The Effect of Aromatherapy on Blood Pressure and Stress Responses by Inhalation and Foot Massage in Patients With Essential Hypertension

Randomized Clinical Trial

■ *Saadet Can Çiçek, PhD, RN* ■ *Şeyma Demir, PhD, RN* ■ *Dilek Yılmaz, PhD, RN*
■ *Aynur Açıkgöz, MSc, RN* ■ *Sedat Yıldız, PhD, DR* ■ *Özgür Mehmet Yis, PhD, DR*

A 3-arm, parallel group, randomized clinical trial examines the effect of aromatherapy through inhalation and foot massage on blood pressure and stress response in patients with essential hypertension. Lavender oil reduced blood pressure, heart rate, serum cortisol, and subjective anxiety in hypertensive patients.

KEY WORDS: *aromatherapy*, *essential hypertension*, *lavender*, *randomized controlled trial*, *stress*

Holist Nurs Pract 2022;36(4):209–222

INTRODUCTION

Hypertension (HT) or increased blood pressure is an important health problem, which is also the main independent risk factor of chronic renal failure and cardiovascular and cerebrovascular diseases.[1,2] Globally, 1.13 billion people had HT in 2015,[3] while increased blood pressure accounts for 10.4 million deaths annually.[4] Nonetheless, it is emphasized that the diagnosis, treatment, and control of essential hypertension (EHT), which is seen in more than 95% of hypertensive people, are below the desired level due to the shortcomings of the health system, especially in primary care.[5]

Stress is a risk factor commonly associated with EHT. Although its etiological effect in the development of HT is known, its prognostic value cannot be ignored.[1,6] Although acute stress contributes to the transient elevation of blood pressure, the relationship has not been fully explained because of the variability of stressors.[6] As for chronic or repetitive stress, the condition has been associated with HT in late life.[4] However, the physiology of stress is clear. Altered activity in the hypothalamic-pituitary-adrenal axis and sympathetic nervous system results in cardiovascular and metabolic disorders.[7] When an organism is confronted with controlled stressors, the circulating levels of catecholamine, corticotropin, and cortisol increase within minutes,[8] which explains the transient increase in heart rate (HR) and blood pressure.[7] Although these appear as an adaptive and protective response of the organism to stressors, frequently repeated responsive conditions of the same type can lead to progressive and irreversible adverse metabolic consequences.[8] Hypertension management focuses primarily on pharmacological treatment and lifestyle modifications.[9] Although

Author Affiliations: Faculty of Health Sciences, Department of Nursing (Drs Can Çiçek and Demir), Internal Medicine Nursing (Dr Demir), Bolu Abant Izzet Baysal University, Bolu, Turkey; Departments of Neurology (Dr Yılmaz), Cardiology (Ms Açıkgöz), and Medical Biochemisty (Dr Yis), Bolu Abant Izzet Baysal University, Izzet Baysal Training and Research Hospital, Bolu, Turkey; and Integrative Medicine Association Physical Therapy, Isparta, Turkey (Dr Yıldız).

The authors thank all the participants.

This study was funded by the Integrative Medicine Association.

Before the study began, ethics committee approval was obtained from the Clinical Research Ethics Committee of Bolu Abant Izzet Baysal University (decision number: 2018/153).

Registration number: NCT04460300.

The authors have disclosed that they have no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

Correspondence: Saadet Can Çiçek, PhD, RN, Department of Nursing, Bolu Abant Izzet Baysal University, Faculty of Health Sciences, Gölköy Campüs, 14280, Bolu, Turkey (saadet.cancicek@ibu.edu.tr).

DOI: 10.1097/HNP.0000000000000526

pharmacological treatments aim to lower blood pressure optimally, they also carry an inherent risk due to their potential side effects.[10] Because of this risk, nonpharmacological methods such as aromatherapy are among the preferred curative approaches for hypertensives in resolving physiological responses associated with stress.

Essential oils are used in aromatherapy to treat minor health problems along with different application methods. Lavender oil (*Lavandula angustifolia*) is widely preferred because of its antibacterial, antifungal, carminative, and anxiolytic properties.[11] The physiological changes in blood pressure and anxiolytic effects of lavender oil have been investigated, especially, in animal studies.[12,13] It was reported that linalool contained in lavender extract had a blood pressure lowering property in terms of its effect on the limbic system, and it was shown that it could reduce anxiety levels with an effect similar to that of the benzodiazepines by increasing the action of γ-aminobutyric acid (GABA-A) receptors in the amygdala.[12] Olfactory stimulation of the oil has been observed to suppress both the sympathetic nerves that innervate the adrenal glands and the renal sympathetic nervous activity, which play an important role in blood pressure regulation in rats.[13]

In human studies, stress responses in hypertensive patients have often been studied by measuring endocrinological stress markers (cortisol, epinephrine, norepinephrine), subjective response (anxiety devices, visual scale), and vital signs (blood pressure, HR, respiratory rate, saturation). A systematic review of 5 studies reported that aromatherapy was an effective approach regarding stress responses in hypertensives.[14] The results of 5 other studies, in which inhalation was conducted, reported significant results in blood pressure,[10,15-18] salivary cortisol,[17] serum cortisol,[16] subjective stress,[16] and HR.[15,16] A significant lowering effect on systolic and diastolic blood pressure was observed according to the findings of a unique study in which aroma massage was applied.[19] The first meta-analysis that investigated the anxiolytic effect of lavender aromatherapy provided strong evidence that it was effective in reducing symptoms associated with anxiety. In addition to the strong effect of lavender aromatherapy on self-rated anxiety, HR, blood pressure, and endocrinological stress markers, inhalation therapy, especially, has been reported to exhibit a large effect size compared with other methods.[20] On the other hand, most of these studies revealed findings obtained from not only lavender but also a mixture of other essential oils (bergamot, ylang-ylang, lemon, etc) with similar effects. The previous 2 studies reported only the unique effect of lavender oil on blood pressure changes.[10,18] However, the variety of oils used and the differences in application methods make it difficult to make a comparison. To illustrate, in clinical studies on hypertensives, the evidence-based results of lavender, including blood pressure, HR, cortisol, and subjective stress responses, have been limited.

In planning this study, the priority was to use lavender in a unique way and to compare 2 different methods (inhalation and foot massage) simultaneously using broad parameters. The research was based on 3 main questions: (1) Is lavender inhalation effective on systolic and diastolic blood pressure, HR, serum cortisol, and subjective anxiety levels in hypertensives? (2) Does lavender foot massage have an impact on parameters? (3) Are inhalation and foot massage superior to each other? Furthermore, it was planned to obtain evidence-based findings with a randomized controlled trial design. In this way, it was thought that methodological dilemmas could be reduced in further research. Therefore, it was aimed to determine the effect of lavender oil on blood pressure and stress responses with this research, which utilized inhalation and foot massage.

