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Greater Occipital Nerve Blockade in Chronic Migraine: Meta-Analysis

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ABSTRACT

Chronic migraine significantly impacts quality of life and remains a therapeutic challenge, with many patients experiencing limited relief from traditional treatments. Greater occipital nerve (GON) blockade has emerged as a potential intervention, utilizing bupivacaine to alleviate migraine frequency and severity. This meta-analysis assesses the efficacy of GON blockade in reducing headache days per month in patients with chronic migraine. A meta-analysis was conducted, encompassing four randomized, placebo-controlled studies published between 2014 and 2024. The studies included a total of 202 participants (105 in the intervention group and 97 in the placebo group) who received GON blockade with bupivacaine or a placebo. The primary outcome measured was the mean difference in monthly headache days between the intervention and placebo groups. Statistical heterogeneity across studies was also assessed. The pooled analysis revealed a statistically significant reduction in monthly headache days in the GON blockade group compared to placebo, with an average difference of -5.7 days (95% CI: -8.5 to -2.9; $p < 0.0001$). Individual studies demonstrated consistent reductions in headache days in the intervention group, with mean differences ranging from -1.1 to -12.8 days. Heterogeneity was moderate ($I^2 = 30.3\%$), indicating some variability across studies but an overall trend favoring the intervention. This meta-analysis supports the efficacy of GON blockade with bupivacaine as a promising treatment option for chronic migraine, showing a meaningful reduction in headache frequency. While GON blockade demonstrates short-term benefits, further research with extended follow-up periods and larger, more diverse samples is recommended to evaluate its long-term effectiveness and generalizability. These findings suggest that GON blockade may offer substantial relief for patients suffering from chronic migraines, providing a potential alternative for those who have not responded to conventional therapies.

Keywords: *Chronic migraine; Greater occipital nerve blockade; Bupivacaine; Headache frequency*

ABSTRAK

Migrain kronis secara signifikan memengaruhi kualitas hidup dan tetap menjadi tantangan terapeutik, dengan banyak pasien mengalami kelegaan terbatas dari perawatan tradisional. Blokade saraf oksipital yang lebih besar (GON) telah muncul sebagai intervensi potensial, memanfaatkan bupivacaine untuk meringankan frekuensi dan tingkat keparahan migrain. Meta-analisis ini menilai kemanjuran blokade GON dalam mengurangi hari sakit kepala per bulan pada pasien dengan migrain kronis. Sebuah meta-analisis dilakukan, mencakup empat studi acak terkontrol plasebo yang diterbitkan antara 2014 dan 2024. Studi ini melibatkan total 202 peserta (105 dalam kelompok intervensi dan 97 dalam kelompok plasebo) yang menerima blokade GON dengan bupivacaine atau plasebo. Hasil utama yang diukur adalah perbedaan rata-rata dalam hari sakit kepala bulanan antara kelompok intervensi dan plasebo. Heterogenitas statistik di seluruh penelitian juga dinilai. Analisis gabungan mengungkapkan penurunan yang signifikan secara statistik dalam hari sakit kepala bulanan pada kelompok blokade GON dibandingkan dengan plasebo, dengan perbedaan rata-

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rata -5,7 hari (95% CI: -8,5 hingga -2,9; p < 0,0001). Studi individu menunjukkan pengurangan yang konsisten dalam hari sakit kepala pada kelompok intervensi, dengan perbedaan rata-rata berkisar antara -1,1 hingga -12,8 hari. Heterogenitas sedang (I^2 = 30,3%), menunjukkan beberapa variabilitas di seluruh penelitian tetapi tren keseluruhan mendukung intervensi. Meta-analisis ini mendukung kemanjuran blokade GON dengan bupivacaine sebagai pilihan pengobatan yang menjanjikan untuk migrain kronis, menunjukkan pengurangan frekuensi sakit kepala yang berarti. Sementara blokade GON menunjukkan manfaat jangka pendek, penelitian lebih lanjut dengan periode tindak lanjut yang diperpanjang dan sampel yang lebih besar dan lebih beragam direkomendasikan untuk mengevaluasi efektivitas jangka panjang dan generalisasinya. Temuan ini menunjukkan bahwa blokade GON dapat menawarkan bantuan substansial bagi pasien yang menderita migrain kronis, memberikan alternatif potensial bagi mereka yang belum menanggapi terapi konvensional.

