ATATÜRK ÜNİVERSİTESİ YAYINLARI
ATATURK UNIVERSITY PUBLICATIONS

RESEARCH ARTICLE / *Araştırma makalesi* DOI: 10.61745/jsmsau.1584825

Propofol vs. Chlorpromazine for Acute Migraine Treatment: Insights from a Prospective Randomized Trial

Akut Migren Tedavisinde Propofol ve Klorpromazin: Prospektif Randomize Bir Çalışma Bulguları

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ABSTRACT

Objective: This study aimed to compare the efficacy of propofol and chlorpromazine in managing acute migraine attacks and to contribute to optimizing the treatment of patients with migraine in the ED.
Methods: This prospective, randomized observational study included 180 migraine patients aged 18–65 presenting to the ED. Patients were randomized into two groups: one received propofol (10 mg every 10 minutes, up to 50 mg), and the other received chlorpromazine (12.5 mg every 20 minutes, up to 37.5 mg). Pain was monitored every 10 minutes using a visual analog scale (VAS).
Results: At admission, the mean VAS score was 8.24 ± 1.72 in the propofol group and 8.83 ± 1.43 in the chlorpromazine group. In the propofol group, the VAS score decreased by 5.19 ± 2.79, 2.66 ± 2.91, and 1.25 ± 2.14 units at the 10^{th}, 20^{th}, and 30^{th} minutes, respectively. In the chlorpromazine group, the VAS score decreased by 4.82 ± 2.99, 2.50 ± 2.93, and 1.03 ± 2.20 units at the 10^{th}, 20^{th}, and 30^{th} minutes, respectively. By the 60^{th} minute, the total VAS reduction was 25.00 ± 12.25 in the propofol group and 23.10 ± 11.40 in the chlorpromazine group. Although pain reduction initially occurred more rapidly in the chlorpromazine group, there was no statistically significant difference between the groups at the 60-minute mark.
Conclusion: Propofol was as effective as chlorpromazine for treating migraines in the ED, with a comparable onset of action and a better side-effect profile.

Keywords: Migraine Attack, Propofol, Chlorpromazine, Acute Migraine Treatment

ÖZ

Amaç: Bu çalışma, akut migren ataklarının yönetiminde propofol ve klorpromazinin etkinliğini karşılaştırmayı ve acil serviste (AS) migren tedavisinin optimize edilmesine katkıda bulunmayı amaçlamıştır.
Yöntemler: Bu prospektif, randomize gözlemsel çalışmada, yaşları 18-65 arasında değişen 180 migren hastası iki gruba randomize edildi. Bir gruba her 10 dakikada bir 10 mg (maksimum 50 mg'a kadar) propofol, diğer gruba ise her 20 dakikada bir 12.5 mg (maksimum 37.5 mg'a kadar) klorpromazin uygulandı. Ağrı, görsel analog skala (VAS) kullanılarak her 10 dakikada bir değerlendirildi.
Bulgular: Başlangıçtaki ortalama VAS skorları propofol grubunda 8,24 ± 1,72, klorpromazin grubunda ise 8,83 ± 1,43 idi. Propofol grubunda VAS skorları 10., 20. ve 30. dakikalarda sırasıyla 5,19 ± 2,79, 2,66 ± 2,91 ve 1,25 ± 2,14 birim azaldı. Klorpromazin grubunda bu azalmalar sırasıyla 4,82 ± 2,99, 2,50 ± 2,93 ve 1,03 ± 2,20 birim olarak ölçüldü. 60. dakikada toplam VAS azalması propofol grubunda 25,00 ± 12,25, klorpromazin grubunda ise 23,10 ± 11,40 olarak belirlendi ve gruplar arasında istatistiksel olarak anlamlı bir fark saptanmadı.
Sonuç: Propofol, AS'de akut migren yönetiminde klorpromazin kadar etkiliydi ve benzer bir etki başlama süresi ile daha iyi bir yan etki profili gösterdi.

Anahtar kelimeler: Migren atağı, propofol, klorpromazin, akut migren tedavisi

This study was conducted as part of a thesis at the University of Health Sciences Kartal, Dr. Lütfi Kırdar Training and Research Hospital.

