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Effect of Aromatherapeutic Lavender Oil on Sleep and Anxiety in Neurological Rehabilitation Patients: Retrospective Study

Aromaterapik Lavanta Yağının Nörolojik Rehabilitasyon Hastalarında Uyku ve Kaygı Üzerine Etkisi: Retrospektif Çalışma

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ABSTRACT Objective: This investigation's objective was to ascertain the effects of Lavandula angustifolia aromatherapy oil on patients undergoing neurological rehabilitation in terms of sleep quality and anxiety levels. It was also aimed to analyze the composition of L. angustifolia oil used in aromatherapy. Material and Methods: Forty-two adults with a diagnosis of spinal cord injury or stroke receiving neurological rehabilitation as inpatients were included in the study and used aromatherapy L. angustifolia oil through inhalation from the inner side of the wrist for 30 days to relieve their anxiety disorders and sleep problems. The Pittsburgh Sleep Quality Index (PSQI) was used to measure the patients' sleep quality, and the Beck Anxiety Inventory (BAI) was used to measure their anxiety levels before and 30 days after the application. Additionally, methods using gas chromatography-mass spectrometry and solid-phase microextraction were utilized to investigate the chromatographic analysis of the used L. angustifolia oil. Results: Comparisons were made between calculated and reported percentages of the remaining constituents, which included eucalyptol, terpinolene, lavandulol and ci, and, as well as the two primary volatile compounds found in L. angustifolia, linally acetate (27.69%) and linalool (29.33%). Conclusion: According to our research, the patients' PSQI and BAI ratings showed a statistically significant improvement after 30 days of L. angustifolia oil aromatherapy application. Therefore, it is considered that L. angustifolia oil aromatherapy can be recommended in patients with sleep and anxiety problems during the neurological rehabilitation process, but there is a need for further comprehensive randomized controlled trials on this subject.

Keywords: Lavandula angustifolia; neurological rehabilitation; sleep; anxiety

ÖZET Amaç: Bu çalışmanın amacı, nörolojik rehabilitasyon sürecindeki hastalarda uyku kalitesi ve anksiyete düzeyi üzerine tamamlayıcı tıpta kullanılan Lavandula angustifolia aromaterapik yağının etkisini ve bileşimindeki maddeleri değerlendirmektir. Gereç ve Yöntemler: Spinal kord varalanması ve inme tanıları ile nörolojik rehabilitasyon süreçleri hastanede yatarak devam eden, anksiyete bozukluğu ve uyku sorunları yaşayan, 18 yaş ve üzeri 42 hastada, aromaterapik L. angustifolia yağı 30 gün boyunca bilek iç yüzüne uygulanıp, inhalasyon yoluyla kullanmış olan hastalar çalışmaya dâhil edildi. Uyku kalitesini ölçmek amacı ile Pittsburgh Uyku Kalitesi İndeksi (PUKİ) ve anksiyete düzeyini belirlemek için Beck Anksiyete Ölçeği (BAÖ) uygulama öncesinde ve 30 gün sonrasında hastalarda değerlendirilmiştir. Ayrıca kullanılan L. angustifolia yağının kromatografik analizi birleşik üst boşluk katı fazlı mikroekstraksiyon ve gaz kromatografisi-kütle spektrometresi yöntemleri ile analiz edilmiştir. Bulgular: L. angustifolia tespit edilen başlıca uçucu bileşikler, linalol (%29,33) ve linalil asetat (%27,69), diğer ana bileşikler terpinolen, cis-ocimene, ökaliptol ve lavandulol literatürle uyumlu olarak sıklık sırasına göre verilmiştir. Sonuc: Çalışmamız sonucunda 30 günlük L. angustifolia yağı aromaterapisinden sonra, PUKİ ve BAÖ'de istatistiksel olarak anlamlı düzeyde iyileşme tespit edilmiştir. L. angustifolia yağı aromaterapisinin nörolojik rehabilitasyon sürecinde uyku ve anksiyete sorunları olan hastalarda önerilebileceği düşünülmüş olup, bu konuda yapılmış randomize kontrollü daha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Lavanta angustifolia; nörolojik rehabilitasyon; uyku; kaygı bozukluğu