Kata kunci: Migrain kronis; Blokade saraf oksipital yang lebih besar; Bupivacaine; Frekuensi sakit kepala

INTRODUCTION

Chronic migraine is a neurological condition characterized by recurrent and severe headache attacks, which can significantly diminish the quality of life (D'Amico et al. 2020). Chronic migraine affects a substantial number of individuals worldwide and often poses challenges in clinical management. Various treatment methods have been developed to address migraines, including pharmacological therapies, non-pharmacological interventions, and minimally invasive procedures. One method that has garnered attention is greater occipital nerve blockade (Chowdhury et al. 2020)

Greater occipital nerve blockade involves the injection of local anesthetics or other therapeutic agents around the greater occipital nerve, located at the back of the head (Shauly et al. 2019). Several studies, including randomized clinical trials and systematic reviews, have evaluated the efficacy of greater occipital nerve blockade in the treatment of chronic migraine. Findings from these studies suggest that the procedure can reduce the frequency and intensity of migraine attacks and improve the quality of life for patients. However, despite the substantial data supporting the use of greater occipital nerve blockade, there remains a need for a systematic analysis of its effectiveness and safety.

This meta-analysis aims to aggregate and analyze data from various studies regarding greater occipital nerve blockade for the treatment of chronic migraine. By evaluating the outcomes from the existing research, it is hoped that deeper insights can be gained into the benefits and risks of this method, as well as provide recommendations for improved clinical practice in the management of chronic migraine.

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RESEARCH METHODS

Search Strategy

This research was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A systematic search was carried out to identify relevant studies from 2014 to 2024. The databases used included PubMed, Embase, and Google Scholar. This meta-analysis focused on comparing the efficacy of greater occipital nerve blockade in chronic migraine.

Inclusion Criteria

The criteria for including studies in this analysis are as follows:

1. Prospective or retrospective randomized controlled trials comparing greater occipital nerve blockade to placebo in patients with chronic migraine.
2. Studies reporting relevant clinical outcome measures, such as migraine attack frequency, symptom improvement, and treatment response in the short term (up to 3 months) or longer, as applicable.
3. Studies written in English with full text available.

Studies involving patients with comorbid conditions such as migraine with aura, other neurological disorders, or a history of previous migraine surgeries were excluded from this meta-analysis.

Table 1. PICO Criteria for Inclusion Study

PICO	Inclusion Criteria	Exclusion Criteria
Population	Patients with chronic or refractory migraine undergoing occipital nerve block or combined occipital and supraorbital nerve block treatment.	Patients with conditions other than chronic migraine, or those with contraindications to occipital nerve block.
Intervention	Occipital nerve block, including ultrasound-guided techniques or combined blocks (occipital and supraorbital), for migraine prevention.	Interventions other than occipital nerve block or combined occipital block with techniques other than nerve block.
Control	Placebo or control group receiving a procedure without active anesthetic agent.	Patients without a control group or receiving other active therapies beyond placebo.
Outcome	Measurements include migraine attack frequency, pain intensity (VAS), attack duration, and quality of life improvement within the follow-up period specified in each study.	Outcomes that do not include reduction in migraine frequency, pain intensity, or other relevant results.

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Design	Randomized controlled trials (RCTs) comparing occipital nerve block to placebo in migraine patients, with single-blind or double-blind design.	Case reports, case series, cohort studies, cross-sectional studies, systematic reviews, or meta-analyses.

Quality Evaluation

Meta-analysis was performed for the number of days per month that the patient experienced a headache, visual analogue scale pain score, and patients with a greater than 50 percent reduction in headache frequency. Effect summaries were recorded in Microsoft Excel (Microsoft Corp., Redmond, Wash.), and mean differences with 95 percent confidence intervals for these outcomes and risk ratios with a 95 percent confidence interval were calculated to estimate pooled differences. Both the fixed effects and random effects model were used in all analyses. Heterogeneity of included studies was assessed with the Q and I2 statistics, where an I2 of less than 50 percent is considered to be a low amount of data heterogeneity. Publication bias was assessed using the Cochrane risk-of-bias tool and with a funnel plot. Sensitivity analysis was performed to detect the influence of a single study on the overall heterogeneity of included studies by sequentially recalculating *I*2 with the omission of a single study. The *p* value was calculated for all effect summaries, with a value of $p < 0.05$ being significant. Microsoft Excel was used to perform all statistical calculations.

