ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

DOI: 10.5336/anesthe.2025-112719

The Role of Inflammatory Markers in Predicting the Effectiveness of Greater Occipital Nerve Block in Chronic Migraine: Retrospective Cohort Study

Kronik Migrende Büyük Oksipital Sinir Bloğunun Etkinliğini Öngörmede İnflamatuar Belirteçlerin Rolü: Retrospektif Kohort Çalışması

Hanzade Aybüke ÜNAL[a], Ersin SÖNMEZ[b], Güngör Enver ÖZGENCİL[a]

[a]Ankara University Faculty of Medicine, Department of Anesthesiology and Reanimation, Ankara, Türkiye
[b]Erciyes University Faculty of Medicine, Department of Anesthesiology and Reanimation, Kayseri, Türkiye

ABSTRACT Objective: This study was aimed to evaluate whether systemic inflammatory markers-specifically the neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and aggregate index of systemic inflammation (AISI)-could serve as reliable predictors in determining the clinical efficacy of greater occipital nerve (GON) block treatment among patients suffering from chronic migraine. **Material and Methods:** This retrospective cohort study included 48 adult patients who had been diagnosed with and who underwent GON block therapy between 2020 and 2025. Each patient received a standardized protocol consisting of seven GON block interventions. The therapeutic response was defined as a reduction of ≥50% in the number of monthly headache days compared to baseline. Demographics and inflammatory indices were derived from the complete blood count (NLR, SII, SIRI, and AISI) were collected and analyzed. The cohort was then divided into responders and non-responders based on clinical outcome. **Results:** A favorable treatment response was observed in 33 (68.7%). No statistically significant differences were found in baseline demographic variables, between the responder and non-responder groups. Similarly, none of the inflammatory markers-NLR, SII, SIRI, and AISI-showed significant differences between the 2 groups (p>0.05). **Conclusion:** The findings of this study suggest that systemic inflammatory markers such as NLR, SII, SIRI, and AISI don't have a significant predictive value in assessing the response to GON block in patients with chronic migraine.

Keywords: Migraine disorders; nerve block; chronic pain; inflammation; biomarkers

ÖZET Amaç: Bu çalışma, kronik migren tedavisinde büyük oksipital sinir [greater occipital nerve (GON)] blokajının etkinliğini öngörmede, sistemik inflamasyon göstergeleri olan nötrofil/lenfosit oranı [neutrophil-to-lymphocyte ratio (NLR)], sistemik immün-inflamasyon indeksi [systemic immune-inflammation index (SII)], sistemik inflamasyon yanıt indeksi [systemic inflammation response index (SIRI)] ve agregat sistemik inflamasyon indeksi [aggregate index of systemic inflammation (AISI)] değerlerinin prediktif rolünü araştırmayı amaçlamaktadır. **Gereç ve Yöntemler:** Bu retrospektif kohort çalışma, 2020-2025 yılları arasında kronik migren tanısıyla GON blokajı uygulanan 48 hastayı içermektedir. Tüm hastalara toplam 7 blok uygulanmış ve tedavi yanıtı, ayda baş ağrısı günlerinde %50 veya daha fazla azalma olarak tanımlanmıştır. Hastaların demografik verileri ve tam kan sayımı üzerinden hesaplanan inflamatuar parametreleri (NLR, SII, SIRI ve AISI) analiz edildi. Sonrasında hastalar klinik yanıta göre yanıtlılar ve yanıtsızlar olarak ayrıldı. **Bulgular:** Hastaların %68,7'si (n=33) tedaviye başarılı yanıt verdi. Yanıt veren ve vermeyen gruplar arasında yaş ve cinsiyeti içeren demografik veriler açısından anlamlı fark bulunmadı. NLR, SII, SIRI ve AISI değerleri açısından da yanıt veren ve vermeyen gruplar arasında istatistiksel fark yoktu (p>0,05). **Sonuç:** NLR, SII, SIRI ve AISI gibi sistemik inflamasyon belirteçleri, GON blok tedavisine yanıtı öngörmede anlamlı bir fark göstermemiştir.

Anahtar Kelimeler: Migren hastalıkları; sinir bloğu; kronik ağrı; inflamasyon; biyobelirteçler

TO CITE THIS ARTICLE:
Ünal HA, Sönmez E, Özgencil GE. The role of inflammatory markers in predicting the effectiveness of greater occipital nerve block in chronic migraine: Retrospective cohort study. Turkiye Klinikleri J Anest Reanim. 2025;23(2):68-73.

