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The effectiveness of supplemental oxygen therapy in patients receiving acute migraine treatment in the emergency department: A randomized clinical trial

[1]Ali Solak *MD*, [1]Gülşah Çıkrıkçı Işık *MD*, [2]Fatma Nur Karaaslan *MD*, [3]Osman Korucu *MD*, [1]Yunsur Çevik *MD*

[1]University of Health Sciences Atatürk Sanatorium Training and Research Hospital, Department of Emergency Medicine, Ankara, Turkey; [2]Emergency Medicine, Soma Public Hospital, Manisa, Turkey; [3]University of Health Sciences Atatürk Sanatorium Training and Research Hospital, Department of Neurology, Ankara, Turkey

Abstract

Background & Objective: Migraine headaches are a frequent reason for emergency department (ED) visits. While oxygen therapy has demonstrated effectiveness for cluster headaches, its role in other primary headaches remains a topic of research. This study aimed to investigate the effectiveness of supplemental oxygen therapy, when added to standard treatments, for pain management in patients presenting to the ED with acute migraine without aura. *Methods:* This study was a randomized, controlled trial. Patients were randomized using the 'Random Allocation' program and divided into two groups. All patients presenting to the ED with migraine without aura received 50 mg dexketoprofen + 10 mg metoclopramide HCl in 100 mL normal saline intravenously as standard treatment. The study group also received humidified oxygen at 10 L/min via a simple face mask for 60 minutes. Data collected included patients' demographic information, pain characteristics, comorbid diseases, medications used, presence of aura, visual analog scale (VAS) scores at 0, 15, 30, and 60 minutes post-treatment, and the need for rescue treatment. *Results:* A total of 160 participants were included: 79 in the oxygen group and 81 in the non-oxygen group. No significant differences were found in demographic data or baseline VAS scores between the groups. VAS scores at 15, 30, and 60 minutes did not show a significant difference between the two groups ($p > 0.05$ for each measurement using either per-protocol [PP] or intention-to-treat [ITT] analysis). One patient in the oxygen group and two patients in the non-oxygen group required rescue treatment, but this difference was not statistically significant ($p = 0.57$).
Conclusion: This study suggests that supplemental oxygen therapy does not augment the effectiveness of conventional migraine treatment. Current evidence is insufficient to support the routine use of oxygen in emergency departments for the management of migraine headaches.

Keywords: Migraine without aura, oxygen inhalation therapy, emergency departments

INTRODUCTION

Background

Primary headaches are a significant reason for emergency department (ED) visits, accounting for approximately 2% of all admissions.[1] The International Classification of Headache Disorders, Second Edition (ICHD-II) categorizes primary headaches into four main groups: migraine, tension-type headache (TTH), cluster headache, and undifferentiated headache.[2] Although tension-type headache is the most common type, it is rarely severe enough to warrant ED treatment unless observed in migraine patients.[3] Migraine accounts for the largest proportion of ED admissions for primary headaches, occurring four times more frequently than non-migraine headaches. Cluster headaches may also lead to ED visits, but their prevalence is less than 0.5%, compared to 12% for migraine.[3] Despite differing underlying pathophysiological mechanisms, the therapeutic management of these

Address correspondence to: Gülşah Çıkrıkçı Işık, MD, University of Health Sciences, Atatürk Sanatorium Training and Research Hospital, Emergency Medicine Department, Ankara / TURKEY. Tel: +90 505 5873436, E-mail: gulsah8676@gmail.com

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disorders in the ED is similar, and they often manifest overlapping responses to treatment. Non-steroidal anti-inflammatory drugs (NSAIDs), neuroleptics, and opioids are commonly used in clinical practice, with intravenous valproic acid also being an option.[3] Intranasal lidocaine, intravenous magnesium sulfate, propofol, and oxygen therapy may also be considered.[3]

