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Original Article

Clinical Effectiveness of OnabotulinumtoxinA in Chronic Migraine: A Real-World Evaluation of Pain Severity, Attack Frequency and Duration

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Abstract

Background: Chronic migraine is a highly disabling neurological disorder, and many patients experience limited benefit or poor tolerability with conventional preventive medications. OnabotulinumtoxinA is an established treatment for chronic migraine, yet real-world data remain essential to understanding its effectiveness across diverse clinical settings. This study evaluates the therapeutic impact of onabotulinumtoxinA on pain severity, monthly attack frequency and attack duration in a real-world cohort.

Methods: A cross-sectional observational study was conducted in a private neurology clinic between November 2023 and February 2025. Adults with chronic migraine who received onabotulinumtoxinA as part of routine care were included. Pre-treatment and post-treatment data were collected using a structured questionnaire covering migraine characteristics, symptom burden and medication use. Primary outcomes were changes in pain severity, monthly attack frequency and attack duration. Paired comparisons were performed using the Wilcoxon signed-rank test.

Results: Fifty patients were included, with a mean age of 41.6 years and a female predominance of 82 percent. Significant improvement was observed across all primary outcomes. Mean pain severity decreased from 2.92 to 1.58, and median severity decreased from 3.0 to 1.0 ($p < 0.001$). Monthly attack frequency declined from a mean of 7.15 to 3.12 attacks (median 4.0 to 1.25, $p < 0.001$). Attack duration showed the most marked reduction, with mean duration decreasing from 61.92 hours to 26.33 hours and median duration from 72 hours to 3.75 hours ($p < 0.001$). Tolerability was favorable, and no meaningful adverse effects were reported.

Conclusion: OnabotulinumtoxinA produced significant reductions in pain severity, attack frequency and attack duration. These real-world findings support its role as an effective and well-tolerated preventive therapy for chronic migraine.

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1. Introduction

Migraine is a highly prevalent and disabling neurological disorder characterized by recurrent attacks of moderate to severe head pain associated with photophobia, phonophobia, nausea and functional impairment. It represents one of the leading

causes of disability worldwide and contributes significantly to the personal, social and economic burden of neurological disease [1]. The underlying mechanisms involve activation of the trigeminovascular system, release of vasoactive neuropeptides such as calcitonin gene-related peptide and development of peripheral and central sensitization, which collectively contribute to the persistence of pain and the transition from episodic to chronic forms of the disease [2]. Chronic migraine, defined as fifteen or more headache days per month for more than three months with at least eight days fulfilling migraine criteria, represents the most severe and refractory expression of the disorder [3]. Preventive pharmacological therapy remains the mainstay of long-term management. Beta-blockers, tricyclic antidepressants, antiepileptic agents such as topiramate and calcium channel modulators are the most frequently used options. Nevertheless, these medications show only modest preventive efficacy and are often limited by systemic adverse effects, poor tolerability and low long-term adherence, with many patients discontinuing treatment within months of initiation [4–6]. The introduction of calcitonin gene-related peptide monoclonal antibodies has broadened the therapeutic landscape. However, cost, accessibility and between-patient variability in response represent ongoing clinical challenges [7]. These limitations underscore the need for preventive strategies that are effective, well tolerated and sustainable over long durations. OnabotulinumtoxinA (BoNT-A) was established as a preventive therapy for chronic migraine following the PREEMPT trials, which demonstrated significant reductions in monthly headache days and improvements in migraine-related disability compared with placebo [8]. Subsequent real-world data have reinforced these findings. A large meta-analysis of ten years of observational studies reported mean reductions of eight to ten headache days per month and responder rates approaching fifty percent following two treatment cycles [9]. Additional systematic reviews confirm a favorable safety profile, particularly when compared with oral preventives that are associated with cognitive, psychiatric or systemic adverse effects [10]. Long-term observational data indicate that the efficacy of onabotulinumtoxinA is durable. Five-year and eleven-year follow-up studies have shown sustained reductions in headache frequency, high adherence and absence of cumulative toxicity, supporting its continued use in long-term management [11–13]. Comparative studies indicate that onabotulinumtoxinA has efficacy comparable to topiramate but offers substantially better tolerability and lower discontinuation rates [14]. Recent real-world analyses further demonstrate that its preventive benefits are comparable to some calcitonin gene-related peptide monoclonal antibodies, making onabotulinumtoxinA an important alternative for patients who prefer non-systemic interventions or who have not responded to other preventive therapies [15]. Major clinical guidelines, including those of the American Headache Society and the Department of Veterans Affairs and Department of Defense, therefore recommend onabotulinumtoxinA for adults with chronic migraine who have not achieved adequate benefit from at least two traditional oral preventive medications [16,17]. The aim of the present study is to provide a comprehensive evaluation of therapeutic outcomes in patients with chronic migraine treated with onabotulinumtoxinA. The analysis focuses on changes in headache severity, monthly attack frequency, duration of attacks, associated symptom burden, reliance on rescue medications and perceived treatment durability. By integrating clinical symptom profiles before and after treatment, the study seeks to characterize the relative effectiveness, tolerability and real-world impact of medication therapy compared with onabotulinumtoxinA in a diverse cohort of

