ARYA Atherosclerosis J

Original Article Open Access

The effect of lavender aromatherapy and acetaminophen as preemptive on comfort and Nitroglycerin-induced headache in acute coronary syndrome

Roghayeh Ezati-Soleiman[1], Arezou Karampourian[2*], Mahnaz Khatiban[3], Leili Tapak[4], Mohammad-Hossein Sayadi[5]

1- Department of Nursing, School of Nursing and Midwifery, Hamadan University of Medical Sciences, Hamadan, Iran
2- Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Urology and Nephrology Research Center, Hamadan University of Medical Science, Hamadan, Iran
3- Department of Nursing, School of Nursing and Midwifery, Mother and Child Care Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
4- Department of Biostatistics, School of Health, Modeling of Non communicable Diseases Research Center, Health Sciences and Technology Research Institute, Hamadan University of Medical Sciences, Hamadan, Iran
5- Cardiologist, Hamadan University of Medical Sciences, Hamadan, Iran

Correspondence:

Arezou Karampourian; Department of Nursing, School of Nursing and Midwifery, Urology and Nephrology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran;
Email: a.karampourian@umsha.ac.ir

Received: 2024-08-16
Accepted: 2025-04-13

How to cite this article:
Ezati-Soleiman R, Karampourian A, Khatiban M, Tapak L, Say MH. **The effect of lavender aromatherapy and acetaminophen as preemptive on comfort and Nitroglycerin-induced headache in acute coronary syndrome.** ARYA Atheroscler. 2025; 21(3): 28-37.

DOI:
https://doi.org/10.48305/arya.2025.42978.2992

Abstract

BACKGROUND: Nitroglycerin (NTG) improves cardiac ischemia, but one of its side effects is headache. This study aimed to compare the effects of lavender aromatherapy and acetaminophen as preemptive interventions on comfort and NTG-induced headache in patients with acute coronary syndrome (ACS).

METHODS: This three-arm randomized clinical trial was conducted on 90 patients divided into three groups of 30. In the acetaminophen group, patients were given 500 mg of oral acetaminophen approximately 15 minutes before IV nitroglycerin infusion. In the lavender group, 15 minutes before nitroglycerin IV infusion, cotton gauze soaked in three drops of 2% lavender essential oil was used. In the control group, patients received routine care for the treatment of NTG-induced headaches. The severity of patients' headaches was evaluated using the visual analog scale (VAS) at 5, 10, 15, and 60 minutes after starting nitroglycerin infusion.

RESULTS: The mean headache intensity at the 60th minute in the lavender and control groups was 1.37 ± 1.10 and 2.50 ± 2.43, respectively, while no headaches were reported in the acetaminophen group. The highest mean pain severity recorded at different times was 2.12 ± 0.86 in the control group. Headache severity varied across the intervention minutes among the three groups ($p < 0.001$). Additionally, post-intervention comfort was significantly higher in the acetaminophen and lavender groups compared to the control group ($p < 0.001$), with a significant difference observed between the groups ($p < 0.001$).

CONCLUSION: The results of this study suggest that acetaminophen can be used as a preemptive agent to reduce NTG-induced headaches and improve the comfort of ACS patients.

Keywords: Headache; Acetaminophen; Analgesics; Aromatherapy; Lavandula; Visual Analog Scale

This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 Unported License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Cardiovascular disease (CVD) is one of the leading causes of death globally[1] and the primary cause of mortality and morbidity in Iran, accounting for 46% of all deaths and 20–23% of the country's disease burden[2]. Out of 17.9 million people who died from CVDs in 2019, 85% succumbed to acute coronary syndrome (ACS)[3]. ACS includes ST-elevation myocardial infarction, non–ST-segment elevation myocardial infarction, and unstable angina, all extensively treated with nitroglycerin[4].

Nitroglycerin, also known as glyceryl trinitrate (GTN), is a medication used to treat and prevent chest pain. This medicine provides immediate relief from angina-related chest pain[5]. NTG induces vasodilation and increases blood flow to the myocardium[6].

Despite the importance of NTG's role in a well-functioning cardiovascular system, headache is the most common side effect of nitrate therapy. NTG-induced headaches are usually severe, throbbing, and persistent, occurring immediately after administration[7-10]. Immediate NTG-induced headaches developing within the first hour of application can be severe and lack typical migraine symptoms[11]. Intravenous nitroglycerin (IV NTG) ordered at 0.5 mcg/kg/min over 20 minutes can produce migraine-like headaches[12]. The majority of patients treated with nitroglycerin experience migraine-like NTG-induced headaches and require analgesics[13]. Unrelieved pain can lead to adverse psychological and physical outcomes in patients. Nurses, along with physicians, play a significant role in managing headaches[14].

Since acetaminophen is a safe and well-tolerated medication, it is used to treat headaches associated with continuous nitroglycerin infusion[15]. Migraine and NTG-induced headaches share some similarities, and some migraine studies have developed nitroglycerin models[10]. These findings can be used to improve the care of ACS patients undergoing intravenous nitroglycerin infusion. In an updated systematic review, the efficacy and tolerability of oral acetaminophen (1,000 mg) were statistically superior to placebo in the treatment of acute migraine in adults, with no serious adverse events[16].

