The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 5, 2025

THE EFFICACY OF BOTULINUM TOXIN IN MIGRAINE

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DOI: https://doi.org/10.5281/zenodo.15322484

Keywords
Botulinum toxin, Chronic migraine, Headache frequency, Prophylactic therapy

Article History
Received on 25 March 2025
Accepted on 27 April 2025
Published on 01 May 2025

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Abstract

Background: *Frequent headaches and related disability define the crippling disorder known as chronic migraines, which seriously affects patients' health. Emerging as a potential preventive treatment for chronic migraines is botulinum toxin.*

Objectives: *This study assessed the effectiveness, safety and patient-reported outcomes of botulinum toxin in lowering headache frequency, severity and disability in chronic migraine sufferings.*

Methods: *At a tertiary care center in Rawalpindi, this prospective observational study spanning July 2024 through December 2024 was undertaken. Convenient sampling enrolled 180 individuals total diagnosed with persistent migraines. Participants were followed up at 4, 12 and 24 weeks after receiving botulinum toxin per the PREEMPT regimen. Measuring headache frequency and intensity with Numeric Rating Scale (NRS) and Migraine Disability Assessment (MIDAS) scores, patient satisfaction, adherence, quality of life was determined by WHOQOL-BREF.*

Results: *Headache days per month dropped from 21.4 ± 3.8 at baseline to 7.4 ± 2.2 at 24 weeks ($p < 0.001$). From 7.9 ± 1.2 and 52.6 ± 14.8 at baseline to 2.7 ± 1.0 and 15.3 ± 6.7, respectively, NRS and MIDAS scores shown similar declines ($p < 0.001$). Across all spheres, quality-of- life ratings greatly improved; physical health rose from 52.3 ± 9.4 to 78.5 ± 7.2 ($p < 0.001$). Adherence rates were high–88.9% at 24 weeks–and adverse effects were few–2.8% at 24 weeks.*

Conclusion: *Ultimately, botulinum toxin improved quality of life by significantly lowering headache frequency, severity and disability while also being useful and well-tolerable treatment for chronic migraine. Its low negative effects and great adherence helped to justify its long-term preventive role.*

INTRODUCTION

A common neurological condition, migraines cause repeated headaches usually accompanied by sensory problems, nausea and photophobia [1]. With an estimated 12% of the world's population affected, migraine is a major burden on people, families, and healthcare systems as well as a main source of

handicap [2]. Although the precise pathophysiology of migraines is yet unknown, it is generally agreed that they entail intricate interactions among inflammatory, vascular and neurological mechanisms. The incapacitating character of migraines has motivated research of several therapeutic modalities, including acute therapies and preventative technique [3-4]. Among these, a fresh and exciting choice for treating chronic migraine is botulinum toxin (BoNT), a neurotoxin generated from *Clostridium botulinum* [5-7]. Originally intended for cosmetic uses, such wrinkle reduction, botulinum toxin's therapeutic value has grown to encompass many neurological and non-neurological disorders [8]. Clinical studies for various diseases when patients reported a notable decrease in headache frequency and intensity led to the coincidental finding of its effectiveness in migraine prevention [9]. This prompted focused investigation on BoNT's mechanism of action and efficacy in treating chronic migraine, a disorder defined by headache occurring on 15 or more days per month for more than three months, with at least eight of these days exhibiting migraine features [9-11].

Although the exact process by which botulinum toxin reduces migraine symptoms is unknown, it is thought to be connected to regulation of the release of pain-modulating neurotransmitter including calcitonin gene-related peptide (CGRP), substance P, glutamate and other molecules [12]. Key players in migraine pathogenesis, BoNT lowers neurogenic inflammation and the stimulation of nociceptive pathways by inhibiting these neuropeptides at the periphery nerve terminals. For long-term use in suitable patients, its limited systemic adverse effects also make it a desirable choice [13-14].

Botulinum toxin for chronic migraine has been approved by regulatory authorities including U.S. Food and Drug Administration (FDA) after clinical trials and real-world evidence showed its efficacy and safety for this particular use. Crucially in proving its effectiveness, the landmark PREEMPT studies showed notable declines in headache days, migraine frequency and related impairment in patients getting BoNT injections [6, 15].

