Original Article

A clinical study on presenting features and prescription pattern for Migraine in a Tertiary care hospital of Eastern India.

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Abstract

Migraine is the leading cause of headache-related disability in the world. There are different pharmacological options to treat acute attack and prophylaxis of Migraine. We conducted a cross-sectional study to observe prescription pattern of migraines in eastern India and find its association with severity of the disease. We collected data from 75 Migraine patients who attended General medicine outpatient department. It was found that Paracetamol and NSAIDs are mainly used to terminate acute attack and Amitriptyline for prophylaxis of Migraine. Multidrug therapy with combinations of antidepressant, anticonvulsant and Flunarizine is used in patients with relatively high Migraine Disability Assessment Score (MIDAS). The prescription pattern we found in our study was found appropriate as per current treatment guidelines.

Keywords: Migraine, MIDAS, NSAIDs, Amitriptyline

1. Introduction

Headache is a common ailment in the general population. Globally, it has been estimated that about 50% of adults suffer from headache at least once within previous year.[1] The types of headaches commonly encountered are Tension headache, Migraine, Trigeminal autonomic or other miscellaneous type. [2] Among them, Migraine is the leading cause of headache-related disability in the world. It is characterized by unilateral episodic cephalalgia in presence or absence of various neurologic dysfunction. Association of nausea, photophobia or phonophobia is common. It is prevalent more in young age group and mostly in women. A recent study in eastern India found Migraine prevalence was 14.12% and showed similar female predominant trend in demography also.[3]

The pharmacological options for termination of acute attack are Paracetamol, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), 5-HT 1B/1D receptor agonists and Dopamine receptor antagonists. For prophylaxis of Migraine Beta Blockers, Antidepressants, Anticonvulsants and Flunarizine are used.[4] There are differences in prescription pattern of Migraine in different countries. A study in Finland showed NSAIDs were prescribed more than Triptans in acute attack.[5] Similar observations were found in a large database-based study in Germany analyzing 56823 prescriptions.[6]

A study in India showed NSAIDs are most commonly used drug for acute attack and beta blockers for prophylactic therapy.[7] We could not any study in eastern India to address the prescription pattern of Migraine of different severity. Therefore, this study is planned with an objective of exploring demographic details and pattern of prescriptions among Migraine patients and to compare it with available guidelines.

Editor's comment

1. Migraine is a common ailment.(14.12% prevalence)
2. Prescription pattern in acute and recurring attacks include cost effective drugs like NSAIDS and Amitryptilline in Eastern India
3. Use of Betablockers and anticonvulsants are less in this study than other countries.

Primary objective of this study was to find prescription pattern to manage acute attack of Migraine and prevent frequent attacks of Migraine and observe the association of prescription pattern with severity of Migraine.

2. Materials and Methods

The cross-sectional observational study was conducted over three months period (August 2019 to October 2019) in the General Medicine Outpatient Department of ESI-PGIMSR and ESIC Medical College, Joka. The study protocol followed the principles expressed in the Helsinki Declaration of 1983 and received prior approval from Institutional Ethics Committee. Informed consents were obtained from all participants. The study population included patients of either sex and age more than 12 years attended General Medicine Outpatient Department with a diagnosis of **'Migraine'** according to International Headache Society Classification characterized by 2 of the following criteria at least Unilateral pain, Throbbing pain, Aggravation by movement, Moderate or severe intensity. It should be accompanied by either Nausea/Vomiting or Photophobia/ Phonophobia.[2] We excluded patients with recent history of CNS infection or any major medical illness such as malignancy, autoimmune disorder and co-existent neurological disorder or a case where attending physician believes any other non-Migraine diagnosis more likely.

We used Non-probability convenient sampling method for

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this study. All the patients matching the inclusion criteria during the study period were included. We could recruit 75 patients during the study period.

Detailed history related to Migraine and other co-morbidities were collected and routine physical examinations were performed for any abnormality. Severity of current episode of headache was assessed using a Visual Analogue Scale of pain by the patient himself. We used **Migraine Disability Assessment Score (MIDAS)** for assessing present disease activity in migraine patients. MIDAS is a questionnaire designed to measure headache-related disability, and to identify patients with high treatment needs.[8] It is a 7-item questionnaire (with 5 scored items) where respondent needs to provide the number of days he suffered from debilitating headache in last 3 months.

The study specific data was collected and entered in a case report form (CRF) specifically designed for this purpose. The data from the CRF were transcribed onto an excel database and analyzed by R version 3.5.1 and R Studio version 1.0.136 (R foundation) statistical software (Language). Data were summarized by routine descriptive statistics and comparison between groups was done using Student's Unpaired t-test for variables showing parametric distribution by Shapiro-Wilk test. For non-parametric data, we used Wilcoxon rank sum test for between group comparison. P value< 0.05 was considered as statistically significant.