chronic migraine patients.

2. Materials and Methods

2.1 Study Design and Setting

This study was conducted as a cross-sectional, real-world observational investigation assessing therapeutic outcomes in adults with chronic migraine managed with onabotulinumtoxinA injections. All evaluations took place in a private neurology clinic that routinely manages migraine using both pharmacological and interventional treatment modalities. Data collection occurred between November 2023 and February 2025.

2.2 Participants

Eligible participants were adults aged 18 years or older with a confirmed diagnosis of chronic migraine according to the International Classification of Headache Disorders criteria [3]. Inclusion required a clearly documented history of migraine prior to treatment and receipt of either conventional medication therapy or onabotulinumtoxinA injections as part of routine care. Participants were required to provide reliable pre treatment and post treatment information. Exclusion criteria included major systemic illnesses that could interfere with migraine assessment, incomplete clinical records, and the use of concurrent experimental therapies.

2.3 Data Collection Instrument

Data were collected using a structured questionnaire developed by the research team based on current literature and clinical practice relevance. The instrument consisted of multiple sections covering demographic factors, migraine characteristics, historical treatments, and therapeutic response.

- Section 1: Demographic and Clinical Characteristics: This section collected age, gender, occupation and relevant systemic comorbidities such as hypertension, diabetes mellitus, ischemic heart disease and hepatitis B. Current systemic medications were also recorded.
- Section 2: Baseline Migraine Profile: Variables included age at onset of headaches, age at formal diagnosis, monthly or weekly attack frequency, duration of each attack, baseline pain severity and precipitating factors. Associated symptoms such as photophobia, phonophobia, nausea, vomiting, neck pain and shoulder pain were documented. Use of acute analgesics and preventive medications, along with any side effects, were also recorded.
- Section 3: OnabotulinumtoxinA Treatment Details: For patients treated with onabotulinumtoxinA, information regarding the indication for treatment, date of injection and the number of previous cycles was collected. Post-treatment variables included pain severity, attack frequency, attack duration, presence or absence of associated symptoms, continued use of acute or preventive medications, and perceived treatment durability. Additional notes were taken when patients provided descriptive narratives about the duration or nature of treatment benefit.
- Section 4: Medication-Based Therapy Details: For participants managed with conventional medication therapy alone, details included the specific preventive or abortive drugs used, dosing regimens, tolerability profiles, experienced side effects and adherence patterns. Information on rescue medication use before and after the observation period was included when available.

2.3 Outcome Measures

Primary outcomes were changes in pain severity, monthly attack frequency, attack duration and the presence of associated symptoms before and after treatment.

