ORIGINAL ARTICLE

The Impact of Aromatherapy with Citrus Aurantium Essential Oil on Sleep Quality in Pregnant Women with Sleep Disorders: A Randomized Controlled Clinical Trial

Freshteh Mohammadi¹, MSc; Maryam Moradi^{1,2}, PhD; Azin Niazi¹, MSc; Jamshid Jamali³, PhD

¹Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran;

²Nursing and Midwifery Care Research Center, Mashhad University of Medical Sciences, Mashhad, Iran; ³Department of Epidemiology and Biostatistics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding Author:

Maryam Moradi, PhD; Nursing and Midwifery Care Research Center, Ebne- Sina Street, Postal code: 91379-13199, Mashhad, Iran

Tel: +98 51 38591511; Fax: +98 51 38597313; Email: moradim@mums.ac.ir

Received: 10 November 2021 Revised: 10 April 2022 Accepted: 16 April 2022

ABSTRACT

Background: Sleep disorders are so prevalent during pregnancy. The present study was conducted to investigate the impact of aromatherapy with Citrus aurantium essential oil on sleep quality in pregnant women with sleep disorders.

Methods: This randomized clinical trial study was conducted on 68 pregnant women in their 28-34 weeks of pregnancy who sufferred sleep disorders and referred to Jiroft health centers in 2021 (January-June). Those meeting the inclusion criteria were divided into the intervention and placebo groups, using random sequence generated through the randomization website. They were given five drops of Citrus aurantium essential oil and the placebo twice a day, every day for one month in the form of facemasks which they inhaled through normal breathing for 20 minutes. Sleep quality was assessed before the intervention and one month after the start of the intervention. The demographic questionnaire and Pittsburgh Sleep Quality Index (PSQI) were used for collecting the data. Data analysis was performed using SPSS 24 software. The Mann–Whitney-U, Wilcoxon and fisher exact tests were carried out. P-value<0.05 was considered statistically significant.

Results: Before the intervention, the mean and standard deviation scores of pregnant women's sleep quality in the intervention (9.89 ± 3.00) and placebo (8.12 ± 2.53) groups were not significantly different (P=0.10). One month after the intervention, the score was significantly lower in the intervention group (4.37 ± 1.85) than the placebo group (8.48 ± 2.62) (P<0.001).

Conclusion: Based on the results of the present study, it seems that aromatherapy with Citrus aurantium essential oil enhances the sleep quality in pregnant women with sleep disorders, so it can be used to diminish sleep disorders in these women.

Trial Registration Number: IRCT20200512047414N1.

Keywords: Aromatherapy, Citrus aurantium, Pregnancy, Sleep, Sleep disorders

Please cite this article as: Mohammadi F, Moradi M, Niazi A, Jamali J. The Impact of Aromatherapy with Citrus Aurantium Essential Oil on Sleep Quality in Pregnant Women with Sleep Disorders: A Randomized Controlled Clinical Trial. IJCBNM. 2022;10(3):160-171. doi: 10.30476/IJCBNM.2022.92696.1900.

INTRODUCTION

Sleep quality dramatically diminishes as pregnancy proceeds. The prevalence increases from 13% in the first trimester to 66% in the third trimester.1 In a systematic review and meta-analysis, it was reported that the prevalence of sleep disorders during pregnancy was 80.8% in Iran.^{1,2} From the 12th week of pregnancy to 2 months after delivery, mothers complain of having trouble going to sleep, frequent sleep disturbances, insomnia, and poor sleep quality.1 Boosted levels of estrogen, progesterone, and cortisol are the hormones affecting sleep patterns during this period. Several emotional factors, e.g. the fear of facing new experiences and acquiring new roles, can lead to sleep disorders.^{3, 4} Insomnia tends to lead to physical and psychological symptoms. Furthermore, sleep disorders can leave an impact on a person's performance and cause mental fatigue, memory issues, lack of concentration, shifts in perception, and impaired judgment.^{5,6} Besides, changes in sleep patterns during pregnancy lead to unfavorable consequences, e.g. fatigue, gestational hypertension, preeclampsia, gestational diabetes, preterm labor, childbirth weight loss, intrauterine death, increased awareness of labor discomfort, and cesarean section.7 In another study, it was reported that sleep disorders in the third trimester of pregnancy are associated with some unfavorable pregnancy aftermaths, including preterm labor.8 In the study, there was a significant relationship between the prevalence of sleep disorders during pregnancy and the rise in labor duration. Also, the prevalence of cesarean birth was higher in women who had endured sleep disorders.9 Prescribing hypnotic/soporific drugs and psychedelics for mothers is prohibited during this period due to the potential side effects they or their infants might face.¹⁰ Non-pharmacological methods and complementary medicine are preferable to medical methods because of the affordability. ease of implementation, non-invasiveness, enhancement of self-confidence, client participation, experience of zero side effects, and

