outpatient department of neurology at a tertiary care teaching hospital. To assess the impact of migraine on Quality of life [QOL] of patients suffering from migraine. **Methods**: This cross-sectional observational study was conducted for 12 weeks. All patients either gender and age were included attending the neurology Outpatient Department and diagnosed to have migraine. Demographic profile of the patient and drug data was collected. Tools of QOL in migraine are included: Migraine disability assessment (MIDAS) score, Headache Disability Index (HDI) score and Headache Impact Test (HIT-6) score. **Results**: Total 65 patients were included; 53 (81.5%) females and 12 (18.5 %) males. Most of the patients were of 21-50 years of age. Precipitating factors were travel (30.77%) followed by mental tension (18.46%) and irregular food intake/ hunger (15.38%). Common symptoms were photophobia (53.8%) and phonophobia (50.7%). Drugs prescribed propranolol 43 (66.1%), amitriptyline (21.5%), naproxen (6.1%) and paracetamol (6.1%). MIDAS score; most patients 36 (55.3%) presented with mild disability. 52 (80%) patients answered that they feel severe migraine pain. **Conclusions**: We observed that migraine is more common in females patients. Most common drugs used alone were propranolol, amitriptyline, naproxen and paracetamol. Most patients felt severe headache which has affected their day-to-day life disabling that it impacted their ability to do even daily routine work.

INTRODUCTION

Migraine is a common neurological disorder associated with a significant disease burden. It affects day to day activities, work, and social and leisure activities which has a massive impact on a person's quality of life (Leonardi M, 2005, Linde M, 2004). It is encountered worldwide including India. Based on large epidemiologic studies from around the world, the prevalence of migraine is about 18% in women and 6% in men (Stovner *et al.*, 2007).It is an episodic headache, become chronic if not treatedpromptly and effectively.

Most often it is poorly diagnosed and managed in developing countries like India. It is characterized by unilateral/bilateral severe pulsating headache accompanied by typical autonomic symptoms such as nausea, vomiting, photo- and phonophobia (Freitag FG, 2007). Treatment of acute attack and prophylactic therapy is important for patients with frequent or long-lasting migraine headache (D'Amico D, 2006, Silberstein SD, 2003, Goadsby P, 2006). Insufficient data are available regarding the utilization pattern of available drugs for the prevention and management of migraine. Neurologists give medication for prophylaxis and management of migraine to increase proper and satisfactory control of headache. Headache control may be achieved by the pharmacological management in most of the patients. Quality of life has been defined as the ability of an individual to play a role in society and to enjoy fully their role

*Corresponding author: **Harsh Joshi**
Junior lecturer, Department of Pharmacology, NHL Municipal Medical College, Ahmedabad, Gujarat

as a citizen, with an independent social status. Migraines can be severe enough to limit sufferers' activities both at work and at home, and there may be significant psychological impact between attacks and thus causing significant lost productivity and decrements in health-related quality of life. hese patients also experience greater emotional distress and disturbed vitality and sleep than non migraineurs, even between attacks (Martin *et al.,* 2000). Substantial research is not done regarding drug utilization and Quality Of Life (QOL) in patients suffering from migraine. This study depicts drug use pattern in patients with migraine in India. Depression, anxiety and various other disorders are very commonly associated with migraine. Research regarding migraine headaches will explore the social network impacts of migraine headache. *Hence, our aim is t*o study drug utilization pattern in patient of migraine in the outpatient department of neurology at a tertiary care teaching hospital. To assess the impact of migraine on Quality of life [QOL] of patients suffering from migraine.

MATERIALS AND METHODS

This cross-sectional observational study was conducted after taking the ethical clearance from the Institutional Ethics Committee (IEC) for 12 weeks. Informed and written consent was obtained from all the patients included in the study.