Correspondence: Ersin SÖNMEZ
Erciyes University Faculty of Medicine, Department of Anesthesiology and Reanimation, Kayseri, Türkiye
E-mail: ersinsonmez@erciyes.edu.tr

Peer review under responsibility of Turkiye Klinikleri Journal of Anesthesiology Reanimation.

Received: 16 Jun 2025 ***Received in revised form:*** 18 Aug 2025 ***Accepted:*** 18 Aug 2025 ***Available online:*** 28 Aug 2025

Migraine is a widespread primary headache disorder, typically presenting as recurrent episodes of unilateral, pulsating pain of moderate to severe intensity. The International Headache Society classifies migraines into two categories: episodic migraine, which happens on less than 15 days per month, and chronic migraine (CM), characterised by headaches on 15 or more days per month for at least 3 months.[1] The global prevalence of migraine is approximately 12%, while CM affects about 2% of the population.[2] CM significantly affects quality of life and presents a considerable financial strain on healthcare costs. Neurogenic inflammation, central sensitization, and dysfunction of the trigeminal system are considered pivotal mechanisms underlying the pathophysiology of migraine, with accumulating evidence indicating a complex bidirectional interaction among these processes.[3] Activation of the trigeminovascular system-accompanied by the release of pro-inflammatory mediators and neuropeptides such as calcitonin gene-related peptide (CGRP) results in vasodilation and perivascular inflammation, which represent key pathophysiological mechanisms in the onset and progression of migraine.[4]

Several systemic inflammatory markers have gained attention in the context of neurological disorders' pathophysiology, including the neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and aggregate index of systemic inflammation (AISI).[5,6] While NLR takes into account neutrophils and lymphocytes, SII, SIRI, and AISI incorporate additional inflammatory cell types such as monocytes and platelets, potentially offering a more comprehensive assessment of systemic inflammatory status.[7,8] Recent findings suggest that AISI could serve as an accurate marker of systemic inflammation and has been linked to outcomes in cardiovascular diseases, cancers, and various neurological conditions disorders.[9-11]

The greater occipital nerve (GON) block has been utilized as an effective prophylactic treatment for CM, mainly through inhibition of trigeminal pain pathways within the trigeminocervical complex and reduction of local inflammation.[12] Injection of local anesthetics, such as lidocaine or bupivacaine, around the GON produces a temporary peripheral nerve blockade, which in turn attenuates central sensitization and inhibits the trigeminovascular system.[13] Despite its clinical efficacy, it remains unclear which patients are most likely to benefit from GON block therapy. To date, only one study has proposed that CGRP levels may serve as a predictive biomarker for GON block efficacy.[14]

In this study we aimed to evaluate the predictive value of systemic inflammatory markers-including NLR, SII, SIRI, and AISI in determining the therapeutic efficacy of GON block in patients with CM. Identifying such biomarkers may enhance patient selection, reduce unnecessary procedures, and support a more personalized approach to migraine management.

MATERIAL AND METHODS

This study was conducted in the Department of Algology of the Faculty of Medicine of Ankara University. Patients who received GON block for the treatment of CM between January 2020-January 2025 at our tertiary headache centre were retrospectively assessed. The study protocol received approval from the Ankara University Human Research Ethics Committee (date: March 18. 2025; no: İ03-233-25) and was carried out in accordance with the principles detailed in the Declaration of Helsinki. The study included patients aged 18 or older who had a CM diagnosis based on International Classification of Headache Disorders-3 criteria and received GON blocks. Exclusion criteria were: presence of renal, hepatic, thyroid, or pulmonary disease; history of malignancy; diagnosis of diabetes mellitus or hypertension; active infection; autoimmune, rheumatologic, or hematologic disorders; cerebrovascular disease (e.g., stroke); and pregnancy. These conditions were excluded to eliminate potential confounding effects on systemic inflammatory markers.

GON BLOCK PROCEDURE

All GON blocks were performed in an outpatient setting by experienced pain specialists using anatomical landmarks. The anatomical target was

identified at the junction of the medial one-third of an imaginary line connecting the occipital protuberance and the mastoid process. At this site 2 mL of 1% lidocaine was injected without the addition of corticosteroids. Each patient received a total of 7 GON blocks: the initial 5 injections were performed at weekly intervals, followed by 2 additional blocks administered at monthly intervals. Informed consent was obtained from all patients prior to the GON block procedure.