The role of oxygen therapy in managing primary headaches was first investigated in the 1940s.[4] Although the exact mechanism of action remains unclear, oxygen has been established as a therapeutic intervention for cluster headaches.[5] The analgesic effect of oxygen in cluster headaches likely results from vasoconstriction in the brain, its anti-inflammatory effect, and the reversal of autonomic nervous system aberrations.[6] In recent years, oxygen therapy has been explored as a potential migraine treatment due to its safety, tolerability, and low cost.[3,7] Abnormal oxygen utilization, tissue hypoxia, and cerebrovascular dysfunction are mechanisms implicated in migraine. Microembolisms and infarcts are other pathophysiologic processes believed to trigger migraines.[8] Animal models of migraine suggest that oxygen therapy can suppress spreading depolarization induced by microembolisms and reduce inflammation and blood-brain barrier damage.[8] There are also reports indicating the efficacy of inhaled oxygen, particularly in migraine patients with accompanying cranial autonomic symptoms.[9] Despite existing publications highlighting its benefits and efficacy, high-level evidence supporting oxygen therapy as a migraine treatment is lacking.[10]

Importance

While the literature includes studies on the efficacy of oxygen therapy for headaches, these studies often include all headache types (cluster, tension-type, migraine) or all migraine patients (with or without aura) without specific differentiation. Our study focused on analyzing acute migraine patients with migraine without aura who presented with a certain severity (VAS score > 40), aiming to demonstrate the contribution of oxygen therapy to standard treatment.

Goals

The aim of this study was to evaluate the effect of oxygen therapy on pain management in acute migraine attacks in the emergency department. Secondary outcomes included the rate of pain relief and the need for additional analgesics.

METHODS

Study design

This prospective randomized clinical study was conducted in the ED of a hospital in the capital of the country, with approval from the local ethics committee and the Turkish Medicine and Medical Device Agency (approval number E-66175679-514.05.02-10157.2), between May 2023 and December 2024. This trial was registered in a clinical trial database (ClinicalTrials.gov under the number NCT05780671).

Study population

Patients admitted to the ED with a primary diagnosis of headache and a prior diagnosis of migraine without aura were eligible for inclusion. Patients who met the International Headache Society's (IHS) 2018 criteria for migraine without aura and had a visual analogue scale (VAS) score above 40 at minute 0 of treatment were included in the study. Inclusion criteria were as follows: patients aged 18 to 65 years with a medical history and ED evaluation confirming migraine-related headache according to the IHS 2018 classification, a VAS score > 40 at the beginning of treatment, and willingness to participate. Only patients who received standard migraine therapy (defined below) and, if necessary, the same rescue therapy were included to avoid drug-related bias. Exclusion criteria included: patients who had taken any analgesic within six hours of admission, patients diagnosed with other types of primary headaches (migraine with aura, migraine status, TTH, trigeminal autonomic cephalalgia, etc.), patients using anticoagulants or with a bleeding diathesis, pregnant or breastfeeding patients, patients with fever, patients diagnosed with secondary headaches, patients with focal neurologic findings, patients with heart, liver, or kidney failure, patients with peptic ulcer, patients with chronic obstructive pulmonary disease, patients with acute coronary syndrome, patients who were not hemodynamically stable, and patients with a history of acute dystonia or akathisia due to metoclopramide.

Randomization and interventions

During the study, patients admitted to the ED with headaches and a history of migraine were initially evaluated by an emergency physician (an emergency medicine specialist) on shift who was not involved in the study. While acknowledging potential variations in treatment regimens, the

standard migraine therapy was generally 50 mg dexketoprofen and 10 mg metoclopramide HCl in 100 cc normal saline intravenously (IV). The routine use of metoclopramide in our ED is based on the frequent association of nausea and/or vomiting with migraine-related headaches (IHS-2018 criteria).

Patients initially evaluated by a physician unaware of their participation and prescribed standard therapy were re-evaluated by the researchers at the treatment zone before medication administration. Patients who met the study's inclusion criteria and consented to participate were enrolled. Written informed consent was obtained from all participants.

Patients were randomized using the "Random Allocation Program Software 1" in a 1:1 ratio. The study group received humidified oxygen at a rate of 10 L/min via a simple face mask for 60 minutes, in addition to standard therapy. A comprehensive data collection form was used to record patients' demographic details, comorbid conditions, pain characteristics, medication usage, and VAS pain scores (0-100) at 0th, 15th, 30th, and 60th minutes post-treatment.