These studies focused on the therapeutic effects of acetaminophen on migraine-like NTG-induced headaches rather than its preventive potential. Traditionally, prophylactic treatment is a crucial element of migraine management[10,17]. However, acetaminophen as a preemptive analgesic for NTG-induced headaches has not been adequately studied. Preemptive acetaminophen analgesia has been shown to significantly reduce the incidence, severity, intensity[18], and duration of post-electroconvulsive therapy (ECT) headaches[19]. However, only one trial was found in which acetaminophen was applied preemptively for NTG-induced headaches in patients with chronic anal fissure who used nitroglycerin 0.4% ointment[20].

Aromatherapy with roses and lavender has been shown to reduce NTG-induced headaches[21].

Among migraine patients, 15-minute aromatherapy with lavender essential oil every other day for four weeks had positive effects on headache disability[22]. Inhalation aromatherapy with lavender essential oil was effective in the acute management of headache attacks in migraine patients[23]. Additionally, lavender plays a role in the prophylactic treatment of migraine, as using lavender for three months reduced the frequency and severity of migraine incidents[24].

The common treatment for headaches in patients receiving nitroglycerin includes both medicinal and non-medicinal approaches. In medical treatment, acetaminophen is used as needed (PRN). However, since the headache occurs before taking the medicine, patients may experience significant pain until the medication reaches its peak effect. Preemptive treatment, whether with or without drug interventions, can be useful in preventing headaches and improving patient outcomes.

To our knowledge, this is the first study to evaluate the preemptive effects of acetaminophen and lavender on NTG-induced headaches in ACS patients. The primary aim

of this study is to compare the efficacy of preemptive analgesia with acetaminophen and lavender aromatherapy in reducing the incidence and intensity of headaches. The secondary aim is to analyze the effects on comfort levels in patients undergoing NTG treatment.

Materials and Methods

Trial Design

This study was a three-arm randomized clinical trial aimed at examining the preemptive effects of acetaminophen and lavender oil on NTG-induced headache and comfort in ACS patients. Participants were recruited between July 2019 and January 2020 from three Coronary Care Units in the teaching hospitals of Hamedan University of Medical Sciences.

Participants and Sample size

Patients newly admitted to the participating CCUs were approached to participate in the study and assessed for eligibility.

A medium effect size of 0.5 standard deviations was anticipated, reflecting a clinically relevant difference in pain intensity. A power of 90% was targeted to maximize the probability of detecting a true difference, if it exists. A significance level of 0.05 was adopted to minimize the risk of Type I error. Three repeated measurements were planned for each participant. An estimated correlation of 0.5 was assumed between the repeated measurements, reflecting moderate correlation[25]. To account for potential attrition, a 10% increase in the sample size was implemented. Therefore, a total sample size of 90 participants (30 per group) was determined to be necessary for the study.

Inclusion criteria: Participants were required to be between 30–60 years old, have a physician's order for 5–10 mcg/minute continuous IV nitroglycerin infusion and 500 mg PO acetaminophen PRN for headache, and have the ability to speak and swallow. Exclusion criteria included a history of sublingual nitroglycerin (SLNTG) use, migraine, chronic headaches, sensitivity to acetaminophen or herbal medicines, olfactory disorders, and nausea.

Exclusion criteria: Patients were excluded if they had a known allergy to nitrate medications or lavender, developed hypotension (systolic blood pressure [SBP] < 100 mmHg) during the study, had inadequate follow-up time (less than one hour after initiation of IV NTG infusion), or experienced uncontrolled symptoms that could affect pain or comfort (such as arrhythmia or heart attack). To minimize contamination bias, patients assigned to different study arms were excluded if their beds were located in the same room.

Using convenience sampling, 90 eligible patients were invited to participate in the study. They were randomly assigned to one of three arms (acetaminophen, lavender essential oil, or control) using permuted block randomization (AABBCC, ABCABC, BBCCAA...), with assignments concealed in paper packets and selected by the nursing officer (Figure 1).

In the acetaminophen group, patients were given 500 mg of oral acetaminophen approximately 15 minutes before IV nitroglycerin infusion. This 15-minute interval was deemed sufficient for the preemptive effects of acetaminophen, as its onset occurs within 15 to 90 minutes[26], and NTG-induced headache typically begins around 20 minutes after IV NTG infusion[12].

Lavender group: About 15 minutes before nitroglycerin IV infusion, a cotton gauze soaked in three drops of 2% lavender essential oil, prepared by Zardband Pharmaceutical Company, was attached to the patient's dress collar. The beneficial effects of inhalation administration of lavender essential oil can be immediate due to the short and direct olfactory pathway to the brain[27]. Positive effects appear within 14, 16, 26, and 30 minutes after starting lavender essential oil aromatherapy[28]. The lavender essential oil used in this study was sourced from a reputable Iranian pharmaceutical company under standardized regulations. Patients were also given deep breathing training.