Study Population

Inclusion criteria: All patients either gender and age attending the neurology Outpatient Department (OPD) at a tertiary care teaching hospital and who are diagnosed with migraine. Patients willing to give informed consent for the study and agreeing to answer questions. related to Quality Of life (QOL).

Exclusion criteria: Subjects with major neurological disorders (e.g. epilepsy, space occupying lesions, neurodegenerative disorders), chronic daily headache (undiagnosed or mixed type) and Substance abuse disorders will be excluded from the study. Patients not willing to give informed consent.

Data collection: A total of 65 patients who were diagnosed with migraine had been enrolled in the study. Patients were diagnosed with migraine (with or without aura) according to the International Classification of Headache Disorder, 2nd edition (ICHD-2) by the same neurologist (Cephalalgia 2004).

Demographic profile of the patient (age and gender), type, etiology of headache, drug data (group and name of the drug, mono or polytherapy, number of drugs / prescription, formulation) was collected in a specially designed Case Record Form [CRF]. The Quality of Life (QOL) was assessed once at the time of enrolment of patients and follow up visits for 12 weeks. Tools of QOL in migraine are included: The questionnaires were also analyzed like Migraine disability assessment (MIDAS) score (Stewart, 1999), Headache Disability Index (HDI) score (Jacobson, 1994), Headache Impact Test (HIT-6) score (Kosinski *et al.,* 2003).

Data analysis: The data will be recorded in Microsoft Excel Worksheet. All data analysis will be performed using Statistical Package for the Social Sciences (SPSS) version 24.0 (IBM Corporation, Armonk, NY, USA). Participant demographics will be analyzed using descriptive statistics and analysis of variance.

RESULTS

The study enrolled 65 patients for duration of 12 weeks. Among the total study population, there were 53 (81.5%) females and 12 (18.5 %) males (Table 1). Most of the patients were from 21-50 years of age. The youngest and the oldest patient in our study were 12 and 72 years old respectively. About 30% patients were obese in our study.

Table1. Demographic profile of the study population with percentage (n=65)

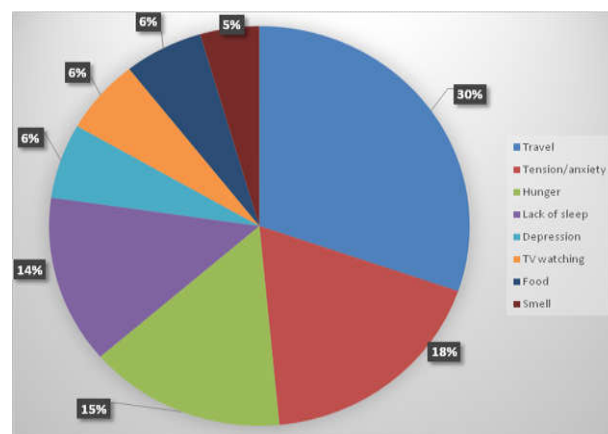| Feature	Male	Female	Total (%)
Gender	12	53	65 (100%)
Mean age (±SD yr)	18.7	19.2	18.9 (7.5)
Mean age of onset (±SD yr)	21.1 (7.4)	20.6 (8.6)	20.8 (8.9)
11-20	2	4	6 (9.23)
21-30	7	10	17 (26.15)
31-40	6	14	20 (30.77)
41-50	4	11	15 (23.08)
51-60	1	4	5 (7.69)
61-70	0	1	1 (1.54)
>70	0	1	1 (1.54)

Figure1. Distribution of precipitating factors for headache (n= 65)

Table 2. Characteristics of migraine headache in study population (n=65)