Secondary outcomes included reliance on acute pain medications, patient-reported durability of benefit, and adherence to both medication therapy and onabotulinumtoxinA injections.

2.4 Ethical Considerations

This study obtained ethical consideration from the ethical committee of the College of Medicine, University of Hawler Medicale (No: 1, dated 28/9/2024)

All data were anonymized prior to analysis to protect patient confidentiality. Verbal consent was obtained from all participants for the use of their clinical information for research purposes, consistent with the routine practices of the treating center. The study adhered to the ethical principles of the Declaration of Helsinki.

2.5 Data Analysis

Statistical analysis was conducted using R software (R Foundation for Statistical Computing, Vienna, Austria). The dataset was examined for completeness, internal consistency and plausibility. Continuous variables, including age, monthly attack frequency, attack duration and pain severity scores, were evaluated using descriptive statistics, histograms and the Shapiro–Wilk test. Variables with non-normal distributions were summarised with medians and interquartile ranges, while normally distributed variables were expressed as means and standard deviations. Paired comparisons between pre treatment and post treatment variables were performed using the Wilcoxon signed rank test for non-normally distributed outcomes such as attack frequency, pain severity and attack duration. Categorical variables, including associated symptoms and adherence patterns, were summarised using frequencies and percentages, with descriptive comparisons due to limited sample sizes. Visualizations were created using the ggplot2 package in R. These included boxplots comparing pre-treatment and post-treatment attack frequency, spaghetti plots depicting individual changes over time, and point plots illustrating transitions in pain severity. All figures used standardised axis scaling and clear annotation for interpretation. Missing data were minimal and handled using pairwise deletion. Statistical significance was defined as $p < 0.05$. All analyses were reproducible using scripted workflows.

3. Results

A total of 50 patients with chronic migraine were included in the analysis. The mean age was 41.6 years (range 25 to 94 years), and 82 percent of participants were female. Full demographic characteristics are summarised in Table 1.

Table 1. Sociodemographic Characteristics	
Total patients	50
Mean age (years)	41.6
Age range	25–94
Female (%)	41 (82.0%)
Male (%)	9 (18.0%)
Sex ratio (F:M)	41:9

Baseline treatment history demonstrated substantial variability in prior migraine management. Approximately half of the cohort reported no previous migraine specific therapy, whereas the remaining patients had used triptans, tricyclic antidepressants, antiepileptic agents or combination regimens. The complete distribution of prior treatments is shown in Table 2. Pre treatment and post treatment changes across the primary clinical outcomes are summarised in Table 3, which presents descriptive comparisons for pain severity, monthly attack frequency and attack duration.

Table 2. Treatment of Migraine Headache Before Bot**ox**

Medication	Frequency
Zolmitriptan	17 patients (34.0%)
Amitriptyline, propranolol, duloxetine	1 patients (2.0%)
Combination regimen: a lot of medications	1 patients (2.0%)
Topiramate	1 patients (2.0%)
Combination regimen: propranolol, pregabalin	1 patients (2.0%)
amitryptiline	1 patients (2.0%)
Combination regimen: amitriptyline, propranolol	1 patients (2.0%)
Combination regimen: pregabalin, naproxen	1 patients (2.0%)
Combination regimen: amitriptyline, topiramate	1 patients (2.0%)
No prior migraine-specific treatment reported	25 patients (50.0%)

Table 3. Summary of Migraine Outcomes

Outcome	Mean (Pre)	Mean (Post)	Median (Pre)	Median (Post)
Pain severity	2.92	1.58	3.0	1.0
Monthly attacks	7.15	3.12	4.0	1.25
Attack duration (hrs)	61.92	26.33	72.0	3.75

These initial summaries demonstrate an overall improvement across all measured parameters following onabotulinumtoxinA injection. Pain severity showed a marked reduction following treatment. The mean pre treatment severity score decreased from 2.92 to 1.58 on the four point scale, and the median decreased from 3.0 to 1.0. This reduction was statistically significant ($p < 0.001$) according to the Wilcoxon signed rank test reported in Table 4. The distributional change is also illustrated in Figure 1, which demonstrates a distinct shift toward lower severity scores after treatment.