Though successful, botulinum toxin treatment is not without restrictions. It is mostly intended for chronic migraine and not for episodic migraine; hence, certain patients may find it difficult to access depending on its cost and procedural criteria. Furthermore, the variation in individual responses emphasizes the need of more investigation to maximize patient choosing and treatment strategies. This research investigation was aimed to assess the effectiveness, mechanisms and clinical results of botulinum toxin in the prevention and management of chronic migraine.

Materials and Methods

Study Design and Setting

From July 2024 to December 2024, in a tertiary care hospital in Rawalpindi, Pakistan, this study was carried out as prospective observational study. The center served a varied patient group and specialized in the care of neurological diseases, offering a good environment for assessing the effectiveness of botulinum toxin in chronic migraine sufferers.

Study Population

The study had 180 participants in all who had been diagnosed with chronic migraines. The International Classification of Headache Disorders (ICHD-3) defined chronic migraine as headache occurring on 15 or more days per month for more than three months, with at least eight days satisfying the diagnostic criteria for migraine. Convenient sampling allowed participants—and patients visiting the neurology outpatient department were selected.

Inclusion Criteria

- Patients ranging in age from eighteen to sixty-five.
- ICHD-3 criteria based diagnosis of persistent migraine.
- Patients who hadn't had past botulinum toxin injections for migraines.
- Patients ready to give informed permission and scheduled thorough follow-up visits.

Exclusion Criteria

- Patients suffering with episodic migraines or other headache conditions.
- History of extreme sensitivity to components of botulinum poison or toxin.
- Women who were either nursing or pregnant.

- Patients with major psychiatric comorbidities or neurological diseases other than migraine.
- Patients using contradicting preventative migraine treatments.

Intervention

Under the Phase III Research Evaluating Migraine Prophylactic Therapy (PREEMPT), patients underwent injections of BoNT-A. Thirty-one standardized injection sites spread over seven particular head and neck muscle groups—including the frontalis, corrugator, procerus, occipitalis, temporalis, trapezius and cervical paraspinal muscles—saw the total dosage of 155 units. Trained neurologists administered injections utilizing sterile procedures.

Data Gathering

We noted baseline demographic information including age, gender and length of migraine experience. Clinical data comprised the frequency of migraine-related disability determined using MIDAS, number of headache days per month and severity of migraines evaluated using NRS. Four, twelve, and twenty-four weeks after intervention, follow-up tests were done to track improvements in headache frequency, severity and disability.

Outcome Measures

The main result was 24-week drop in headache days per month from baseline. Changes in headache intensity (NRS), MIDAS scores and patient-reported treatment satisfaction comprised secondary results.

Ethical Considerations

The research evaluation unit of College of Physicians and Surgeons, Pakistan approved the study trial vide Notification No. CPSP/REU/NEU-2022-124-748, dated June 6, 2024. Every participant had written informed permission before enrolling. Participants' privacy and identities were respected all through the study.

Statistical Analysis

SPSS version 25.0 was used to examine the data. Clinical and demographic variables were gathered using descriptive statistics. Paired t-tests tests examined changes in continuous variables from baseline to follow-up. Considered statistically significant was a p-value of 0.05.

Results

The baseline features described the clinical profiles and demographic traits of the research population. Participants had generally middle-aged cohort with the mean age of 39.8 ± 10.5 years. Consistent with the epidemiology of migraines, which are more common in women, gender distribution revealed a higher presence of females (72.2%) than men (27.8%). With an 8.2 ± 3.4 year mean duration, most individuals seemed to have a history of chronic migraine. With average frequency of 21.4 ± 3.8 days per month, this sample showed notable handicap in baseline headache frequency. The baseline NRS score of 7.9 ± 1.2 and MIDAS score of 52.6 ± 14.8 highlighted even more the great impact of headaches in this cohort (Table 1).