Treatment was considered successful if the patient's VAS score decreased by 50% after one hour. If this was not the case, patients received rescue treatment consisting of tramadol 100 mg intravenously in saline. VAS scores of patients receiving rescue therapy were recorded again at the 120th minute.

Outcomes

The primary outcome was defined as the absolute changes in headache scores between the groups at 0 and 60 minutes. Secondary endpoints included the extent of pain relief (≥50% reduction in initial VAS) and the need for additional analgesics. Changes in headache scores between the groups at 15 and 30 minutes were also measured.

The headache severity of all patients was assessed using the Visual Analog Scale (VAS), where 0 points indicated no pain and 100 points indicated the worst possible pain. After explaining the scale to our patients, they were asked to mark the point that best represented the intensity of the pain they were experiencing with a pencil. Subsequently, the marked point was measured with a ruler and recorded. These measurements were taken at the time of admission, as well as at 15, 30, and 60 minutes after treatment, and at 120 minutes for patients who required additional rescue treatment.

The study was analyzed by using two different approaches. First, per protocol (PP) analysis was performed including only those participants who completed the study according to the predefined protocol. This approach is beneficial for understanding the efficacy of the treatment as per the established protocol. Secondly, intention-to-treat analysis (ITT) was performed. For ITT analysis, we implemented the last observation carried forward method to address any missing patient responses. As a result, for those participants who withdrew from the study before the primary outcome measurement at 60 minutes, their last recorded VAS scores were used as their final observations in the analysis. ITT analysis minimizes the impact of lost follow-up data or treatment deviations, thereby reflecting real-world applicability.

Sample size estimation

The sample size of this study was calculated with the G-Power for Mac OS X (version 3.1.9.2; UniversitatDüsseldorf, Germany) program. Considering the minimum VAS difference suggested by Todd et al. in their migraine studies, a power calculation was made to detect a 13-unit VAS difference between the groups at the 60th minute of treatment.[11] Based on previous studies the standard deviation (SD) value was accepted as 28.[12] As a result, the sample size of this study was determined as 74 patients for each group, with a type-1 error of 5% and a type-2 error of 20%. Considering possible protocol deviations, it was decided to include a total of 160 patients, with 80 patients per group for the per-protocol analysis cohort. A larger number of patients were randomized to achieve this target after anticipated withdrawals. (Figure 1).

Statistical analyzes

Statistical analyses were conducted using jamovi version 2.6 (The jamovi project, Sydney, Australia). Quantitative (continuous/discrete) data were typically expressed as mean (SD) or median (IQR), while qualitative (categorical) data were expressed as number (%). The T-test was used for normally distributed parameters in pairwise group comparisons. Chi-square test or Fisher's exact test was used to compare categorical variables. All hypothesis tests were two-tailed and considered significant at a p-value < 0.05.

RESULTS

A total of 213 patients were initially evaluated for headache presentations consistent with migraine. Of these, 5 were excluded due to a diagnosis of migraine with aura, 1 was excluded due to secondary headache (subarachnoid hemorrhage), 6 were excluded because they had used analgesics before presenting to the emergency department, 10 had comorbid conditions as specified in the exclusion criteria, and 22 declined to participate in the study. In the oxygen therapy group, 3 patients withdrew from the study before completing the one-hour treatment period, while 6 patients in the control group also exited the study prematurely (these patients were included in the ITT analysis). A total of 79 patients in the oxygen group and 81 patients in the control group completed the protocol and were included in the PP analysis. (Figure 1).

The demographic composition of the study population is outlined in Table 1. The sample included 138 (86.3%) female patients. The mean age of the patients was 37.5 years (±10.7). Pain characteristics and VAS scores before the treatment were similar between the groups. Pain scores at 15, 30 and 60 minutes were similar in the groups receiving and not receiving oxygen, and no significant difference was found between the groups ($p > 0.05$ for each measurement) either on PP analysis or ITT analysis (figure 2 and 3). Delta VAS scores (difference between 0th minute VAS score and 15th, 30th, and 60th minutes VAS scores) are tabulated. The rate of pain reduction was similar between the groups. The number of patients who needed rescue treatment was 1 in the group receiving O2 and 2 in the group not receiving O2. The pain of these patients regressed after rescue treatment. (Table 2).