METHODS

Trial design

This was a randomized, controlled, 3-arm parallel-group study conducted in Turkey. The CONSORT statement was adopted for the study design and reporting.[21]

Participants and setting

The study was conducted with patients recruited from the cardiology, neurology, and internal medicine clinics of 2 public hospitals in Bolu, Turkey, from November 2018 to May 2020. Eligible patients were all adults aged 18 years or older with a diagnosis of EHT for at least 6 months, not currently receiving anxiolytic or hypnotic therapy, or not using any herbal treatment to lower blood pressure. Exclusion criteria were being diagnosed with asthma or chronic obstructive pulmonary disease, undergoing dialysis treatment, and having a known allergy to lavender.

The trial was approved by the university's clinical research ethics committee (reference number, 2018/153) and the Ministry of Health. The trial is registered at ClinicalTrials.gov, number NCT04460300. Patients approved their participation with written consent before the study.

Sample size and randomization

G*Power was used to calculate the sample size based on serum cortisol levels from prior research with a 2-sided 5% significance level, a power of 80%, and 0.39 effect size,[16] and a sample size of 23 patients per arm was needed. A total of 69 patients were recruited and allocated in a 1:1:1 ratio into one of the following 3 groups: inhalation, foot massage, and usual care (n = 23/per arm). For allocation of the participants, a computer-generated list of random numbers using simple randomization procedures was used. Patients were assigned to groups by 2 researchers and the randomization list was saved. Opaque, sealed envelopes containing sequential numbers (I1, I2, … FM1, FM2, … UC1, UC2, etc) were prepared for each arm. The clinical nurse was asked to choose one of the envelopes and the patient was allocated to the group written on the envelope. Outcome measures (blood pressure and stress responses) were carried out by another researcher blinded to the groups. Clinical nurses and laboratory technicians, with patients assigned independently to the groups, were blinded to the groups.

Interventions

Inhalation group

First, a smell test was performed on the patients assigned to this group. Lemon and peppermint extracts, which were shown to have no irritant effects, were applied separately in both nostrils for 2 minutes. If the smells were distinguished by the patient, the inhalation protocol was used. The inhalation protocol was administered 3 times every other day (eg, Monday, Wednesday, Friday) between 7 AM and 8 AM in the morning. The researcher placed 5 drops of lavender oil directly onto a sterile gauze cloth and placing it about 10 cm away, asked the patient to inhale it for 5 minutes.

Foot massage group

First, a skin test was performed on the patients assigned to this group. A few drops of lavender oil were applied to the inner wrist and held for about 1 hour. If the skin did not develop sensitivity, the massage protocol was used. The foot massage was applied according to the Swedish massage protocol, which is a complementary method that is believed to provide relaxation and therefore reduce blood pressure caused by stress.[22] It is highly preferred because it is not associated with any severe side effects and is a painless, gentle technique performed without applying force.[23] The massage protocol was applied 3 times every other day (eg, Monday, Wednesday, Friday) between 7 AM and 8 AM in the morning. The massage was applied with 10 drops of lavender oil (5 drops per foot) for 20 minutes: 10 minutes per foot. During the application, 20 techniques, each of which lasts for 30 seconds, were used: (1-2) touching: dorsiflexion to feet and plantar flexion, (3) stretching and relaxing the leg, (4) shaking, (5) compression of the solar plexus, (6) grasping the foot with both hands and making toe shifts, (7) thumb-walking along the metatarsals, (8) vibration with compression, (9) simultaneous circular movements to the soles and top of the feet using the 5 fingers, (10) thumb stroking to the plantar surface of the foot, (11) circular movements around the malleolus and Achilles tendon with the fingers, (12) palmar kneading, (13) rotating to all-of-5 toes, (14) rotation and stretching of each toe, (15) foot and ankle rotations, (16) spinal twist, (17) adduction and abduction, (18) press and slide the knuckles from the thumb side to the little finger, (19) effleurage on the feet, and (20) tapping.

Usual care group

Patients in this group received routine treatment and care from the clinic where they were followed up. No other intervention was done by the researchers. Patients were visited 3 times every other day between 7 AM and 8 AM and measurements were made.

Outcome measures

Blood pressure

Following the first admission, after resting for at least 10 minutes in a quiet room, blood pressure was measured in both arms using a digital sphygmomanometer. Further follow-up was made using the arm with the higher measurement. Besides, the measurements were taken 10 minutes after each intervention for both the inhalation and foot massage groups. Both systolic BP (SBP) and diastolic BP (DBP) were recorded. The digital sphygmomanometer

was suitable for calibration procedures without any doubt in reading.

Stress responses

Heart rate

After at least 10 minutes of rest, the apical pulse was counted for 1 minute using a stethoscope and recorded.

Serum cortisol

According to the circadian rhythm, the serum cortisol level is at the diurnal peak between 6 AM and 8 AM.[24] Considering the rapid change in concentrations, cortisol measurements were made on the blood samples taken within 5 minutes following the administration between these hours. For cortisol measurement, blood samples were collected in yellow-capped serum separation tubes (5-mL BD Vacutainer SST II Advance Plus Blood Collection Tubes [lot 7327531; Becton Dickinson, Plymouth, United Kingdom]) within 5 minutes following an antecubital vein cannulation after an overnight fast. Serum cortisol was measured in the serum obtained by centrifugation in the laboratory using the Architect i2000SR System (Abbott Laboratories, Illinois) device.

Subjective stress response

The Turkish version of the Spielberger State-Trait Anxiety Inventory was used to assess subjective stress.[25] It has 2 separate scales: state and trait anxiety, each of which comprises 20 items and 4-point Likert type. The state section determines how individuals feel at the moment while the trait anxiety scale determines the individual's predisposition to respond anxiously to certain situations. The state anxiety scale consists of 10 items (1, 2, 5, 8, 10, 11, 15, 16, 19, and 20) while the trait anxiety scale consists of 7 items (21, 26, 27, 30, 33, 36, and 39) expressing a negative statement and reverse-scored. In the scoring of the scale, the total weighted score of the reverse-worded items is subtracted from the total weighted score obtained from direct-worded items and a constant value is added to this difference. This value is 50 for the state anxiety scale and 35 for the trait anxiety scale. The total score of the scales ranges between 20 and 80. High scores indicate a high level of anxiety. The Cronbach α coefficient in this study was found to be 0.87 for the trait anxiety scale and 0.90 for the state anxiety scale.