Control group: Patients received routine care for nitroglycerin-induced headaches. This meant that 500 mg of acetaminophen was

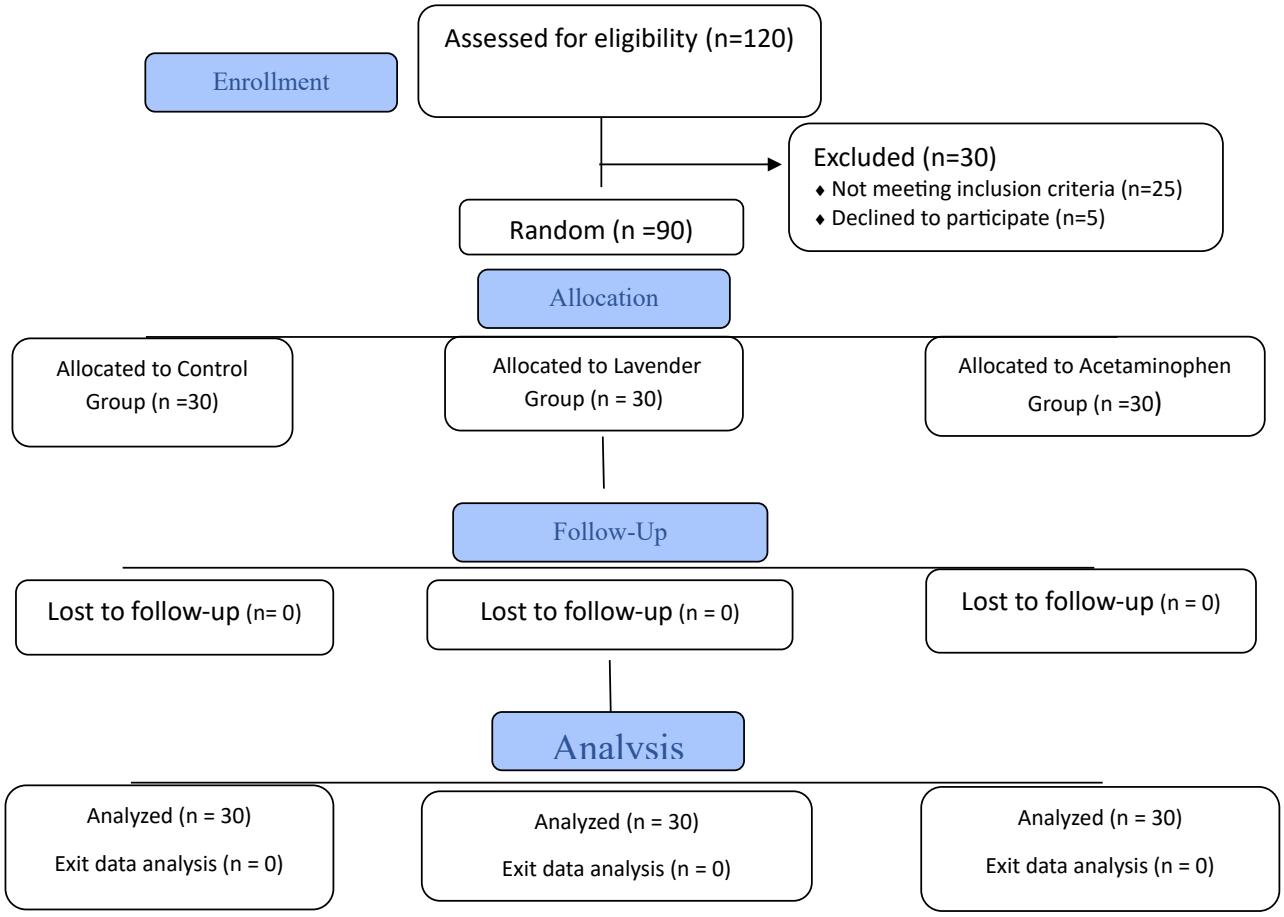

Figure 1. CONSORT Diagram

administered after the nitroglycerin infusion whenever the patient expressed a headache.

All patients received routine CCU care and nitroglycerin infusion management. They remained on complete bed rest (CBR) in a semi-sitting position (45°). None had consumed alcohol, and none reported headaches at the time of enrollment. ACS patients received a 5–10 µ/min IV nitroglycerin infusion, which was continued until chest pain resolved or hypotension occurred (SBP < 100 mmHg). Researchers provided simple and comprehensive instructions to patients regarding the visual analog scale at the time of enrollment.

It should be noted that the patients were unaware of their allocated group. As they rated their NTG-induced headaches, the non-blinded assessor ensured accurate reporting without under- or overestimating symptoms.

Outcome Measures

- **Demographic and clinical characteristics checklist:** This checklist includes age, BMI, gender, marital status, occupation, education level, history of smoking, disease, or opium use, nitroglycerin dose, hemodynamic parameters, and narcotic medication use.
- **Headache severity:** Measured using a 0–10 visual analog scale (VAS), where 0 indicates "no pain at all" and 10 represents "the worst pain imaginable"[29]. NTG-induced headaches usually occur immediately after administration[30], within the first hour of NTG application[11], specifically 20 minutes after IV NTG infusion[12]. Patients' VAS scores were recorded at 5, 10, 15, and 60 minutes after the start of nitroglycerin infusion.
- **Comfort measurement:** VAS for comfort assessment[31] was completed 15 minutes before and 60 minutes after the start of nitroglycerin

infusion. The scale consists of a 10 cm horizontal line ranging from 0 to 10, where 0 indicates complete discomfort and 10 represents complete comfort.

- **Checklist for painkiller administration and vital signs:** Completed from the start of the injection until the end of the study.