DISCUSSION

This study evaluated the efficacy of oxygen therapy, administered with dexketoprofen and metoclopramide, for acute migraine management without aura. Our findings indicated that oxygen treatment did not significantly impact pain intensity, as assessed by the Visual Analog

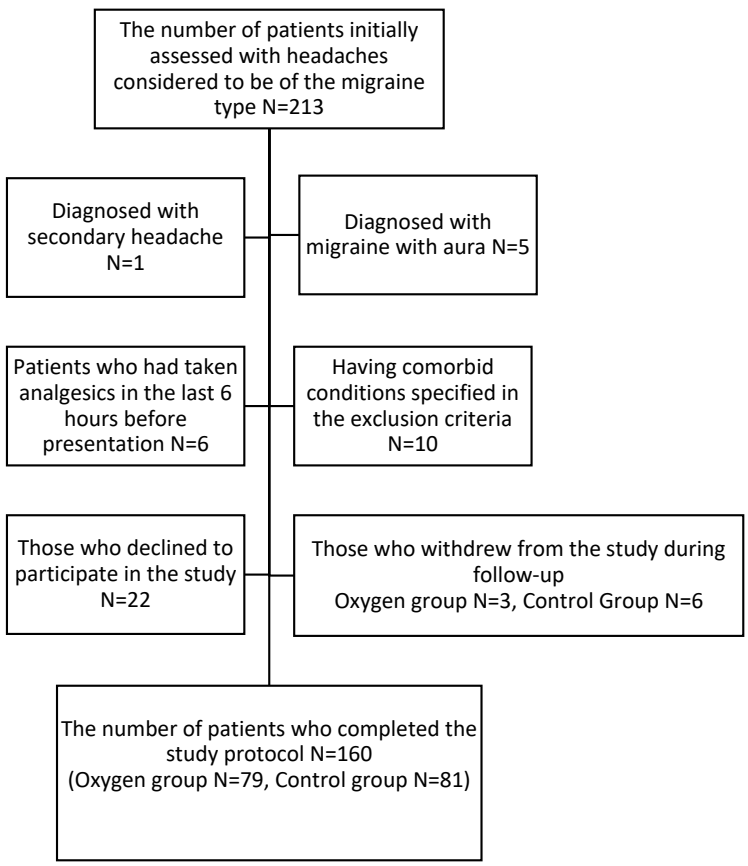

Figure 1. Patients flow chart

Table 1: General characteristics and baseline VAS scores of the participants according to treatment groups

PP analysis	Oxygen Receiving Group N=79	Control Group N=81	Differences proportions or mean/median with 95%CI a,b
Female Gender	67 (84.8%)	71 (87.7%)	0.06 (-0.16 to 0.28)
Age	37.8 ± 11.5	37.2 ± 9.9	-0.6 (-4 to 2.7)
Accompanied symptoms			
Nausea / Vomiting	71 (44.4%)	74 (46.3%)	0.04 (-0.22 to 0.3)
Photophobia	52 (32.5%)	54 (33.8%)	0.01 (-0.15 to 0.17)
Phonophobia	50 (31.3%)	43 (26.9%)	-0.1 (-0.26 to 0.05)
VAS score on admission	78.3 ± 16.9	77.2 ± 16.8	-1.04 (-6.3 to 4.21)

* Frequency data are shown as n and %; data that fit the normal distribution are shown as mean ± standard deviation.

Scale (VAS) at 15, 30, and 60-minute intervals. Additionally, no significant difference was observed between treatment groups regarding the proportion of patients requiring rescue treatment. These findings suggest that adding oxygen therapy does not provide significant advantages in managing acute migraine headaches when used with conventional therapeutic agents.