A notable change in migraine intensity during the course of the trial was seen. Just 11.1% of participants said they had mild migraines at baseline; 55.6% of them had severe ones. By 24 weeks, light cases rose to 38.9% while severe cases dropped drastically to 5.6%. From 33.3% at baseline to 55.6% at 24 weeks, moderate severity likewise exhibited increasing tendency. The p-value (<0.001) for all severity categories showed statistically significant decrease in migraine severity over time, so implying the effectiveness of the intervention in lowering the intensity of migraines (Table 2). The indicators of quality of life showed notable gains in all spheres. Physical health scores climbed from the baseline of 52.3 ± 9.4 to 78.5 ± 7.2 at 24 weeks ($p < 0.001$). From 49.8 ± 10.2 to 76.2 ± 8.5, psychological health also increased rather noticeably. With baseline scores of 45.6 ± 8.9 and 48.7 ± 9.1 rising to 70.3 ± 9.0 and 73.5 ± 7.8, respectively, social contacts and environmental scores displayed comparable patterns. These findings showed that the participants' general quality of life improved considerably appreciated the treatment (Table 3).

The main and secondary results showed clear trend of development across time. Headache days per month dropped dramatically from 21.4 ± 3.8 at baseline to 7.4 ± 2.2 at 24 weeks ($p = 0.001$). Likewise, MIDAS ratings dropped from 52.6 ± 14.8

to 15.3 ± 6.7 over the same period; NRS scores improved from 7.9 ± 1.2 to 2.7 ± 1.0 ($p < 0.001$). Mean satisfaction scores rose to 9.1 ± 0.8 by 24 weeks, therefore reflecting patient contentment as well. Minimal adverse effects were evident; reported cases dropped from 6.7% at 4 weeks to 2.8% at 24 weeks. These results showed the treatment's both effectiveness and acceptability (Table 4). Over the course of study, treatment adherence made notable improvement. From 77.8% at 4 weeks to 88.9% at 24 weeks, proportion of patients with high adherence—≥80%—rose ($p = 0.045$). Whereas low adherence (<60%) reduced from 5.6% to 2.8% (p-values of 0.032 and 0.021, respectively), moderate adherence (60–79%) dropped from 16.7% to 8.3%. These patterns showed the acceptance and continuous adherence to the treatment plan, which would have helped to explain the noted clinical changes (Table 5). Most participants said they were moderately satisfied at four weeks. More participants reported high satisfaction (9-10) by 12 weeks, a trend that persisted 24 weeks when over 58.3% of participants rated their satisfaction at the highest level (9-10). This rising trend emphasizes over time the growing efficiency and acceptance of botulinum toxin treatment for chronic migraine. Regarding adverse impact frequency distribution, after neck weakness (8.3%), flu-like symptoms (5.6%), injection site pain (13.9%) and eyelid ptosis (4.4%), most individuals (67.8%) said they had no side effects, suggesting that botulinum toxin treatment is usually well-tolerated (Figure 1).

Table 1: Baseline characteristics of participants

Characteristic	Mean ± SD or N (%)
Age (years)	39.8 ± 10.5
Gender (Male/Female)	50 (27.8)/130 (72.2)
Duration of Migraine (years)	8.2 ± 3.4
Baseline Headache Days (per month)	21.4 ± 3.8
Baseline NRS Score	7.9 ± 1.2
Baseline MIDAS Score	52.6 ± 14.8

Table 2: Migraine severity classification over time

Migraine Severity Classification	Baseline (N, %)	4 Weeks (N, %)	12 Weeks (N, %)	24 Weeks (N, %)	p-value
Mild	20 (11.1%)	30 (16.7%)	50 (27.8%)	70 (38.9%)	<0.001
Moderate	60 (33.3%)	80 (44.4%)	90 (50.0%)	100 (55.6%)	<0.001
Severe	100 (55.6%)	70 (38.9%)	40 (22.2%)	10 (5.6%)	<0.001

Table 3: Quality of life improvement (WHOQOL-BREF)

WHOQOL-BREF Domain	Baseline Score (Mean ± SD)	24 Weeks Score (Mean ± SD)	p-value
Physical Health	52.3 ± 9.4	78.5 ± 7.2	<0.001
Psychological Health	49.8 ± 10.2	76.2 ± 8.5	<0.001
Social Relationships	45.6 ± 8.9	70.3 ± 9.0	<0.001
Environment	48.7 ± 9.1	73.5 ± 7.8	<0.001