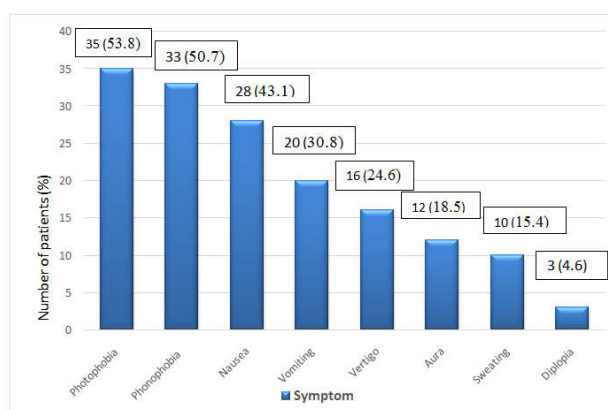| Parameter	No of patients (n=65)	Percentage (%)
Location		
Unilateral	29	44.6
Bilateral	33	50.7
Unilateral changing site	3	4.6
Pulsatile	40	61.5
Constricting	5	7.7

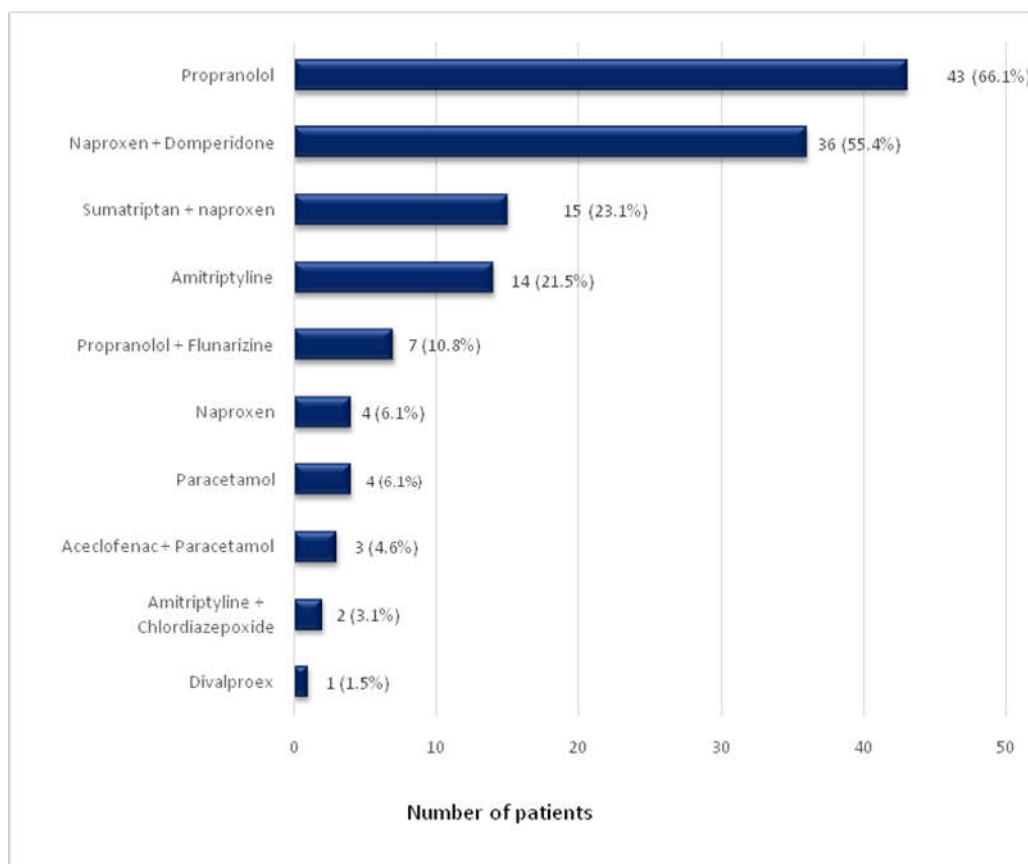**Figure 2. Various symptoms in patients of migraine (N=65)**

Figure 3. Drug utilization pattern among prescribed drugs

Table 3. Analysis of prescriptions for therapy in migraine

Parameter	Number
Total no. of drugs prescribed	145
Total no. of drugs prescribed through oral route	145
Average no. of drugs prescribed per prescription	2.23
Drugs prescribed by generic name	20%
Number of fixed dose combinations	63 (43.4%)