The efficacy of oxygen therapy in cluster headache has been confirmed.[5] However, there are conflicting results about its efficacy in migraine-type headaches, and its possible mechanism of action is not fully elucidated. Proposed mechanisms include inhibition of the cranial parasympathetic pathway or trigeminoautonomic reflex, modulation of neurotransmitters or neuropeptides (such as calcitonin gene-related peptide), suppression of neurogenic plasma protein extravasation, and cerebral artery vasoconstriction.[13] Additionally, cortical depression spreading in the brain due to hypoxia plays a role in the pathogenesis of aura in seizures and migraines. It is thought that hyperoxia may effectively alleviate migraine by preventing this cortical depression.[14] Wang *et al*. investigated migraine patients with patent foramen ovale (PFO), suggesting that PFO with hypoxia due to venous blood mixing may be the cause of migraine. They claimed that normobaric oxygen treatment may attenuate headaches by correcting hypoxemia in patients with PFO.[15]

In a randomized, placebo-controlled study of 64 attacks in 22 migraine patients, adult migraineurs self-administered high-flow oxygen or medical air (10-15 L/min) via face mask in a blinded fashion, starting soon after symptom onset for 30 minutes.[8] Participants were instructed to record the severity of headache, nausea, and visual symptoms on visual analogue scales at regular intervals up to 60 minutes. Oxygen therapy did not result in any significant differences in pain scores at 15 and 30 minutes compared with room air. However, oxygen therapy significantly reduced pain severity scores (0-1) at 60 minutes (24% versus 6%, p = 0.05). Additionally, it alleviated nausea (42% versus 23%, p = 0.08) and visual disturbances (36% versus 7%, p = 0.004). Participants were asked to refrain from utilizing any other symptomatic migraine treatment.[8] Moreover, in contrast to our study, exclusion was not determined by VAS value, and the study encompassed migraine attacks of all severity levels. It is possible that co-administration of NSAIDs in our study may have masked our observation of the possible efficacy of oxygen therapy.

Shah *et al*. hypothesized that cooling of the nasal passages via trans-nasal gas therapy may play a role in migraine pain relief.[14] For this study, subjects were randomized into nasal high-flow dry oxygen, dry air, humidified oxygen, or humidified air (control) at 15 liters per minute for fifteen minutes. Compared to the control arm, all therapeutic arms showed significantly greater pain score reduction and photosensitivity at 2 hours of therapy with dry oxygen, dry air and humidified oxygen. When evaluating this study's results, one should consider the groups' small and unequal sample sizes. The trans-nasal delivery and consequent cooling of the nasal tissues may explain the positive results as compared to our negative study findings.

Özkurt *et al*. conducted a study in Turkey, including all primary headaches admitted to the emergency department, treating one group with 100% oxygen at 15 L/min with a non-rebreathing mask, while the other group received room air as a

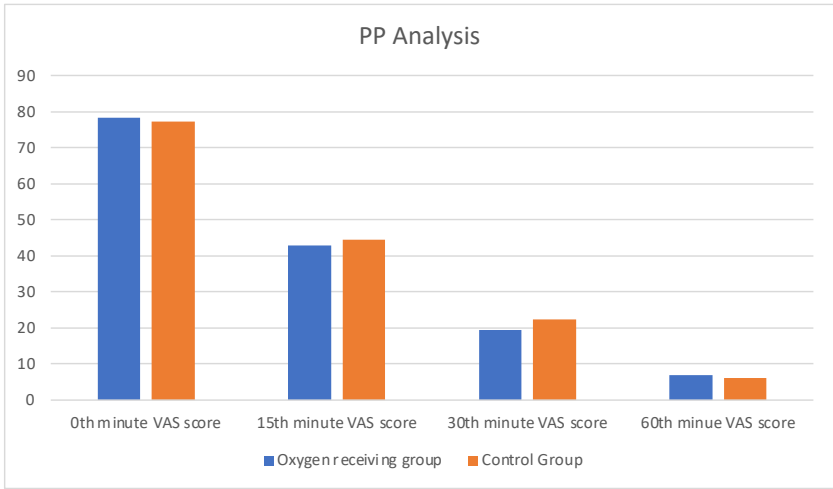

Figure 2. Per protocol analysis of the Visual Analog Scale (VAS) scores at 0th, 15th, 30th and 60th minutes of treatment in the oxygen receiving group and the control group.