Received/ Geliş Tarihi 15.11.2024
Revision request/Revizyon Talebi 26.11.2024
Accepted/Kabul Tarihi 18.12.2024
Publication Date/Yayın Tarihi 28.12.2024

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Cite this article: Saglam SS, Guneysel O. Propofol vs. Chlorpromazine for Acute Migraine Treatment: Insights from a Prospective Randomized Trial. *Atatürk Univ Fac Med J Surg Med Sci*. 2024;3 (3): 56-64

INTRODUCTION

It is estimated that approximately 240 million people worldwide experience approximately 1.4 billion migraine attacks annually. [1] According to World Health Organization reports, migraine is ranked 25th among diseases causing labor loss. [2] In a prevalence study conducted by Stewart et al. in 1992, they detected that one out of every four people in the United States had at least one migraine attack per year. [3] While prevalence studies conducted in Turkey are useful in determining fighting strategies against migraine, the lifetime prevalence of migraine in Turkey is 16%. [4]

Headaches are broadly divided into primary and secondary types. Primary headaches include migraines, trigeminal autonomic cephalalgia, and other primary headaches, whereas secondary headaches result from distinct pathological processes or brain-independent organic disorders. [5] Migraines, often characterized by recurring similar attacks with a family history, may present with aura, which includes visual anomalies such as scintillation scotomas (flare/spark-shaped scotomas) or notched lines. [5] Complicated migraines are marked by neurological findings like hemiparesis, paresthesia, ophthalmoplegia, and aphasia. [5]

Although the pathophysiology of migraine, a theory based on neuronal events, has become prominent in recent years, no consensus has been reached regarding its pathophysiology. [6, 7] Modern imaging methods have made it possible to demonstrate that primary headaches are of structural origin. Therefore, evidence showing the association of migraine and cluster headaches with vascular dilatation and neuronal structures has increased. [6- 8]

Currently, migraine is classified into clinical practice and scientific studies according to The International Classification of Headache Disorders, 3rd edition). [5] Accordingly, the treatment of migraine, which deteriorates quality of life, begins with a correct diagnosis. After the diagnosis is made, the clinician prepares a treatment plan considering the type, character, frequency of migraine attacks, additional illnesses, and current medications of the patient. [8-10]

Pharmacological treatment for migraines may be acute or prophylactic. Acute treatment aims to decrease or stop the progression of headache after it has begun. Acute treatment drugs can be divided into two categories: migraine-specific and non-specific. Migraine-specific drugs include ergot derivatives and triptans. Medications that are not specific to migraine but are still in use include analgesics, antiemetics, anxiolytics, NSAIDs, steroids, major tranquilizers, and opiates. [11] On the other hand, prophylactic treatment aims to reduce the frequency and severity of the expected attacks, even if there is no headache at that time. Acute treatment is appropriate for most patients even if they receive prophylactic treatment. Acute treatment should not be administered more than three times per week to prevent rebound headaches. Owing to the diversity of patients presenting with migraine attacks, clinicians have difficulty choosing treatment. This study aimed to contribute to the termination of migraine attacks and the use of Propofol and Chlorpromazine in Emergency Department.

METHODS

This study was approved by the Scientific Research Evaluation and Support Committee of the University of Health Sciences Kartal Dr. Lütfi Kırdar Training and Research Hospital (Ethics Committee No: 89513307/1009/370, Date: 09.12.2014). This was a prospective, randomized, observational, single-blind study. The study population included patients admitted to the Health Sciences Kartal Dr. Lütfi Kırdar Training and Research Hospital Emergency Department between January 1 and May 1, 2015. Patients who were admitted to the emergency department with headache, who had been diagnosed with migraine, or who had a medical history and neurological examination at the time of admission, met the International Headache Society Migraine Diagnostic Criteria, and whose complaints persisted for more than 4 hours were included in this study. A flowchart of our patients is shown in Figure 1.

Inclusion criteria: Patients aged between 18-65 years and patients with moderate or severe pain despite the administration of oral non-steroidal anti-inflammatory drugs (NSAIDs) in the last two hours or 30 min after intramuscular NSAIDs (75 mg Diclofenac Sodium) were administered in our emergency department were included.