Data collection

Demographic characteristics and HT-related data were obtained through interviews before the random allocation of patients. A short questionnaire was prepared by the researchers with the following questions: (1) age, (2) gender, (3) smoking habit, and (4) antihypertensive medication duration. Data collection times of the aromatherapy and the usual care groups varied as follows:

Blood pressure (SBP/DBP) and HR

Data were collected at baseline (T0), first intervention pre- (T1) and posttest (T2), the second pre- (T3) and posttest (T4), the third pre- (T5) and posttest (T6) for both inhalation and foot massage groups, and at baseline (T0), first follow-up (T1, T2), the second follow-up (T3, T4), and the third follow-up (T5, T6), twice every other day (eg, Monday, Wednesday, Friday) and between 7 AM and 8 AM for the usual care group. All groups were measured 7 times.

Serum cortisol

Data were collected at baseline (T0), within 5 minutes as the posttest of each intervention (T2, T4, T6) for both the inhalation and foot massage groups, and at baseline (T0), the third follow-up (T6) between 7 AM and 8 AM for the usual care group. The aromatherapy groups were measured 4 times while the usual care group was measured twice.

Subjective stress response: trait and state anxiety

Trait anxiety was measured only at baseline (T0) for all 3 groups, and state anxiety at baseline (T0) and the third follow-up (T6).

Statistical methods

Data were analyzed using the Statistical Package for the Social Sciences (IBM SPSS 26.0). Descriptive statistics were used to describe the basic characteristics of the patients. All variables were normally distributed according to the normality test in which skewness and kurtosis were used. One-way analysis of variance and χ^2 tests were used to compare basic group differences. The differences between the groups related to blood pressure (SBP, DBP) and stress responses (HR, serum cortisol, state anxiety) were analyzed by repeated-measures analysis of variance. A Greenhouse-Geisser correction was used if Mauchly's test showed that sphericity could

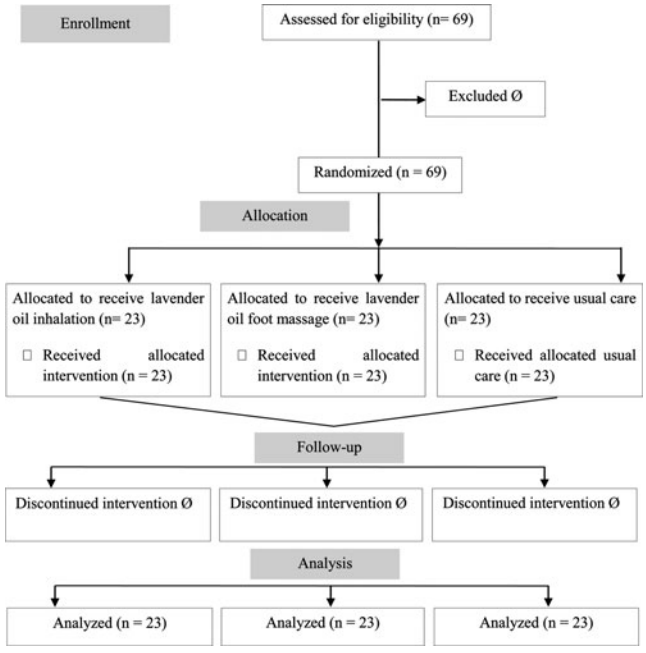

FIGURE 1. Flow diagram.

not be assumed. If the homogeneity of variances between the groups could not be assumed, the Games-Howell test was performed for post hoc analysis. Paired-samples *t* test was used for within-group comparisons and independent-samples *t* test for pre- and posttest comparisons between groups. Outcome analyses were conducted on the basis of the intention-to-treat principle. *P* value of .05 was considered statistically significant.

RESULTS

A flowchart shows the allocation of patients to the trial (Figure 1). Finally, 69 patients were included in the study. The baseline characteristics of the patients are shown in Table 1. Among the patients, the majority were 65 to 79 years of age (n = 45), male (n = 37), not a smoker (n = 59), and suffering from HT for more than 10 years (n = 38). The baseline scores were similar with no significant difference between the groups in terms of demographic and HT-related characteristics. At the beginning of the study, all 3 groups were comparable since there were no statistically significant differences in outcome variables (Table 1).

TABLE 1. Baseline Characteristics of the Patients (N = 69)

	Foot Massage (n = 23)		Inhalation (n = 23)		Control (n = 23)			
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	χ^2	***P***
Age, y								
≤65	6	26.1	6	26.1	7	30.4	4.55	.336[a]
66-79	15	65.2	15	65.2	10	43.5		
≥80	2	8.7	2	8.7	6	26.1		
Age, mean (SD)	68.43 (8.93)		70.82 (8.96)		72.13 (10.76)		0.87	.420[b]
Gender								
Male	13	56.5	10	43.5	14	60.9	1.51	.469[a]
Female	10	43.5	13	56.5	9	39.1		
Smoke								
Yes	3	13.0	4	17.4	3	13.0	0.23	.890[a]
No	20	87.0	19	82.6	20	87.0		
Antihypertensive medication, y								
<10	14	60.9	8	34.8	9	39.1	3.63	.163[a]
≥10	9	39.1	15	65.2	14	60.9		
Outcome variables	**Mean (SD)**		**Mean (SD)**		**Mean (SD)**		***F***	***P***
Systolic BP (mm Hg)	139.00 (10.97)		138.08 (14.55)		134.04 (22.99)		0.54	.581[b]
Diastolic BP (mm Hg)	74.56 (6.86)		71.43 (14.12)		67.39 (11.81)		2.31	.107[b]
Heart rate (min)	82.78 (7.54)		80.08 (8.65)		79.86 (7.79)		0.94	.395[b]
Serum cortisol (μg/dL)	12.59 (5.87)		13.07 (3.96)		12.80 (5.95)		0.05	.955[b]
Trait anxiety	46.86 (6.64)		45.17 (7.56)		45.04 (8.02)		0.43	.651[b]
State anxiety	42.30 (14.68)		40.04 (11.13)		41.00 (7.53)		0.22	.800[b]

Abbreviation: BP, blood pressure.
[a]Chi-square test.
[b]One-way analysis of variance.

Tables 2 to 5 show comparisons of changes over time in outcome variables, both between and within groups. The group and time interaction was significant for all outcome variables measured at the time points from T0 to T6 (G*T; $P < .05$). In post hoc analyzes, the only significant difference on SBP was between the inhalation and usual care groups at the T6 point (15.08; 95% confidence interval [CI], 4.64-25.52). On DBP, inhalation compared with usual care was significant at times T2, T3, and T6; foot massage was at T3 and T6. The highest mean differences of both groups occurred at the T6 (inhalation, 15.52; 95% CI, 9.37-21.66; foot massage, 12.52; 95% CI, 6.37-18.66). Results of the within-group comparisons showed significant differences in both SBP and DBP from T0 to T6 ($P < .05$). For SBP and DBP, respectively, foot massage decreased by 7.65 mm Hg and 11.82 mm Hg, inhalation by 11.73 mm Hg and 13.47 mm Hg, while usual care resulted in an increase of 4.39 mm Hg and 4.60 mm Hg (Tables 2 and 3; Figure 2a and b).