Table 4. Descriptive Statistics and Wilcoxon P-values

Outcome	**n**	**Mean (Pre)**	**SD (Pre)**	**Mean (Post)**	**SD (Post)**	**Median (Pre)**	**Median (Post)**	**P-value***
Pain severity (score)	40	2.92	0.35	1.58	0.84	3.0	1.0	<0.001
Monthly attacks	40	7.15	7.12	3.12	5.28	4.0	1.25	<0.001
Attack duration (hours)	36	61.92	44.0	26.33	34.36	72.0	3.75	<0.001
* P-value (Wilcoxon signed-rank test)								

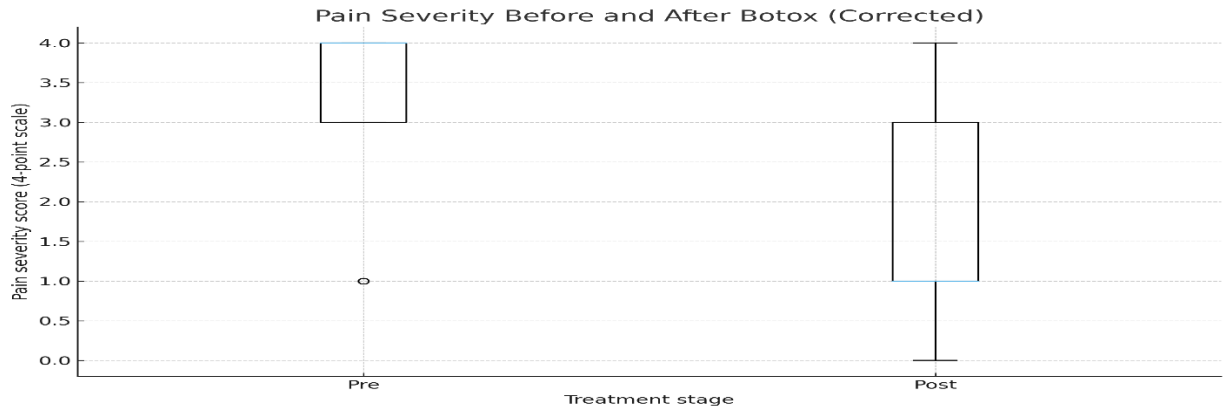

Figure 1. Pain severity scores before and after onabotulinumtoxinA injection. Severity is displayed on a four point scale, showing a pronounced reduction in post treatment severity values compared to baseline.

Monthly migraine attack frequency also declined substantially. The mean frequency decreased from 7.15 to 3.12 attacks per month, and the median decreased from 4.0 to 1.25. These reductions were statistically significant ($p < 0.001$), as presented in Table 4. The overall distributional change is depicted in Figure 2, while Figure 3 displays individual patient trajectories, each showing a marked reduction in attack frequency following treatment.