FOLLOW-UP AND EVALUATION OF TREATMENT RESPONSE

Patients were followed up for a period of 3 months following the initial GON block procedure. Treatment efficacy was assessed based on the reduction in the number of headache days per month a positive response was identified as at least a 50% reduction in headache days compared to baseline.

DATA COLLECTION

Age, sex, headache days per month, and blood results, were retrospectively obtained from medical records. Systemic inflammatory indices (NLR, SII, SIRI, AISI) were calculated as described using baseline complete blood count results before GON block administration.[15] The following formulas were used:

- NLR=Neutrophil count/lymphocyte count
- SII=(Platelet count×neutrophil count)/lymphocyte count
- SIRI=(Neutrophil count×monocyte count)/lymphocyte count
- AISI=(Neutrophil count×monocyte count×platelet count)/lymphocyte count

STATISTICAL ANALYSIS

The data analysis was performed with IBM SPSS Statistics (Version 29.0.1 for MacOS, Armonk, NY, IBM Corp, USA). Data were shown as units (n), percentages (%), mean±standard deviation, median, and interquartile range. The normality of quantitative variables was evaluated with the Shapiro-Wilk test and Q-Q plots. Age, NLR, SII, SIRI, and AISI, were compared using the independent samples t-test. Fisher's exact test was employed to analyze gender and Numeric Rating Scale reduction as categorical variables.

RESULTS

A total of 67 patients who received GON block for the treatment of CM were identified. Following the application of predefined inclusion and exclusion criteria, 48 patients were considered eligible and included in the final analysis. The remaining 19 patients were excluded due to factors such as missing follow-up data, comorbidities affecting inflammatory markers, or non-compliance with the study protocol. Among the 48 analyzed patients, 33 were classified as treatment responders, whereas 15 were categorized as non-responders. There were no statistically significant differences in age or gender distribution between responders and non-responders (Table 1). Similarly, no significant differences were observed in baseline levels of NLR, SII, SIRI, or AISI between the 2 groups (p>0.05) (Table 2).

TABLE 1: Comparison of demographic variables

	Treatment response			
	Responders	Non-responders	Test statistics	
Variables	(n=33)	(n=15)	Test value	p value
Age (years)	45.1±9.8	42.7±11.5	t=-0.749	0.458
Gender (female/male)	30/3	12/3	-	0.36*

Data presented as mean±standard deviation or numbers; *Fisher's exact test; t: Independent samples t-test

TABLE 2: Comparison of baseline inflammatory markers

	Treatment response			
	Responders	Non-responders	Test statistics	
Variables	(n=33)	(n=15)	Test value	p value
NLR	1.78±0.51	1.80±0.37	t=0.158	0.875
SII	485.27±167.96	514.54±109.90	t=0.616	0.541
SIRI	1.06±0.51	0.90±0.27	t=-1.185	0.242
AISI	287.29±130.18	257.13±82.48	t=-0.823	0.415

Data presented as mean±standard deviation or median (interquartile range); t: Independent samples t-test; NLR: Neutrophil-to-lymphocyte ratio; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; AISI: Aggregate index of systemic inflammation

DISCUSSION

In this study, we investigated whether inflammatory markers had any impact on treatment response in patients with CM who underwent GON block. Pre-procedural blood samples were analyzed to calculate systemic inflamatory indices including the NLR, SII, SIRI, and AISI. Our results revealed no statistically significant differences in these baseline inflammatory markers between patients who achieved ≥50% reduction in headache days and those who did not.

Inflammation is a key factor in triggering and exacerbating numerous neurologic diseases, such as migraines, seizures, strokes, as well as neurodegenerative diseases like Alzheimer's and Parkinson's. Increasing evidence support that the interplay between neural and immune systems is crucial in the pathophysiology of these brain disorders.[16] Neuroinflammation, or neurogenic inflammation, contributes significantly to migraine pathophysiology. It involves the release of neuropeptides such as CGRP, substance P, and neurokinin A from trigeminal nerves, leading to sensitization of meningeal nociceptors. This process is modulated by both pro- and anti-inflammatory cytokines, which influence pain perception. Although a systemic pro-inflammatory state is frequently observed in migraineurs, its exact role in lowering the activation threshold of the trigeminovascular system remains unclear. These findings highlight migraine as a complex neuro-glio-vascular disorder driven in part by inflammatory mechanisms.[5]