agreeableness to mothers and fetuses. Various complementary treatments such as progressive muscle relaxation,¹¹ massage therapy,¹ music therapy,¹² yoga, and aromatherapy can help reduce sleep disorders in pregnant women. Some of these methods, though beneficial, have limitations of their own. For instance, not all patients can take part in workout or yoga sessions.¹³ Aromatherapy is a supplementary method utilizing essential oils to prevent and cure diseases that can influence the mind, body, and soul.14 Citrus aurantium, commonly known as bitter orange, belongs to the Citrus genus and the Rutaceae family.15 Ingredients of Citrus aurantium include compounds such as linalool, linalool acetate, limonene, coumarin, and a variety of flavonoids. These compounds activate the GABAergic system. Gammaaminobutyric acid (GABA) is considered an inhibitory neurotransmitter at nervous synapses. It is primarily secreted by nerve endings in the spinal cord, cerebellum, or other basal ganglia in the brain. GABA is one of the most crucial inhibitory chemical mediators in the nervous system and is thought to be among the neurons involved in sleep. 16 Linalool and linalyl acetate have sedative and narcotic effects, respectively. Flavonoid and phenolic by-products exert their hypnotic and anti-anxiety effects through the GABA receptor. They are known as natural benzodiazepines.¹⁷ The study revealed that the aqueous extract of Citrus aurantium increased the sleep duration and decreased the anxiety levels in rats.¹⁸ Another study investigated the impact of Citrus aurantium essential oil on hospitalized patients with cardiovascular diseases (CVD), reporting that it lessened the sleep latency, increased sleep depth, reduced nocturnal disturbances to half, enhanced sleep duration, improved sleep quality, and boosted daytime freshness.¹⁹ No adverse effect or health hazard was found at the therapeutic doses of C. aurantium plant.20 Eventually, given the prevalence of sleep disorders in pregnant women, the negative impacts the disorders have on maternal and fetal health, sedative effects of Citrus aurantium compounds, limitation of research studies exploring the impact of Citrus aurantium on pregnancy-related sleep disorders, and different causes of insomnia in pregnant women, as opposed to other groups, the present study was designed to investigate the impact of aromatherapy with Citrus aurantium essential oil on sleep quality in pregnant women with sleep disorders.

MATERIALS AND METHODS

The present study was a two-group placebo controlled clinical trial carried out on 68 pregnant women with sleep disorders who referred to Jiroft health centers (Two centers of districts 1 and 3 and from each one 2 health centers were chosen) in 2021 (January-June).

To determine the sample size, we used the formula for comparing two means from two independent samples based on the values of the parameters Pittsburgh Sleep Quality Index (PSQI) Score obtained in the pilot study on 10 participants. Based on the pilot study, the mean difference of the PSQI score before and after the study in the intervention and control groups was 2.32±2.93, 0.19±3.02, respectively. As a result, the size of each group was determined as 32 individuals per group based on type I error or alpha 0.05, and power of 80; considering a 20% dropout rate, we included 38 people in each group (76 people in total).

$$n = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^{2} (s_{1}^{2} + s_{2}^{2})}{(\bar{x}_{2} - \bar{x}_{1})^{2}} =$$

$$\frac{(1.96 + 0.84)^2(2.93^2 + 3.02^2)}{(2.32 - 0.19)^2} = 32$$

The inclusion criteria were basic literacy, Iranian nationality, residence in Jiroft, sleep quality scores above 5 from the PSQI Questionnaire, 28-34 weeks of pregnancy, single pregnancy as opposed to a twin pregnancy, no olfactory dysfunction (obtaining a score of more than 3 in the mental olfactory training section or more than 2.9 in the specific olfactory sections

or more than 3.7 in the olfactory quality of life section of the Passwald questionnaire), cold symptoms, no medical disorders (e.g. epilepsy, coagulation disorders, diabetes, heart disease, kidney disease), no sleep disorders pre-pregnancy and no medical records of mental illnesses according to the Depression, Anxiety and Stress Scale - 21 Items (DASS-21) questionnaire (severe or very severe depression/anxiety/stress, depression score less than 21, anxiety score less than 15 and stress score less than 26), no accidents and major stressful events (including death of a family member, separation from the spouse, severe conflicts with spouse, expulsion and bankruptcy) in the last 6 months, and no habits of smoking, alcohol consumption or substance abuse. Lack of willingness to continue participation in the study, hospitalization, allergic reactions to Citrus aurantium essential oil or almond oil during the study, irregular and ill-timed medication administration, and the use of other treatments to prevent sleep disorders (Pharmacological and/or non-pharmacological treatments), and preterm delivery during the study were the exclusion criteria.