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The clinical indicators of a stroke, one of the most prevalent cerebrovascular illnesses in the general population, involve signs of a localized (or global) impairment of brain function that appear quickly and remain for more than 24 hours or cause death. According to the definition of the World Health Organization, it can be of hemorrhagic, thrombotic, or embolic origin without other obvious explanation than vascular origin.¹ Although strides have been made in stroke treatment, monitoring, and recovery, it is remaining the leading cause of impairment in the aged population.²

Spinal cord injury (SCI) is another neurological problem that often occurs due to traumatic causes, can cause serious changes in human life, and has high morbidity and mortality. The incidence of spinal cord injuries in the world is estimated to be around 15-40/1,000,000.³ The aim of neurological rehabilitation programs after stroke and SCI is to increase patients' quality of life, maximize their level of physical independence, and provide psychological support to help them regaintheir place in society. Insomnia and anxiety complaints, which are common in patients undergoing neurological rehabilitation, can adversely affect the physical therapy and rehabilitation process. During the course of neurological rehabilitation, sleeping pills, antidepressants, and anxiolytics are typically administered to lessen these problems. However, these drugs also have side effects in some patients. Therefore, recently, there has been an increasing trend toward complementary therapies. As one of these complementary methods, lavender oil, an aromatherapeutic agent, has been the subject of many studies due to its analgesic and antiinflammatory properties, as well as anxiolytic and sleep-regulating effects.⁴ Lavandula angustifolia oil has been approved as herbal medicine by the Agency European Medicines for the treatment of stress and anxiety. It has also been reported that L. angustifolia oil creates physical and psychological calmness and relieves individual anger and fatigue.⁵ 1,8-cineole (eucalyptol), linalool, perillyl alcohol, and at least 100 other recognized chemicals are found in L. angustifolia oil. The U.S. Food and Drug Administration has declared it to be "generally safe" for eating. L. angustifolia is also called medicinal

lavender. It is a plant with woody tones, a light and clear scent, semi-bushy,blue-colored flowers, found naturally in the mountainous regions of the Northern Mediterranean.⁶ This investigation looked at how patients responded to *L. angustifolia* aromatherapy oil undergoing neurological rehabilitation in terms of anxiety levels and sleep quality.

MATERIAL AND METHODS

The patient records from the Polyclinic for Physical Therapy and Rehabilitation of Adana City Training and Research Hospital with a diagnosis of stroke and SCI between June 1, 2020, and April 1,2021, were screened. The following inclusion criteria were used:

-Age over 18 years,

-Being admitted to an inpatient neurological rehabilitation program,

-Having sleep and anxiety problems,

-The physician's recommendation, using *L. an*gustifolia aromatherapy oil by applying it on theinner side of the wrist and sniffing it for 10 minutes at 8 p.m. every evening under the supervision of anurse, in addition to receiving routine clinical care, and use the Beck Anxiety Inventory (BAI) to measure anxiety levels before and after 30 days of inpatient care, as well as the Pittsburgh Sleep Quality Index (PSQI) to measure sleep quality. The patients' age, height, weight, and gender characteristics are given in Table 1. Pregnant and lactating women and patients using drugs foranxiety and sleep disorders were excluded from the study.

The frequency of the patients' anxiety symptoms was assessed using the Turkish version of BAI before and 30 days after the application.⁷ The BAI is a 21-item Likert-style rating scale with scores ranging from 0 to 3. A high overall score reflects the person's high level of anxiousness. Low anxiety is indicated by a score of 0-21, moderate anxiety by 22-35, and high anxiety by 36 and higher.⁸

The patients' sleep quality was evaluated using PSQI, which was developed by Buysse et al.⁹ The validity and reliability assessments of this scale's Turkish translation were completed by Ağargün et al.¹⁰ PSQI consists of 24 questions evaluating sleep qual-