3. Results

The study population included 75 patients with diagnosis of Migraine recruited from General Medicine Outpatient Department of ESI-PGIMSR and ESIC Medical College, Joka, West Bengal, India. Most of the patients were female (n = 71, 94.7%) around 40 years of age. Baseline parameters in **Table 1** shows mean duration of present episode were 4.13 days and mean duration of disease was 7.87 years.

Parameters	Mean (Standard Deviation) N=75
Age in years	38.6 (12.0)
Current headache episode duration in days	4.13 (2.02)
Total disease duration in years	7.87 (4.92)
Pulse rate (per minute)	76.8 (8.95)
Systolic Blood Pressure	117 (5.79)
Diastolic Blood Pressure	76.9 (3.98)

Table 1: Baseline parameters of study participants

Mean severity of headache by a self-scored visual analogue scale was 6.79 with a standard deviation of 2.29 indicating most of the patients suffered from severe headache. **Table 2** shows the characteristics of migraine in study participants. It was commonly associated with nausea (59%), photophobia (82.7%) or phonophobia (773%). Majority of the subjects reported 'throbbing' type of unilateral headache which sometimes aggravated by movement.

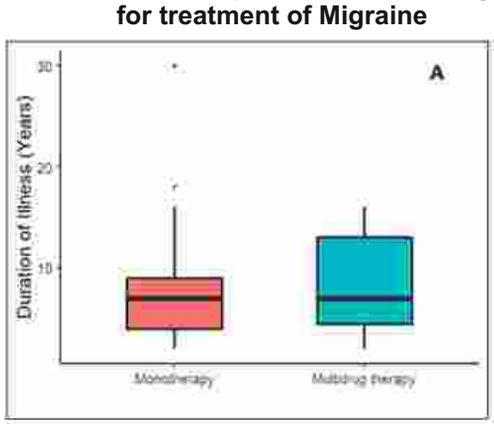
Table 3 shows the prescription pattern of migraine therapy. Drugs to control acute attack were required for 21.3% cases. Amitriptyline was the mainstay of migraine prophylaxis

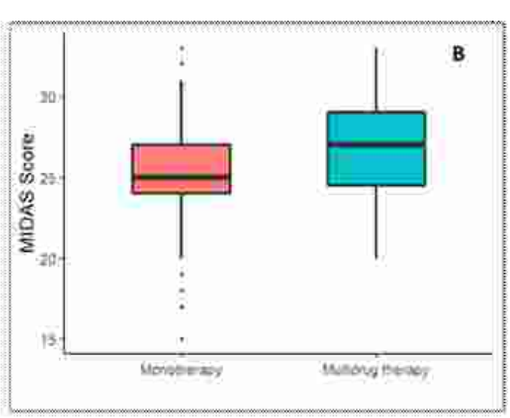
Presenting Symptoms	Number (Percent) N=75
Unilateral headache:	45 (60.0%)
Throbbing:	63 (84.0%)
Aggravated by movement:	47 (62.7%)
Nausea:	59 (78.7%)
Vomiting:	44 (58.7%)
Photophobia:	62 (82.7%)
Phonophobia:	58 (77.3%)
Scalp tenderness:	19 (25.3%)
Light headedness:	3 (4.00%)
Visual disturbance:	2 (2.67%)
Convulsion:	0 (0%)
Vertigo:	73 (97.3%)
Aura:	51 (68.0%)
Family history:	22 (29.3%)

Table 2: Characteristics of headache of study participants

Pharmacotherapy	Number (Percent) N=75
Drugs to control acute attack (Paracetamol/NSAIDs):	16 (21.3%)
Beta Blocker (Propranolol):	9 (12.0%)
Amitriptyline:	68 (90.7%)
Anticonvulsant (Sodium Valproate):	12 (16.0%)
Flunarizine:	8 (10.7%)
Any other drug	0 (0%)

Table 3: Prescription pattern of drugs for treatment of Migraine





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Questionnaire componentof MIDAS Score	Overall N=75 Mean (SD)	Monotherapy N=52 Mean (SD)	Multi-drug therapy N=23 Mean (SD)	p-value (Student' s t-test)
1. On how many days in the last 3 months did you miss work or school because your headaches?	6.49 (2.31)	6.23 (2.01)	7.09 (2.84)	0.200
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches?	4.47 (1.73)	4.44 (1.59)	4.52 (2.04)	0.869
3. On how many days in the last 3 months did you not do household work because of your headaches?	4.91 (1.76)	4.87 (1.68)	5.00 (1.98)	0.778
4. How many days in the last 3 months was your productivity in household work reduced by half of more because of your headaches?	5.05 (1.98)	4.87 (1.93)	5.48 (2.06)	0.234
5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?	4.64 (1.78)	4.56 (1.59)	4.83 (2.17)	0.597
MIDAS Score	**25.6 (3.88)**	**25.0 (3.86)**	**26.9 (3.64)**	**0.041**

Table 4: MIDAS score in study participants. Mean values of Individual item and total MIDAS score are higher in multidrug therapy group than monotherapy group.

prescribed to about 90% of study participants. Beta blocker Propranolol was used for 12% of cases and anticonvulsant like Sodium Valproate for 16% of cases. Flunarizine was used in 10.7% of cases. 23 patients (30.66%) required more than one drug as prophylaxis and Amitriptyline was commonly combined with Valproate.