Exclusion criteria: Patients under the age of 18 or over 60 years; pregnancy or suspected pregnancy; patients who took migraine-specific 5-HT receptor agonists (triptan derivative), narcotic analgesics, or sedative medications in the last 24 hours; patients diagnosed with malignancy; patients with conditions that constitute contraindications or patients with soy allergy; and patients with any of the following vital signs (body temperature <36 °C or> 38 °C, systolic blood pressure <90 mmHg or > 150 mmHg).

Study design: Age, sex, and the presence of previous migraine diagnoses were recorded. The severity of pain at the beginning was evaluated via a 10 cm equally divided

"Visual Analogue Scale (VAS)". [1] Participants indicated the severity of pain by marking the appropriate number on the scale.

The randomization process was conducted using a computer-based random number generator to ensure unbiased group allocation. Participants were assigned to the propofol or chlorpromazine group in a 1:1 ratio. To maintain balance between the groups, stratified randomization was used based on age and sex to ensure equal distribution of these characteristics in both groups. The group assignment was concealed from the emergency department personnel by using sealed opaque envelopes, which were drawn by personnel blinded to the study.

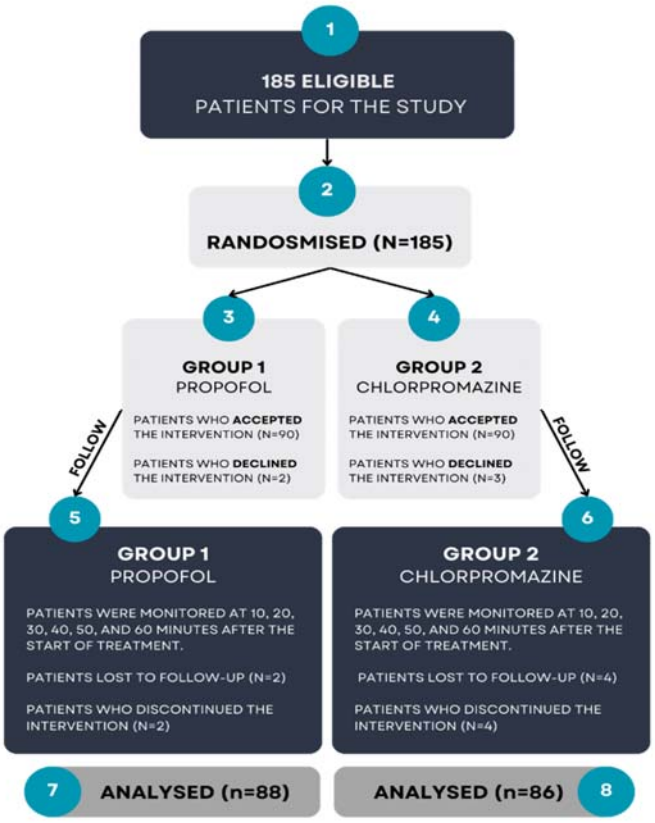

Figure 1: The Flowchart graph of the patients and study

After group allocation, the patients were placed in stretchers in the observation room, and vascular access was established using a 20-gauge catheter from the right antecubital vein in the supine position. Continuous monitoring of pulse and oxygen saturation was performed, and arterial blood pressure was measured at five-minute intervals.

In the propofol group, participants received 10 mg of intravenous propofol at 10-minute intervals, with a maximum dose not exceeding 50 mg. In the chlorpromazine group, 12.5 mg of chlorpromazine was dissolved in 20 cc of saline (0.9%) and administered intravenously over one minute at 20-minute intervals, with a maximum dose not exceeding 37.5 mg.

Study Termination Criteria Pain severity was assessed before each drug dose: In patients with a severity of two or less out of 10 points, the target was considered achieved, and the study was terminated. The study was terminated in the following situations.

1. Patients with low oxygen saturation, blood pressure, and pulse abnormalities.
2. Patients with allergic reactions, or developed akathisia, sedation or anxiety
3. Patients who do not want to continue treatment for any reason.

Participant Interests and Funding Disclosure: None of the participants in this study had any financial or personal interest related to the drugs or treatments evaluated. The study was conducted independently without any external funding or sponsorship from pharmaceutical companies or other institutions. All authors declare that they have no conflicts of interest related to the content of this manuscript.