TABLE 1: Comparison of some demographic and clinical characteristics of the groups.				
Patient group (n=42)				
Age (year) (X±SD)	50.37±	50.37±18.35		
BMI (kg/m ²) (X±SD)	26.02±	26.02±3.76		
Gender (n, %)				
Female	16	45.7		
Male	19	54.3		
Diagnosis (n, %)				
SCI	16	45.7		
CVD	19	54.3		
Additional disease (n, %)				
None	21	60.0		
Hypertension	12	34.3		
Diabetes mellitus	2	5.7		

SD: Standard deviation; BMI: Body mass index; SCI: Spinal cord injury; CVD: Cardiovascular disease.

ity within the last month. While the patient answers 19 of the self-report questions, the patient's spouse or roommate answers the final 5 questions, which are used for clinical information only and are not scored. The score ranges from 0 to 21 points.

The aromatherapy *L. angustifolia* oil mixture to be used in the study was prepared by adding 1 mL of *L. angustifolia* oil (Art de huile lavender aromatherapy code for oil product licenses and permits: İstanbul Provincial Directorate of Agriculture, E-97834074-399-2344860) to 10 mL of olive oil. Only *L. angustifolia* oil can be toxic to the skin, so it is mixed with olive oil, which is a stable oil. For 30 days, the patients inhaled two drops of this mixture for 10 minutes from a distance of approximately 10 cm from the nose under the supervision of a nurse.

To identify the volatile ingredients in lavender oil, the Horticulture Department at Çukurova University utilized methods for gas chromatographymass spectrometry and headspace solid-phase microextraction. To extract the essential oils from lavender oil, the oil was treated 20 minutes at 3°C with 5 M CaCl2 on a magnetic stirrer and typical glass vessel with headspace (Supelco, 23 mm 75 mm). Three replications were used in the analysis. Using an SPME needle, polydimethylsiloxane absorbed the volatiles (Supelco, Bellefonte, PA). For the separation of volatiles, a PerkinElmer GC (USA) (Clarus 600) outfitted with an HP-5 MS (30 m 0.25 mm 0.25 µm) fused-silica capillary column. Helium was used as the carrier gas (0.6 mL/min). The temperature for the injection port was fixed at 280°C. The column was initially heated to 40°C for 2 minutes, after which the temperature was increased to 250°C at a rate of 5°C/minute, where the sample was kept for 20 minutes. By acquiring their mass spectra and using the NIST, Wiley, and taste libraries in accordance with their retention durations, compounds were identified. Categorical data were expressed as numbers and percentages, whereas continuous variables were expressed as mean, standard deviation, and median (minimum-maximum) values. The normality of continuous variables was examined using the Kolmogorov-Smirnov goodness-of-fit test. Data having a normal distribution were compared between 2 independent groups using the independent-samples t-testand between 2 dependent groups using the paired-samples t-test. In order to compare categoricaldata, the chi-square test was used. The Pearson correlation test was used to see whether there is alinear relationship between the scales. The SPSS version 26.0 was used to conduct statistical analyses (NY, USA, Armonk, IBM Corporation). The accepted statistical significance as p < 0.05.

The study was initiated with the approval of Adana Research and City Hospital Clinical Research Ethics Committee (date: April 8, 2021, no: 1364). The Declaration of Helsinki's ethical guidelines and principles were followed during every procedure. Patients were not given a written informed consent form because the study was retrospectively planned.

RESULTS

Of the 42 patients included in the study, 16 (45.7%) were female and 19 (54.3%) were male. Sixteen (45.7%) patients were diagnosed with SCI and 19 (54.3%) with stroke. The mean overall age was 50.37 ± 18.35 years, and the mean body mass index was 26.02 ± 3.76 . Forty percent of the patientshad an additional disease (Table 1).

