Original Article

Use of Different Drugs in Migraine

Comparison of Treatment Response of Different Drugs in Common Migraine

Salman Khan, Imran Ahmad, Muhammad Jalil, Ibrar Saleem, Fawad Ahmad and Khuram Haq Nawaz

ABSTRACT

Objective: The study was carried out to assess and contrast the efficacy of different pharmacological interventions in individuals who have received the diagnosis of common migraine.

Study Design: A longitudinal observational cohort research study

Place and Duration of Study: This study was conducted at the Department of Neurology, Pak Emirates Military Hospital in Rawalpindi from Jan 2022 to Jan 2023.

Methods: The cohort comprised 234 individuals diagnosed with common migraine according to the criteria of International Classification of Headache Disorders (ICHD-3). The medication regimens of the patients, which included Tricyclic antidepressants, Topiramate, beta-blockers, calcium channel blockers and antiepileptics, were utilized to classify them. The evaluation of treatment response was conducted at one, three, and six months after treatment using Migraine Treatment Response Score (MTRS).

Results: The study revealed that females comprised the majority at 65.8%. The average age of the participants was 40±12 years. Over the course of six months, Tricyclic antidepressants demonstrated the most substantial enhancement in MTRS, as evidenced by scores increasing from 4.5±1.2 to 5.8±1.0 ($p<0.05$). Significant declines in frequency and intensity of attacks were noted in response to Tricyclic antidepressants: the former decreased by 4±2 to 2±1, while latter decreased by 7±2 to 4±2 ($p<0.05$). Although improvements in attack frequency and severity were observed across all drug classes, Tricyclic antidepressants exhibited the most significant efficacy. 50% of antiepileptic-treated patients reported being affected post-treatment, with Tricyclic antidepressants influencing 28%.

Conclusion: After six-month evaluation of medications examined, Tricyclic antidepressants demonstrated the highest level of efficacy in management of common migraines. However, symptom relief was observed in all drug categories to varying degrees, emphasizing the importance of tailoring treatment plans to patient-specific characteristics.

Key Words: Antidepressants; Antiepileptics; Beta-Blockers; Calcium Channel Blockers.

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INTRODUCTION

Migraine is a neurovascular disorder that causes significant global burden, characterized by recurrent episodes of severe cephalalgia that affect millions of people, majority of whom are women [1]. These episodes are characterized by intense, pulsating pains that are typically localized to one side of cranium.

Department of Neurology, Pak Emirates Military Hospital, Rawalpindi.

Correspondence: Dr. Salman Khan, Trainee Neurology, Pak Emirates Military Hospital, Rawalpindi.
Contact No: 03339698830
Email: salman.imdc1@gmail.com

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Nausea, vomiting and an acute sensitivity to light and sound are frequent accompanying symptoms[2]. Numerous victims encounter auras, which manifest as visual impairments or blind areas, serving as indicators of impending assault. Migraines may persist for several hours to days, causing significant impairment to an individual's daily functioning. While the precise mechanism underlying migraines remains unknown, it is hypothesized that they are caused by secretion of inflammatory mediators in the vicinity of cranial nerves and blood vessels.

Migraines have consequences that extend beyond mere physical distress; they impose substantial socio-economic burden through the hindrance of work performance and personal relationships[3]. Migraine is often neglected and inadequately managed, resulting in significant number of individuals being compelled to endure the agony without any alleviation. Nevertheless, ongoing progress in migraine research is revealing more about the disorder's biological foundations and potential treatments, providing glimmer of hope for

individuals afflicted with this incapacitating condition and enhancing their quality of life[4-5].