As shown in **Figure 1A**, total duration of illness was similar in patients receiving multidrug therapy (Median = 7 years, IQR = 5 year) and monotherapy (Median = 7 years, IQR = 8.5 years) and as expected, difference was not statistically significant (p-value = 0.526, Wilcoxon rank sum test).

But there was a significant difference in total MIDAS score between monotherapy and multidrug therapy group (p-value = 0.041, Student's Independent t-test). (**Figure 1B**) Difference between individual components of MIDAS has been shown in **Table 4**. All the items have higher mean value in multidrug therapy group, but the difference was not statistically significant.

Figure1: Box and Whisker's plot showing relation of Duration of illness (1A) and MIDAS Score (1B) with drug therapy. The box and whisker plots denote median, interquartile range and range. The dots indicate outlier values

4. Discussion

Migraine is a common public health problem affecting all parts of society including all vulnerable sections of the population. In a developing country like India, new high cost therapy is inaccessible to those who require them the most. Prevalence and impact of migraine has been studied in Government based health studies in USA has shown women predominance particularly burdensome on female of child-bearing age. A study was carried out in medical students in our country where 42% fulfilled the IHS criteria of migraine.[9,10]

The demographics in this study is similar to other studies of Migraine patients conducted in India. Females of reproductive age group were more commonly affected by the condition.[7,11] We found unilateral headache associated with nausea, photophobia and phonophobia and duration of headache episodes more than 72 hours in most of the patients. All these findings were consistent with several migraine studies.[3,4,11,13] However, we found very high prevalence of migraine with aura (68%) in our study where most resources report this below 30%. A pan-India cross-sectional study reported mean MIDAS score of 27.28 which indicates most of the patients suffered from

moderate to severe migraine (Grade 3 and 4). [8,13] We found overall MIDAS score of 25.6 (SD = 3.88) which was close to their observation.

In our study, Paracetamol and NSAIDs were most common drug used to terminate acute attack and Amitriptyline (90.7%) for prophylaxis of Migraine followed by Valproate, Propranolol and Flunarizine. This trend is evidently different from other studies in India where beta-blockers are mainstay of therapy for prevention of acute episode rather than antidepressants. [7,13])Use of beta-blocker is more common in other developed countries like Germany, USA and Australia.[6,12,14] However, cost-effective studies showed Amitriptyline is most cost-effective drug for migraine prophylaxis.[15,16] This might be a reason for such high prescription rate of this drug here in eastern zone of India.

In a cross-sectional study, Jena et al. Reported 44.7% of migraine patients received (n = 882) more than one anti-migraine drugs for prevention of recurrent attacks. (7)We could not find any study comparing the severity of Migraine with polypharmacy. In our study, 30.66% patients were on multi-drug therapy who had significantly more MIDAS score than those on monotherapy (p value = 0.041). However, total duration of disease was not significantly different between two groups. It can be assumed that progression of disease requiring multi-drug therapy does not depend upon the duration of disease, but extent of disability caused by it.

5. Limitations

Association of comorbid conditions and adverse effect profile of the drugs could not be analyzed due to small sample size for time and resource constraints.

6. Conclusions

In eastern India, medications used to treat acute attack and prophylaxis of Migraine were found appropriate as per current treatment guidelines. Mostly cost-effective drugs like Paracetamol and Amitriptyline were prescribed and multi-drug therapy were given to patients with higher disability measured by MIDAS score.

Conflict of interest none.

Funding none.