Heart rate was significant for inhalation compared with usual care only at T6 (5.17; 95% CI, 0.07-10.27; $P = .046$); the mean differences of the 2 groups were similarly significant in the within-group comparisons, resulting in a decrease of 5.08/min with inhalation and an increase of 3.17/min with usual care (Table 4 and Figure 2c). Table 5 shows the serum cortisol and state anxiety levels measured at 2 time points (T0-T6). Serum cortisol level revealed significant mean differences in the inhalation group compared with usual care in the posttest (T6) (4.25; 95% CI, 1.02-7.48; $P = .008$), whereas state anxiety demonstrated significant mean differences in the foot massage group compared with usual care (7.52; 95% CI, 2.19-12.84; $P = .003$). Serum cortisol level decreased from T0 to T6 with inhalation and foot massage, respectively, by 3.27 μg/dL ($P < .001$), 2.65 μg/dL ($P < .001$) in within-group comparisons, and increased by 1.25 μg/dL in the usual care group ($P < .001$) (Table 5 and Figure 3a). State anxiety levels were statistically significant with an average tendency to decrease 11.22 with foot massage ($P < .001$) and 4.60 with inhalation ($P = .005$), while the decrease of 0.18 in the usual care group was not significant ($P = .909$) (Table 5 and Figure 3b).

DISCUSSION

Essential hypertension, which is prevalent all over the world, is an important risk factor for cardio- and cerebrovascular diseases. For this reason, it is crucial to keep EHT under control. Essential hypertension is primarily treated with medication, diet, and exercise. In addition, lifestyle changes (smoking cessation, weight reduction, salt restriction, stress management, etc) are recommended.[3] One recent global guideline mentions complementary and alternative therapies, highlighting the need for supporting evidence for HT control.[4] Aromatherapy is one of these complementary therapies with its increasing use in HT management. In the present study, the effect of aromatherapy through inhalation and foot massage on blood pressure and stress response in patients with EHT was investigated.

Research variables included stress responses along with blood pressure. Stress response parameters were HR, serum cortisol, and state anxiety. Furthermore, trait anxiety was initially measured once to evaluate the individual's predisposition to respond anxiously to certain situations. The main premise was the contribution of long-term and persistent stress to hemodynamic and metabolic processes that can affect prognosis in hypertensives.[6] Hence, the findings indicate that trait anxiety levels of individuals in all 3 groups may be considered to be slightly above the average level. This can be interpreted as the tendency of the patients in the present study to perceive their conditions as slightly more stressful than others. Naturally, the predisposition to stress may lead to the activation of the hypothalamic-pituitary-adrenal axis, causing elevated blood pressure, increased HR, or variable serum cortisol levels in study groups.[7] It is also predictable that subjective anxiety may be experienced more frequently and intensely than others.[25]

In this study, both within-group and between-group differences were determined in terms of outcome variables of aromatherapy applied 3 times with lavender. Apparently, based on research questions, the significant effects of inhalation on objective measures (blood pressure, HR, and serum cortisol) and foot massage on subjective measurements (state anxiety) were revealed. Diastolic BP was the common variable in which both applications were effective compared with the usual care. Furthermore, significant changes in outcome variables were found to be largely due to lavender inhalation rather than foot massage. Another important finding of the study was related to the effect size of aromatherapy on outcome variables. In fact, it was determined that both time and group $\times$ time interaction revealed statistical significance

TABLE 2. The Effects of Lavender Oil Aromatherapy on Systolic Blood Pressure at the 7 Time Points (N = 69)

	Foot Massage (n = 23) Mean (SD)	Inhalation (n = 23) Mean (SD)	Usual Care (n = 23) Mean (SD)	Usual Care Versus Foot Massage		Usual Care Versus Inhalation		Foot Massage Versus Inhalation	
				Mean Difference (95% CI)	*P*	Mean Difference (95% CI)	*P*	Mean Difference (95% CI)	*P*
T0	139.00 (10.97)	138.08 (14.55)	134.04 (22.99)	4.95 (−8.10 to 18.01)	.624	− 1.04 (−14.89 to 12.80)	.982	3.91 (−5.33 to 13.15)	.563
T1	137.43 (11.46)	130.65 (15.33)	130.56 (21.22)	− 6.86 (−19.20 to 5.46)	.370	− 0.08 (−13.37 to 13.20)	.999	6.78 (−2.92 to 16.49)	.218
T2	134.73 (11.40)	126.65 (15.63)	132.13 (19.69)	− 2.60 (−14.21 to 8.99)	.847	5.47 (−7.26 to 18.21)	.553	8.08 (−1.73 to 17.90)	.124
T3	136.13 (11.81)	129.30 (13.72)	132.43 (23.31)	− 3.69 (−17.07 to 9.68)	.778	3.13 (−10.66 to 16.92)	.845	6.82 (−2.33 to 15.99)	.179
T4	132.78 (12.87)	125.60 (13.88)	131.86 (22.30)	− 0.91 (−14.05 to 12.22)	.984	6.26 (−7.11 to 19.63)	.494	7.17 (−2.40 to 16.75)	.176
T5	135.08 (11.65)	127.65 (14.54)	136.56 (16.46)	1.47 (−8.67 to 11.63)	.935	8.91 (−1.24 to 19.06)	.097	7.43 (−2.71 to 17.58)	.193
T6	131.34 (10.79)	123.34 (15.12)[a]	138.43 (17.56)[b]	7.08 (−3.35 to 17.52)	.241	15.08 (4.64 to 25.52)	**.003**[a,b]	8.00 (−2.43 to 18.43)	.165
F/*P* (within-group)	13.90 **(<.001)**	10.98 **(<.001)**	3.54 **(.009)**						
Differences in the means[c]	7.65	11.73	− 4.39						
Group (3)[d] Time (7)	Group: 1.30 (0.280); time: 8.36 **(<0.001)**; G*T: 6.65 **(<0.001)**								

Abbreviation: CI, confidence interval.
[a]Inhalation: significant difference (Tukey test, or Games-Howell test; $P < .05$).
[b]Usual care: significant difference (Tukey test, or Games-Howell test; $P < .05$).
[c]Differences in the means within-group (initial and final comparisons) (paired-samples *t* test).
[d]Repeated-measures of analysis of variance.