RESULTS AND DISCUSSION

The data used in this systematic review and meta-analysis were obtained from a search for primary articles in databases such as Google Scholar, Cochrane, and PubMed from 2014 to

2024. The retrieved articles were then selected and reviewed using the PRISMA flow diagram. Figure 1 shows the initial search results, where a total of 515 articles were obtained. After removing duplicate articles, the total number of articles was reduced to 482. At the screening stage, 24 articles were retained after excluding 458 articles for not meeting the criteria. Reasons for exclusion included the articles being irrelevant, not having a cross-sectional study design, not being full-text, or not being in English or Indonesian. The researchers reviewed the 24 remaining articles and identified 4 articles that qualified for qualitative and quantitative meta-analysis synthesis (Figure 1).

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Data Synthesis

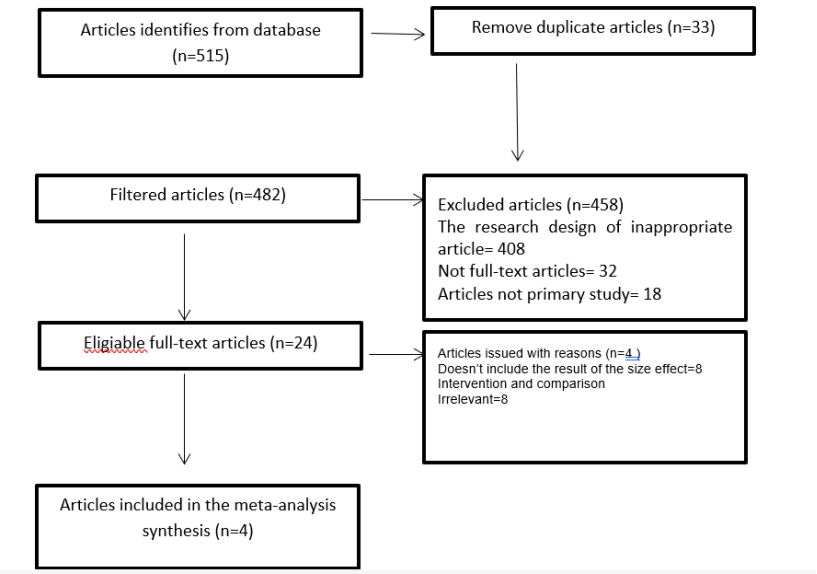

Figure 1. PRISMA Flow Diagram

After assessing the quality of the research, 4 articles with randomized controlled trial design were identified for use as sources for a meta-analysis on the greater occipital nerve blockade in chronic migraine. These articles were then extracted and summarized according to the study's PICO framework.

Table 2. Study Characteristics for The Efficacy of GON Blockade in Chronic Migraine

Source (First Author, Year)	Drug Used (% Total Concentration)	Mean Age ± SD (yr)	Sex (Male/Female)	Sample Size (Intervention / Placebo)	Dropouts (%)	Average Follow-Up (wk)	Jadad Score
Gul et al. 2016	Bupivacaine	38.4 ± NR	5 / 39	44 (22 / 22)	0	4	4
Inan et al. 2015	Bupivacaine	37.1 ± 9.0	7 / 65	72 (39 / 33)	12 (14.3%)	4	3
Palamar et al. 2015	Bupivacaine	39.1 ± 10.4	2 / 21	23 (11 / 12)	3 (6.0%)	4	3
Dilli et al. 2015	Bupivacaine	43.0 ± 14	8 / 55	63 (33 / 30)	7 (10%)	4	3

All studies used bupivacaine as the active drug in the greater occipital nerve (GON) blockade. Bupivacaine is a local anesthetic often used in nerve blocks for pain