In the present study, the data collection tools were a demographic questionnaire which included Gestational Age, Pregnant Woman's Age, Gravida, Number of Labors/ Para, Number of Abortions, Number of Children, Number of Stillbirths, Length of Marriage, History of infertility, Length of infertility, Antenatal Care Frequency, The interval between the current pregnancy and the previous pregnancy, Education Level, Spouse's Education Level, Occupation, PSQI, Pusswald Olfactory Dysfunction Questionnaires, and DASS-21. The PSQI Questionnaire was developed in 1989 by Buysse et al. It basically has 9 items, but because Question 5 itself contains 10 subitems, the entire questionnaire has 19 items. This questionnaire has 7 component scores: mental quality of sleep, delay in falling asleep, sleep duration, sleep efficiency, sleep disorders, use of sleeping pills, and

daily functional disorders. The 19 selfrated questions are grouped to form seven component scores. Each component score is rated on a 4-point Likert scale from 0 to 3, and the total score of this questionnaire ranges from 0-21, but a total score higher than 5 in the whole questionnaire means poor sleep quality. Buysse et al. (1989) have confirmed the validity and reliability of the questionnaire.²¹ This questionnaire's reliability was calculated in a study conducted in Germany (r=0.87). Validity analyses showed high correlations between PSQI and sleep log data and lower correlations with polysomnography data. A PSQI global score >5 resulted in a sensitivity of 98.7 and specificity of 84.4 as a marker for sleep disturbances in insomnia patients versus the controls.²²

Farahi Moghadam et al. (2012) assessed the reliability of the PSQI-P in terms of internal consistency and corrected item-total correlation. Internal consistency analysis showed that Cronbach's alpha was 0.77. To assess the construct validity of the PSQI-P, we used General Health Questionnaire -12, as a measure of general psychopathology, because "difficulty with sleep is one of the earliest manifestations of psychopathology"; the results showed an acceptable correlation (0.54) between these two tools.²³ In the present study, reliability was confirmed through the internal consistency method with a Cronbach's alpha of 0.75. For analysis of validity, ANCOVA test was used to compare the patient groups for PSQI global and component scores, and the control subjects differed from all patient groups (t=9.31 and 4.50, respectively; both P<0.001). The Pusswald questionnaire contains 12 questions and 3 subscales: the one-item subjective olfactory capability scale (SOC), the five-item self-reported capability of perceiving specific odors scale (SRP), and the six-item olfactory-related quality of life (ORQ) scale, no olfactory dysfunction (obtaining a score of more than 3 in the mental olfactory training section or more than 2.9 in the specific olfactory sections or more than 3.7 in the olfactory quality of life section of

the Passwald questionnaire). Pusswald et al. (2012) confirmed the scientific validity and reliability of the questionnaire with a Cronbach's alpha of 0.85. The Cronbach's alpha values were determined at 0.93 and 0.95 for the SOC and SRP scales, respectively. The validity of the *self-reported olfactory* functioning (ASOF) was determined using discriminant and convergent techniques. The first approach was to determine the ASOF's discriminative power by comparing ASOF score profiles between the healthy controls and patients with olfactory dysfunction. All the three scales significantly discriminated between patients with olfactory dysfunction and healthy controls.²⁴ In the present study, reliability was confirmed through the internal consistency method with a Cronbach's alpha of 0.86. The DASS-21 self-reporting questionnaire was developed by Lovibond and Lovibond in 1995. This study showed that there were satisfactory psychometric properties, and the factor structure was substantiated both by exploratory and confirmatory factor analysis (CFA).25 The questionnaire was validated as a screening tool to measure the symptoms of depression, anxiety, and stress in both community setting and under clinical conditions. The exploratory factor analysis revealed three underlying factors which explained 41.3% item variance. Confirmatory factor analysis of the questionnaire was also performed, showing strong evidence of the stability of the scale over time.²⁶ Asghari et al. (2008) translated the DASS-21 questionnaire and validated the Persian version in a sample of Iranian population. In their study, a 3-factor model was supported by CFA data. Convergent and divergent validityes were performed and the validity of the Persian version of the DASS 21 questionnaire was confirmed. The internal consistency (Cronbach alpha=0.94) and test-retest reliability (ICC=0.77) suggested a satisfactory reliability.²⁷ The DASS-21 questionnaire offers four options: normal, mild, moderate, severe, and very severe. Each item is scored on a 4-point Likert scale ranging from 0 ("did not apply to me at all")

to 3 ("applied to me very much"). According to the DASS-21 questionnaire, the scores of depression, based on the normal, mild, moderate, severe, and very severe types, were 0-9,10-13, 14-20, 21-27, and more than 28. The scores for anxiety were 0-7, 8-9, 10-14, and 19-15, respectively, and more than 20, and for stress 0-14, 15-18, 19-25, 26-33, and greater than 33, respectively. In the present study, reliability was confirmed through the internal consistency levels with Cronbach's alpha values of 90%, 91%, and 83% for depression, anxiety, and stress, respectively.

Sampling was carried out through the multi-stage sampling technique. First, two out of six healthcare centers of districts number 1 and 3 of Jiroft were selected as a cluster through a lottery with a coin; then, four healthcare units covered by each of these two centers (two bases from each one) were chosen according to the ratio of the patients and their collaboration in carrying out the study. The required permits for data gathering were obtained. Afterward, pregnant women who referred to those centers were selected through convenient sampling. After introducing the research, clarifying the objectives, and obtaining informed written consent from the subjects to participate, if the individuals met the inclusion criteria, the demographic questionnaire DASS-21, Pusswald's Olfactory Disorder Questionnaire, and the PSQI Questionnaire were selfreportedly filled out by them. Women who acquired a sleep quality score more than 5, a score more than 3 in the SOC, a score more than 2.9 in the SRP, and a score more than 3.7 in the ORO in Pusswald's Olfactory Disorder Questionnaire and had no severe and very severe levels of stress, anxiety, and depression according to the DASS-21 questionnaire, (depression score less than 21, anxiety score less than 15, and stress score less than 26) were selected as the study samples. The allocation of pregnant women to the two groups of intervention and placebo was done randomly with a random sequence generated through the site www.randomization.com