Statistical Analysis

The NCSS (Number Cruncher Statistical System) 2007 program (Kaysville, Utah, USA) was used for statistical analysis. When evaluating study data, student's t test was used to compare quantitative data showing normal distribution as well as descriptive statistical methods (Mean, Standard Deviation, Median, Frequency, Ratio, Minimum, and Maximum) and Mann Whitney U test was used for those who did not show normal distribution. Fisher's exact test and Yates continuity correction test were used to compare the qualitative data. Statistical significance was set at $P < .05$.

RESULTS

In our study, there were 180 patients, of whom 39 (21.7%) were male and 141 (78.3%) were female. Their ages ranged from 18 to 59 years old. The mean age was 38.58 ± 10.81 years. A total of 103 (52.7%) patients were previously diagnosed with migraine by a neurologist, and 77 (42.8%) cases had an unknown diagnosis of migraine but met the criteria. In addition to headaches, nausea was present in 103 patients (57.2%), vomiting in 25 (13.9%), photophobia

in 61 (33.9%), and phonophobia in 25 (13.9%). In 50 patients (27.8%), there were additional complaints. After treatment, no side effects occurred in 115 patients (63.9%) but occurred in 65 patients (36.1%). The side effects were as follows: nausea, 2 (1.1%); vomiting, 2 (1.1%); dizziness, 37 (20.6%); hypotension, 22 (12.2%); allergic reaction, 3 (1.7%); dystonic reaction, 6 (3.3%); and sedation, 17 (9.4%). The mean age and sex distribution of the patients were not statistically different between the groups (P >.05). The rates of migraine diagnosis did not differ significantly between the groups (P >.05). The rate of comorbidities was not significantly different between groups (P > .05). There was no statistically significant difference between the groups in terms of success rates after treatment (P > .05). Statistically significant differences were detected between the groups in terms of the incidence of side effects (P = .044; P <.05). The dystonic reaction rate was significantly higher in the chlorpromazine group than in the propofol group (P =,029; P <,05). The demographic and clinical data of the patients are presented in Table 1.

The initial VAS scores in the chlorpromazine group were significantly higher than those in the propofol group (P = .012 and P < .05, respectively).
There was no statistically significant difference between the groups in terms of the VAS scores at 10th, 20th, 30th, 40th, 50th and 60th minutes (P > .05).
When the times, which VAS scores of cases were reduced to 2 and below, evaluated according to groups, in propofol group that time was average of 25.00 ± 12.25 minutes and in chlorpromazine group was average of 23.10 ± 11.40 minutes. There was no statistically significant difference between the two groups in terms of the reduction times of VAS to ≤ 2 (P > .05). Figure 2 shows the evaluation of VAS measurements during follow-up according to group and The evaluation of VAS Measurements during follow-up according to groups is shown in Table 2.

The decrease in VAS levels at 10th 30th 40th and 50th minutes in the chlorpromazine group was significantly higher than that in the propofol group (P < .05). The decrease in VAS levels in the chlorpromazine group at the 20th and 60th min when compared to the baseline was higher than that in the propofol group, but the difference was not significant (P = .076, P = .067; P > .05).

The evaluation of VAS scores during Follow-ups according to group is shown in Table 3. The distribution of the VAS changes is shown in Figure 3.