TABLE 3. The Effects of Lavender Oil Aromatherapy on Diastolic Blood Pressure at the 7 Time Points (N = 69)

	Foot Massage (n = 23) Mean (SD)	Inhalation (n = 23) Mean (SD)	Usual Care (n = 23) Mean (SD)	Usual Care Versus Foot Massage		Usual Care Versus Inhalation		Foot Massage Versus Inhalation	
				Mean Difference (95% CI)	*P*	Mean Difference (95% CI)	*P*	Mean Difference (95% CI)	*P*
T0	88.30 (10.50)	86.95 (9.24)	84.39 (15.70)	−3.91 (−13.51 to 5.69)	.586	−2.56 (−11.85 to 6.72)	.779	1.34 (−5.73 to 8.43)	.889
T1	83.00 (7.63)	82.65 (8.57)	83.04 (14.27)	−0.04 (−8.23 to 8.32)	.999	0.39 (−8.09 to 8.87)	.993	0.34 (−5.46 to 6.15)	.998
T2	79.56 (6.75)	76.30 (8.17)[a]	84.82 (13.11)[b]	5.26 (−2.28 to 12.81)	.217	8.52 (0.65 to 16.39)	**.031**[a,b]	3.26 (−2.10 to 8.63)	.313
T3	77.08 (6.74)[c]	74.26 (7.26)[a]	86.34 (11.64)[b]	9.26 (2.39 to 16.12)	**.006**[b,c]	12.08 (5.09 to 19.07)	**<.001**[a,b]	2.82 (−2.18 to 7.84)	.367
T4	78.60 (7.57)	75.69 (11.04)	79.56 (12.71)	0.95 (−6.58 to 8.50)	.949	3.86 (−4.65 to 12.39)	.518	2.91 (−3.89 to 9.71)	.555
T5	81.21 (6.73)	75.39 (10.25)[a]	83.43 (12.14)[b]	2.21 (−4.87 to 9.31)	.726	8.04 (−0.01 to 16.09)	.050	5.82 (−0.41 to 12.06)	.071
T6	76.47 (7.18)[c]	73.47 (8.19)[a]	89.00 (10.39)[b]	12.52 (6.37 to 18.66)	**<.001**[b,c]	15.52 (9.37 to 21.66)	**<.001**[a,b]	3.00 (−3.14 to 9.14)	.475
F/*P* (within-group)	21.13 **(<.001)**	16.91 **(<.001)**	4.42 **(.008)**						
Differences in the means[d]	11.82	13.47	−4.60						
Group (3)[e] Time (7)	Group: 3.30 **(0.043)**; Time: 17.88 **(<0.001)**; G*T: 9.02 **(<0.001)**								

Abbreviation: CI, confidence interval.
[a]Inhalation: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[b]Control: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[c]Foot massage: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[d]Differences in the means within-group (initial and final comparisons) (paired-samples *t* test).
[e]Repeated-measures analysis of variance.

TABLE 4. The Effects of Lavender Oil Aromatherapy on Heart Rate at the 7 Time Points (N = 69)

	Foot Massage (n = 23) Mean (SD)	Inhalation (n = 23) Mean (SD)	Usual Care (n = 23) Mean (SD)	Usual Care Versus Foot Massage		Usual Care Versus Inhalation		Foot Massage Versus Inhalation	
				Mean Difference (95% CI)	*P*	Mean Difference (95% CI)	*P*	Mean Difference (95% CI)	*P*
T0	82.78 (7.54)	82.95 (7.20)	79.86 (7.79)	−2.91 (−8.23 to 2.40)	.393	−3.08 (−8.40 to 2.23)	.351	−0.17 (−5.49 to 5.14)	.997
T1	83.86 (6.73)	82.17 (7.86)	79.82 (8.12)	−4.04 (−9.41 to 1.32)	.176	−2.34 (−7.72 to 3.02)	.550	1.69 (−3.67 to 7.06)	.731
T2	81.82 (6.24)	79.82 (7.58)	79.17 (7.58)	−2.65 (−7.72 to 2.41)	.426	−0.65 (−5.72 to 4.41)	.949	2.00 (−3.06 to 7.06)	.613
T3	83.21 (6.48)	79.69 (5.97)	79.69 (8.27)	−3.52 (−8.45 to 1.41)	.209	0.01 (−4.93 to 4.93)	.999	3.52 (−1.41 to 8.45)	.209
T4	82.21 (7.29)	79.21 (6.42)	80.52 (7.79)	−1.69 (−6.78 to 3.39)	.705	1.30 (−3.78 to 6.39)	.813	3.00 (−2.08 to 8.08)	.340
T5	84.69 (7.83)	80.56 (6.40)	81.34 (7.29)	−3.34 (−8.43 to 1.74)	.263	0.78 (−4.30 to 5.87)	.928	4.13 (−0.96 to 9.22)	.134
T6	82.34 (7.70)	77.86 (6.07)[a]	83.04 (7.72)[b]	0.69 (−4.40 to 5.79)	.943	5.17 (0.07 to 10.27)	**.046**[a,b]	4.47 (−0.61 to 9.57)	.096
F/*P* (within-group)	2.35 (.094)	9.49 **(<.001)**	4.62 **(.001)**						
Differences in the means[c]	0.43	5.08	−3.17						
Group (3)[d] Time (7)	Group: 1.22 **(0.330)**; Time: 4.32 **(0.002)**; G*T: 5.53 **(<0.001)**								

Abbreviation: CI, confidence interval.
[a]Inhalation: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[b]Control: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[c]Differences in the means within-group (initial and final comparisons) (paired-samples *t* test).
[d]Repeated-measures analysis of variance.

TABLE 5. The Effects of Lavender Oil Aromatherapy on Serum Cortisol and State Anxiety at the Different Time Points (N = 69)

	Serum Cortisol (μg/dL)									State Anxiety								
	Foot Massage (n = 23) Mean (SD)	Inhalation (n = 23) Mean (SD)	Usual Care (n = 23) Mean (SD)	Usual Care Versus Foot Massage Mean Difference (95% CI)	*P*	Usual Care Versus Inhalation Mean Difference (95% CI)	*P*	Foot Massage Versus Inhalation Mean Difference (95% CI)	*P*	Foot Massage (n = 23) Mean (SD)	Inhalation (n = 23) Mean (SD)	Usual Care (n = 23) Mean (SD)	Usual Care Versus Foot Massage Mean Difference (95% CI)	*P*	Usual Care Versus Inhalation Mean Difference (95% CI)	*P*	Foot Massage Versus Inhalation Mean Difference (95% CI)	*P*
T0	12.92 (5.85)	13.07 (3.96)	12.80 (5.95)	−0.12 (−3.90 to 3.64)	.996	−0.27 (−0.04 to 3.49)	.983	−0.14 (−3.91 to 3.62)	.995	42.30 (14.68)	40.04 (11.13)	41.00 (7.53)	−5.17 (−11.88 to 1.53)	.162	−0.78 (−7.49 to 5.92)	.958	4.39 (−2.31 to 11.09)	.266
T1	n/a	n/a	n/a							n/a	n/a	n/a						
T2	13.49 (7.57)	12.81 (3.88)	n/a					0.68 (−2.89 to 4.25)	.702	n/a	n/a	n/a						
T3	n/a	n/a	n/a							n/a	n/a	n/a						
T4	12.47 (6.65)	12.60 (3.95)	n/a					−0.13 (−3.38 to 3.12)	.936	n/a	n/a	n/a						
T5	n/a	n/a	n/a							n/a	n/a	n/a						
T6	10.27 (5.27)[a]	9.79 (3.09)[b]	14.05 (5.51)[c]	3.77 (−0.08 to 7.64)	.056	4.25 (1.02 to 7.48)	**.008**[b,c]	0.47 (−2.88 to 3.83)	.939	31.08 (8.61)[a]	35.43 (8.15)	40.82 (9.40)[c]	7.52 (2.19 to 12.84)	**.003**[a,c]	3.82 (−1.49 to 9.14)	.204	−3.69 (−9.01 to 1.62)	.226
F or *t*/*P* (within-group)	25.45 (<**.001**)	45.30 (<**.001**)	3.89 (**.001**)							6.19 (<**.001**)[f]	2.15 (**.043**)[f]	1.40 (0.174)[f]						
Differences in the means[d]	2.65	3.27	−1.25							10.52	2.43	−2.17						
Group (3)[e] Time (2)	Group: 1.11 (0.334); Time: 95.43 (<**0.001**); G*T: 78.71 (<**0.001**)									Group: 1.22 (0.301); Time: 36.01 (< **0.001**); G*T: 13.03 (< **0.001**)								