for 76 people in two groups of A and B. The mentioned site provided a sequence of these codes (6 blocks of 4) for the sample size. This sequence was kept in a sealed envelope. When each research unit met the inclusion criteria, the envelope was opened, and the subject was allocated to the intervention or placebo group, based on the code. Codes A and B were assigned to two groups (citrus essential oil and placebo) through a lottery.

To prepare the medication, we purchased dried orange blossoms from the health centers approved by the School of Persian and Complementary Medicine of the Ferdowsi University of Mashhad. Once Mashhad Pharmacological Research Center of Medicinal Plants determined and approved the plant species, a herbarium code (3-67-1) was assigned to it. The plant was then pulverized and soaked in neutral carrier oil (sweet almond oil). The process took 7 days. Afterward, the plant was filtered, and the derived oil was once again soaked with the same amount of the initial plant for another week. After the second week, the resulting oil, which was saturated with essential oil, was prepared. Then, the oil containing the essence was packed in dark cans with specific labels after refining. The cans containing placebo, which was neutral, odorless, sweet almond oil, were prepared in the same manner. To determine the markers of the Citrus aurantium essential oil, Mashhad TESTA Company standardized the oil containing the essence through the gas chromatography method. The predominant compound identified in the essential oil was linalool (47.2%).

The participants in both intervention and placebo groups were given facemasks induced with either 5 drops^{21, 24} of Citrus aurantium essential oil or the placebo essential oil (sweet almond oil). They put on the masks twice a day (in the morning and before going to bed at night), every day for one month. Each time they inhaled the substances for 20 minutes²⁸ through normal breathing. The masks were provided for them for a month. Each participant was given a checklist for inhaling essential oil,

either Citrus aurantium or placebo (including frequency of use, any allergy, or reason for lack of use). Moreover, weekly follow-up phone calls kept reminding the participants of using the intervention and placebo. Moreover, the potential side effects were elaborated on, the satisfaction level was kept in check, and the exclusion criteria were reviewed during the study. The intervention was finished after one month. During an in-person meeting, one month after the start of the intervention, the research units were asked to fill out the sleep quality questionnaire again.

At first, 76 subjects were included in the study, but finally 8 of them were excluded from the study. The 5 excluded participants were in the Citrus aurantium group (3 due to inaccessibility mid-study and 2 due to ill-timed usage), and 3 excluded participants were in the placebo group (1 due to unwillingness to continue participation and 2 due to ill-timed usage). Finally, the results of the study on 68 individuals as the final study sample were analyzed and compared (Figure 1). The collected data were analyzed using SPSS Statistics Software (version 24). Descriptive statistics including frequency,

mean and standard deviation were used to describe the characteristics of the research units. The Kolmogorov-Smirnov test was used to determine data normality. The Mann–Whitney U and Wilcoxon tests were utilized to analyze the non-normal data. Fisher's exact test was used for nominal variables. P-value<0.05 was considered statistically significant.

The current study was approved by the ethics committee of Mashhad University of Medical Sciences with the code of IR.MUMS. NURSE.REC.1399.056. The research units were assured that their names will not be mentioned in the study and that they can leave the study whenever they wished with no effect on their pregnancy care.

RESULTS

In the present study, the mean age of the participants was 26.75±4.70 years. In the intervention group, 9 (27.30%) and in the control group 7 (20%) were nulliparous, which were homogeneous (P=0.24). There was no statistically significant difference in the distribution of other demographic and

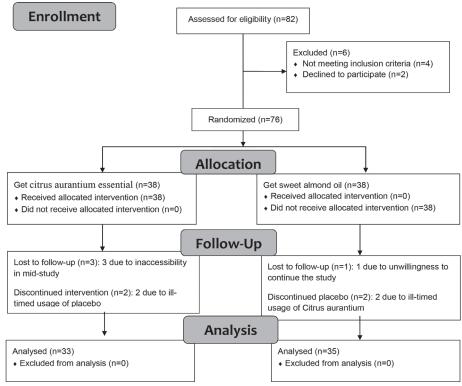


Figure 1: CONSORT flowchart of the participants of the study

contextual variables between the intervention and placebo groups, and the two groups were homogeneous in this regard (P<0.05). The majority of the participants in the current study had high school diploma and were housewives in the intervention and placebo groups, respectively (Table 1).