Significant advancements have been made in the treatment of migraines over the last few decades. Historically, treatment approaches for migraines have been divided into two categories: acute and preventive. Acute strategies seek to alleviate or terminate ongoing attacks, while preventive strategies strive to diminish the frequency and intensity of migraines[6]. Acute treatments comprise the variety of pharmaceutical interventions, including Topiramate, ergots, antiemetics and basic analgesics. In addition to calcium channel blockers, antiepileptic drugs, beta-blockers and antidepressants, preventive treatments have expanded to include monoclonal antibodies that target calcitonin gene-related peptide (CGRP) pathway[7]. Nevertheless, patient response to these interventions is extraordinarily variable and decision-making continues to be empirical, frequently predicated on trial and error[8].

Through the assessment of response to various treatments, potential biomarkers of response can be identified, thereby augmenting the accuracy of migraine management. This is consistent with the rapidly expanding domain of pharmacogenomics, which utilizes the genetic underpinnings of drug response to customize therapeutic interventions[9-10].

The objective of this study was to investigate the varying responses of common migraine patients to different medication treatments and to identify potential contributors to this variability, such as genetic predispositions, comorbid conditions, and phenotypic manifestation of the migraine.

METHODS

The research described herein was undertaken at Pak Emirates Military Hospital in Rawalpindi for the duration of one year, specifically from Jan 2022 to Jan 2023. The study population comprised 234 individuals who were diagnosed with common migraine as defined by ICHD-3[11]. Age between 18 and 65 years, migraine diagnosis spanning at least one year, and minimum of one migraine episode per month during the previous three months constituted the inclusion criteria. Exclusion criteria for this study included patients who presented with chronic migraine, secondary headache disorders or significant comorbidities including cardiovascular disease, renal impairment or hepatic dysfunction.

Intervention Procedure: The medication regimen administered to patients was utilized to classify them into the following categories: Tricyclic antidepressants, Topiramate, beta-blockers, calcium channel blockers and antiepileptic pharmaceuticals. The treatment regimen was in accordance with standard clinical practice guidelines[12].

Data Collection: Clinical and baseline demographic information, including age, gender, migraine frequency, duration and intensity was gathered. The evaluation of treatment response was conducted using MTRS, which was recorded at three, one, and six months after treatment commenced. Through clinical evaluations and patient self-reports, adverse effects were documented.

Outcome Measures: At each time point, primary outcome indicator was change in MTRS. The frequency of migraine attacks, alterations in the severity of attacks and occurrence of treatment-related adverse events constituted secondary outcomes.

Statistical Analysis: The data were analyzed with version 25.0 of SPSS. Descriptive statistics were utilized to provide the summary of sample's demographic and clinical attributes. Using repeated measures ANOVA for continuous variables and Chi-square test for categorical variables, treatment responses were compared. A p-value below 0.05 was deemed to indicate statistical significance.

Ethical Approval: Following evaluation and approval by Institutional evaluation Board of Pak Emirates Military Hospital, Rawalpindi, study protocol was implemented. All procedures conducted in this study adhered to the ethical guidelines set forth by the institutional research committee, Helsinki Declaration of 1964 and comparable standards of ethics.

RESULTS

The analysis comprised 234 patients who were diagnosed with common migraine. The average age of these patients was 40±12 years. The participants were predominantly composed of females (65.8%), with only slight variations observed among the treatment groups. The antidepressant cohort comprised participants having age of 43±15, whereas CGRP inhibitor group comprised patients of age 38±11 years. The mean number of migraine attacks per month was four, with CGRP inhibitor and beta-blocker groups experiencing fewer attacks (3±1). The mean duration of migraine history was 9±7 for antiepileptic users, while antidepressant users reported the minimum duration of 5 years. The migraine intensity exhibited mean value of 7±2. It is worth mentioning that antiepileptic groups documented reduced intensity 8±2 and 8±1, respectively, in contrast to the Tricyclic antidepressants group (Table 1).