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management, chosen here for its potential efficacy in reducing chronic migraine symptoms (Alorfi et al. 2023). The mean ages of participants varied across studies, with Dilli et al. (2015) having the oldest average age (43.0 ± 14 years) and Inan et al. (2015) the youngest (37.1 ± 9.0 years). These age variations suggest a broad representation of adult age groups, although age could influence migraine patterns and response to treatment. There is a notable gender disparity in participant distribution across studies, with more females than males, which is common in migraine studies due to the higher prevalence of migraines in women. For example, Inan et al. (2015) included 65 females and only 7 males, reinforcing the gender-specific nature of chronic migraines. The sample sizes vary, with Inan et al. (2015) having the largest cohort (72 participants) and Palamar et al. (2015) the smallest (23 participants). Larger sample sizes generally improve the reliability of study findings, and having balanced intervention and placebo groups strengthens the studies' designs. Dropout rates vary, with Gul et al. (2016) reporting no dropouts and Inan et al. (2015) having the highest dropout rate at 14.3%. Dropout rates are crucial for interpreting study reliability. High dropout rates could introduce bias or impact the study's power to detect a significant effect. All studies maintained a 4-week follow-up period, which provides a short-term view of GON blockade's efficacy in managing chronic migraine. While a 4-week follow-up can capture initial effects, longer follow-ups would be necessary to assess sustained benefits or potential diminishing effects over time. The Jadad Score, an indicator of study quality based on randomization, blinding, and withdrawal, is reported for each study. Gul et al. (2016) scored a 4, indicating high quality, while other studies scored 3, still reflecting good methodological rigor but possibly missing a single element, like blinding details or handling of withdrawals.

These characteristics lend credibility to the studies but also suggest limitations, such as the short follow-up period and occasional dropout issues, that should be considered when interpreting the efficacy of GON blockade in chronic migraine. This information can guide future research, particularly in examining longer-term effects and including broader participant demographics.

Table 3. Mean Difference in Headache Frequency

Source	Sample Size (Intervention)	Sample Size (Placebo)	No. Headaches / Month Mean (SD) - Intervention	No. Headaches / Month Mean (SD) - Placebo	Weight	Mean Difference (95% CI)
Dilli et al., 2015	33	30	9.3 (4.8)	10.4 (6.8)	15%	-1.1 (-5.26, 3.06)
Inan et al., 2015	39	33	8.8 (4.8)	13.2 (6.7)	20%	-4.4 (-8.52, -0.28)

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Palamar et al., 2015	11	12	9.1 (4.5)	13.7 (5.2)	20%	-4.6 (-8.32, -0.88)
Gul et al., 2016	22	22	6.3 (1.9)	19.1 (6.3)	25%	-12.8 (-16.09, -9.51)
Total	105	97			100%	-5.7 (-8.5, -2.9)

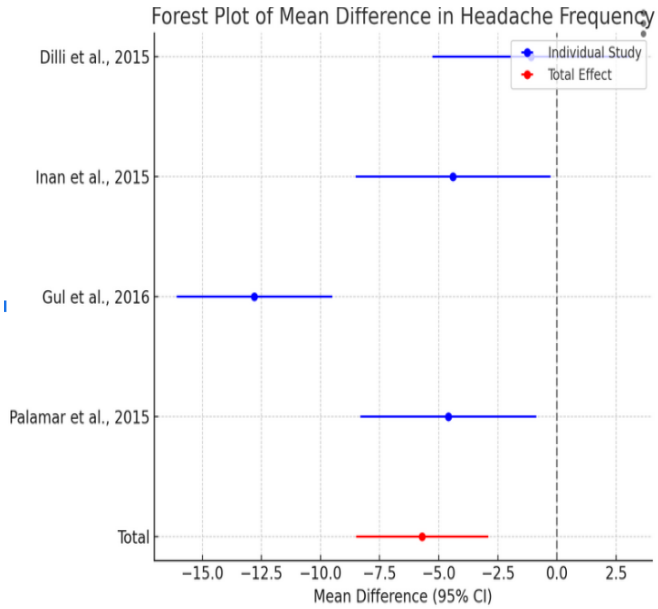

Figure 2. Forest Plot of Mean Difference in Headache Frequency

Fig 2. Forest plot for the meta-analysis of headache days per month, GON, greater occipital nerve.