Before the intervention, the mean total score of sleep quality in pregnant women showed no statistically significant difference between the two groups; hence, they were homogeneous. However, after the intervention, the Mann-Whitney test revealed that the difference was statistically significant (P<0.001), indicating the effectiveness of the intervention in the Citrus aurantium group. Besides the sleep total score, the sleep domains were investigated as well. Once the impact of the initial heterogeneity was disregarded in some domains, the Citrus aurantium group

Maniahla

was significantly different from the placebo group one month after the intervention in 6 domains (subjective sleep quality, sleeps latency, sleeps duration, habitual sleep efficiency, Daytime Dysfunction, and sleep disturbances) (P<0.05). In the domain of Use of Sleep-Promoting Medication, comparison between groups showed no statistically significant difference (P>0.05). Regarding the intragroup comparison, the Wilcoxon test showed that only in the Citrus aurantium group, the mean score was significantly lower in PSQI Score and domains of Subjective Sleep Quality, Sleep Latency, Sleep Duration, Sleep Efficiency, Sleep Disturbances (P<0.001), and in domains of Daytime Dysfunction (P=0.001) one month after the intervention (Table 2). However, there was no difference in the domain of Use of Sleep-Promoting Medication (P>0.999).

Table 1: Demographic characteristics of pregnant women in the intervention and control groups

Variable		Intervention	Control	_ P value
		Mean±SD	Mean±SD	
Pregnant Woman's Age(year)		27.11±4.55	26.36±4.89	0.51*
Gravida		2.86±1.73	2.88±1.78	0.12*
Number of Labors /Para		1.49±1.35	1.45±1.39	0.73*
Number of Abortions		1.49±1.36	1.45±1.39	0.95*
Number of Children		0.31 ± 0.68	0.48 ± 0.76	0.93*
Number of Stillbirths		1.37±1.16	1.24±1.17	0.23*
Length of Marriage (year)		0.14 ± 0.49	0.12 ± 0.42	0.60*
Length of Infertility(year)		6.89±3.88	5.42±3.10	0.97*
Gestational Age(week)		31.0 ± 0.93	27.0 ± 0.72	0.08*
The interval between the current pregnancy and		5.31±1.53	5.85 ± 1.94	0.33*
the previous pregnar	ncy(year)			
		N(%)	N(%)	
Education Level	Elementary School	7(21.20)	8(22.90)	0.21**
	Intermediate School	7(21.20)	4(11.40)	
	High school Diploma	11(33.30)	16(45.70)	
	Associate Degree &	8(24.20)	4(11.40)	
	Bachelor's Degree			
	Master's Degree & Above	0(0.00)	3(8.60)	
Spouse's	Elementary School	8(24.20)	9(25.70)	0.47**
Education Level	Intermediate School	3(9.10)	6(17.10)	
	High school Diploma	16(48.50)	11(31.40)	
	Associate Degree &	6(18.20)	7(20)	
	Bachelor's Degree			
	Master's Degree & Above	0(0)	2(5.70)	
Occupation	Housewife	26(78.80)	27(77.10)	> 0.999**
	Student	0(0)	1(2.90)	
	Self-Employed	3(9.10)	2(5.70)	
	Government Employee	4(12.10)	5(14.30)	
*N (VVII : 4 4	**F:-1			

^{*}Mann-Whitney test, **Fisher's exact test

Table 2: Mean and standard deviation of sleep quality scores in the intervention and control groups before and after the intervention

Variable		Intervention	Control	P value*
		Mean±SD	Mean±SD	
Subjective Sleep	Pre-intervention	1.91±0.818	1.52±1.03	0.01
Quality	Post-intervention	0.49 ± 0.51	2.88 ± 8.65	< 0.001
	Difference	-1.43 ± 0.92	1.36 ± 7.85	< 0.001
P value**		< 0.001	0.59	
Sleep Latency	Pre-intervention	2.03±0.86	1.79±0.89	0.22
	Post-intervention	1.14±0.77	2.70±4.254	< 0.001
	Difference	-0.89±0.68	0.91±3.84	< 0.001
P value**		< 0.001	0.01	
Sleep Duration	Pre-intervention	2.14±0.810	1.70±1.47	0.018
	Post-intervention	1.00 ± 0.73	3.82 ± 13.17	0.006
	Difference	-1.14 ± 0.60	2.12 ± 12.01	< 0.001
P value**		< 0.001	0.31	
Sleep Efficiency	Pre-intervention	1.09±0.89	1.12±1.17	0.78
	Post-intervention	0.23 ± 0.80	0.85 ± 0.80	< 0.001
	Difference	-0.86±0.85	-0.27±0.91	0.001
P value**		< 0.001	0.08	
Sleep	Pre-intervention	1.37±0.55	1.85±1.20	0.01
Disturbances	Post-intervention	0.91 ± 0.45	1.55 ± 0.56	< 0.001
	Difference	-0.46 ± 0.61	-0.30±1.16	0.04
P value**		< 0.001	0.10	
Use of Sleep-	Pre-intervention	0.00 ± 0.00	0.36±2.09	0.30
Promoting	Post-intervention	0.00 ± 0.00	0.06 ± 0.35	0.30
Medication	Difference	0.00 ± 0.00	-0.30±1.74	0.30
P value**		>0.999	0.31	
Daytime	Pre-intervention	1.40 ± 0.98	1.21±1.14	0.34
Dysfunction	Post-intervention	0.60 ± 0.65	1.48 ± 0.87	< 0.001
	Difference	-0.80 ± 0.96	0.27 ± 1.04	< 0.001
P value**		0.001	0.03	
PSQI Score	Pre-intervention	9.89±3.00	8.12±2.53	0.10
	Post-intervention	4.37±1.85	8.48±2.62	< 0.001
	Difference	-5.51±2.36	0.36±1.93	< 0.001
P value**		< 0.001	0.12	