Data analysis

Data were analyzed using SPSS Statistics version 23. Chi-square tests were used to compare categorical variables (e.g., gender, marital status) among the three groups. One-way ANOVA was employed to compare continuous variables (e.g., age, BMI) among the three groups.

Repeated-measures analysis of covariance (RM-ANCOVA) was conducted to assess the effect of the three interventions (acetaminophen, lavender essential oil, and control) on pain intensity, controlling for baseline pain intensity and relevant covariates such as blood pressure, heart rate, and narcotic medication use.

To further explore group differences in pain intensity over time, repeated-measures analysis of variance (RM-ANOVA) was performed. Post-hoc pairwise comparisons with Bonferroni correction were used to identify significant differences between groups at specific time points. Cochran's Q test was applied to compare the incidence of headaches among patients over time.

A significance level of 0.05 was used for all statistical tests.

Ethical approval

The study was performed following the Declaration of Helsinki. The Research and Technology Vice-chancellor of Hamadan University of Medical Sciences approved the study (9710256335) after the Ethical Committee approval (IR.UMSHA.REC.1397.409) and registration on the Iranian Registry of Clinical Trials (IRCT20180927041157N1). The written consents were signed by the patients after clarifying the aims and objectives of the study and their right to decline the study without any negative consequences.

Results

The results showed that the patients in all three groups were homogeneous in terms of gender, marital status, occupation, and education (Table 1). However, the three groups were heterogeneous in terms of nitroglycerin dose ($P < 0.05$), diastolic blood pressure ($P < 0.05$), mean arterial pressure ($P < 0.05$), and narcotic medication use ($P < 0.001$)

The results showed that the highest frequency of headache among the three groups occurred in the control group. In the control group, the frequency of headache at 5, 10, 15, and 60 minutes was 16.67%, 26.67%, 50%, and 66.67%, respectively. The frequency of headache varied at the 5th, 10th, 15th, and 60th minutes of the intervention among the three groups ($p < 0.001$). Moreover, pairwise comparisons using Bonferroni-adjusted p-value ($P = 0.787$) indicated no statistically significant differences in headache frequency at the 60th minute of intervention between the lavender and control groups.

The results also showed that headache intensity was highest in the control group. In the control group, the average headache intensity at 5, 10, 15, and 60 minutes was 2.50 ± 2.43, 2.50 ± 3.06, 1.43 ± 2.52, and 0.87 ± 2.13, respectively. The average headache intensity varied at the 5th, 10th, 15th, and 60th minutes of intervention among the three groups ($p = 0.012$).

Additionally, the highest headache duration was observed in the control group. In the control group, the average headache duration at 5, 10, 15, and 60 minutes was 1,031.1 ± 1,090.0, 210.9 ± 275.1, 90.1 ± 160.5, and 50.0 ± 113.7 minutes, respectively. The average headache duration varied at the 5th, 10th, 15th, and 60th minutes of intervention among the three groups ($p = 0.005$) (Table 2).

Moreover, repeated measures analysis of covariance, as well as multiple comparisons of average headache duration and severity between time points, were provided in Table S1 to Table S4 (see Supplementary File 1).

Table 1. Demographic data among acetaminophen, lavender, and control groups

Variables		Acetaminophen (n=30)	Lavender (n=30)	Control (n=30)	P-value
Age, year, M± SD		69.60±10.73	63.43±13.87	63.33±12.86	0.092 [1]
BMI, kg/m², M± SD		27.37±6.94	25.55±2.83	28.26±6.36	0.176 [1]
Gender, n(%)	**Male**	15 (50.00)	19 (63.33)	19 (63.33)	0 .480 [2]
	Female	15 (50.00)	11 (36.67)	11 (36.67)	
Married, n(%)		29 (96.67)	23 (76.67)	29 (96.67)	0 .078 [3]
Occupied, n(%)		8 (26.67)	11 (36.67)	17 (56.67)	0 .054 [2]
Education, n(%)	**Illiterate**	20 (66.67)	21 (70.00)	16 (53.34)	0.410 [3]
	High school	8 (26.67)	9 (30.00)	13 (43.33)	
	Academic	2 (6.66)	0 (0.00)	1 (3.33)	
Smoking, n(%)		7 (23.33)	10 (33.33)	7 (23.33)	0 .600 [2]
History of Diseases, n(%)		19 (63.33)	13 (43.33)	15 (50.00)	0.287 [2]
History of Opium, n(%)		6 (20.00)	2 (6.67)	2 (6.67)	0.205 [3]
Nitroglycerine Dose; mg/min, n(%)	**5**	13 (43.33)	23 (76.67)	15 (50.00)	0.037 [2]
	10	14 (46.67)	7 (2333)	14 (46.67)	
	15	3 (10.00)	0 (0.00)	1 (3.33)	
Hemodynamic parameters, n(%)	**SBP**	150.70±30.85	139.10±19.42	146.17±24.80	0.211 [1]
	DBP	89.57±19.30	82.03±12.95	93.30±17.40	0.036 [1]
	PR	79.53±21.01	75.47±9.12	80.27±17.97	0.494 [1]
	T	36.93± .20	36.88± .19	36.96± .31	0.490[1]
	RR	18.90± 1.30	18.57± .86	18.07± 1.80	0.066 [1]
	MAP	109.77± 21.98	99.42± 17.16	110.9± 19.39	0.049 [1]
	SaO_2	95.17± 3.67	96.50± 2.16	95.36± 7.02	0.503 [1]
Narcotic Medication, n(%)	**No**	30 (100.00)	24 (80.00)	13 (43.33)	<0.001 [2]
	Yes	0 (0.00)	6 (20.00)	17 (56.67)	