Table 1: The demographic and clinical data of the patients

Variables		Total Patients (n=180)	Propofol Group (n=90)	Chlorpromazine Group (n=90)	*P*
Age (years)		38.58±10.81	38.48±10.75	38.68±10.93	.902
Gender	Male	39 (21,7)	20 (22.2)	19 (21.1)	1.000
	Female	141 (78,3)	70 (77.8)	71 (78.9)	
Migraine Diagnosis	No	77 (42,8)	63 (70.0)	56 (62.2)	.270
	Yes	103 (52,7)	27 (30.0)	34 (37.8)	
Additional complaints	Nausea	103 (52,7)	51 (56.7)	52 (57.8)	.880
	Vomiting	25 (13,9)	10 (11.1)	15 (16.7)	.389
	Photophobia	61 (33,9)	34 (37.8)	27 (30.0)	.270
	Phonophobia	25 (13,9)	17 (18.9)	8 (8.9)	.085
	No additional complaints	50 (27,8)	23 (25.6)	27 (30.0)	.618
Side effects	No	115 (63,9)	64 (71.1)	51 (56.7)	**.044**
	Yes	65 (36,1)	26 (28.9)	39 (43.3)	
Types of side effects	Nausea	2 (1,1)	1 (1.1)	1 (1.1)	1.000
	Vomiting	2 (1,1)	2 (2.2)	0 (0.0)	.497
	Vertigo	37 (20,6)	16 (17.8)	21 (23.3)	**.461**
	Hypotension	22 (12,2)	10 (11.1)	12 (13.3)	.820
	Allergic reaction	3 (1,7)	1 (1.1)	2 (2.2)	1.000
	Dystonic reaction	6 (3,3)	0 (0.0)	6 (6.7)	**.029**
	Sedation	17(9,4)	6 (6.7)	11 (12.2)	.308

Values are presented as number (%) or mean ± standard deviation (SD). P <.05 indicates statistical significance.

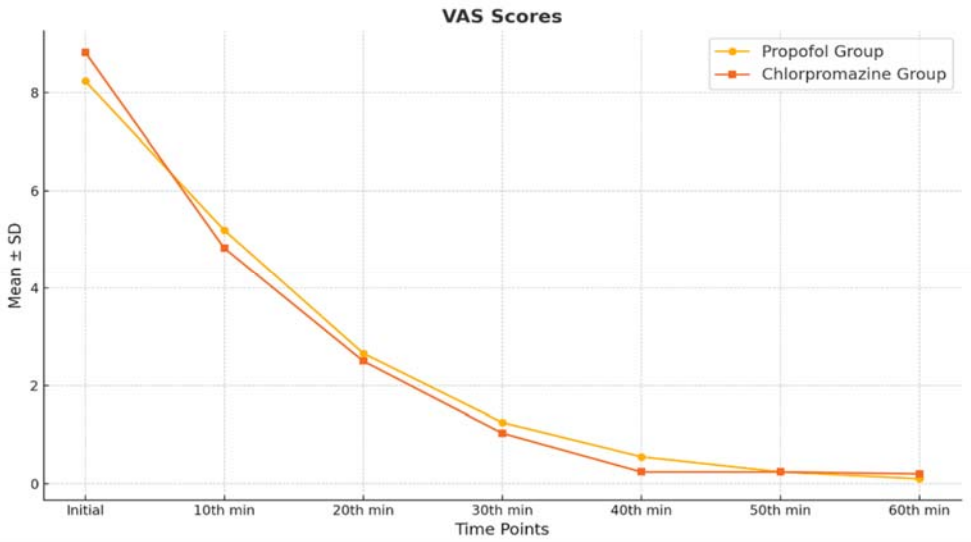

Figure 2: Evaluation of VAS measurements during follow-up according to groups

Table 2: Evaluation of VAS Measurements during Follow-up according to Groups.

		n	Propofol Group	n	Chlorpromazine Group	[e] *P*
Initial	Min-Max (Median)	90	3-10 (8.00)	90	5-10 (10.00)	*.012**
	Mean ± SD		8.24±1.72		8.83±1.43	
10.min	Min-Max (Median)	90	0-10 (5.00)	90	0-10 (5.00)	*.395*
	Mean ± SD		5.19±2.79		4.82±2.99	
20.min	Min-Max (Median)	90	0-10 (1.00)	90	0-10 (1.00)	*.701*
	Mean ± SD		2.66±2.91		2.50±2.93	
30.min	Min-Max (Median)	90	0-9 (0.00)	90	0-10 (0.00)	*.455*
	Mean ± SD		1.25±2.14		1.03±2.20	
40.min	Min-Max (Median)	90	0-8 (0.00)	90	0-6 (0.00)	*.723*
	Mean ± SD		0.55±1.46		0.24±0.90	
50.min	Min-Max (Median)	90	0-6 (0.00)	90	0-10 (0.00)	*.873*
	Mean ± SD		0.24±0.90		0.24±1.28	
60.min	Min-Max (Median)	90	0-6 (0.00)	90	0-10 (0.00)	*.495*
	Mean ± SD		0.10±0.71		0.20±1.22	
VAS<2 Reach Time (min)	Min-Max (Median)	88	10-60 (20.00)	88	10-60 (20.00)	*.317*
	Mean ± SD		25.00±12.25		23.10±11.40	