Abbreviations: CI, confidence interval; n/a, not applicable.
[a]Foot massage: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[b]Inhalation: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[c]Control: Significant difference (Tukey test, or Games-Howell test; $P < .05$).
[d]Differences in the means within-group (initial and final comparisons) (paired-samples *t* test).
[e]Repeated-measures analysis of variance.
[f]Independent-samples *t* test.

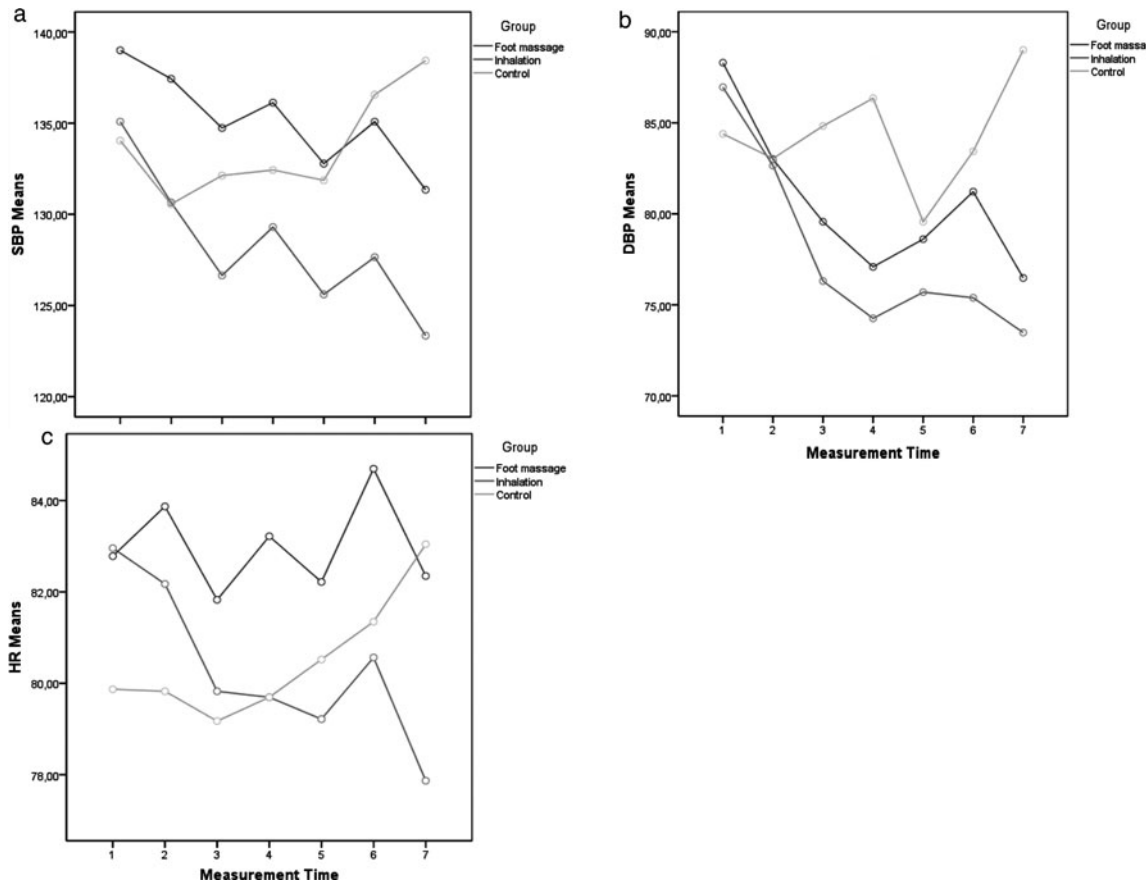

FIGURE 2. Trends in blood pressure and heart rate changes between groups at the 7 time points: (a) systolic BP (mm Hg), (b) diastolic BP (mm Hg), and (c) heart rate (min). BP indicates blood pressure; HR, heart rate; DBP, diastolic BP; SBP, systolic BP.

in the primary analyses. Compared with usual care, the aromatherapy groups showed significant differences in the T6 point, reflecting only the third posttreatment in all but DBP. In terms of DBP, similar changes between groups were observed after the first application.

It is known that higher levels of both SBP and DBP (SBP >120 mm Hg, DBP >80 mm Hg) are associated

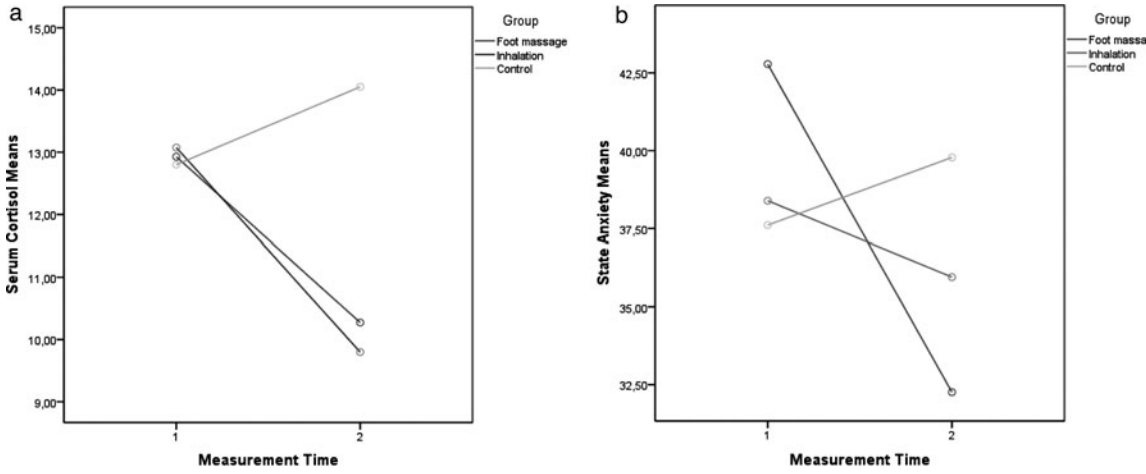

FIGURE 3. Trends in serum cortisol and state anxiety changes between groups at the 2 time points (initial and final): (a) serum cortisol (μg/dL) and (b) state anxiety.

