

The Effect of Combined Inhalation Aromatherapy with Lemon and Peppermint on Nausea and Vomiting of Pregnancy: A Double-Blind, Randomized Clinical Trial

Abstract

Background: Nausea and vomiting are almost inevitable features of pregnancy which have a serious impact on the quality of life of pregnant women. This study aimed to determine the effects of combined inhalation aromatherapy with lemon and peppermint on nausea and vomiting of pregnancy. **Materials and Methods:** The parallel randomized clinical trial was conducted on 90 pregnant women suffering from nausea and vomiting of pregnancy referred to health centers in Birjand-Iran- from February 2015 to August 2016. Participants were randomly divided into two groups. The combined lemon and peppermint essential oils were used as an inhaler for the intervention and the placebo for the control group. Both groups were trained to place three drops of the solution onto a cotton ball and keep it in a 3-cm distance of their nose. The intensity of nausea, vomiting and fatigue was assessed through 24-hour Pregnancy Unique Quantization of Emesis (PUQE-24) questionnaire and Fatigue Severity Scale (FSS), respectively. **Results:** Mean (SD) scores of nausea and vomiting intensity before the intervention and on the first day of intervention were not significantly different between the two groups, but became significant on the second, third, and fourth days of intervention. The results showed that the effect of time on the mean intensity of nausea and vomiting was significant in the aromatherapy group ($F_{2,84} = 22.92, p < 0.001$) but was not significant in the placebo group ($F_{2,78} = 0.26, p = 0.836$). **Conclusions:** The combined lemon and peppermint aromatherapy could reduce mild to moderate intensity of nausea and vomiting during pregnancy.

Keywords: Aromatherapy, nausea, peppermint, pregnancy

Introduction

Nausea and vomiting are typical and almost inevitable features of pregnancy complain, with an estimated prevalence 35% to 91% in pregnant women.^[1,2] Remarkable physical and psychological effects exist in women who experience these symptoms, along with significant constraints in the lifestyle of pregnant women, which have a serious impact on the family quality of life, ability to perform daily activities, social function and the stress level of pregnant women. The psychological effects in women may cause some women decide to terminate the pregnancy.^[1-4]

The reason for Nausea and Vomiting in Pregnancy (NVP) is still unknown. Therefore, a wide variety of treatments have been used empirically. Many therapeutic methods, including pharmaceutical and non-pharmaceutical interventions, have

been proposed for NVP.^[2] Concerns about the adverse effects of using chemical drugs on the fetus have compelled women to try Complementary and Alternative Medicine (CAM) to treat nausea and vomiting. However, wider knowledge is required on the safety of using CAM during pregnancy.^[4-6]

Aromatherapy is one of the common types of medications that is recommended by midwives. This is a branch of herbal medicine that exploits the medicinal aspects of essential oils.^[4] One of the herbs used in aromatherapy is a special type of lemon, *Citrus Limon*, from the Rutaceae family. One of the therapeutic effects of lemon essential oil is NVP relief.^[7-9] The results of a clinical trial showed that lemon aroma was effective in reducing the NVP.^[9] The peppermint, *Mentha x Piperita*, from the Mint family, is one of the other herbs used in aromatherapy.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Safajou F, Soltani N, Taghizadeh M, Amouzesi Z, Sandrous M. The effect of combined inhalation aromatherapy with lemon and peppermint on nausea and vomiting of pregnancy: A double-blind, randomized clinical trial. *Iran J Nurs Midwifery Res* 2020;25:401-6.

Submitted: 15-Apr-2019. **Revised:** 19-Feb-2020. **Accepted:** 04-Jul-2020. **Published:** 01-Sep-2020.