[e]MannWhitney U Test * *P* <.05

DISCUSSION

The pathophysiology of migraine is not fully understood, and as such, a single indispensable drug for acute migraine attack treatment is yet to be developed. Researchers continue to search for the “ideal medication” that can rapidly terminate migraine attacks with minimal side effects, high efficacy, low interaction potential with other drugs, and convenience for both patients and clinicians. However, it is evident that the search for such ideal medications will continue for some time.

In this study, we compared the effects of "propofol," which has gained popularity for its analgesic properties in recent years, with "chlorpromazine," a well-established option for migraine attack management. Our findings demonstrate that propofol is as effective as chlorpromazine in terminating migraine attacks. Although chlorpromazine initially provided faster relief within the first few minutes, there was no statistically significant difference between the two drugs in terms of the overall efficacy at the end of one hour. Furthermore, propofol exhibited a more favorable side effect profile than chlorpromazine, making it a safer option.[12]

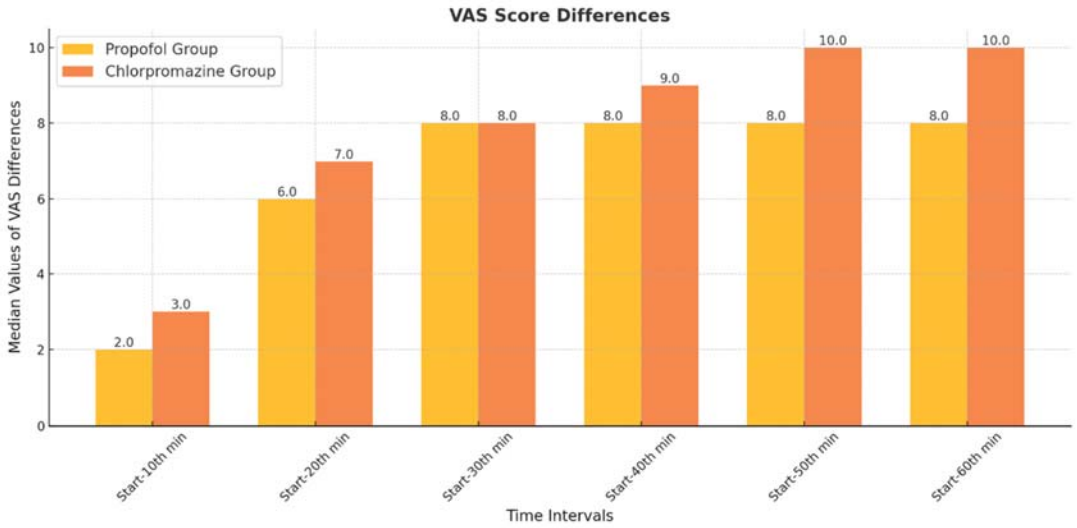

Figure3: Distribution of VAS changes

Table 3: Evaluation of VAS Levels during Follow-ups according to Groups

		Propofol Group(n=90)	Chlorpromazine Group(n=90)	[e] *P*
Initial-10.min	Min-Max (Median)	0-9 (2.00)	-1-10 (3.00)	***0.017****
	Mean ± SD	3.06±2.45	4.01±2.90	
Initial -20.min	Min-Max (Median)	0-10 (6.00)	-1-10 (7.00)	***0.076***
	Mean ± SD	5.59±2.84	6.35±2.88	
Initial -30.min	Min-Max (Median)	0-10 (8.00)	0-10 (8.00)	***0.023****
	Mean ± SD	6.97±2.57	7.83±2.35	
Initial -40.min	Min-Max (Median)	1-10 (8.00)	0-10 (9.00)	***0.031****
	Mean ± SD	7.67±2.19	8.43±1.99	
Initial-50.min	Min-Max (Median)	3-10 (8.00)	0-10 (10.00)	***0.042****
	Mean ± SD	7.98±1.90	8.63±1.80	
Initial-60.min	Min-Max (Median)	3-10 (8.00)	0-10 (10.00)	***0.067***
	Mean ± SD	8.11±1.80	8.67±1.77	