with an increased risk of cardiovascular disease. The recommended target BP is less than 120 mm Hg and less than 80 mm Hg for SBP and DBP, respectively.[9] It is seen that the initial SBPs of the patients are in the elevated BP category (120-139 mm Hg) according to cardiac guidelines while their DBPs are in the normal BP (<80 mm Hg) category. Although the inhalation group was associated with a significant decrease for both SBP and DBP compared with the usual care group at the T6 time point, the highest mean difference between the groups was also at this time point. Similarly, the highest significant difference of foot massage for DBP was seen in T6 compared with usual care. On the other hand, although it was seen that both aromatherapy methods decreased SBP and DBP in within-group measurements, it was found that the higher mean difference was achieved by inhalation. To illustrate, the mean SBP levels in the inhalation group approached the acceptable levels recommended in cardiac guidelines.[9] In contrast, the usual care group experienced an increase in BP levels. Although some previous study findings seem to be consistent with the results of this study,[10,16,19] it is observed that researchers would rather use a mixture of oils than the unique effect of lavender. A study conducted with lavender inhalation, which was very similar in design to the current study, was associated with a reduction in SBP and DBP over 14 days.[10] As reported by Prusinowska and Smigielski,[26] the blood pressure lowering effect of lavender oil inhalation was emphasized since it is a smooth muscle relaxant that inhibits the contraction response of acetylcholine and histamine. Furthermore, it has been proposed that massage improves systemic and lymphatic blood flow by stimulating the vasomotor nerves, which causes increased vasodilation; thus, promoting blood pressure regulation.[27] On the other hand, it could be argued that blood pressure changes occur more prominently through inhalation than massage stimulation since inhalation causes the rapid arrival of olfactory stimulation to the limbic system and sensory responses within seconds.[11]

As a result of the study, HR and serum cortisol were significantly different in the inhalation group compared with usual care after 3 administrations (T6), while state anxiety was different in the usual care compared with foot massage group at the same time point. Similarly, in the within-group comparisons for HR and serum cortisol, the highest mean difference was a result of lavender inhalation. As expected, this difference was greatest thanks to foot massage regarding state anxiety. These results are consistent with the same parameters of the 3-arm study conducted by Hwang[16] with hypertensive patients using blended oil inhalation. The studies that reported a significant correlation with the result of a decrease in HR include that of Sayorwan et al[28] in which 4 sessions were conducted with healthy volunteers and that of Ziyaeifard et al[29] in which single-session lavender inhalation tests were conducted before coronary angiography for immediate effect. The current research findings are supported by these studies showing that lavender oil can promote HR regulation by causing a decrease in adrenocorticotropic hormone, epinephrine, and adrenaline levels through the activity of parasympathetic nervous system, which decreases the activity of the sympathetic nervous system. On the other hand, it has been reported that the reduction in HR may occur thanks to the sedative effect based on the pleasant and unpleasant odor of essential oils.[28] In this study, the fragrance preferences of the patients for the essential oil were not taken into account just as their positive or negative opinions associated with lavender. Although the comparison of the 2 interventions reveals the superiority of HR inhalation over foot massage, the placebo effect on relief should not be ignored. For this reason, a multiarm trial design that could be implemented in advanced research can contribute to the solution of this problem.

One of the studies that focused on cortisol in hypertensives reported that blending oil inhalation in experimental groups resulted in a 0.8 μg/dL decrease in serum cortisol and a 0.02 μg/dL decrease in saliva cortisol, which demonstrated a significant difference.[16,17] These results indicate that lavender aromatherapy may have an anxiolytic effect through the inhibition of sympathetic nerves that innervate the adrenal glands, thus regulating cortisol release, which is an endocrinological stress marker. Although inhalation and foot massage both contribute to a significant reduction in serum cortisol, the superiority of inhalation in this study is supported by the results of a previous analysis.[20] On the other hand, state anxiety scores decreased significantly in both intervention groups and foot massage with lavender was found to be superior to inhalation with a decrease of 6.9 within the group. In fact, it was an unexpected result for researchers. The reason for this is that the difference of inhalation was observed in all other stress parameters together with blood pressure. Therefore, a similar effect would be expected on subjective anxiety scores. Nevertheless, a previous

meta-analysis confirmed the superiority of inhalation over other modes of administration in terms of the measurements of subjective anxiety.[20] At this point, 2 dilemmas have arisen for researchers. Unlike other parameters, state anxiety was not measured in the intervention groups during the period following each aromatherapy session. The reason for this was the increased likelihood of biased answers due to the retention of questions in a test conducted at short time intervals. In this way, it remains unclear exactly when the earliest subjective response to inhalation or foot massage was actually given. The second is that along with the physiological effects of lavender, foot massage functions as a touch therapy with an additional treatment, thereby mentally relaxing the patients. Nevertheless, linalool and linalyl acetate contained in lavender extract apparently have a soothing and relaxing effect by increasing the function of GABA-A receptors.[11]

Limitations of the research

During the planning and conduct of this research, researchers experienced a few limitations. First, the study sample consisted of hypertensive individuals hospitalized in various clinics (cardiology, neurology, internal medicine) of 2 different centers. Because of the limited number of EHT patients reached during the required intervention or follow-up period in one unique clinic, the included patients were a mix of groups treated for different reasons or procedures. In such an environment, it should not be ignored that the adaptive responses of patients and stressors may vary. Second, the diversity of antihypertensive drugs prescribed to patients, especially those that may cause blood pressure and HR variability, was not taken into account in order to avoid sample size limitations while planning the study. Third, the research was carried out with short-term intervention procedures in a hospital environment with various diagnosis, treatment, and care processes as well as physical and psychological effects caused by environmental change. Thus, only instantaneous changes in result parameters were observed. In fact, it may be more beneficial to obtain long-term results of lavender aromatherapy as a supportive method in a patient group expected to adhere to lifestyle changes and medication. Therefore, further research can evaluate the efficacy of lavender both outside the hospital and through longer-term interventions.