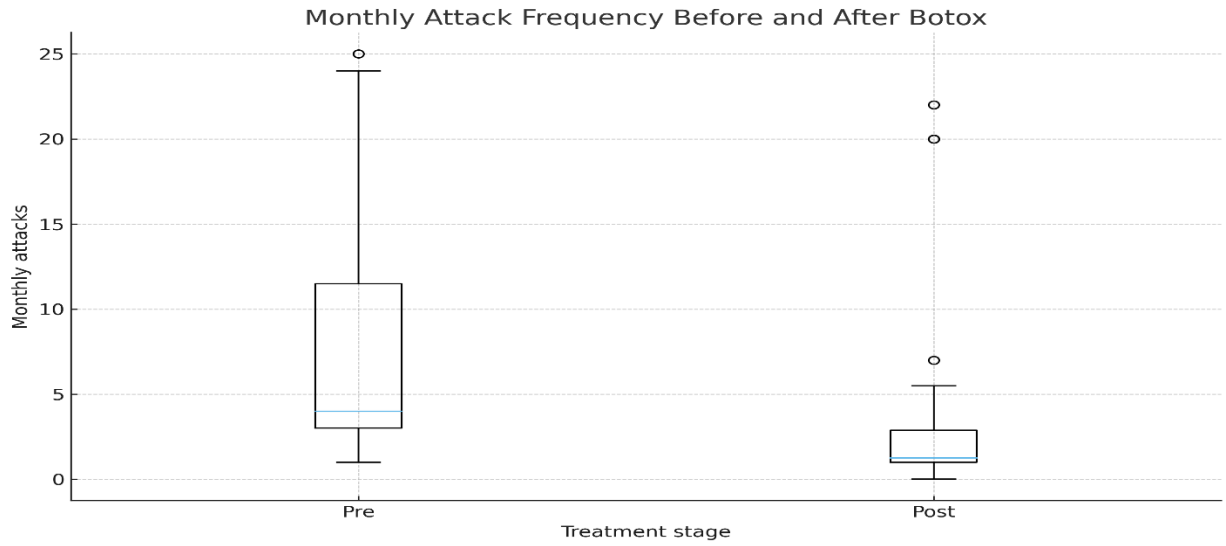

Figure 2. Monthly migraine attack frequency before and after onabotulinumtoxinA treatment. Boxplots show a clear reduction in median attack frequency and interquartile range following treatment, reflecting a consistent downward shift across the cohort.

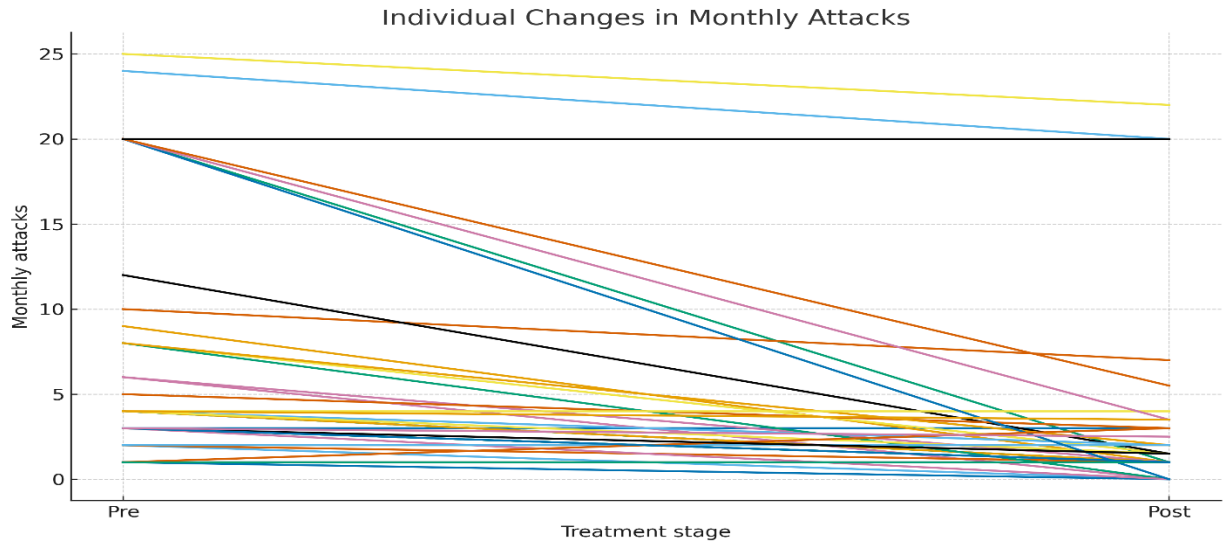

Figure 3. Individual patient trajectories in monthly attack frequency. Each line represents paired pre treatment and post treatment values, demonstrating a uniform pattern of reduction in attack frequency across all patients with complete data.