Tricyclic antidepressants demonstrated consistent superior efficacy in treatment of migraines throughout the six-month study period. Response scores improved significantly from 4.5±1.2 at one month to 5.8±1.0 at six months ($p<0.05$). The mean response scores of Topiramate, beta-blockers, calcium channel blockers and antidepressants all increased moderately with time; however, none of these medications achieved the same level of effectiveness as Tricyclic antidepressants. With antiepileptics, least improvement was observed. The results of statistical analysis revealed that differential treatment responses became more significant as the

time points progressed; the p-values decreased from 0.045 at one month to 0.001 at six months, indicating the distinct trends (Table 2). Following treatment with Tricyclic antidepressants, there was notable decrease in frequency and severity of migraine attacks. Specifically, frequency of attacks decreased from 4±2 to 2±1 ($p<0.05$), while severity decreased from 7±2 to 4±2 ($p<0.05$). Topiramate also reduced assault frequency and severity by significant margins, from 4.2 to 3.1 ($p<0.05$) and 7.1 to 5.2 ($p<0.05$), respectively. Although beta-blockers did not have significant impact on attack frequency, they did marginally reduce severity from 7.3 to 6.3% ($p<0.05$). The frequency and severity of calcium channel blockers were reduced from 4.2 to 3.1 ($p<0.05$) and 7.2 to 5.0 ($p<0.05$), respectively, bearing positive albeit less pronounced impact. Antiepileptics demonstrated efficacy by reducing the frequency by 5±3 to 4±2 ($p<0.05$) and severity by 8±1 to 6±2 ($p<0.05$). Antidepressants demonstrated a modest benefit by reducing severity from 6±3 to 5±2 ($p<0.05$) and frequency from 4±2 to 3±1 ($p<0.05$). Statistical improvements in both frequency and severity were observed across all pharmacological categories following treatment, with Tricyclic antidepressants demonstrating the greatest efficacy (Table 3). 50% who were prescribed antiepileptics. Topiramate influenced 38% of the patients, while beta-blockers influenced 45%. 30% of the patients were affected by Tricyclic antidepressants and Calcium Channel Blockers (Figure 1).

Table No. 1: Baseline demographic and clinical characteristics of participants

Variable	Total (N=234)	Tricyclic antidepressants	Topiramate	Beta-Blockers	Calcium Channel Blockers	Antiepileptics
Age (Mean±SD) years	40±12	38±11	39±10	41±14	40±12	37±9
Female n(%)	154 (65.8)	22 (68.8)	25 (64.1)	28 (70)	26 (65)	15 (62.5)
Migraine frequency/month (Mean±SD)	4±2	3±1	4±2	3±1	4±2	5±3
Migraine duration (Mean±SD) years	7 ±5	6±4	7±6	6±3	7±5	9±7
Migraine intensity (Mean±SD)	7±2	6±2	7±1	7±3	7±2	8±1

Table No. 2: Migraine Treatment Response Score (MTRS) at each time point

Time Point	Tricyclic antidepressants	Topiramate	Beta-Blockers	Calcium Channel Blockers	Antiepileptics	p-value
1 Month	4.5±1.2	4.0±1.3	3.5±1.2	3.8±1.4	2.5±1.3	0.045*
3 Months	5.2±1.1	4.5±1.1	4.0±1.3	4.2±1.2	3.0±1.4	0.012*
6 Months	5.8±1.0	5.0±1.2	4.5±1.1	4.7±1.1	3.5±1.5	0.001*

*indicated the significant values

Table No. 3: Frequency and severity of migraine attacks post-treatment

Drug Category	Baseline Attack Frequency	Post-Treatment Attack Frequency	p-value	Baseline Attack Severity	Post-Treatment Attack Severity	p-value
Tricyclic antidepressants	4±2	2±1	0.001*	7±2	4±2	0.001*
Topiramate	4±2	3±1	0.012*	7±1	5±2	0.018*
Beta-Blockers	3±1	3±1	0.020*	7±3	6±3	0.053
Calcium Channel Blockers	4±2	3±1	0.045*	7±2	5±2	0.051
Antiepileptics	5±3	4±2	0.031*	8±1	6±2	0.045*