Farzaneh Safajou^{1,2},
Narges Soltani³,
Mohsen
Taghizadeh⁴,
Zahra Amouzesi^{5,6},
Maryam Sandrous⁷

¹Student Research Committee, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran, ²Ghaen Faculty of Nursing and Midwifery, Birjand University of Medical Sciences, Birjand, Iran, ³Instructor of Midwifery, Birjand University of Medical Sciences, Birjand, Iran, ⁴Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, Iran, ⁵Faculty of Nursing and Midwifery, Surgery and Trauma Research Center, Birjand University of Medical Sciences, Birjand, Iran, ⁶PhD Student in Medical Education, Isfahan University of Medical Sciences, Isfahan, Iran, ⁷Midwife, Birjand University of Medical Sciences, Birjand, Iran

Address for correspondence:

Dr. Zahra Amouzesi,
Ghafari Street, Faculty of
Nursing and Midwifery,
Birjand University of Medical
Sciences, Birjand, Iran.
E-mail: zam9039@gmail.com

Access this article online

Website: www.ijnmrjournal.net

DOI: 10.4103/ijnmr.IJNMR_11_19

Quick Response Code:



It has analgesic, anti-microbial, anti-parasitic properties and is used for many therapeutic purposes such as tiredness, tension headaches, and NVP.^[10-12] In this regard, the results of a clinical trial showed that mixing two essential oils of lavender and peppermint could reduce the intensity of nausea episodes, increase energy levels, and decrease fatigue during pregnancy.^[11] Joulae-rad's study examined (2018) the effect of aromatherapy with peppermint essential oil on the NVP intensity and showed that despite a significant decrease in the NVP intensity in each intervention group, this lessening in two groups was not statistically significant and the effect of inhalation aromatherapy with peppermint essential oil on the reduce of NVP intensity was similar to the placebo group.^[13]

In spite of the fact that lemon and peppermint inhalation aromatherapy alone was effective in diminishing NVP, more investigation in this field is required. With respect to safety, more clinical trials are required to assess their side effects. On the other hand, to provide adequate evidence on the effects of combined inhalation aromatherapy, high-quality methodological studies such as clinical trials are necessary. Given that aromatherapy, among other forms of CAM, is one of the ways which the majority of midwives in Iran prefer to use it due to positive experiences and acceptance of these methods^[14] as well as the widespread use of the CAM methods, especially herbal remedies, and inadequate evidence of the effectiveness and safety of medicinal herbs during pregnancy are the cases which require further attention. Since more research is needed to determine the prevalence, safety, efficacy, and economic benefits of using these methods,^[13] so this study was conducted to investigate the effects of combined lemon and peppermint inhalation aromatherapy on the NVP.

Materials and Methods

This study was a Parallel Randomized controlled trial (IRCT2014062914324N2). Conducted in two health centers in Birjand from February 2015 to August 2016, using convenience sampling. The sample size was calculated 45 people in each group by using the formula for comparing the means, the data which were obtained from the study of Yavari Kia^[9] and taking into account $\alpha = 0.05$, test power of 90% and with a probability of 10% drop-out [Figure 1].

Random allocation was done using the database on www.random.org and through six blocking methods with the allocation ratio of 1:1 and dark and similar packaged glass containers sequentially numbered from 1 to 90. For allocation concealment, all of these steps, from blocking to glass numbering, were executed by a person uninvolved in the study. Also, the researcher and the participants were kept blind.

Inclusion criteria were the gestational age of 6–16 weeks with mild to moderate nausea and vomiting (scores in