Table 4. Migraine disability assessment (MIDAS) score

MIDAS GRADE	Disability	MIDAS SCORE	Patient Frequency
I	Little or no disability	0-5	7(9.2%)
II	Mild disability	6-10	36 (55.3%)
III	Moderate disability	11-20	20(30.7 %)
IV	Severe Disability	21+	2 (3.07%)

Table 5. Headache Disability Index (HDI) score

HDI percentage	Disability	Patient frequency
10-28%	Mild disability	11(16.9%)
30-48%	Moderate disability	33(50.7%)
50-68%	Severe Disability	18(27.6%)
>=72%	Complete Disability	3(4.6%)

Table 6. Headache Impact Test (HIT) score

		Total number of patients (N = 65)				
		Never	Rarely	Sometimes	Very often	Always
Q-1	How often is the pain severe?	0	2	11	36	16
Q-2	How often do headaches limits daily activities ?	0	8	25	29	3
Q-3	When you have a headache, do you wish you could lie down?	0	0	0	40	25
Q-4	In the past 4 weeks, have you felt too tired due to headaches?	0	0	59	3	3
Q-5	In the past 4 weeks, have you felt fed up or irritated due to headaches?	0	0	15	26	24
Q-6	In the past 4 weeks, how often did headaches limit your ability ?	0	18	35	10	2

A number of precipitating factors were observed (Figure1). Amongst these, the commonest was travel (30.77%) followed by mental tension (18.46%), irregular food intake/ hunger (15.38%), lack of sleep (13.85%), depression (6.15%) and excessive TV watching (6.15%). Some patients reported, precipitation of attacks by certain foods (fish, cheese, and cold drinks), perfumes, agarbatti, petrol, phenyl and cigarette smoke. In this study, about 51% patients had bilateral headache while 45% patients had unilateral headache. Few patients reported that they initially had unilateral headache but it changes side with duration. Most of the patients (61.5%) had pulsatile headache. (Table-2) In our study the majority of patients had photophobia (53.8%) and phonophobia (50.7%) as their migraine symptoms. Patients also experienced symptoms like nausea (43.1%), vomiting (30.8%), vertigo (24.6%), aura (18.5%) and sweating (15.4%). The details of the symptoms experienced by the study population are presented in the Figure-2.

Most common drugs used alone were propranolol 43 (66.1%). It is followed by amitriptyline (21.5%), naproxen (6.1%), paracetamol (6.1%) and divalproex (1.5%). Many drugs were prescribed in combinations/ polytherapy like Naproxen + Domperidone (55.4%), Sumatriptan + naproxen (23.1%), Propranolol + Flunarizine (10.8%) and Aceclofenac + Paracetamol (4.6%). (Figure-3). We had also analyzed the prescriptions in various parameters as depicted in table-5. Total 145 drugs were prescribed to 65 patients. Average number of drugs prescribed per prescription was 2.23. About 20% drugs were prescribed by generic name. In total 63 (43.4%) drugs were given as fixed dose combinations. (Table-3). Health-related quality of life (HRQoL) in patients with migraine is done to assess the effect of migraine and its treatment on patients' HRQoL to measure three meaningful dimensions: Role function-restrictive, Role function preventive and Emotional function.

The quality of life in accordance with MIDAS score is represented in Table 4.MIDAS grade is given according to MIDAS score. Most patients presented with mild disability i.e. 36 patients (55.3%) followed by moderate disability (20 patients; 30.7%). Seven patients (9.2%) had little or no disability. Only 2 patients (3.07%) had severe disability. Table 5 depicts Headache disability index (HDI) score in 65 patients of our study. Most patients were presented with moderate disability (33 patients; 50.7%) with an HDI percentage in the range of 50-68% followed by 18 patients (27.6%) who had severe disability in the range of 50-68%.Total 11 patients (16.9%) were presented with mild disability. Only 3 patients (4.6%) had HDI percentage>=72% with complete disability. Headache Impact Test (HIT) score was also calculated as depicted table-6. Many patients (52; 80%) answered that they feel severe migraine pain. About 100% patients wish they could lie down during attack of migraine. 50 patients felt fed up or irritated due to migraine pain (Table-6).