*indicated the significant values

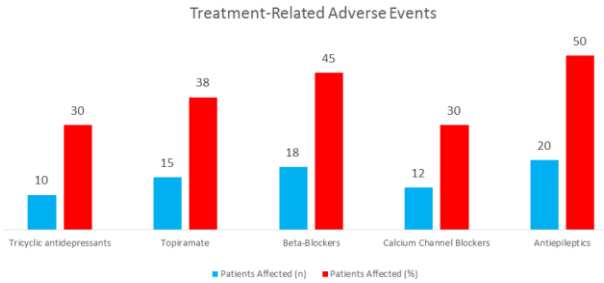

Figure No. 1: Incidence of Treatment-Related Adverse Events.

DISCUSSION

The current investigation examined the relative efficacy of different medications in managing patients with common migraines for a duration of six months. A significant finding was the notable effectiveness of Tricyclic antidepressants, especially when evaluated for extended periods of time, which suggests they have the potential to be a formidable tool for managing migraines[13].

The study's female participants comprised the majority (65.8%), which is consistent with previous research indicating that migraines are more prevalent among women than men[14]. The age discrepancies observed among various drug categories, specifically in the CGRP inhibitor group in comparison to the antidepressant cohort, may be attributed to pharmacokinetic and adverse effect profiles of the drugs, which may have an impact on prescribing practices[15].

Tricyclic antidepressants exhibited the most substantial decrease in both the frequency and severity of migraine attacks; nevertheless and Topiramate also demonstrated noteworthy effectiveness. The reason for this is their firmly established functions in the treatment of acute migraines[7]. Further corroboration of prior research underscores the importance of extended treatment durations for thorough evaluation, as evidenced by the upward trend in response scores for the majority of pharmaceuticals over time[16].

Consistent with previous research[17], beta-blockers substantially diminished the severity of attacks while having only the marginal effect on their frequency. Although noteworthy, advantages associated with calcium channel blockers, antiepileptics, and antidepressants were comparatively subdued. The risk-benefit ratio of these treatments should be diligently assessed, particularly when prescribing for extended periods of time, in light of these findings[17].

The observed reduction in migraine intensity among the antiepileptic groups, as opposed to the Tricyclic antidepressants and antidepressants, could potentially be attributed to the distinct mechanisms of action exhibited by these pharmaceuticals. In contrast, antiepileptics alter neurotransmitter release by modulating voltage-gated sodium and calcium channels[18].

Additionally, improvements in both frequency and severity were observed across all pharmacological categories following treatment, according to the study. This consistency indicates that although certain drug categories may provide more substantial benefits, all drug categories offer some degree of alleviation. In contrast, the fact that Tricyclic antidepressants exhibited the greatest efficacy highlights their increasing significance in the treatment of migraines. The relatively low proportions of Tricyclic antidepressants in the sample may be attributed to their recent introduction to the market or possible financial obstacles[19]. Conducting additional randomized controlled trials would be advantageous in solidifying these findings.

CONCLUSION

In contrast to other drug classes, Tricyclic antidepressants significantly diminished the frequency and severity of migraine attacks. Nevertheless, despite the potential of Tricyclic antidepressants as primary therapeutic intervention, each drug class exhibited varying levels of alleviation, underscoring the significance of individualized treatment strategies. In order to customize therapeutic interventions for migraines, patient-specific factors, potential medication interactions, and adverse effects must be considered owing to the wide array of migraine manifestations and triggers.

Author's Contribution:

Concept & Design of Study:	Salman Khan
Drafting:	Imran Ahmad, Muhammad Jalil
Data Analysis:	Ibrar Saleem, Fawad Ahmad, Khuram Haq Nawaz
Revisiting Critically:	Salman Khan, Imran Ahmad
Final Approval of version:	Salman Khan

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