The post-treatment PSQI and BAI scores $(4.31\pm2.28 \text{ and } 16.42\pm10.99, \text{ respectively})$ were found to be statistically significantly lower compared to the pre-treatment scores $(11.45\pm3.07 \text{ and } 11.45\pm3.07 \text{ and } 11.$

	TABLE 2: Comparison of the PSQI and BAI scores before and after treatment. Before treatment (X±SD) After treatment (X±SD) p value				
	PSQI	11.45±3.07	4.31±2.28	<0.001*	
	BAI	28.11±14.15	16.42±10.99	<0.001*	

*Paired samples t-test; PSQI: Pittsburgh Sleep Quality Index; BAI: Beck Anxiety Inventory; SD: Standard deviation.

 28.11 ± 14.15 , respectively) (p<0.001 and p<0.001, respectively) (Table 2).

Subjective sleep quality, sleep latency, sleep length, habitual sleep efficiency, sleep disruption, use of sleep medicine, and daytime dysfunction on the PSQI scale all showed statistically significant improvements following therapy (p<0.001).

The volatile compounds of lavender oil used in the inpatient clinic are presented in Table 3.

DISCUSSION

In patients with stroke and SCI receiving neurological rehabilitation frequently experience sleep disorders and anxiety symptoms, which may adversely affect their treatment process. In the literature, we did not find any study evaluating the effects of *L. angustifolia* aromatherapy on sleep quality and anxiety in patients undergoing neurological rehabilitation. In recent studies, it has been shown that *L. angustifolia* oil, whichis used in aromatherapy treatment, is effective in chronic pain, anxiety, and sleep disorders.

L. angustifolia contains the main components of anxiolytic effective linalool and linalyl acetate, whose pharmacological mechanisms are still being investigated in aromatherapy. Linalool is the most effective component in anxiolytic activity, and linalyl acetate increases this effect.^{11,12} In the *L. angustifolia* oil used in our study, the linalool level was found to be 29.33%, and the linalyl acetate level 27.69%.

In a randomized controlled study consisting of 70 patients diagnosed with cancer, a statistically significant improvement was found in anxiety levels in the lavender aromatherapy group.¹³ Chioca et al. suggested that the anxiolytic effect of inhaled *L. angustifolia* essential oil was through the serotonergic system.¹⁴ Supporting this result, López et al. determined that the anxiolytic effect of *L. angustifolia* es-

Compound name	RT	%	RI
Total ketones		1.58	
2-Propanone (CAS)	2.337	0.92	831
Camphor (CAS)	18.259	0.66	1,522
Total alcohols		40.60	
1-Hexanol (CAS)	13.789	0.25	1,359
3-Octanol (CAS)	14.958	0.62	1,399
1-Octen-3-ol	16.535	1.25	1,459
cis-Linalool oxide	17.052	0.40	1,477
Linalool	19.446	29.33	1,568
Lavandulol	22.453	2.91	1,687
alpha-Terpineol	22.93	1.92	1,706
Nerol (CAS)	25.301	0.23	1,807
trans-Geraniol	26.357	0.47	1,855
Eucalyptol	9.731	3.22	1,214
Total ester		32.29	
Acetic acid, butyl ester (CAS)	6.221	0.19	1,083
Butanoic acid, butyl ester (CAS)	10.146	0.66	1,230
Acetic acid, hexyl ester (CAS)	11.761	0.53	1,286
3-Octanyl acetate	13.473	0.68	1,348
2-methyl- hexyl ester (CAS), Propanoic acid	13.62	0.29	1,354
Oct-1-en-3-yl acetate	14.74	1.00	1,392
Butanoic acid, hexyl ester (CAS)	15.756	0.94	1,430
Linalyl acetate	19.968	27.69	1,588
Geranyl acetate	24.401	0.31	1,769
Total terpenes		25.53	
Alpha-pinene	5.002	0.93	1,030
I-Phellandrene	5.13	0.56	1,036
Camphene (CAS)	5.879	0.61	1,069
Delta-3-carene	8.114	0.41	1,158
Beta-myrcene	8.679	0.58	1,177
1,7,7-trimethyl, Bicyclo[2.2.1]hept-2-ene	9.575	2.50	1,208
<i>cis</i> -Ocimene	10.82	3.86	1,255
Gamma-terpinene	10.993	0.45	1,261
Alpha-terpinolene	11.991	0.45	1,261
2,6-dimethyl-2,4,6-octatriene	14.533	0.38	1,385
Terpinolene	20.918	13.59	1,626
Santalene	20.234	1.21	1,597