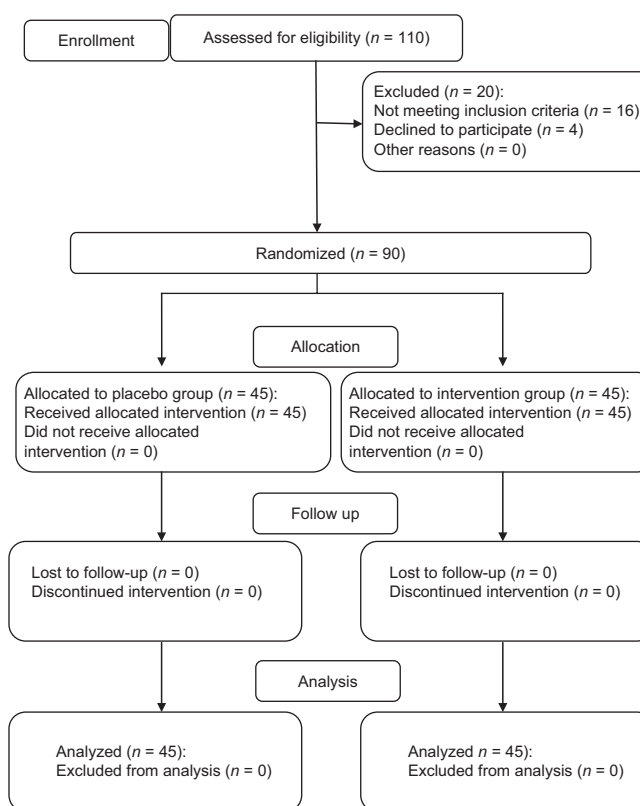


Figure 1: Flowchart of the participants

3–12 in 24-hour Pregnancy Unique Quantization of Emesis; PUQE-24), reading and writing literacy, singleton pregnancy without symptoms of threatened abortion, no smoking, no taking anti-nausea drug within the last 24 hours, no history of mental illness or disastrous events within the past 6 months, no problems with the olfactory system according to the patient history taking and no history of digestive diseases or any other illness, including nausea and vomiting. Hypersensitivity or intolerance to the drug was used in the study were considered as exclusion criteria in the study.

The drugs which were used in this study were made in dark-colored glasses with a dropper. The drug was used in the intervention group contained 10 cc of lemon and peppermint essential oil at a concentration of 10%, containing 5% lemon essential oil and 5% peppermint essential oil (Barij Essence Co., Iran). The control group received a placebo with the same color and concentration as the original drug of the same company. The placebo was prepared with propylene glycol base with a very small amount (as much as micrograms) of essential oil in order to create a sense of aromatic substances.

Both groups were trained to place three drops of the solution onto a cotton ball when feeling nausea within 4 days of treatment and keep it in 3-cm distance of their nose, then breathe three times deeply through the nose,^[15] repeat the same action after 5 minutes if necessary^[9] and close the lid of glass container firmly after using and retain

it away from light. The same cotton balls were given to the participants of both groups. In order to provide the same recommendations for changing nutrition and effective lifestyle in reducing nausea and vomiting, they were given to all mothers in form of a pamphlet and were asked to follow them during treatment.

In this study, the data collection tool was questionnaires. The first part, demographic characteristics and pregnancy information, was completed prior the intervention. The second part was the 24-hour Pregnancy Unique Quantization of Emesis (PUQE-24) that consists three questions that measure the duration of nausea, the frequency of vomiting, and the frequency of retching in the last 24 hours through a five-point Likert scale. The range of scores is between 3 and 15, indicating ≤ 6 as mild, 7–12 as moderate, and ≥ 13 as severe nausea and vomiting.^[16] This questionnaire was completed by the participants before the intervention and during four days of intervention (once a day). The validity and reliability of this instrument in Iran have also been confirmed in the study of Yavari Kia (Cronbach's alpha = 0.81).^[9] The third section was the Fatigue Severity Scale (FSS). This questionnaire was designed in 1989 to measure the severity of fatigue in patients with multiple sclerosis as well as lupus and consists 9 questions, each question was given a seven-point Likert scale, indicating 1 as strongly disagree and 7 as strongly agree. The range of scores was from 9 to 63 and the total score was obtained from the sum of scores, < 36 indicated as no fatigue and ≥ 36 as further examination by the physician was needed.^[17] The validity and reliability of this questionnaire in Iran were confirmed by Azimian in 2013 (Cronbach's alpha = 0.96 and ICC = 0.93).^[18] The questionnaire was also completed, in this study, once before the intervention and another time after the end of the intervention. In the fourth section, the questionnaire (researcher-made) contained questions such as side effect assessment, patient satisfaction with treatment, preference of this type of treatment and adherence to nutritional recommendations and lifestyle changes, and was completed only after the end of four-day treatment. During these four days, the participants were contacted twice on the telephone to ensure the intervention was implemented and their possible questions were being answered.