^{*}Mann-Whitney test, **Wilcoxon

DISCUSSION

The results demonstrated a statistically significant difference in the mean scores of the PSQI between the two groups of Citrus aurantium essential oil and placebo one month after the beginning of the intervention. Subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, and daytime dysfunctions significantly improved in the Citrus aurantium essential oil group compared with the placebo group. A study compared the effects of lavender and bitter orange on the sleep quality in postmenopausal women; it was shown

that bitter orange and lavender significantly improved the mean sleep score compared with the control group.²⁹ It should be noted that the intervention was conducted orally for 8 weeks, while in the present study aroma was used for 4 weeks. Therefore, Citrus aurantium improves the sleep quality both when used orally and in aromatherapy. This result can be explained by the fact that the linalool in Citrus aurantium, which interacts with GABA receptors in the central nervous system, has a sedative action.³⁰ A study aoolied aromatherapy with two drops of 10% Citrus aurantium essential oil for 20 minutes for three consecutive nights in the

elderly with heart failure, showing that the intervention had an impact on the overall quality of sleep, sleep latency, wake-up time, get-up time, daytime amount of sleep, the individual's feeling after waking up, sleep satisfaction, and difficulty falling asleep,³¹ which are consistent with the results of the present study; however, in our study aroma was used for 4 weeks on pregnant women. This result can be explained by the linalool in Citrus aurantium.¹⁶

Another study assessed the impact of aromatherapy with Citrus aurantium essence on sleep quality in people with type 2 diabetes. Participants underwent aromatherapy with 8 drops of 20% Citrus aurantium essential oil for three consecutive nights in the intervention group. There was a significant difference between the mean scores of total sleep quality, sleep latency, and subjective sleep quality in the intervention group pre- and post-aromatherapy. Furthermore, the mean scores of sleep quality for questions related to sleep latency, sleep disturbance frequency, ease of getting back to sleep, and total sleep quality showed an increase and henceforth an improvement in the intervention group as opposed to the placebo group.³² This result is consistent with the findings of the present study; despite the differences in the study population, type of questionnaires used, the drug improved the women's sleep quality. However, the participants in the present study did not suffer from any mental or physical diseases. Another study carried out aromatherapy with 10% Citrus aurantium essential oil for three consecutive nights. The results suggested a boost in sleep quality in the following areas: the participants' sleep quality the night before, sleep disturbance frequency, sleep satisfaction the night before, and time taken to get back to sleep.19 A study reported that the mean score of sleep quality in the group who used aromatherapy with Citrus aurantium 50% essence was significantly different from the placebo group. Therefore, Citrus aurantium essence had a positive impact on sleep quality in patients with acute coronary syndrome.33 In the present study, a statistically significant difference was observed between the mean scores of all investigated items, except for the scope of drug use in the Citrus aurantium group post-intervention versus pre-intervention. Likewise, regarding the intergroup study, the mean total score of the PSQI was significantly different between the two groups.

According to research studies, Citrus aurantium extract is composed of the following compounds: a wide range of hydrocarbons (35%) and terpene alcohols (47%), e.g. linalool, geraniol, nerol, flavonoids and their acetates, nerolidol (6%), and indole (7 to 11%). Linalool acts as a sedative in the central nervous system through interaction with the GABA receptor.³²⁻³⁴ Flavonoids also act as benzodiazepine receptor agonists and possess sedative qualities.35 Limonene, a major component of Citrus aurantium extract, reduces the simultaneous and collective activity of the neurons in the central nervous system. This compound can bind to GABA receptors and lead to the release of GABA neurotransmitters. Therefore, it is concluded that limonene brings about antianxiety and hypnotic effects by influencing the gabaergic system and suppressing the central nervous system.³⁶ These cases can explain the reason behind the findings of the present study and the impact of Citrus aurantium essential oil on improving the sleep quality.

In a study which utilized aromatherapy with 10% Citrus aurantium essential oil for three nights, the substance successfully improved the sleep quality of the elderly. However, the total score of sleep quality, scores of subjective sleep quality, sleep effectiveness, and daily dysfunction were significantly better in the rose oil group than the Citrus aurantium essential oil group.³⁷ Perhaps the decrease in the efficiency of Citrus aurantium essential oil can be attributed to the research method which was carried out periodically and without a control group. A study which evaluated the impact of acupressure on patients with CVD contrasted to aromatherapy with Citrus aurantium essential oil revealed that Citrus aurantium essential oil had no impact on improving the sleep quality of

the patients. The ineffectuality of Citrus aurantium essential oil in the research study can be attributed to the short duration of the intervention (one night), the amount and dosage of the applied essential oil (two drops of 10% essential oil), unpleasant odor of the oil for several patients, study population, and dissimilar sleep qualities in patients.³⁸

One of the most important strengths of this study was conducting the intervention by using Citrus aurantium essential oil in helping to improve the sleep quality of pregnant women with sleep disorders. On the other hand, this study had some limitations that should be considered to generalize its results. One limitation of the study was the infeasibility of blinding due to the evident odor of Citrus aurantium essential oil. Another limitation was the difference between the individuals' attitude about aromatherapy and the effect of undiagnosed physical or mental illness; however, randomly assigning the participants to two groups of placebo and intervention might have controlled this concern to some extent.