[e]MannWhitney U Test * *P* <.05

The International Headache Society recommends acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) for mild-to-moderate migraine attacks, whereas 5-HT1 agonists (triptans) are recommended for more severe cases. [13] Given the high prevalence of migraine, numerous studies have investigated acute headache management in patients presenting to the emergency department (ED) with migraine attacks. Some studies have highlighted the importance of aggressive intravenous pain management in acute migraine attacks. [14]

In our study, the age and gender demographics in both the chlorpromazine and propofol groups were consistent with previous literature. [15-18] The first study to assess the efficacy of chlorpromazine in headache management was conducted by Iserson et al. [18] Their study, which lacked a control group, indicated that a dose of 1 mg/kg of chlorpromazine achieved the highest degree of pain relief. Ninety-six percent of the patients reported complete pain relief within the first minute, with 92% remaining pain-free for an entire day. However, 18% of patients experienced orthostatic hypotension and 11% developed symptomatic side effects. [19] Iserson's study successfully drew attention to the potential of chlorpromazine in headache relief.

Subsequent placebo-controlled studies, such as those by McEwen et al. and Bigal et al., have further investigated the efficacy of chlorpromazine. [20, 21] McEwen et al. found that 1 mg/kg intramuscular (IM) chlorpromazine was superior to imatinib in 1 mg/kg normal saline (47.4% vs. 23.5%; *P* = .18). Patients receiving chlorpromazine also had a significantly lower need for additional narcotic analgesics than those administered normal saline, although they experienced higher rates of imbalance and systolic blood pressure drops. [20] Bigal et al. demonstrated that 0.1 mg/kg intravenous (IV) chlorpromazine provided a significantly higher percentage

of complete pain relief at one hour compared to placebo, particularly in patients with aura. [22]

Studies comparing chlorpromazine to other active agents have provided relevant insights. For instance, Lane et al. reported that 0.1-0.3 mg/kg IV chlorpromazine was more effective in pain reduction than 0.4 mg/kg IV meperidine combined with 25 mg IV dimenhydrinate (70.6% vs. 44.5%; *P* <.05). [22] Similarly, Bell et al. found chlorpromazine to be more effective than lidocaine and dihydroergotamine in migraine management, with a headache termination rate of 79.5% compared with 50% and 36.7%, respectively (*P* <.05). [23] Our findings align with these results, as 96.7% of the patients in the chlorpromazine group experienced complete pain relief, a result comparable to that of Iserson et al. and exceeding the success rates reported by Bigal et al.
Chlorpromazine has a well-documented side effect profile, with common adverse effects including dizziness, hypotension, sedation, and dystonic reactions. [24, 25] In our study, dizziness and hypotension were the most frequent side effects in both the treatment groups. Although sedation and dystonic reactions were more prevalent with chlorpromazine, these adverse effects were managed with rest and isotonic fluid supplementation, and no permanent effects were observed.

The efficacy of propofol in treating migraine was initially discovered incidentally by Krusz et al. during regional anesthesia, marking a significant milestone in migraine management. [26] Since then, multiple studies have tested propofol for migraines and other headache disorders, yielding positive outcomes. The precise mechanism of action of propofol in migraine is not fully understood; however, possible mechanisms include gamma-aminobutyric acid-A (GABA-A) receptor stimulation, sympathetic activity inhibition, nitric oxide release stimulation, and N-methyl-d-aspartate receptor suppression. [26] Folkerts et al. observed in 1995 that propofol effectively terminated migraine attacks in a patient undergoing electroconvulsive therapy, further supporting its potential for migraine treatment. [27]