SBP= Systolic Blood Pressure DBP=Diastolic Blood Pressure PR= Pulse Rate T=Temperature RR=Respiratory Rate MAP=Mean Arterial Pressure SaO2= Arterial Oxygen Saturation
[1]: ANOVA [2]: Chi-square [3]: Fisher's Exact Test

Table 2. Comparing headache over time among three groups

Variables	Groups		Minutes after intervention				P value
			5th	**10th**	**15th**	**60th**	
Frequency of Headache,	Acetaminophen, n (%)		0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	-
	Lavender, n (%)		0 (0.00)	0 (0.00)	0 (0.00)	19 (63.33)	<0.001 [1***]
	Control, n (%)		5 (16.67)	8 (26.67)	15 (50.00)	20 (66.67)	<0.001 [1***]
P value[3]	unadjusted		0.010	< 0.001	<0 .001	<0.001	
P value[4]	adjusted£		0.014	<0.001	<0.001	<0.001	
Intensity of Headache	Acetaminophen, M± SD		0.00±0	0.00±0	0.00±0	0.00±0	0.012 [2*]
	Lavender, M± SD		0.00±0	0.00±0	0.00±0	1.37±1.10	
	Control, M± SD		0.87±2.13	1.43±2.52	2.50±3.06	2.50±2.43	
P value[5]	unadjusted		0.009	<0.001	<0.001	<0.001	
P value[6]	adjusted£		0.022	<0.001	<0.001	<0.001	
Duration of Headache (Seconds)	Acetaminophen M± SD		0.00±0	0.00±0	0.00±0	0.00±0	0.005 [2**]
	Lavender	M± SD	0.00±0	0.00±0	0.00±0	449.7±462.19	
		Median (Q3-Q1)	-	-	-	746.75-0	
	Control	M± SD	50.0±113.7	90.1±160.5	210.9±275.1	1031.1±1090.0	
		Median Q3-Q1	-	-	300-0	2175-0	
P value[5]	unadjusted		<0.014	< 0.001	< 0.001	<0.001	
P value[6]	adjusted£		0.014	<0.001	<0.001	<0.001	

[1]: Cochran's Q Test
[2]: RMANCOVA= Repeated-measures analysis of covariance after adjusting the patients' narcotic medication doses, diastolic blood pressure, and nitroglycerine doses;
3: Chi-square test 4: Logistic Regression 5: ANOVA 6: ANCOVA *: P<0.05, **P<0.01, ***P<0.001
£: Adjustment was done for patients' narcotic medication doses, diastolic blood pressure, and nitroglycerine doses and MAP

Table 3. Comparing of patients' comfort in acetaminophen, lavender, and control groups

Comfort	Before M± SD	After M± SD	P value[1]
Acetaminophen	4.08±2.07	9.37±0.93	<0.001
Lavender	2.78±1.22	8.40±1.30	<0.001
Control	6.43±1.63	3.09±2.01	<0.001
P value [2]	<0.001	<0.001	
P value [3]	<0.001	<0.001	

[1]: Paired t-test [2]: ANOVA (unadjusted P-value) [3]: ANCOVA (adjusted P-value)

Table 4. Pairwise Comparisons of Mean Comfort Using the Bonferroni test

Dependent Variable: Comfort	Group (I)	Group (J)	Mean Difference (I-J)	Std. Error	P value[1]	P value[2]
Before intervention	Acetaminophen vs.	Lavender	1.31	0.43	0.009	0.010
	Acetaminophen vs.	Control	-2.35	0.43	<0.001	<0.001
	Lavender vs.	Control	-3.66	0.43	<0.001	<0.001
After intervention	Acetaminophen vs.	Lavender	1.03	0.40	0.038	0.032
	Acetaminophen vs.	Control	6.16	0.41	<0.001	<0.001
	Lavender vs.	Control	5.13	0.52	<0.001	<0.001

* The mean difference is significant at the 0.05 level. [1]: obtained from ANOVA; [2]: obtained from ANCOVA (adjusted P-value for controlling confounders including the patients' narcotic medication doses, diastolic blood pressure, and nitroglycerine doses and MAP as well as comfort level before intervention (for after intervention))

The results showed that the comfort after the intervention in the two groups of acetaminophen and lavender was more than the control group (p <0.001). The lowest comfort was in the control group (3.09±2.01), while the highest comfort was in the acetaminophen group (9.37±0.93). The comfort was significantly different, even after adjusting the narcotic medication doses, headache severity, and nitroglycerine doses. The comfort in the two groups of acetaminophen and lavender was higher than in the control group (p <0.001). The average comfort in three groups after intervention was 9.37±0.93, 8.40±1.30, and 3.09±2.01 respectively (Table 3).