placebo.[16] The study included 204 patients (102 in each group) and reported significant improvements in VAS scores at 15 and 30 minutes in oxygen-treated patients compared with the placebo group. At 30 minutes, 72% of patients in the oxygen group and 86% of patients in the placebo group requested analgesic medication ($p = 0.005$). This study included all types of headache, and only 27% of patients were classified as migraine patients. Moreover, no additional therapeutic interventions beyond oxygen supplementation and room air were administered. Although the VAS score decreased significantly more in the oxygen group than in the placebo group, analgesics were still requested by 72% of patients in the oxygen group at the thirtieth minute, indicating that oxygen therapy alone is insufficient to effectively manage pain.

A recent study on the efficacy of high and medium flow oxygen therapy in primary headaches administered 4 different treatments for 4 different attacks in 104 patients: high-flow oxygen (15 L/min oxygen), medium flow oxygen (8 L/min oxygen), high-flow room air as placebo (15 L/min room air), and medium-flow room air as placebo (8 L/min room air).[17] VAS scores of patients receiving oxygen therapy were significantly lower than those given placebo at all control points (15, 30, and 60 minutes) ($p < 0.001$). No statistically significant difference was

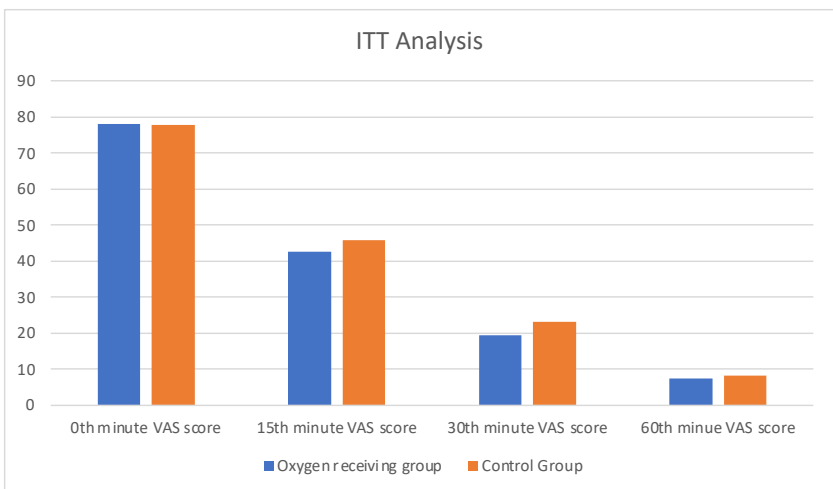

Figure 3. Intention to treat analysis of the Visual Analog Scale (VAS) scores at 0th, 15th, 30th and 60th minutes of treatment in the oxygen receiving group and the control group.

Table 2: VAS scores and rescue treatment need in oxygen receiving group and control group

PP analysis	Oxygen Receiving Group N=79	Control Group N=81	Differences proportions or mean/median with 95%CI a,b	P value
0th minute VAS score	78.3 ± 16.9	77.2 ± 16.8	-1.04 (-6.3 to 4.21)	0.69
15th minute VAS score	42.9 ± 26.5	44.5 ± 24.2	1.59 (-6.33 to 9.52)	0.69
30th minute VAS score	19.5 ± 21.7	22.3 ± 27.3	2.74 (-4.98 to 10.45)	0.48
60th minute VAS score	6.95 ± 13.3	6.22 ± 15	-0.72 (-5.16 to 3.71)	0.74
Rescue treatment needed	1 (1.3%)	2 (2.5%)	0.16 (-0.37 to 0.70)	
Delta VAS scores				
Delta VAS at 15th min	35.4 ± 26.9	32.7 ± 22.4	-2.63 (-10.36 to 5.08)	
Delta VAS at 30th min	58.7± 25.7	54.9 ± 28.5	-3.78 (-12.26 to 4.69)	
Delta VAS at 60th min	71.3 ± 20.3	71 ± 20.1	-0.31 (-6.62 to 5.99)	
ITT analysis	**Oxygen Receiving Group N=82**	**Control Group N=87**	**Differences proportions or mean/median with 95%CI a,b**	
0th minute VAS score	78.1 ± 17.1	77.8 ± 16.6	-0.26 (-5.38 to 4.85)	
15th minute VAS score	42.7 ± 26.8	45.7 ± 24.4	3 (-4.77 to 10.78)	
30th minute VAS score	19.4 ± 21.8	23.2 ± 28.1	3.77 (-3.89 to 11.44)	
60th minute VAS score	7.3 ± 14	8.26 ± 18.7	0.95 (-4.07 to 5.99)	
Rescue treatment needed	1 (1.2%)	2 (2.3%)	0.15 (-0.38 to 0.69)	
Delta VAS scores				
Delta VAS at 15th min	35.4 ± 27.8	32.1 ± 22.2	-3.27 (-10.91 to 4.35)	
Delta VAS at 30th min	58.6± 26	54.6 ± 29	-4.04 (-12.42 to 4.32)	
Delta VAS at 60th min	70.8 ± 21.1	69.5 ± 22	-1.22 (-7.78 to 5.32)	