7. References

1. World Health Organisation. Headache disorders [Internet]. [cited 2020 Feb 12]. Available from: https://www.who.int/news-room/fact-sheets/detail/headache-disorders
2. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018 Jan 25;38(1):1211.
3. Ray B, Paul N, Hazra A, Das S, Ghosal M, Misra A, et al. Prevalence, burden, and risk factors of migraine: A community-based study from Eastern India. Neurol India. 2017;65(6):1280.
4. Goadsby PJ. Migraine and Other Primary Headache Disorders. In: Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 20th ed. McGraw-Hill Education; 2018. p. 3096108.
5. Sumelahti M-L, Mattila K, Sillanmäki L, Sumanen M. Prescription patterns in preventive and abortive migraine medication. Cephalalgia. 2011 Dec 13;31(16):165963.
6. Jacob L, Kostev K. Prescription Patterns and the Cost of Migraine Treatments in German General and Neurological Practices. Pain Pract. 2017 Jul;17(6):74752.
7. Jena S., Jena M, Dash M, Mishra S, Behera IC. Migraine: Pattern of prescription & adverse drug reaction profile in a tertiary care teaching hospital. J Pharm Sci Res. 2015;7(3):1116.
8. Stewart WF, Lipton RB, Kolodner KB, Sawyer J, Lee C, Liberman JN. Validity of the Migraine Disability Assessment (MIDAS) score in comparison to a diary-based measure in a population sample of migraine sufferers. Pain. 2000 Oct;88(1):4152.
9. Menon B, Kinnera N. Prevalence and characteristics of migraine in medical students and its impact on their daily activities. Ann Indian Acad Neurol. 2013 Apr;16(2):221.
10. Burch R, Rizzoli P, Loder E. The Prevalence and Impact of Migraine and Severe Headache in the United States: Figures and Trends From Government Health Studies. Headache J Head Face Pain. 2018 Apr;58(4):496505.
11. Panda S, Tripathi M. Clinical profile of migraineurs in a referral centre in India. J Assoc Physicians India. 2005;
12. Shao E, Hughes J, Eley R. The presenting and prescribing patterns of migraine in an Australian emergency department: A descriptive exploratory study. World J Emerg Med. 2017;8(3):1706.
13. Singh S, Sarda K, Hegde R. A pan-india study to assess the quality of life, symptom profile and management trends in patients with migraine: A cross-sectional study. J Assoc Physicians India. 2017
14. Takaki H, Onozuka D, Hagihara A. Migraine-preventive prescription patterns by physician specialty in ambulatory care settings in the United States. Prev Med Reports. 2018 Mar 1;9:627.
15. Linde M, Steiner TJ, Chisholm D. Cost-effectiveness analysis of interventions for migraine in four low- and middle-income countries. J Headache Pain. 2015;
16. Yu J, Smith KJ, Brixner DI. Cost effectiveness of pharmacotherapy for the prevention of migraine: a Markov model application. CNS Drugs. 2010 Aug;24(8):695712.

Legends

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LEARNING POINTS ON MIGRAINE

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- The term migraine is derived from the Greek word “hemikranios” which means 'half head'.
- The migraine attack can consist of up to four phases: the premonitory phase, aura, headache phase, and postdrome.
- The lifetime prevalence of migraine is about 33% in women and 13% in men.
- 2% of the general population has “chronic migraine,” meaning that they have headaches on at least 15 days per month including at least 8 days per month on which they have symptoms of fullblown migraine attacks
- The most commonly identified migraine attack triggers include emotional stress, fluctuating female hormones,missed meals, weather factors, sleep disturbance, odours, certain visual stimuli, alcohol, muscle tension, physical exercise, and being overheated.
- The most frequent prodromal symptoms include fatigue, mild cognitive dysfunction, irritability, neck pain, light and noise sensitivity, blurred vision, excessive yawning and excessive thirst.
- Visual aura,sensory aura.language aura,motor aura and brainstem aura can occur in decreasing order of frequency
- Headache phase - Severe unilateral throbbing pain that is exacerbated by routine physical activities associated with hypersensitivity to visual, auditory, olfactory and somatosensory stimuli,nausea,vomiting,neck pain and dizziness
- Untreated, the migraine headache phase usually lasts from 4 to 72 hours, with the majority subsiding within a day or after a night's sleep.
- When the migraine attack lasts for longer than 72 hours, “status migrainosus” is diagnosed.
- Migraine postdrome - fatigue, mild cognitive dysfunction,atypical mood, generalized weakness, feeling dizzy, neck stiffness,light and sound hypersensitivity, and excessive thirst
- Attention should be paid to examination of the temporal arteries,fundoscopy, cervical and cranial muscles, blood pressure and temporomandibularjoint in any patient with headache to rule out secondary causes
- Pathophysiology of migraine Vascular vs Neuronal vs CGRP (calcitonin gene related peptide) theory
- NSAIDS and triptans for acute attack.
- Prophylactics antidepressants, beta blockers,calcium channel blockers and anticonvulsants.
- Important associations of migraine : vertigo, seizures and stroke.
- Menstrual migraine : Hormonal pills and Magnesium may be useful in addition to the usual medications.
- Migraine and pregnancy - Paracetamol for mild to moderate attacks; Severe attacks IV magnesium sulphate/ IV methylprednisolone/ IV opioids/ IV neuroleptics may be tried.

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