Table 4 presents the results of the Tukey test for post-hoc analysis, highlighting significant differences in mean comfort levels across the Acetaminophen, Lavender, and Control groups at both pre- and post-intervention stages. Prior to the intervention, both Acetaminophen (p = 0.009) and Lavender (p < 0.001) groups reported significantly higher comfort levels compared to the Control, with the Lavender group showing the largest difference. Therefore, the level of comfort before intervention was adjusted for calculation of P-values after intervention. Post-intervention, comfort levels further increased in both treatment groups, with Acetaminophen demonstrating the highest improvement, showing a significant mean difference of 6.27 points compared to the Control (p < 0.001) and a modest yet significant advantage over Lavender (p = 0.035). The Lavender group also maintained a significant increase in comfort over the Control (p < 0.001). These findings suggest that both Acetaminophen and Lavender interventions effectively enhanced comfort, with Acetaminophen showing a slightly stronger impact.

Discussion

The study aimed to compare the effects of lavender aromatherapy and acetaminophen as preemptive treatments for comfort and NTG-induced headache in ACS patients. The results showed that headache severity was lowest and comfort highest in the acetaminophen group, followed by the lavender group. Both acetaminophen and lavender effectively reduced headaches in ACS patients.

Gallelli examined the effects of acetaminophen and ibuprofen on children's migraines, showing that both groups experienced a significant reduction in pain frequency[32]. Acetaminophen,

used as preemptive analgesia, has significantly decreased the incidence and severity of post-electroconvulsive therapy (ECT) headaches[18] as well as the intensity and duration of post-ECT headaches[19]. Prior et al. conducted a placebo-controlled trial of acetaminophen for migraine treatment, demonstrating its effectiveness in relieving migraine headaches[33].

Tasan conducted a study to evaluate the effects of lavender oil inhalation on pain intensity during vascular access in hemodialysis patients, revealing that lavender inhalation significantly reduced pain severity[34]. Rafie investigated lavender essential oil as a migraine prevention treatment, finding that it decreased both the frequency and severity of migraine episodes[35].

Karaman explored lavender aromatherapy for pain relief in surgical patients, showing that pain scores in the lavender group were significantly lower than in the control group[36]. However, Ebrahimi Hoshyar's study found that Transcutaneous Electrical Nerve Stimulation (TENS) more effectively reduced post-cesarean section pain than lavender[37].

Ali et al.'s study confirmed that lavender is effective in controlling headaches[38]. Sasannejad examined lavender essential oil for migraine treatment and found that inhalation of lavender is a safe and effective therapy for acute migraine management[39]. Mashouf discovered that lavender aromatherapy helps alleviate restlessness and agitation in mechanically ventilated patients[40].

Bikmoradi assessed the effects of inhaled lavender aromatherapy on stress and vital signs in coronary artery bypass surgery patients, showing that lavender had a significant impact on stress reduction[41]. Ziyaeifard's study demonstrated that lavender significantly reduces anxiety and pain in patients before and after coronary angiography[42].

Conclusion

The results of this study suggest that acetaminophen can be used as a preemptive agent to reduce NTG-induced headaches and improve the comfort of ACS patients.

Limitations

One of the limitations of this study was the individual differences and psychological conditions of the participants, which had an effect on the results and were beyond the control of the researchers. We also did not measure headaches beyond one hour after IVNTG infusion. On the other hand, small sample size and the possible psychological influence of researcher presence on participant pain reporting are other limitations of the study.

Acknowledgements

This study is the result of a master's thesis in nursing. The authors thank all the patients and nurses participating in the study. We also thank the Vice Chancellor for Research.

Conflict of interests

The authors declare no conflict of interest.

Funding

The study was financially supported by Hamadan University of Medical Sciences.

Author's Contributions

Study Conception or Design: RES; AK; MKS
Data Acquisition: RES; MHS
Data Analysis or Interpretation: LT
Manuscript Drafting: RES; AK; MK
Critical Manuscript Revision: AK; LT
All authors have approved the final manuscript and are responsible for all aspects of the work.

References

1. Li S, Wu Y, Du X, Li X, Patel A, Peterson ED, et al. Rational and design of a stepped-wedge cluster randomized trial evaluating quality improvement initiative for reducing cardiovascular events among patients with acute coronary syndromes in resource-constrained hospitals in China. Am Heart J. 2015 Mar;169(3):349-55. https://doi.org/10.1016/j.ahj.2014.12.005
2. Sarrafzadegan N, Mohammmadifard N. Cardiovascular Disease in Iran in the Last 40 Years: Prevalence, Mortality, Morbidity, Challenges and Strategies for Cardiovascular Prevention. Arch Iran