* Frequency data are shown as n and %; data that fit the normal distribution are shown as mean ± standard deviation. Comparison between groups was performed by Fischer exact test and Student t test.

observed between high-flow and medium-flow treatments. Conversely, patients receiving placebo treatment exhibited a higher analgesic demand at the 30-minute mark and a greater likelihood of readmission to the emergency department. However, analyzing the results revealed that over 65% of patients receiving oxygen therapy required analgesics within 30 minutes. This supports the conclusion that oxygen therapy alone is insufficient for pain management as mentioned above.

Bennett *et al*., in their meta-analysis, examined the role of hyperbaric oxygen therapy (HBOT) in migraine.[10] They showed that HBOT was effective in relieving migraine headaches compared to sham therapy (relative risk 5.97). On the other hand, there was no evidence that HBOT could reduce the requirement for rescue medication or reduce the incidence of nausea and vomiting. Poor availability and high treatment costs limit this treatment's applicability in acute migraine attacks.

The extant literature includes studies with heterogeneous samples in which migraines with aura were included, or all primary headaches were analyzed. In this respect, the present study provides more specific information and contributes to the existing literature by analyzing migraine patients without aura with a VAS score above 40 mm. While publications exist on the possible benefits of oxygen in migraine patients (as mentioned above), oxygen therapy alone does not provide effective pain control. In light of our findings, we are of the opinion that oxygen does not provide an additional contribution to standard migraine headache treatments and that there is insufficient evidence for its routine use. Further research employing diverse application types, varying durations, and across different populations is necessary.

The primary limitation of our study is that it was a single-centre study in a tertiary hospital. Consequently, the generalizability of the results is limited. Second, the non-blinded nature of the study could introduce bias, as both patients and clinicians were aware of the treatment assigned, potentially influencing the reporting of outcomes and treatment responses. This lack of blinding may

have affected patient expectations and perceptions of pain relief. The inclusion of only patients diagnosed with migraine without aura can also be considered a limitation of the study. While the specificity of our patient population enhances the value of our research in demonstrating the effectiveness of oxygen therapy in this particular group, the exclusion of other types of migraines prevents us from assessing the potential efficacy of oxygen in different migraine attacks.

In conclusion, our study investigated the efficacy of oxygen administered as an adjunct to standard migraine headache treatment in the emergency department. No statistically significant differences were found in terms of pain control between the study groups. While studies demonstrate the potential benefits of oxygen administration alone in migraine headaches, our findings suggest that it does not augment the effectiveness of conventional migraine treatment. The available data does not provide sufficient support for the routine use of oxygen in emergency departments for migraine headaches.

DISCLOSURE

Ethics: Ethics committee approval was received for this study from the ethics committee of Atatürk Sanatorium Training and Research Hospital, Ankara, Turkey. Informed Consent: Written informed consent was obtained from patients who participated in this study.