Conclusion

Based on the results of the present study, it seems that using aromatherapy with Citrus aurantium essential oil increases the sleep quality of pregnant women with sleep disorders. Therefore, the usage of Citrus aurantium essential oil is recommended in this regard. Furthermore, it does not cause the side effects of synthetic medications, and it is also widely accessible and financially economic. The results of the current study can be used as a scientific source for further inquiries on the impacts of Citrus aurantium essential oil on improving the sleep quality. It is highly suggested that further research should be conducted on the impact of Citrus aurantium essential oil on sleep disorders in the first trimester of pregnancy and compared with other herbal aromatherapy as well.

ACKNOWLEDGMENTS

The present paper is the result of a research

project that was ratified by the Vice-Chancellor for Research and Student Research Committee of Mashhad University of Medical Sciences with the code of 990754. This study was financially supported by Mashhad University of Medical Sciences.

Conflicts of Interest: None declared.

REFERENCES

- 1 Bazrafshan MR, Ghorbani Z. The Effect of slow stroke back massages on anxiety among primigravid women. Hayat. 2010;16:34-40. [In Persian]
- 2 Arfaie K, Nahidi F, Simbar M. A qualitative investigation on mothers' perception of socioeconomic determinants of induced anxiety during pregnancy. Payesh. 2018;17:657-65. [In Persian]
- 3 Facco FL, Grobman WA, Kramer J, et al. Self-reported short sleep duration and frequent snoring in pregnancy: impact on glucose metabolism. American Journal of Obstetrics and Gynecology. 2010;203:142. e1-5.
- 4 Kaveh M, Kashi AM, Sadegi K, Forghani F. Pregnancy in non-communicating rudimentary horn of a unicornuate uterus. International Journal of Fertility & Sterility. 2018;11:318-20.
- 5 Gulia KK, Kumar VM. Sleep Deprivation during Pregnancy: The Cost of Ignorance. SM Journal of Sleep Disorders. 2016;2:1004.
- 6 Okun ML, Kiewra K, Luther JF, et al. Sleep disturbances in depressed and nondepressed pregnant women. Depression and Anxiety. 2011;28:676-85.
- 7 Gordon A, Raynes-Greenow C, Bond D, et al. Sleep position, fetal growth restriction, and late-pregnancy stillbirth: the Sydney stillbirth study. Obstetrics & Gynecology. 2015;125:347-55.
- 8 Najar S, Sharafi F, Afshari P, Haghighizadeh MH. The relationship between sleep disorders during pregnancy and premature labor and low birth weight.

- Iranian Journal of Obstetrics, Gynecology and Infertility. 2017;20:44-9. [In Persian]
- 9 Raiesifar Z, Kamangar S, Tahery N, et al. The relationship between sleep disorders in the last month of pregnancy and the length of labor and mode of delivery in pregnant women referring to Abadan Taleghani Hospital in 2017. Iranian Journal of Obstetrics, Gynecology and Infertility. 2019;22:53-9. [In Persian]
- 10 Bacaro V, Benz F, Pappaccogli A, et al. Interventions for sleep problems during pregnancy: a systematic review. Sleep Medicine Reviews. 2020;50:101234.
- 11 Shobeiri F, Manoucheri B, Parsa P, Roshanaei G. Effects 13 counseling and sole reflexology on fatigue in pregnant women: a randomized clinical trial. Journal of Clinical and Diagnostic Research. 2017;11:QC01-4.
- 12 Liebman SS, MacLaren A. The effects of music and relaxation on third trimester anxiety in adolescent pregnancy. Journal of Music Therapy. 1991;28:89-100.
- 13 Tayebi A, Dehkordi Ak, Ebadi A, et al. The effect of aromatherapy with lavender essential oil on depression, anxiety and stress in hemodialysis patients: A clinical trial. Evidence Based Care Journal. 2015;5:65-74. [In Persian]
- 14 Sharifipour F, Mirmohammad Ali M, Hashemzadeh M. Comparison of the effect of Citrus arantium and Salvia officinalis aroma on post-cesarean section pain. Iranian Journal of Obstetrics, Gynecology and Infertility. 2017;20:41-9. [In Persian]
- 15 Chan YY, Li CH, Shen YC, Wu TS. Anti-inflammatory principles from the stem and root barks of Citrus medica. Chemical and Pharmaceutical Bulletin. 2010;58:61-5.
- 16 Menichini F, Loizzo MR, Bonesi M, et al. Phytochemical profile, antioxidant, anti-inflammatory and hypoglycemic potential of hydroalcoholic extracts from Citrus medica L. cv Diamante flowers, leaves and fruits at two maturity stages. Food and Chemical Toxicology. 2011;49:1549-55.