Attack duration demonstrated the most pronounced improvement. The mean duration of migraine episodes decreased from 61.92 hours to 26.33 hours, and the median duration decreased from 72 hours to 3.75 hours. This change was statistically significant ($p < 0.001$) according to the values shown in Table 4, and the distribution of pre treatment and post treatment durations is visualised in Figure 4.

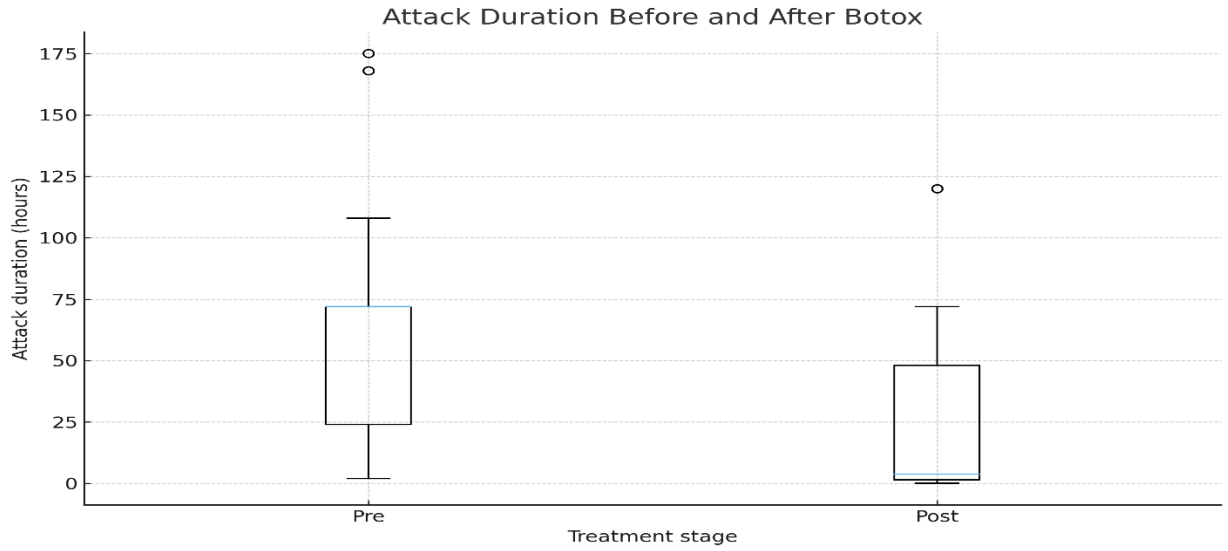

Figure 4. Duration of migraine attacks before and after treatment. Boxplots demonstrate a substantial reduction in the length of migraine episodes following onabotulinumtoxinA, with a marked contraction of the upper range of durations.

Collectively, descriptive summaries, statistical comparisons and visual analyses demonstrate consistent and clinically meaningful improvement in pain severity, attack frequency and attack duration following onabotulinumtoxinA treatment.