The primary outcome of this study was to compare the severity of nausea and vomiting after intervention in both groups and the secondary outcome was to measure the fatigue intensity.

The normality of data was evaluated using the Kolmogorov-Smirnov test. Data were analyzed by SPSS 16 (IBM Incorporation, Chicago, IL), using descriptive statistics and independent t-test, Mann-Whitney, Chi-square and repeated measures ANOVA tests.

Ethical considerations

All stages of the study have been approved by the Ethics Committee of Birjand University of Medical Sciences. All participants signed written informed consent after enrolling in the study.

Results

This study evaluated 45 pregnant women with NVP in each group [Figure 1]. The two groups were homogeneous with regard to demographic and pregnancy variables and there was no significant difference between the two groups in terms of these variables. The pregnancy and demographic characteristics of the studied mothers are presented in Table 1.

The results showed that the mean scores of nausea and vomiting intensity before the intervention and on the first day of that were not significantly different between the two groups, but were significant on the second, third and fourth days of intervention [Table 2]. The repeated measures ANOVA test results indicated that the effect of time on the intensity mean of nausea and vomiting was significant in the intervention group so that the intensity of nausea and vomiting was decreased in the intervention group with time, but not significant in the placebo group [Table 2].

There was no significant difference in fatigue intensity mean score between the two groups before and after the intervention [Table 3]. After the intervention, there was a significant difference between the two groups in terms of patient satisfaction with treatment, the preference of this type of treatment and adherence to nutritional recommendations and lifestyle changes during the course of treatment [Table 4]. Participating mothers in both groups did not mention a problem or complication during the treatment period.

Discussion

In this study, there was a significant difference in the mean intensity of nausea and vomiting in the second, third and fourth days of intervention between the two groups. However, some studies reported the efficacy of lemon and peppermint for reducing the NVP, but clinical trials are very limited in this regard.^[7,14,19] The results of the study by Yavari Kia *et al.* also indicated that inhalation aromatherapy with lemon reduced the intensity of nausea and vomiting in the second and fourth days of intervention.^[9] In another study, combined inhalation aromatherapy (lavender and peppermint) was used to reduce the NVP, and the results demonstrated that the intensity of nausea and vomiting was decreased in the course of 3 days after intervention.^[11] However, the results of a study by Pasha, who used four drops of peppermint essential oil in a water bowl before bedtime, reported that the intensity of nausea and vomiting in the peppermint aromatherapy group was reduced, but was not statistically significant. This difference can be due

Table 1: Pregnancy and demographic characteristics in two study groups

Variable	Intervention group Mean (SD) or No. (%)	Control group Mean (SD) or No. (%)	t, Z, χ^2	df	p
Age (Year)	27.15 (5.11)	26.13 (4.56)	1	88	0.320*
Education					
Elementary	3 (6.70)	4 (8.90)	-0.73		0.461**
Middle school	8 (17.80)	5 (11.10)			
Diploma	14 (31.10)	12 (26.70)			
University	20 (44.40)	24 (53.30)			
Occupation					
Householder	38 (84.40)	36 (80)	4.38	2	0.112****
Employed	7 (15.60)	5 (11.10)			
Work at home	0 (00)	4 (8.90)			
Income					
Income less than expend	11 (24.40)	7 (15.60)	0.11	1	0.735***
Income equal to expend	31 (68.90)	34 (75.60)			
Income more than expend	3 (6.70)	4 (8.90)			
Gestational age (week)	11.11 (2.97)	10.45 (3.12)	1.02	88	0.310*
Gravidity	2.02 (1.01)	1.75 (1.73)	1.30	88	0.197*
Taking medication (before intervention)					
Yes	11 (24.40)	11 (24.40)			1.000****
No	34 (75.60)	34 (75.60)			
Name of medication (before intervention)					
Ondansetron	7 (63.60)	8 (72.70)	2.35		0.781*****
Metoclopramide	1 (9.10)	2 (18.20)			
Ginger	2 (18.2)	0 (00)			
Vit B6	1 (9.10)	1 (9.10)			