CONCLUSION

Lavender oil reduced blood pressure, HR, serum cortisol, and state anxiety in hypertensive patients. Lavender inhalation was uniquely superior to foot massage in objective measurements (blood pressure, HR, serum cortisol). In contrast, foot massage was more dominant in subjective measurements (state anxiety). In conclusion, it could be argued that lavender aromatherapy is a method that can contribute to disease management for hypertensive patients, complementary to pharmacological treatment. Aromatherapy should be supported by appropriate health policies, and health professionals should be trained to teach, encourage, and support hypertensive patients with the self-administration of aromatherapy.

REFERENCES

1. Liu MY, Li N, Li WA, Khan H. Association between psychosocial stress and hypertension: a systematic review and meta-analysis. *Neurol Res.* 2017;39(6):573-580. doi:10.1080/01616412.2017.1317904.
2. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. *Lancet*. 2017;389(10064):37-55. doi:10.1016/S0140-6736(16)31919-5.
3. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39(33):3021-3104. doi:10.1093/eurheartj/ehy339.
4. Unger T, Borghi C, Charchar F, et al. 2020 International society of hypertension global hypertension practice guidelines. *Hypertension*. 2020;75(6):1334-1357. doi:10.1161/HYPERTENSIONAHA.120.15026.
5. World Health Organization. *Global status report on noncommunicable diseases 2014*. https://www.who.int/nmh/publications/ncd-status-report-2014/en/. Published 2014. Accessed December 22, 2020.
6. Sparrenberger F, Cichelero FT, Ascoli AM, et al. Does psychosocial stress cause hypertension? A systematic review of observational studies. *J Hum Hypertens*. 2009;23(1):12-19. doi:10.1038/jhh.2008.74.
7. Porth CM. *Essentials of Pathophysiology: Concepts of Altered Health States*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
8. Brotman DJ, Golden SH, Wittstein IS. The cardiovascular toll of stress. *Lancet*. 2007;370(9592):1089-1100. doi:10.1016/S0140-6736(07)61305-1.
9. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Hypertension*. 2018;71(6):e13-e115. doi:10.1161/HYP.0000000000000065.
10. Gultom AB, Ginting S, Silalahi EL. The influence of lavender aroma therapy on decreasing blood pressure in hypertension patients. *Int J Public Health Sci.* 2016;5(4):470-478. doi:10.11591/ijphs.v5i4.4853.
11. Cavanagh HM, Wilkinson JM. Biological activities of lavender essential oil. *Phytother Res.* 2002;16(4):301-308. doi:10.1002/ptr.1103.
12. Chioca LR, Ferro MM, Baretta IP, et al. Anxiolytic-like effect of lavender essential oil inhalation in mice: participation of serotonergic but not

GABAA/benzodiazepine neurotransmission. *J Ethnopharmacol*. 2013; 147(2):412-418. doi:10.1016/j.jep.2013.03.028.
13. Tanida M, Niijima A, Shen J, Nakamura T, Nagai K. Olfactory stimulation with scent of lavender oil affects autonomic neurotransmission and blood pressure in rats. *Neurosci Lett*. 2006;398(1-2):155-160. doi:10.1016/j.neulet.2005.12.076.
14. Hur MH, Lee MS, Kim C, Ernst E. Aromatherapy for treatment of hypertension: a systematic review. *J Eval Clin Pract*. 2012;18(1):37-41. doi:10.1111/j.1365-2753.2010.01521.x.
15. Cha JH, Lee SH, Yoo YS. Effects of aromatherapy on changes in the autonomic nervous system, aortic pulse wave velocity and aortic augmentation index in patients with essential hypertension. *J Korean Acad Nurs*. 2010;40(5):705-713. doi:10.4040/jkan.2010.40.5.705.
16. Hwang JH. The effects of the inhalation method using essential oils on blood pressure and stress responses of clients with essential hypertension. *Taehan Kanho Hakhoe Chi.* 2006;36(7):1123-1134. doi:10.4040/jkan.2006.36.7.1123.
17. Kim IH, Kim C, Seong K, Hur MH, Lim HM, Lee MS. Essential oil inhalation on blood pressure and salivary cortisol levels in prehypertensive and hypertensive subjects. *Evid Based Complement Alternat Med*. 2012;2012:984203. doi:10.1155/2012/984203.
18. Suidah H, Murtiyani NM, Fibriana LP, Lestari YA, Kushayati N. The effectiveness of lavender aromatherapy in changing blood pressure in middle age with primary hypertension in Mojokerto Regency of East Java Province. *Adv Soc Sci Res J.* 2018;5(3):19-26. doi:10.14738/assrj.53.4114.
19. Ju MS, Lee S, Bae I, Hur MH, Seong K, Lee MS. Effects of aroma massage on home blood pressure, ambulatory blood pressure, and sleep quality in middle-aged women with hypertension. *Evid Based Complement Alternat Med*. 2013;2013:403251. doi:10.1155/2013/403251.
20. Kang HJ, Nam ES, Lee Y, Kim M. How strong is the evidence for the anxiolytic efficacy of lavender? systematic review and meta-analysis of randomized controlled trials. *Asian Nurs Res (Korean Soc Nurs Sci)*. 2019;13(5):295-305. doi:10.1016/j.anr.2019.11.003.
21. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c869. doi:10.1136/bmj.c869.
22. Fritz S. *Mosby's Fundamentals of Therapeutic Massage.* St Louis, MO: Mosby Elsevier; 2012.
23. Braun MB, Simonson SJ. *Introduction to Massage Therapy.* 2nd ed. Philadelphia, PA: Lippincott Williams &Wilkins; 2008.
24. Katsu Y, Iguchi T. Cortisol. In: Takei Y, Ando H, Tsutsui K, eds. *Handbook of Hormones: Comparative Endocrinology for Basic and Clinical Research.* San Diego, CA: Elsevier Science & Technology; 2015:533-534.
25. Öner N, Le Compte A. *Handbook of State-Trait Anxiety Inventory*. Istanbul, Turkey: Boğaziçi University Publications; 1983.
26. Prusinowska R, Śmigielski KB. Composition, biological properties and therapeutic effects of lavender (Lavandula angustifolia L). A review. *Herba Polonica*. 2014;60(2):56-66. doi:10.2478/hepo-2014-0010.
27. Beck MF. *Theory and Practice of Therapeutic Massage*. Clifton Park, NY: Milady; 2010.
28. Sayorwan W, Siripornpanich V, Piriyapunyaporn T, Hongratanaworakit T, Kotchabhakdi N, Ruangrungsi N. The effects of lavender oil inhalation on emotional states, autonomic nervous system, and brain electrical activity. *J Med Assoc Thai*. 2012;95(4): 598-606.
29. Ziyaeifard M, Zahedmehr A, Ferasatkish R, et al. Effects of lavender oil inhalation on anxiety and pain in patients undergoing coronary angiography. *Iranian Heart J*. 2017;18(1):44-50.