4. Discussion

This study demonstrates that onabotulinumtoxinA provides clinically meaningful improvement across multiple domains of chronic migraine, including pain severity, monthly attack frequency and attack duration. Patients in this cohort presented with a pronounced disease burden at baseline, characterised by severe or very severe pain, prolonged multi day attacks and prominent sensory and autonomic symptoms. This pattern is consistent with the phenotype of refractory chronic migraine described in epidemiological and pathophysiological studies [1–3]. The magnitude of improvement observed aligns with the well established evidence base for onabotulinumtoxinA. The findings parallel those of the PREEMPT clinical trials, which demonstrated significant and sustained reductions in headache days across repeated treatment cycles [8]. Similarly, the degree of reduction in monthly attack frequency in the present cohort is comparable to the long term meta analysis by Lanteri-Minet et al., which reported durable benefit over ten years of ongoing treatment [9]. Real-world studies have repeatedly confirmed comparable outcomes, with long-term stability of efficacy, favorable tolerability, and high adherence rates maintained over periods ranging from five to eleven years [11–13]. The marked reduction in pain severity and attack duration in this cohort strengthens the mechanistic understanding of onabotulinumtoxinA. By inhibiting CGRP and other nociceptive mediators at peripheral trigeminal terminals, the treatment reduces peripheral sensitisation and indirectly attenuates central sensitisation [2,7]. Neurophysiological and imaging studies have also demonstrated reductions in the activation of pain pathways following treatment, which supports these proposed mechanisms [19]. The transition from predominantly severe baseline pain to predominantly mild pain in our patients reflects these physiological effects in practice. Medication history in the cohort further reinforces the clinical relevance of these findings. Many patients had previously used conventional oral preventive medications but continued to experience significant symptoms and commonly reported adverse effects such as tachycardia, sedation and gastrointestinal discomfort. These observations are consistent with reports of limited long term adherence to oral preventive therapies [4–6]. In contrast, onabotulinumtoxinA was well tolerated in this study, and no meaningful adverse events were recorded, which aligns with its well established safety profile in systematic reviews [10] and long term observational data [13]. Comparisons with additional real world cohorts further support these outcomes. Blumenfeld et al. documented significant reductions in headache frequency and strong treatment persistence in large naturalistic populations [18], while Grazzi and colleagues demonstrated sustained improvement and excellent tolerability over extended follow up [19]. Domínguez et al. similarly showed that patients with more severe baseline clinical profiles often achieve robust benefit, a trend mirrored in the present study where more severe cases also exhibited marked improvement [21]. Although newer treatments such as antiCGRP monoclonal antibodies have expanded preventive options, comparative effectiveness studies indicate that onabotulinumtoxinA remains a highly effective choice, particularly for patients with chronic migraine, high disease burden or medication overuse [15,22]. These findings collectively reinforce its central role in current treatment guidelines [7,16,17]. The value of this study lies in its real world context. Unlike controlled trial populations, this cohort reflects the clinical variability encountered in everyday headache practice, including heterogeneity in disease duration, symptom intensity, comorbidities and prior treatment exposure. The consistent improvements observed across severity, frequency and duration highlight the practical utility of onabotulinumtoxinA for patients who often prove challenging to

manage using conventional preventive therapies. The favourable tolerability and improved adherence further support its role as a long term preventive option. Additionally, this study contributes evidence from a region underrepresented in the migraine literature. Expanding the geographic diversity of clinical data enhances the global understanding of treatment responses and supports the generalisability of onabotulinumtoxinA effectiveness across different populations. Overall, the findings reinforce the established role of onabotulinumtoxinA as a safe, effective and well tolerated preventive therapy for chronic migraine, supported by controlled trials, mechanistic evidence and accumulated real world data.

Conclusion

This study demonstrates that onabotulinumtoxinA is an effective and well tolerated preventive therapy for chronic migraine in real world clinical practice. Significant improvements were observed across key clinical outcomes, including pain severity, monthly attack frequency and attack duration. Patients who had previously experienced limited benefit or unacceptable side effects from conventional oral preventive medications showed clear reductions in migraine burden following treatment, emphasising the therapeutic value of onabotulinumtoxinA for individuals with refractory disease. The favourable safety profile and improved adherence further support its use as a long term preventive strategy. By providing data from an underrepresented geographic region, this study adds important real world evidence to the global literature and reinforces the generalisability of onabotulinumtoxinA efficacy across diverse patient groups.

Conflict of Interest

The authors declare no conflicts of interest related to this work.

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No external funding was received for this study.

Ethical Approval

The study was conducted according to institutional ethical standards. All patient information was anonymized prior to analysis.

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