*Independent *t*-test. **Mann-Whitney. ***Linear by linear Chi-square. ****Chi-square. *****Fisher exact test

Table 2: Comparison of mean (SD) scores of nausea and vomiting intensity in the two study groups before the intervention and within four days of intervention

Variable	Intervention group mean (SD)	Control group mean (SD)	t	df	p
Before intervention	7.91 (2.20)	7.46 (2.08)	0.98	88	0.328
First day	7.11 (2.20)	7.61 (2.47)	-1.01	87	0.315
Second day	6.13 (2.09)	7.61 (2.29)	-3.17	87	0.002
Third day	5.66 (2.00)	7.56 (2.54)	-3.92	87	<0.001
Fourth day	5.66 (2.08)	7.34 (2.84)	-3.17	87	0.002
ANOVA with repeated measures	$F=22.92$ $df=2.84$, $p<0.001$	$F=0.26$ $df=2.78$, $p=0.836$			

*Independent sample *t*-test

Table 3: Comparison of the mean (SD) score of fatigue intensity before and after the intervention

Variable	Intervention group	Control group	Independent sample <i>t</i> -test
Before intervention	37.42 (8.95)	36.66 (9.63)	$t=-1.03$ $df=87$, $p=0.302$
After intervention	35.73 (9.71)	37.93 (10.23)	
Paired <i>t</i> -test	$t=1.21$, $df=44$, $p=231$	$t=-0.98$ $df=43$, $p=331$	

to differences in the method of study, as the aim of this study was to reduce the frequency of nausea and vomiting in the morning. For this purpose, the peppermint essential oil was used during the nighttime sleep. On the other hand, the type of instrument used in this study was different as the Visual Analogue Scale (VAS) was used to measure the intensity of nausea and vomiting^[20] and we used a tool designed specifically for nausea and vomiting of pregnancy.

Our results contradict the result of Jolaerad *et al.* They carried out a RCT in which used inhalation aromatherapy with peppermint to reduce the NVP. Based on the results, the effect of aromatherapy with peppermint was similar to that of placebo. This could be due to the combination of aromatherapy in our study.^[13]

The aromatherapy with peppermint has been also used to reduce postoperative nausea and vomiting, as well as to

Table 4: Comparison of satisfaction with treatment, preference of the type of treatment and adherence to nutritional and lifestyle recommendations

Variable	Intervention group No. (%)	Control group* No. (%)	χ^2	df	p
The satisfaction of the treatment					
Yes	17 (37.80)	7 (15.90)	11.55	2	0.003
Partly	24 (53.30)	21 (47.70)			
No	4 (8.90)	16 (36.40)			
Prefer this type of treatment					
Yes	35 (77.80)	23 (52.30)	6.37	1	0.012
No	10 (22.20)	21 (47.70)			
Adhere to nutritional & lifestyle recommendations					
Yes	27 (60.0)	17 (38.60)	4.06	1	0.044
No	18 (40)	27 (61.40)			

*Valid percent reported because of missing data

attenuate nausea and vomiting caused by chemotherapy. The results of a review article showed that the inhalation aromatherapy with peppermint may reduce the intensity of postoperative nausea and vomiting as well as oncology patients.^[4] However, Hines believed that there was inadequate evidence to support the effectiveness of inhalation aromatherapy with peppermint to reduce postoperative nausea and vomiting, although its use is not harmful.^[21]