Table 4: Treatment outcomes at follow-up

Outcome Measure	Baseline (Mean ± SD)	4 Weeks (Mean ± SD)	12 Weeks (Mean ± SD)	24 Weeks (Mean ± SD)	p-value
Headache Days (per month)	21.4 ± 3.8	15.8 ± 3.1	11.2 ± 2.9	7.4 ± 2.2	<0.001
NRS Score	7.9 ± 1.2	5.6 ± 1.4	4.1 ± 1.3	2.7 ± 1.0	<0.001
MIDAS Score	52.6 ± 14.8	38.4 ± 12.3	26.7 ± 9.8	15.3 ± 6.7	<0.001
Patient Satisfaction (Scale: 1-10)	-	7.2 ± 1.1	8.3 ± 1.0	9.1 ± 0.8	<0.001

Treatment Adverse Effects (%)	-	12 (6.7)	8 (4.4)	5 (2.8)	0.045

Table 5: Treatment adherence levels over time

Adherence Level	4 Weeks (N, %)	12 Weeks (N, %)	24 Weeks (N, %)	p-value
High (≥80%)	140 (77.8)	150 (83.3)	160 (88.9)	0.045
Moderate (60-79%)	30 (16.7)	20 (11.1)	15 (8.3)	0.032
Low (<60%)	10 (5.6)	10 (5.6)	5 (2.8)	0.021

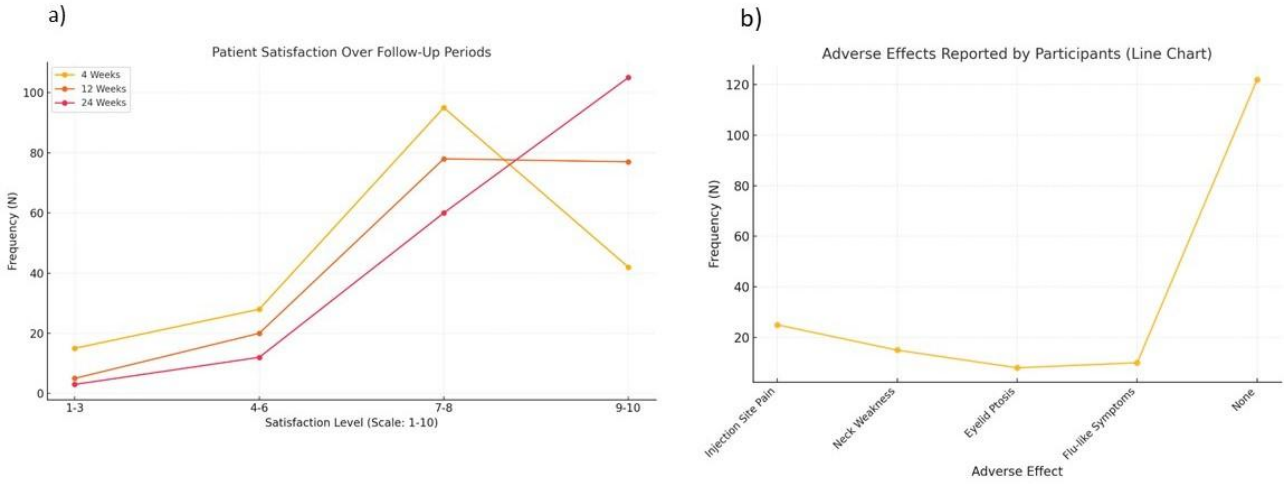

Figure 1: Trends in patient satisfaction and adverse effects of botulinum toxin therapy

(a) Patient satisfaction levels over follow-up periods (4, 12, and 24 weeks), measured using a satisfaction scale (1-10).

(b) Frequency of adverse effects reported by participants following botulinum toxin therapy, categorized by specific adverse effects.

Discussion

This study assessed the effects on quality of life, treatment adherence and adverse effects of botulinum toxin in lowering the frequency, severity and impairment related with chronic migraines. The findings showed notable increase in all assessed criteria, therefore supporting current knowledge and offering fresh analysis on the application of botulinum toxin for migraine control.

The decrease in headache days—from 21.4 ± 3.8 at baseline to 7.4 ± 2.2 at 24 weeks—showcases the therapeutic value of botulinum toxin in controlling chronic migraines. This is consistent with results from the PREEMPT studies, which showed treated individuals had a comparable decrease in headache days [16-17]. Further underlining the clinical advantages are the drop in severe migraines from 55.6% at baseline to 5.6% after 24 weeks and the comparable rise in mild and moderate instances. Our investigation showed steady efficacy with repeated treatments based on slow gains over time.