Following Krusz et al., subsequent studies evaluated propofol in refractory migraine cases. [14] For example, Drummond and Scher administered 1 mg/kg IV propofol to two patients and achieved significant pain relief, although airway complications required intervention. [28] Similarly, Mosier et al. observed that a single 1 mg/kg bolus of propofol significantly reduced VAS scores in four patients, with mild sedation observed in all cases. [29] These findings suggest that, although propofol administration carries some risks, it can be safely managed in an emergency setting with appropriate precautions. Ward et al. also reported positive outcomes in their Australian study, where IV propofol achieved complete pain relief in 11 of 15 patients and reduced pain in the remaining patients, who expressed satisfaction with the treatment. [30]

In our study, we adopted the dosing protocol used by Soleimanpour et al., which included administering 10 mg of IV propofol at 10-minute intervals. Similar to Soleimanpour's findings, our results showed that pain reduction with propofol was significant within the first 20 min and slowed thereafter. VAS scores decreased to 2 or lower within 25 min in the propofol group and 23 min in the chlorpromazine group, with no statistically significant difference between the groups.

Our findings support propofol as an effective alternative to chlorpromazine for migraine management in the ED, with a more favorable side-effect profile. Although further studies are necessary to refine dosing and monitor safety, the unique mechanism of action and rapid efficacy of propofol suggest that it may play an increasingly important role in migraine management.

Our study has certain limitations that should be considered when interpreting the results. First, the sample size was relatively small and drawn from a single center, which may limit the generalizability of the findings to broader populations. Second, the study was conducted in an emergency department setting, and the findings may not fully reflect the outcomes in other clinical environments, such as primary care or specialized migraine clinics. Third, while randomization and stratification were employed to reduce potential biases, the possibility of residual confounding cannot be completely excluded. Finally, the self-reported nature of the Visual Analogue Scale (VAS) for pain assessment introduces a subjective component that might affect the reliability of pain measurements. Future studies involving larger sample sizes and multi-center designs are warranted to validate these findings and provide more robust and generalizable conclusions.

CONCLUSION

In our study, chlorpromazine maintained its current position as an effective treatment option for migraine attacks, in accordance with the literature. However, although the guidelines still do not include propofol in attack treatment, it has been found that propofol reduces headache quickly, effectively, and has a low side-effect profile, as similar studies have indicated. When compared

to chlorpromazine, the effect of propofol started statistically significantly later, but there was no significant delay in clinical and patient expectations. Propofol reaches this goal within 25 minutes. We believe that propofol can be used safely in the treatment of migraine and headache in emergency departments and pain centers

Ethics Committee Approval: This study was approved by the Scientific Research Evaluation and Support Committee of the University of Health Sciences Kartal Dr. Lütfi Kırdar Training and Research Hospital (Ethics Committee No: 89513307/1009/370, Date: 09.12.2014).
Informed Consent: Written informed consent was obtained from all participants after providing information about the study. Voluntary participation was emphasized, and patients who declined to participate were excluded from the study.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept – SSS; Design – SSS; Supervision – OG; Resources – SSS; Data Collection and/or Processing – SSS; Analysis and/or Interpretation – OG; Literature Search – SSS; Writing Manuscript – SSS; Critical Review – OG.
Conflict of Interest: The authors have no conflicts of interest to declare.
Financial Disclosure: The authors declared that this study has received no financial support.

Etik Komite Onayı: Çalışmamız Sağlık Bilimleri Üniversitesi Kartal Dr. Lütfi Kırdar Eğitim ve Araştırma Hastanesi Bilimsel Araştırma Değerlendirme ve Destekleme Kurulu tarafından onaylanmıştır (Etik Kurul No: 89513307/1009/370, Tarih: 09.12.2014).
Hasta Onamı: Written informed consent was obtained from all participants after providing information about the study. Voluntary participation was emphasized, and patients who declined to participate were excluded from the study.
Hakem Değerlendirmesi: Dış bağımsız.
Yazar Katkıları: Fikir- SSS; Tasarım-SSS; Denetleme-OG; Kaynaklar-SSS; Veri Toplanması ve/veya İşlemesi-SSS; Analiz ve/ veya Yorum-OG; Literatür-SSS; Yazıyı Yazan-SSS: Eleştirel İnceleme-OG:
Çıkar Çatışması: Yazarlar, çıkar çatışması olmadığını beyan etmiştir.
Finansal Destek: Yazarlar, bu çalışma için finansal destek almadığını beyan etmiştir.

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