Several studies have investigated hematological and inflammatory parameters in patients with migraine. Evrin and Katipoglu reported significant differences in hemoglobin and hematocrit levels in migraine patients compared to healthy subjects, However, no statistically significant differences were observed in platelet counts or mean platelet volume between the groups.[17] Similarly, Sarıcam demonstrated significant elevations in inflammatory markers, including C-reactive protein (CRP), NLR, platelet-to-lymphocyte ratio, and lymphocyte-to-monocyte ratio in migraineurs compared to controls.[18] Yucel et al. also reported increased levels of CRP and D-dimer in individuals with migraine. Consistently, other studies have found CRP concentrations to be significantly higher in migraineurs than in healthy subjects.[19,20] In contrast, Bastuğ Gül et al. observed significantly higher platelet counts in migraine patients but found no notable differences in other hematological parameters. The increase in platelet count was attributed to the inflammatory mechanisms involved in migraine, as platelets can release pro-inflammatory mediators such as thromboxane.[21] Supporting this, Karabulut et al. reported increased platelet counts among migraine patients suggesting that elevated circulating platelet levels reflects the inflammation in both cerebral and extracerebral neurovascular structure.[22]

The therapeutic efficacy of the GON block in treating migraines are primarily attributed to its modulation of the trigeminovascular system. The GON, which is a sensory branch of the second cervical nerve (C2), shares an anatomical connection with the trigeminal nucleus caudalis in the brainstem.[23] This overlap enables interactions between the cervical and trigeminal afferents, which can lead to the activation and sensitization of peripheral nociceptors, as well as promoting the release of inflammatory mediators. Proinflammatory cytokines, which enhance inflammatory responses and modulate proinflammatory activity, play critical role in the regulation of pain.[5] A previous study investigating the role of inflammatory markers in the effectiveness of GON block reported that patients with elevated levels of baseline CGRP exhibited a reduced response to the intervention. The same study demostrated that GON block was associated with a reduction in CGRP levels, and that a baseline CGRP concentration below 250 pg/mL correlated with a more favorable clinical response. The authors suggested that this finding may be attributed to the influence of CGRP on the trigeminal caudal nucleus and the C1-C2 levels of the spinal cord, which are involved in the transmission of pain signals to the thalamus and higher cortical areas.[14] In the present study no significant association was found between the inflammatory markers mentioned earlier and the clinical response to GON block. Our research has

certain limitations; the retrospective design, single-center setting, and relatively small sample size may have influenced the generalizability of the findings. Although conditions and diseases that could potentially affect inflammatory markers were excluded, further large-scale, multicenter prospective studies are warranted to validate these findings and provide more comprehensive and generalizable results.

CONCLUSION

GON block is a well-established and effective treatment modality for CM. Our findings showed no statistically significant relationship between baseline levels of inflammatory markers and treatment outcomes. These findings suggest that the efficacy of the GON block might not depend on systemic inflammatory status; nevertheless, additional prospective and controlled studies are necessary to confirm these insights.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Hanzade Aybüke Ünal;* ***Design:*** *Hanzade Aybüke Ünal;* ***Control/Supervision:*** *Güngör Enver Özgencil;* ***Data Collection and/or Processing:*** *Ersin Sönmez;* ***Analysis and/or Interpretation:*** *Hanzade Aybüke Ünal, Ersin Sönmez;* ***Literature Review:*** *Hanzade Aybüke Ünal;* ***Writing the Article:*** *Hanzade Aybüke Ünal, Ersin Sönmez;* ***Critical Review:*** *Güngör Enver Özgencil.*

REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders. 3rd ed. Cephalalgia. 2018;38(1):1-211. [Crossref] [PubMed]
2. Buse DC, Manack AN, Fanning KM, Serrano D, Reed ML, Turkel CC, et al. Chronic migraine prevalence, disability, and sociodemographic factors: results from the American Migraine Prevalence and Prevention Study. Headache. 2012;52(10):1456-70. [PubMed]
3. Zhang XC, Strassman AM, Burstein R, Levy D. Sensitization and activation of intracranial meningeal nociceptors by mast cell mediators. J Pharmacol Exp Ther. 2007;322(2):806-12. [Crossref] [PubMed]
4. Charles A. The pathophysiology of migraine: implications for clinical management. Lancet Neurol. 2018;17(2):174-82. [PubMed]
5. Lee SH, Kim JH, Kwon YS, Sohn JH. Role of peripheral inflammatory markers in patients with acute headache attack to differentiate between migraine and non-migraine headache. J Clin Med. 2022;11(21):6538. [Crossref] [PubMed] [PMC]
6. Göçmen A, Gesoglu Demir T. The aggregate index of systemic inflammation as a predictor of mortality in stroke patients. Cureus. 2024;16(7):e64007. [PubMed] [PMC]
7. Xiu J, Lin X, Chen Q, Yu P, Lu J, Yang Y, et al. The aggregate index of systemic inflammation (AISI): a novel predictor for hypertension. Front Cardiovasc Med. 2023;10:1163900. [Crossref] [PubMed] [PMC]
8. Wang RH, Wen WX, Jiang ZP, Du ZP, Ma ZH, Lu AL, et al. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Front Immunol. 2023;14:1115031. [PubMed] [PMC]
9. Huang YW, Zhang Y, Feng C, An YH, Li ZP, Yin XS. Systemic inflammation response index as a clinical outcome evaluating tool and prognostic indicator for hospitalized stroke patients: a systematic review and meta-analysis. Eur J Med Res. 2023;28(1):474. [Crossref] [PubMed] [PMC]
10. Ye Z, Hu T, Wang J, Xiao R, Liao X, Liu M, et al. Systemic immune-inflammation index as a potential biomarker of cardiovascular diseases: a systematic review and meta-analysis. Front Cardiovasc Med. 2022;9:933913. [PubMed] [PMC]
11. Zhou Q, Su S, You W, Wang T, Ren T, Zhu L. Systemic inflammation response index as a prognostic marker in cancer patients: a systematic review and meta-analysis of 38 cohorts. Dose Response. 2021;19(4):15593258211064744. [Crossref] [PubMed] [PMC]
12. Shauly O, Gould DJ, Sahai-Srivastava S, Patel KM. Greater occipital nerve block for the treatment of chronic migraine headaches: a systematic review and meta-analysis. Plast Reconstr Surg. 2019;144(4):943-52. [PubMed]
13. Ashkenazi A, Blumenfeld A. OnabotulinumtoxinA for the treatment of headache. Headache. 2013;53 Suppl 2:54-61. [Crossref] [PubMed]
14. Abbas A, Moustafa R, Shalash A, Haroun M, Amin R, Borham S, et al. Serum CGRP changes following ultrasound-guided bilateral greater-occipital-nerve block. Neurol Int. 2022;14(1):199-206. [PubMed] [PMC]
15. Liu H, Dong H, Guo M, Cheng H. Association between inflammation indicators (MLR, NLR, SII, SIRI, and AISI) and erectile dysfunction in US adults: NHANES 2001-2004. J Health Popul Nutr. 2024;43(1):169. [Crossref] [PubMed] [PMC]

16. Lénárt N, Brough D, Dénes Á. Inflammasomes link vascular disease with neuroinflammation and brain disorders. J Cereb Blood Flow Metab. 2016;36(10):1668-85. [PubMed] [PMC]

17. Evrin T, Katipoglu B. Evaluation of hematological parameters in migraine attack in emergency room. Annals of Medical Research. 2019;26(7):1384-7. [Link]

18. Sarıcam G. Relationship between migraine headache and hematological parameters. Acta Neurol Belg. 2021;121(4):899-905. [Crossref] [PubMed]

19. Yucel Y, Tanriverdi H, Arıkanoglu A, Varol S, Kaplan I, Akil E, et al. Increased fibrinogen, D-dimer and galectin-3 levels in patients with migraine. Neurol Sci. 2014;35(4):545-9. [PubMed]

20. Yildiz BT, Koca TT. Is migraine an inflammatory event? Which inflammatory markers can we use for migraine? Annals of Medical Research. 2019;26(6):973-5. [Link]

21. Bastuğ Gül Z, Gül M, Gözübatık Çelik RG, Soysal A. New indicator of inflammation in migraine: red blood cell distribution. Haydarpaşa Numune Med J. 2021;61(2):166-71. [Link]

22. Karabulut KU, Egercioglu TU, Uyar M, Ucar Y. The change of neutrophils/lymphocytes ratio in migraine attacks: a case-controlled study. Ann Med Surg (Lond). 2016;10:52-6. [PubMed] [PMC]

23. Martami F, Razeghi Jahromi S, Togha M, Ghorbani Z, Seifishahpar M, Saidpour A. The serum level of inflammatory markers in chronic and episodic migraine: a case-control study. Neurol Sci. 2018;39(10):1741-9. [PubMed]