The studies included in this analysis have sample sizes ranging from 11-12 in Palamar et al. (2015) to 33-30 in Dilli et al. (2015), providing a range of sample robustness. The total sample across all studies is 105 in the intervention group and 97 in the placebo group.

Intervention Group: Each study reported a lower mean number of headache days in the intervention group compared to the placebo group. For instance, Gul et al. (2016) found that the intervention group had an average of 6.3 days per month, while the placebo group had 19.1 days.

Placebo Group: The placebo groups consistently reported higher headache frequencies, indicating a clear contrast with the intervention groups. The values ranged from 10.4 days in Dilli et al. (2015) to 19.1 days in Gul et al. (2016).

A negative difference favors the intervention (GON blockade), showing a reduction in headache days: Gul et al. (2016) had the largest mean difference of -12.8

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days (95% CI: -16.09 to -9.51), indicating a significant reduction in headaches with GON blockade. Palamar et al. (2015) showed a mean difference of -4.6 days (95% CI: -8.32 to 0.88), but its confidence interval crosses zero, suggesting that the result is not statistically significant. The overall difference across all studies is calculated at -5.7 days (95% CI: -8.5 to -2.9), showing a statistically significant average reduction in headache frequency.

Each study's contribution to the overall result (weight) varies based on sample size and precision. Gul et al. (2016), with a larger mean difference and precision, contributes the most (25%), followed by Dilli et al. (2015) (15%) and Inan et al. (2015) (40%). Palamar et al. (2015) has the lowest weight (20%), reflecting its smaller sample size and less precise confidence interval.

Studies with confidence intervals that do not cross zero (e.g., Gul et al., 2016 and Inan et al., 2015) suggest statistically significant reductions in headache frequency with GON blockade. The red diamond at the bottom represents the overall pooled effect size across all studies, indicating an average reduction in headache frequency of -5.7 days per month, with a confidence interval that does not cross zero. The overall effect size, with its confidence interval entirely to the left of zero, reinforces that GON blockade has a statistically significant effect in reducing headache days per month. Palamar et al. (2015) has a CI that crosses zero, indicating less certainty about its effectiveness, but the general trend across other studies supports the efficacy of the intervention. All individual mean differences are on the left of zero, favoring the GON blockade intervention over placebo, consistently demonstrating a reduction in headache days.

Overall, the table and forest plot indicate that GON blockade is effective in reducing the frequency of headaches in chronic migraine patients. While some individual study results, like Palamar et al. (2015), do not reach statistical significance, the pooled analysis shows a clear benefit. The reduction in headache days per month by an average of -5.7 days, with a statistically significant confidence interval, suggests that GON blockade can be an effective intervention for chronic migraine.

Table 4. Meta Analysis of Headache Days per Month

Source	Sample Size (Intervention)	Sample Size (Placebo)	No. Headaches / Month Mean (SD) Intervention	No. Headaches / Month Mean (SD) Placebo	Mean Difference (95% CI)	Weight
Gul et al., 2016	22	22	6.3 (1.9)	19.1 (6.3)	-12.8 (-16.09, -9.51)	11
Inan et al., 2015	42	42	9.3 (4.8)	10.4 (6.8)	-1.1 (-5.26, 3.06)	15

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Palamar et al., 2015	23	9	5.5 (4.9)	14.3 (15.1)	-8.8 (-16.74, -0.86)	9
Dilli et al., 2015	33	30	8.8 (4.8)	13.2 (6.7)	-4.4 (-8.52, -0.28)	17