Med. 2019 Apr 1;22(4):204-10.
3. WHO. Cardiovascular diseases (CVDs) https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds): World Health Organization; 2021 [updated 11 June 202120 Sep 2021].
4. Makki N, Brennan TM, Girotra S. Acute coronary syndrome. J Intensive Care Med. 2015;30(4):186–200. https://doi.org/10.1177/0885066613503294
5. Boden WE, Padala SK, Cabral KP, Buschmann IR, Sidhu MS. Role of short-acting nitroglycerin in the management of ischemic heart disease. Drug Des Devel Ther. 2015 Aug 19;9:4793-805. https://doi.org/10.2147/dddt.s79116
6. Ferreira JC, Mochly-Rosen D. Nitroglycerin use in myocardial infarction patients. Circ J. 2012;76(1):15-21. https://doi.org/10.1253/circj.cj-11-1133
7. Pradhan AA, Bertels Z, Akerman S. Targeted Nitric Oxide Synthase Inhibitors for Migraine. Neurotherapeutics. 2018 Apr;15(2):391-401. https://doi.org/10.1007/s13311-018-0614-7
8. Demartini C, Greco R, Zanaboni AM, Sances G, De Icco R, Borsook D, et al. Nitroglycerin as a comparative experimental model of migraine pain: From animal to human and back. Prog Neurobiol. 2019 Jun;177:15-32. https://doi.org/10.1016/j.pneurobio.2019.02.002
9. Divakaran S, Loscalzo J. The Role of Nitroglycerin and Other Nitrogen Oxides in Cardiovascular Therapeutics. J Am Coll Cardiol. 2017 Nov 7;70(19):2393-410. https://doi.org/10.1016/j.jacc.2017.09.1064
10. Caudle RM, Caudle SL, Flenor ND, Rohrs EL, Neubert JK. Pharmacological Characterization of Orofacial Nociception in Female Rats Following Nitroglycerin Administration. Front Pharmacol. 2020 Dec 3;11:527495. https://doi.org/10.3389/fphar.2020.527495
11. Bagdy G, Riba P, Kecskeméti V, Chase D, Juhász G. Headache-type adverse effects of NO donors: vasodilation and beyond. Br J Pharmacol. 2010 May;160(1):20-35. https://doi.org/10.1111/j.1476-5381.2010.00643.x
12. Wei DY, Goadsby PJ. Comprehensive clinical phenotyping of nitroglycerin infusion induced cluster headache attacks. Cephalalgia. 2021 Jul;41(8):913-33. https://doi.org/10.1177/0333102421989617
13. Sureda-Gibert P, Romero-Reyes M, Akerman S. Nitroglycerin as a model of migraine: Clinical and preclinical review. Neurobiol Pain. 2022 Sep 27;12:100105. https://doi.org/10.1016/j.ynpai.2022.100105
14. Glowacki D. Effective pain management and improvements in patients' outcomes and satisfaction. Crit Care Nurse. 2015 Jun;35(3):33-41. https://doi.org/10.4037/ccn2015440
15. Karsan N, Bose PR, Thompson C, Newman J, Goadsby PJ. Headache and non-headache symptoms provoked by nitroglycerin in migraineurs: A human pharmacological triggering study. Cephalalgia. 2020 Jul;40(8):828-41. https://doi.org/10.1177/0333102420910114
16. Derry S, Moore RA. Paracetamol (acetaminophen) with or without an antiemetic for acute migraine headaches in adults. Cochrane Database Syst Rev. 2013 Apr 30;2013(4):CD008040. https://doi.org/10.1002/14651858.cd008040.pub3
17. D'Amico D, Tepper SJ. Prophylaxis of migraine: general principles and patient acceptance. Neuropsychiatr Dis Treat. 2008 Dec;4(6):1155-67. https://doi.org/10.2147/ndt.s3497
18. Isuru A, Rodrigo A, Wijesinghe C, Ediriweera D, Premadasa S, Wijesekara C, et al. A randomized, double-blind, placebo-controlled trial on the role of preemptive analgesia with acetaminophen [paracetamol] in reducing headache following electroconvulsive therapy [ECT]. BMC Psychiatry. 2017 Jul 28;17(1):275. https://doi.org/10.1186/s12888-017-1444-6
19. Kertesz DP, Trabekin O, Vanetik MS. Headache treatment after electroconvulsive treatment: a single-blinded trial comparator between eletriptan and paracetamol. J ECT. 2015 Jun;31(2):105-9. https://doi.org/10.1097/yct.0000000000000179
20. Berry SM, Barish CF, Bhandari R, Clark G, Collins GV, Howell J, et al. Nitroglycerin 0.4% ointment vs placebo in the treatment of pain resulting from chronic anal fissure: a randomized, double-blind, placebo-controlled study. BMC Gastroenterol. 2013 Jul 1;13:106. https://doi.org/10.1186/1471-230x-13-106
21. Moradi M, Jalili F, Basiri-Moghadam M, Basiri-Moghadam K. Comparing the effect of aromatherapy with lavender and rose essential oils on the prevention of headache induced by infusion of nitroglycerin in cardiac care unit. J Isfahan Med Sch. 2022;40(670):300-60. https://doi.org/10.48305/jims.v40.i670.0300
22. Jafari-Koulaee A, Khenarinezhad F, Sharifi Razavi A, Bagheri-Nesami M. The effect of aromatherapy with Lavender essence on depression and headache disability in migraine patients: A randomized clinical trial. J Med Plants. 2019;18(70):162-72. http://dx.doi.org/10.29252/jmp.2.70.162
23. Sasannejad P, Saeedi M, Shoeibi A, Gorji A, Abbasi M, Foroughipour M. Lavender essential oil in the treatment of migraine headache: a placebo-controlled clinical trial. Eur Neurol. 2012;67(5):288-91. https://doi.org/10.1159/000335249
24. Rafie S, Namjoyan F, Golfakhrabadi F, Yousefbeyk F, Hassanzadeh A. Effect of lavender essential oil as a prophylactic therapy for migraine: A randomized controlled clinical trial. J Herb Med. 2016;6(1):18-23.