RT: Retention time; RI: Retention index.

sential oil was due to the antagonism effect of linalool and linalyl acetate on the N-methyl-D-aspartate receptor and the affinity of linalool to bind to the serotonin transporter.¹⁵ Selective serotonin reuptake inhibitors (SSRIs) have a similar effect by preventing the reuptake of serotonin into the cell. However, SSRIs can cause side effects, such as sleep and sexual problems and suicidal tendencies. No side effects were observed in any of the patients in our study. According to a review, *L. angustifolia* oil works through a similar mechanism as benzodiazepines to boost the action of gamma-aminobutyric acid in the amygdala. Benzodiazepines can cause sedation, attention deficit and ataxia.⁵ In our study, sedation was observed in patients with sleep problems.

The effect of orally administered silexan, a patented active ingredient produced from *L. angusti-folia* flowers, on anxiety and sleep disorders was evaluated in patients without psychiatric and neurological disorders. According to the Hamilton Anxiety Rating Scale and PSQI scores, silexan was reported to have sedative and anxiolytic activity.¹⁶ In our study, the application of *L. angustifolia* through inhalation from the skin were evaluated with BAI and PSQI in patients receiving neurological rehabilitation, and it was found to be have an effect on sleep and anxiety, which is in agreement with the literature.

In a randomized controlled clinical study, Lillehei et al. applied an empty pad to the chest area at night in one group and a lavender inhalation pad in the other group, and determined that lavender had an effect on balancing the sleep cycle and permanently increasing sleep quality.¹⁷

In a double-blind, randomized controlled study conducted in postmenopausal women with sleep disorders, L. angustifolia was administered to a group (n=17) for 29 days, and sunflower oil to another group (n=18) by inhalation. General sleep quality (p<0.001), depression levels (p=0.025), and polysomnography data (p=0.002) showed a significant improvement in the L. angustifolia group.¹⁸ It was found in a meta-analysis of three randomized controlled studies that lavender utilized in various forms, including aromatherapy, cream, and tea, improved postpartum moms' sleep quality.¹⁹ In another study, sleep disturbance and anxiety, which are common in patients with fibromyalgia, adversely affecting their quality of life, were found to be significantly improved by L. angustifolia aromatherapy. In this study, in agreement with the literature, a statistically significant improvement was detected in the PSQI scale evaluating subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorder, use of sleep medication, and daytime dys-function (p<0.001) and BAI (p<0.001) after the *L. angustifolia* aromatherapy oil application, and no side effect was observed in any of the patients.²⁰

CONCLUSION

In line with these findings, *L. angustifolia* oil aromatherapy can be recommended as a complementary medicinal application that is effective in anxiety and sleep disorders and has a low risk of side effects in patients undergoing neurological rehabilitation. However, further extensive studies are needed to confirm our findings.

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Conflict of Interest

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

Authorship Contributions

Idea/Concept: Gülşah Yaşa Öztürk, Nilüfer Aygün Bilecik; Design: Gülşah Yaşa Öztürk, Sedat Yıldız; Control/Supervision: Gülşah Yaşa Öztürk, Nilüfer Aygün Bilecik, Sedat Yıldız; Data Collection and/or Processing: Gülşah Yaşa Öztürk, Nilüfer Aygün Bilecik, Sedat Yıldız; Analysis and/or Interpretation: Gülşah Yaşa Öztürk, Nilüfer Aygün Bilecik, Sedat Yıldız; Literature Review: Gülşah Yaşa Öztürk, Sedat Yıldız, Nilüfer Aygün Bilecik; Writing the Article: Gülşah Yaşa Öztürk, Nilüfer Aygün Bilecik; Critical Review: Sedat Yıldız, Nilüfer Aygün Bilecik; References and Fundings: Sedat Yıldız, Nilüfer Aygün Bilecik.

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