In this study, the effect of time was significant on the mean intensity of nausea and vomiting in the intervention group, in contrast to the control group, and the intensity of nausea and vomiting was decreased with time. In the study of Pasha and Yavari Kia, the intensity of nausea and vomiting in both groups was decreased with time. Although this decrease was higher in the intervention group than in the control group, there was no significant difference between the two groups in this regard.^[9,20] In the study of Jolaeerad, the intensity of nausea and vomiting in both groups was decreased during the intervention, but there was no significant difference between the two groups.^[13] Although, the author stated that this decrease in both groups was due to the effects of respiratory techniques (three deep breaths through the nose), we also used similar respiratory techniques in both groups. As a result, further research is needed in this area.

The results of the present study indicated that the combined aromatherapy had no effect on fatigue intensity. Fatigue, like nausea and vomiting, is one of the most common problems in women in the first trimester of pregnancy,^[22] and the results of studies showed that the NVP intensity can be directly related to the fatigue intensity during pregnancy.^[23,24] Contrary to this study, the results of a study by Abdel Ghani, who used peppermint and lavender aromatherapy, showed that combined inhalation aromatherapy reduced the fatigue intensity after the intervention.^[11] Perhaps this difference was due to differences in the type of drugs used in the study of Abdel Ghani, as the author said that this effect was more likely to result from the lavender intervention.

In this study, the participants in the intervention group were more satisfied with the treatment than the control group, as far as they preferred this method to the anti-nausea pills. Participants in both groups did not report any side effects during the intervention. Regarding the satisfaction, similar results were reported in Yavari Kia and Joulaeerad's study. The satisfaction of treatment in the intervention group was reported in 50 and 60.7% of patients in the two above studies, respectively. No adverse effects were reported in the Yavari Kia 's study, but in the Joulaeerad's, 4 patients in the intervention group and one in the control group reported complications such as headache, dizziness, and shortness of breath, all resolved within 24 hours.^[9,13] This difference might be due to the different combinations of drugs were used in our study.

The impossibility of examining the maternal and neonatal outcomes of the participants and the lack of control over their psychological state during the intervening days is one of the limitations of this study. According to the Cochrane review, there was little evidence that non-pharmacological methods were effective in reducing the NVP.^[2] As a result, more studies are needed in this area to recommend this method as an effective method for pregnant women.

Conclusion

Combined inhalation aromatherapy with lemon and peppermint can be recommended as an inexpensive and affordable method to reduce mild to moderate nausea and vomiting of pregnancy in women who are reluctant to use chemical drugs.

Acknowledgments

The authors would like to appreciate and thank the Research and Development Unit of Barij Essence Pharmaceutical Company for assisting in the preparation and formulation of the drug and placebo, as well as the Deputy of Research of Birjand University of Medical Sciences (NO: 1393-04-02) and all those who helped us to collect data.

Financial support and sponsorship

Birjand University of Medical Sciences

Conflicts of interest

Nothing to declare.