- 17 Chhikara N, Kour R, Jaglan S, et al. Citrus medica: nutritional, phytochemical composition and health benefits a review. Food & Function. 2018;9:1978-92.
- 18 Abbasnia VS. The effect of Citrus Aurantium flowers aqueous extract on sleeping time and the level of anxiety in mice. Journal of Birjand University of Medical Sciences. 2016;23:307-14. [In Persian]
- 19 Zeighami R, Mohamadi hariry F, Jalilolghadr S, Alipour haidari M. Investigating the effect of "Citrus Aurantium" aroma on sleep quality of patients hospitalized in the coronary care unit (CCU). Complementary Medicine Journal. 2014;4:720-33. [In Persian]
- 20 Kaats GR, Miller H, Preuss HG, Stohs SJ. A 60day doubleblind, placebo-controlled safety study involving Citrus aurantium (bitter orange) extract. Food and Chemical Toxicology. 2013;55:358-62.
- 21 Buysse DJ, Reynolds III CF, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Research. 1989;28:193-213.
- 22 Backhaus J, Junghanns K, Broocks A, et al. Test–retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. Journal of Psychosomatic Research. 2002;53:737-40.
- 23 Moghaddam JF, Nakhaee N, Sheibani V, et al. Reliability and validity of the Persian version of the Pittsburgh Sleep Quality Index (PSQI-P). Sleep and Breathing. 2012;16:79-82.
- 24 Pusswald G, Auff E, Lehrner J. Development of a brief self-report inventory to measure olfactory dysfunction and quality of life in patients with problems with the sense of smell. Chemosensory Perception. 2012;5:292-9.
- 25 Lovibond PF, Lovibond SH. The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behaviour Research

- and Therapy. 1995;33:335-43.
- 26 Brown TA, Chorpita BF, Korotitsch W, Barlow DH. Psychometric properties of the Depression Anxiety Stress Scales (DASS) in clinical samples. Behaviour Research and Therapy. 1997;35:79-89.
- 27 Asghari A, Saed F, Dibajnia P. Psychometric properties of the Depression Anxiety Stress Scales-21 (DASS-21) in a non-clinical Iranian sample. International Journal Psychology. 2008;2:82-102.
- 28 Igarashi T. Physical and psychologic effects of aromatherapy inhalation on pregnant women: a randomized controlled trial. Journal of Alternative and Complementary Medicine. 2013:19:805-10.
- 29 Kamalifard M, Farshbaf-Khalili A, Namadian M, et al. Comparison of the effect of lavender and bitter orange on sleep quality in postmenopausal women: a triple-blind, randomized, controlled clinical trial. Women & Health. 2018;58:851-65
- 30 Karadag E, Samancioglu S, Ozden D, Bakir E. Effects of aromatherapy on sleep quality and anxiety of patients. Nursing in Critical Care. 2017;22:105-12.
- 31 Arab Firouzjaei Z, Illali ES, Taraghi Z, et al. The effect of Citrus aurantium aroma on sleep quality in the elderly with heart failure. Journal of Babol University of Medical Sciences. 2019;21:181-7.
- 32 Abdollahi F, Mohaddes Ardebili F, Najafi Ghezelje T, Hosseini F. The Effect of Aaromatherapy with Bitter orange extract on Sleep quality in Patient with type 2 diabetic. Complementary Medicine

- Journal. 2017;7:1851-1861. [In Persian]
- 33 Gharaee R, Saghi N, Nasiri M, Kheyrabadi A. A comparative study on the effects of aromatherapy with orange and citrus aurantium extracts on sleep quality in patients with acute coronary syndrome. Koomesh. 2020;22:275-81. [In Persian]
- 34 Milanos S, Elsharif SA, Janzen D, et al. Metabolic products of linalool and modulation of GABAA receptors. Frontiers in Chemistry. 2017;5:46.
- 35 Vandebroek I, Picking D. Popular Medicinal Plants in Portland and Kingston, Jamaica. Swiss: Springer cham; 2020.
- 36 Abbasnejad M, Keramat B, Mahani E, Rezaeezade-Roukerd M. Effect of hydromethanolic extract of sour orange flowers, Citrus aurantium, on pentylentetrazole induced seizure in male rats. Journal of Babol University of Medical Sciences. 2012;14:20-8. [In Persian]
- 37 Khalili Z, Taraghi Z, Ilali E, Mousavinasab N. Comparison of the effect of aromatherapy with essential of Damask Rose and Citrus aurantium on the sleep quality of the elderly people. Journal of Nursing and Midwifery Sciences. 2021;8:9-14.
- 38 Asgari MR, Vafaei-Moghadam A, Babamohamadi H, et al. Comparing acupressure with aromatherapy using Citrus aurantium in terms of their effectiveness in sleep quality in patients undergoing percutaneous coronary interventions: A randomized clinical trial. Complementary therapies in clinical practice. 2020;38:101066.