DISCUSSION

We have studied 65 patients in the neurology OPD. Among the total study population, there were 53 (81.5%) females and 12 (18.5 %) males. The Female to male ratio in our study was 4.4:1. It is very higher than a study done in India by Subhransu *et al* which observed female to male ratio was 2.1:1. (Ware JE, 2000, Subhransu Jena *et al.,* 2015).

The literature from various studies from western society also suggests, migraine is more frequent in the female population. (Stewart W F, 1992, Silberstein SD, 2000)In a study conducted by Richard B Lipton et al., the prevalence of migraine among females was found to be 18.2% and that in males was 6.5% (Richard B L, 2001). In another study found that the prevalence of migraine was high in women in reproductive age group. This predominance can be attributed to the hormonally driven changes in females. (Silberstein SD, 2000).In the present study, majority of patients (20; 30.77%) were in the age group 31-40 years followed by 21-30 years (17; 26.15%). This is almost similar to a study by Ramesh et al showed age range of 21 -30 (44.6%) followed by 31 -40 (31%). (Ramesh et al., 2014)Although it is more common in young age, it can affect children also. The youngest patient was 12 year old. It is also observed that it is common in obese patients. Prevalence of obesity in our population was 30 percent. Obesity may be one factor which can lead to migraine. Many patients were obese, therefore controlling weight may have a significant impact on migraine.

Trigger factors are also important for migraine as these may be helpful as indicators to treat the cause and severity of migraine attack. The common precipitating factors in our study were travel (30.77%), anxiety/ mental tension (18.46%), irregular food intake/ hunger (15.38%), lack of sleep (13.85%), depression (6.15%) and excessive TV watching (6.15%). These results are similar to a study revealed various trigger factors like travel (78.02%) followed by tension, hunger, skipped meal, fasting, insomnia, depression (Subhransu Jena *et al.,* 2015). Travel has a significant impact over the occurrence of migraine. Thirty percent patients reported that they develop migraine episodes during travel. It may be related to physical and mental stress occurring during the travel period (Bener, 2000). A proper uninterrupted sleep or some amount of rest in between work period may decrease its frequency (Stewart *et al.,* 1991).

Watching television for long hours is associated with migraine. This was common in children. This form of migraine headache can be prevented easily (Bener, 2000. Certain foods and perfumes lead to migraine inour study. Some patients reported, precipitation of attacks by certain foods (fish, cheese, cold drinks), perfumes, agarbatti, petrol, phenyl and cigarette smoke also. This is similar in other studies also (Stewart *et al.,* 1991). So, avoiding these factors is useful to prevent migraine. In this study, about 50.7% patients have bilateral headache. The nature of headache is mostly pulsatile (61.5). A study reported (26.7%) patients experienced unilateral pain and 40.2% patients with bilateral pain. 71.5% patients felt pulsatile pain. (Subhransu Jena, 2015) Most patients had photophobia (53.8%) and Phonophobia (50.7%) as their migraine symptoms. Other symptoms were nausea (43.1%), vomiting (30.8%). In a study conducted by Ramesh et al., phonophobia (91.3%) and photophobia (74.8%) were more frequently seen symptoms than the other symptoms. (Ramesh et al., 2014) In another study by Richard B L, the most frequently reported symptoms were in the order, pulsatile pain (85%), photophobia (80%) and phonophobia (76%) (Richard B L, 2001). For prophylaxis of migraine, propranolol is most frequently used. Studies have shown Beta blocker (60-80%) were effective in reducing attack frequency by more than50%. (Silberstein SD, 2002) Although propranolol is the most commonly prescribed drug in this class, there is no evidence of difference in efficacy between propranolol and other ß- blockers (atenolol,