References

1. Khresheh R. How women manage nausea and vomiting during pregnancy: A Jordanian study. *Midwifery* 2011;27:42-5.
2. Matthews A, Haas DM, O'Mathúna DP, Dowswell T, Doyle M. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database Syst Rev* 2014;3:CD007575.
3. Jarvis S, Nelson-Piercy C. Management of nausea and vomiting in pregnancy. *BMJ* 2011;342:1407-12.
4. Lua PL, Zakaria NS. A brief review of current scientific evidence involving aromatherapy use for nausea and vomiting. *J Altern Complement Med* 2012;18:534-40.
5. Steel A, Adams J, Sibbritt D, Broom A. The outcomes of complementary and alternative medicine use among pregnant and birthing women: Current trends and future directions. *Womens Health* 2015;11:309-23.
6. Dante G, Pedrielli G, Annessi E, Facchinetti F. Herb remedies during pregnancy: A systematic review of controlled clinical trials. *J Matern Fetal Neonatal Med* 2013;26:306-12.
7. Arias BA, Ramón-Laca L. Pharmacological properties of citrus and their ancient and medieval uses in the Mediterranean region. *J Ethnopharmacol* 2005;97:89-95.
8. Setzer WN. Essential oils and anxiolytic aromatherapy. *Nat Prod Commun* 2009;4:1305-16.
9. Yavari Kia P, Safajou F, Shahnazi M, Nazemiyeh H. The effect of lemon inhalation aromatherapy on nausea and vomiting of pregnancy: A double-blinded, randomized, controlled clinical trial. *Iran Red Crescent Med J* 2014;16:e14360.
10. Yıldırım M, Desdicioğlu R, Kara H, Avşar A. The use of herbal supplements in pregnancy. *Ankara Med J* 2016;16:225-31.
11. Ghani RMA, Ibrahim ATA. The effect of aromatherapy inhalation on nausea and vomiting in early pregnancy: A pilot randomized controlled trial. *J Nat Sci Res* 2013;3:10-22.
12. Keifer D, Ulbricht C, Abrams TR, Basch E, Giese N, Giles M, *et al.* Peppermint (*Mentha piperita*): An evidence-based systematic review by the Natural Standard Research Collaboration. *J Herb Pharmacother* 2007;7:91-143.
13. Joulaeeraad N, Ozgoli G, Hajimehdipoor H, Ghasemi E, Salehimoghaddam F. Effect of aromatherapy with peppermint oil on the severity of nausea and vomiting in pregnancy: A single-blind, randomized, placebo-controlled trial. *J Reprod Infertil* 2018;19:32-8.
14. Fahimi F, Hrgovic I, El-Safadi S, Münstedt K. Complementary and alternative medicine in obstetrics: A survey from Iran. *Arch Gynecol Obstet* 2011;284:361-4.
15. Lane B, Cannella K, Bowen C, Copelan D, Nteff G, Barnes K, *et al.* Examination of the effectiveness of peppermint aromatherapy on nausea in women post-C-section. *J Holist Nurs* 2012;30:90-104.
16. Ebrahimi N, Maltepe C, Bournissen FG, Koren G. Nausea and vomiting of pregnancy: Using the 24-hour Pregnancy-Unique Quantification of Emesis (PUQE-24) scale. *J Obstet Gynecol Can* 2009;31:803-7.
17. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale: Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989;46:1121-3.
18. A'zimian M, Fallah-Pour M, Karimlou M. Evaluation of reliability and validity of the Persian version of Fatigue Severity Scale (FSS) among persons with multiple sclerosis. *Arch Rehabil* 2013;13:84-91.
19. Koç Z, Sağlam Z, Topatan S. Determination of the usage of complementary and alternative medicine among pregnant women in the Northern Region of Turkey. *Collegian* 2016;24:533-9.
20. Pasha H, Behmanesh F, Mohsenzadeh F, Hajahmadi M, Moghadamnia AA. Study of the effect of mint oil on nausea and vomiting during pregnancy. *Iran Red Crescent Med J* 2012;14:727-30.
21. Hines S, Steels E, Chang A, Gibbons K. Aromatherapy for treatment of postoperative nausea and vomiting. *Cochrane Database of Systematic Reviews*. 2018.
22. Nazik E, Eryılmaz G. Incidence of pregnancy-related discomforts and management approaches to relieve them among pregnant women. *J Clin Nurs* 2014;23:1736-50.
23. van Lier D, Manteuffel B, Dilorio C, Stalcup M. Nausea and fatigue during early pregnancy. *Birth* 1993;20:193-7.
24. Reeves N, Potempa K, Gallo A. Fatigue in early pregnancy: An exploratory study. *J Nurse Midwifery* 1991;36:303-9.