Financial support: None

Conflict of interest: None

REFERENCES

1. Şafak S, Çorbacioğlu ŞK, Korucu O, Emektar E, Çevik Y. Comparison of ibuprofen and dexketoprofen in the management of migraine-related headache in the emergency department. *Notfall Rettungsmed* 2022; 25(Suppl 2): 31-7. DOI:10.1007/s10049-022-01105-w
2. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 2nd edition. *Cephalalgia* 2004; 24(Suppl 1): 2-150. doi: 10.1111/j.1468-2982.2003.00824.x.
3. Green MW. The emergency management of headaches. *Neurologist* 2003;9(2):93-8. doi:10.1097/01.nrl.0000051443.03160.72
4. Alvarez WC, Mason AY. Results obtained in the treatment of headache with the inhalation of pure oxygen. *Mayo Clin Proc* 1940;15:616-8.
5. Cohen AS, Burns B, Goadsby PJ. High-flow oxygen for treatment of cluster headache: A randomized trial. *JAMA* 2009;302:2451-7. doi: 10.1001/jama.2009.1855.
6. Saeedi M, Shahvaran SM, Ramezani M, Rafiemanesh H, Karimialavijeh E. Comparing the effects of 3 oxygen delivery methods plus intravenous ketorolac on primary headaches: A randomized clinical trial. *Am J Emerg Med* 2020;38(1):55-9. doi:10.1016/j.ajem.2019.04.018
7. Ciarambino T, Sansone G, Menna G, *et al*. Oxygen therapy in headache disorders: A systematic review. *Brain Sci* 2021;11(3):379. doi:10.3390/brainsci11030379
8. Singhal AB, Maas MB, Goldstein JN, *et al*. High-flow oxygen therapy for treatment of acute migraine: A randomized crossover trial. *Cephalalgia* 2017;37(8):730-6. doi:10.1177/0333102416651453
9. Jürgens TP, Schulte LH, May A. Oxygen treatment is effective in migraine with autonomic symptoms. *Cephalalgia* 2013;33(1):65-7. doi: 10.1177/0333102412465206.
10. Bennett MH, French C, Schnabel A, Wasiak J, Kranke P, Weibel S. Normobaric and hyperbaric oxygen therapy for the treatment and prevention of migraine and cluster headache. *Cochrane Database Syst Rev* 2015;2015(12):CD005219. doi:10.1002/14651858.CD005219.pub3
11. Todd KH, Funk JP. The minimum clinically important difference in physician-assigned visual analog pain scores. *Acad Emerg Med* 1996;3:142-6.
12. Friedman B, Garber L, Yoon A, *et al*. Randomized trial of IV valproate vs metoclopramide vs ketorolac for acute migraine. *Neurology* 2014;82:976-83. doi: 10.1212/WNL.0000000000000223.
13. Akerman S, Holland PR, Lasalandra MP, Goadsby PJ. Oxygen inhibits neuronal activation in the trigeminocervical complex after stimulation of trigeminal autonomic reflex, but not during direct dural activation of trigeminal afferents. *Headache* 2009;49:1131-43. doi: 10.1111/j.1526-4610.2009.01501.x.
14. Shah R, Assis F, Narasimhan B, *et al*. Trans-nasal high-flow dehumidified air in acute migraine headaches: a randomized controlled trial. *Cephalalgia* 2021;41:968-78. doi: 10.1177/0333102421997766.
15. Wang M, Lan D, Dandu C, Ding Y, Ji X, Meng R. Normobaric oxygen may attenuate the headache in patients with patent foramen povale and migraine. *BMC Neurol* 2023;23(1):44. doi: 10.1186/s12883-023-03059-z.
16. Ozkurt B, Cinar O, Cevik E, *et al*. Efficacy of high-flow oxygen therapy in all types of headache: a prospective, randomized, placebo-controlled trial. *Am J Emerg Med* 2012;30(9):1760-4. doi:10.1016/j.ajem.2012.02.010
17. Kaçer İ, Çağlar A. High or mid-flow oxygen therapy for primary headache disorders: A randomized controlled study. *Am J Emerg Med* 2023;68:138-43. doi: 10.1016/j.ajem.2023.03.037.