metoprolol or bisoprolol). (Rapoport A, 2008) Among antidepressant, amitriptyline was most commonly used. Most commonly used drugin our study was propranolol (43; 66.1%) patients followed by amitriptyline (21.5%), naproxen (6.1%), paracetamol (6.1%) and divalproex (1.5%). Silberstein et al showed beta blockers (60-80%) were effective in reducing attack frequency by more than50% patients (Silberstein SD , 2002). In our study, for acute attack, NSAIDs alone were prescribed in 80% of cases either alone or in combination with ergots and triptans cases. For acute therapy sumatriptan was used in 23.1%cases. NSAIDs are a usual first-line therapy for mild to moderate migraine. naproxen for moderate to severe migraine showed effective forshort-term pain relief. (Suthisisang *et al.,* 2007). Paracetamol was found to be effective in reducing headache. (Meredith, 2003) The practice parameters by the American Academy of Neurology recommend sumatriptan, ergotamine and its derivatives to be more effective than NSAIDs for acute attack.(Silberstein SD,2000) Higher use of NSAIDs in this study could be due to easy availability and less cost.

European study, by order of frequency, the prophylactic treatments administered were topiramate (43%), β-blockers (18%), flunarizine (17%), amitriptyline (14%). (López Hernández *et al.,* 2009). A France study revealeddihydroergotamine and β-blockers were most commonly used in migraine prophylaxis. (Lantéri-Minet, 2000). Many drugs were prescribed in combinations polytherapy like Naproxen + Domperidone (55.4%) and Sumatriptan + naproxen (23.1%). Patients were given on an average of 2.23 drugs per prescription. In 43.4% cases, drugs were given as fixed dose combinations. This is similar to a study by Subhransu et al. (Subhransu Jena, 2015).

In our study, Most of patients (36;55.3%) presented with mild disability as per total MIDAS score. A similar study reported that 44.5% patients hadmild disability MIDAS total score. (M Jamil Laghari, 2012). Dwajani. S found that57.72% patients had mild disability MIDAS score. In this study, moderate disability is seen in 20 patients (30.7%) which is higher than a study by Dwajani S (13.01%) (Dwajani, 2014) Most patients said that their headache was severe and it affected their day-to-day life. They get agitated and angry very easily. According to Headache Disability Index (HDI) score, most patients were presented with moderate disability (33 patients; 50.7%) with an HDI percentage in the range of 50-68%. This is similar to a study by Brandes et al. (Brandes *et al.,* 2004). We had also calculated Headache Impact Test (HIT) score. Total 6 questions to be asked. Most of the patients answered very often and sometimes. On literature search, this is the first study to score HIT score in migraine patients of India. To our knowledge, this is the first study involves drug utilization pattern and various quality of life indicators in patients of migraine. It is very important to improve the therapeutic outcomes and the overall quality of life of patients suffering from migraine, the proper education about their disease, medication and life style changes are very much essential.

Conclusion

We observed that migraine is more common in females and obese patients. The common precipitating factors were travel, anxiety/ mental tension and irregular food intake/ hunger. Most common drugs used alone were propranolol, amitriptyline, naproxen and paracetamol. Many drugs were prescribed in combinations/ polytherapy like Naproxen + Domperidone and

Sumatriptan + naproxen. Most patients felt severe headache which has affected their day-to-day life. They get agitated and angry very easily. They were unable to sleep properly at night. They generally felt tired. Most patients reiterated that they felt better while lying down over the bed and while taking rest. Migraine control may be achieved by the pharmacological management, decreasing weight and regular food habit. *Further studies with more patients and for more duration are required to identify prescription pattern and quality of life.*

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