All spheres of WHOQOL-BREF evaluation revealed notable increases in quality of life; physical and psychological health showed the most clear changes. These results lined up with those of Skevington et al. (2004), who noted improved patient-reported results in chronic migraine sufferers given botulinum toxin [18]. The noted changes in social contacts and environmental contentment further emphasized the whole advantages of this treatment, which go beyond mere symptom management to include more general psychological effects. Given that chronic migraines

are well documented to seriously compromise quality of life (Escher et al., 2017) [6].

From 52.6 ± 14.8 to 15.3 ± 6.7, the improvement in NRS ratings—from 7.9 ± 1.2 at baseline to 2.7 ± 1.0 at 24 weeks—reflected both the symptomatic relief and functional recovery attained with botulinum toxin treatment. MIDAS scores reflected also the symptomatic relief and functional recovery attained with botulinum toxin treatment. These results are better than those documented with oral preventive drugs such topiramate, which are sometimes limited by side effects and adherence problems [19]. Particularly for patients who suffer from unbearable side effects with conventional pharmacologic treatments, our findings highlighted botulinum toxin's possible preferable prophylactic role for chronic migraine.

Rising from 77.8% at 4 weeks to 88.9% at 24 weeks, high adherence rates pointed to great tolerability and acceptability of botulinum toxin treatment. Long-term treatment efficacy in chronic diseases like migraines depends mostly on adherence [20]. The great patient satisfaction ratings (9.1 ± 0.8 at 24 weeks) supported even further the acceptance of this therapy approach. These results stressed the need of patient-centered care and the part minimally invasive treatments play in improving compliance and satisfaction.

The most prevalent adverse effects—which were minor and transient—were neck weakness (8.3%) and injection site soreness (13.9%). These results lined up with earlier research showing low rates of major side effects linked to botulinum toxin [21]. The change in adverse effect frequency over time—from 6.7% at 4 weeks to 2.8% at 24 weeks—may indicate better patient adaptation to the therapy or administration methods. Botulinum toxin is a reasonable long-term treatment choice with this good safety profile. Our results are consistent with and expand the corpus of data supporting botulinum toxin as a successful preventative treatment for chronic migraineurs. Although PREEMPT trials remain the gold standard, our extensive analysis offered more exact picture of treatment efficacy and adherence across time. For example, although Ruschel and Jesus, (2024) found a 50% decrease in headache days, our study showed a 65.4% decrease after 24 weeks most likely because of variations in population characteristics or adherence policies [1]. Furthermore, our results supported the conclusions of Silberstein et al. (2000) [22], who underlined the enhancements in quality of life related to botulinum toxin, thereby adding data particular to low-resource healthcare environments. Particularly in patient's refractory to conventional pharmaceutical prophylaxis, persistent decrease in headache frequency, severity and disability emphasized the promise of botulinum toxin as a cornerstone therapy for chronic migraines [6, 22]. The notable quality-of-life enhancements noted further support its usage in complete migraine control. Furthermore underlined by the high rates of adherence and satisfaction are the requirement of patient-centric methods in the management of chronic diseases by including treatments that not only work but also fit for patients.

The thorough evaluation of this study—which combines patient-reported data with clinical results—is one of its main strengths. The results get strength from the planned design and longitudinal follow-up. Using convenient sampling method, however, would restrict generalizability since participants from one tertiary care facility might not reflect the larger migraine prevalence. Furthermore, the absence of a control group forbids clear causal conclusions even if the obtained results match accepted knowledge. Future studies should try to include other demographics and investigate the long-term effectiveness and safety of botulinum toxin in therapy of chronic migraine. Comparative research comparing botulinum toxin versus more recent preventative treatments, including calcitonin gene-related peptide inhibitors, are justified to define its respective advantages.

Conclusion

This study showed that botulinum toxin is safe and efficient treatment for persistent migraines, so greatly lowering headache frequency, intensity and related impairment. High treatment adherence, low adverse effects and improvements in quality of life pointed to its fit as a long-term therapeutic choice. The findings provided evidence of real-world adherence trends and increasing efficacy across time. Particularly in patient's refractory to conventional pharmaceutical treatments, these results suggested the inclusion of

botulinum toxin into regular clinical practice for therapy of chronic migraine.

Conflict of Interest: None.

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