https://doi.org/10.1016/j.hermed.2016.01.003
25. Zarifnejad G, Eshghi E, Mirhaghi A, Ghorbanzadeh H. The effect of aromatherapy with lavender essential oil in treatment of headache due to nitroglycerine infusion in patients admitted to cardiac emergency department. Complement Med J. 2015;5(3):1248–57.
26. Katzung BG, Vanderah TW. Basic & clinical pharmacology. 15th ed. New York: McGraw-Hill Education; 2020.
27. Erdő F, Bors LA, Farkas D, Bajza Á, Gizurarson S. Evaluation of intranasal delivery route of drug administration for brain targeting. Brain Res Bull. 2018 Oct;143:155-70. https://doi.org/10.1016/j.brainresbull.2018.10.009
28. Shimizu K, Gyokusen M, Kitamura S, Kawabe T, Kozaki T, Ishibashi K, et al. Essential oil of lavender inhibited the decreased attention during a long-term task in humans. Biosci Biotechnol Biochem. 2008 Jul;72(7):1944-7. https://doi.org/10.1271/bbb.70835
29. Heller GZ, Manuguerra M, Chow R. How to analyze the Visual Analogue Scale: Myths, truths and clinical relevance. Scand J Pain. 2016 Oct;13:67-75. https://doi.org/10.1016/j.sjpain.2016.06.012
30. Kim JT, Ren CJ, Fielding GA, Pitti A, Kasumi T, Wajda M, et al. Treatment with lavender aromatherapy in the post-anesthesia care unit reduces opioid requirements of morbidly obese patients undergoing laparoscopic adjustable gastric banding. Obes Surg. 2007 Jul;17(7):920-5. https://doi.org/10.1007/s11695-007-9170-7
31. Trimmel M, Trimmel K. Rating comfort and every-day mood states (TRIM-S): comparing Likert scales with visual analog scales (VAS) and relations to cardiovascular response. Ergonomics Open J. 2017;10:14–28. https://doi.org/10.2174/1875934301710010014
32. Gallelli L, Avenoso T, Falcone D, Palleria C, Peltrone F, Esposito M, et al. Effects of acetaminophen and ibuprofen in children with migraine receiving preventive treatment with magnesium. Headache. 2014 Feb;54(2):313-24. https://doi.org/10.1111/head.12162
33. Prior MJ, Codispoti JR, Fu M. A randomized, placebo-controlled trial of acetaminophen for treatment of migraine headache. Headache. 2010 May;50(5):819-33. https://doi.org/10.1111/j.1526-4610.2010.01638.x
34. Taşan E, Ovayolu O, Ovayolu N. The effect of diluted lavender oil inhalation on pain development during vascular access among patients undergoing haemodialysis. Complement Ther Clin Pract. 2019 May;35:177-82. https://doi.org/10.1016/j.ctcp.2019.02.010
35. Rafie S, Namjoyan F, Golfakhrabadi F, Yousefbeyk F, Hassanzadeh A. Effect of lavender essential oil as a prophylactic therapy for migraine: A randomized controlled clinical trial. Journal of Herbal Medicine. 2016;6(1):18-23. https://doi.org/10.1016/j.hermed.2016.01.003
36. Karaman T, Karaman S, Dogru S, Tapar H, Sahin A, Suren M, et al. Evaluating the efficacy of lavender aromatherapy on peripheral venous cannulation pain and anxiety: A prospective, randomized study. Complement Ther Clin Pract. 2016 May;23:64-8. https://doi.org/10.1016/j.ctcp.2016.03.008
37. Ebrahimi-Hoshyar A, Hosein Rezai H, Gahani Y, Kazemi M, Monfared S. Comparative study of two methods of lavender essential oil aromatherapy with nerve electrical stimulation on pain after cesarean section. Iranian Journal of Obstetrics, Gynecology and Infertility. 2015;18(146):6-12.
38. Ali B, Al-Wabel NA, Shams S, Ahamad A, Alam Khan S, Anwar F. Essential oils used in aromatherapy: A systemic review. Asian Pacific Journal of Tropical Biomedicine. 2015;5(8):601-11. https://doi.org/10.1016/j.apjtb.2015.05.007
39. Sasannejad P, Saeedi M, Shoeibi A, Gorji A, Abbasi M, Foroughipour M. Lavender essential oil in the treatment of migraine headache: a placebo-controlled clinical trial. Eur Neurol. 2012;67(5):288-91. https://doi.org/10.1159/000335249
40. Mashouf S, Aflaki M, Esmaeilpour Zanjani S, Mojab F. The Effects of Aromatherapy by Lavender Oil on Agitation and Hemodynamic Parameters in Mechanically Ventilated Patients in ICU. Trad Integr Med. 2017;2(3):119-28.
41. Bikmoradi A, Seifi Z, Poorolajal J, Araghchian M, Safiaryan R, Oshvandi K. Effect of inhalation aromatherapy with lavender essential oil on stress and vital signs in patients undergoing coronary artery bypass surgery: A single-blinded randomized clinical trial. Complementary therapies in medicine. 2015;23(3):331-8.
42. Ziyaeifard M, Azarfarin R, Aghdaii N, Alizadehasl A, Massoumi G, Alavi M, et al. Effects of lavender oil inhalation on anxiety and pain in patients undergoing coronary angiography. Iran Heart J. 2017;18(1):44–50.