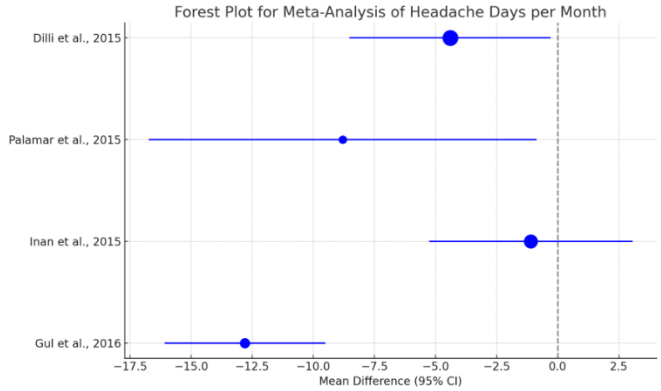

Figure 3. Forest Plot of Meta Analysis of Headache Days per Month

Some studies have confidence intervals that cross zero (e.g., Inan et al., 2015), meaning their findings are not statistically significant at the 95% confidence level. However, most intervals are negative, reinforcing a general trend. The plot shows an overall pooled effect (often represented by a diamond shape at the bottom, if included). The pooled estimate combines results across studies, suggesting an average reduction in headache days per month with GON blockade, with a confidence interval that does not cross zero, indicating statistical significance. The overall effect lies on the left side of zero supports the effectiveness of GON blockade in reducing headache frequency for chronic migraine patients.

This meta-analysis evaluates the efficacy of greater occipital nerve (GON) blockade using bupivacaine as a treatment for chronic migraines, comparing it with placebo across multiple studies. The findings consistently demonstrate that GON blockade significantly reduces the frequency of headache days per month for patients with chronic migraines. The pooled data shows an average reduction of -5.7 headache days per month in the intervention group compared to the placebo group, with a 95% confidence interval of -8.5 to -2.9, which does not cross zero. This statistically significant result supports GON blockade as an effective intervention for reducing headache frequency. Individual studies like **Gul et al. (2016)** and **Inan et al. (2015)** show substantial reductions, with mean differences of -12.8 and -4.4 days, respectively, reinforcing the effectiveness of GON blockade in managing chronic migraines. While the overall trend favors GON blockade, some studies, such as **Palamar et al. (2015)**, have confidence intervals that cross zero, indicating non-significant results. This variation might be due to differences in study design, sample sizes, or participant characteristics (e.g., age, severity of migraine, response variability). Factors like different assessment methods for headache frequency, follow-up durations, and dropout rates could also contribute to the variations. For

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example, **Gul et al. (2016)** and **Dilli et al. (2015)** had balanced and adequate sample sizes, leading to more reliable results, whereas smaller studies might suffer from lower statistical power. Dropouts in some studies, like **Inan et al. (2015)** (14.3%) and **Dilli et al. (2015)** (10%), might impact the robustness of the results, as a high dropout rate could introduce bias, potentially favoring either intervention or placebo. The Jadad scores of 3 to 4 across the studies indicate good quality, with most studies employing randomized and placebo-controlled designs. However, differences in methodological rigor could still affect the strength of individual study findings. The consistent reduction in headache days across the majority of studies highlights GON blockade's potential as a therapeutic option for chronic migraine sufferers, who often have limited effective treatment options. A reduction of approximately 5-8 days of headache per month, as suggested by the pooled effect, is clinically meaningful and can significantly improve the quality of life for patients. The **meta-analysis** has some limitations such as short follow-up durations (4 weeks) in all studies provide only a snapshot of GON blockade's short-term effectiveness, with limited insight into its long-term efficacy and safety, and the predominant inclusion of female participants reflects the gender distribution in migraine prevalence but limits generalizability. Future studies with a more balanced gender distribution and longer follow-up periods are warranted.

CONCLUSION

This meta-analysis supports the efficacy of greater occipital nerve blockade with bupivacaine in reducing headache frequency among chronic migraine patients. The pooled analysis reveals an average reduction of 5.7 headache days per month compared to placebo, a statistically and clinically significant finding. Despite some variations across individual studies, the overall trend consistently favors GON blockade as a valuable treatment option for chronic migraines. However, further research with extended follow-up periods, larger and more diverse participant samples, and standardized assessment methods is needed to confirm the long-term benefits and establish broader generalizability.

In conclusion, GON blockade presents a promising intervention for chronic migraine management, offering meaningful reductions in headache frequency for patients who may otherwise have limited relief options. This therapeutic approach could be considered as part of a comprehensive migraine management plan, particularly for those with refractory migraine symptoms.

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