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Original Research Paper

The effect of aromatherapy with bitter orange (*Citrus aurantium*) extract on anxiety and fatigue in type 2 diabetic patients

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ABSTRACT

Objective: Studies have shown some complementary therapies to be effective in the management of diabetes and its comorbidities. The present study was conducted to evaluate the effect of an aromatherapy extract on anxiety and fatigue in type 2 diabetic patients.
Methods: 60 type 2 diabetic patients were randomly assigned in two groups: patients in the intervention group received bitter orange (*Citrus aurantium*) extract inhalation aromatherapy for three consecutive nights before sleeping, whereas patients in the control group received usual care. Patients' level of anxiety and fatigue was recorded before and after intervention using Visual Analog Scale (VAS).
Results: The mean score of anxiety in patients in the intervention group before and after intervention were 63.13 ± 40.42 and 52.9 ± 3.57, respectively ($P < 0.001$). The mean score of anxiety in patients in control group before and after intervention were 56.73 ± 39.52 and 56.6 ± 3.93, respectively ($P = 0.468$). The mean score of fatigue in patients in intervention group before and after intervention were 65.7 ± 39.63 and 63 ± 3.93, respectively. The mean score of fatigue in patients in control group before and after intervention were 56.5 ± 43.15 and 56.26 ± 4.28, respectively ($P = 0.436$).
Conclusion: The use of bitter orange extract inhalation aromatherapy is a potentially effective intervention to relive type 2 diabetics' anxiety and fatigue. Further study in this regards are recommended.

1. Introduction

Over the past thirty years, the international community has witnessed a 4-fold increase in diabetes [1]. In 2018, one in every 11 adults suffered from diabetes, of which 90% was type 2 diabetes [1]. It is estimated that in the year 2035, approximately 592 million people will have diabetes [2]. Diabetes is particularly common in Asian countries [1]. The prevalence of diabetes in Iran was evaluated between the years 2005 and 2011, and more than 4 million people in Iran were diagnosed with diabetes in 2011, a 35% increase compared to 2005 [3]. Diabetes is the ninth leading cause of death in the world, with cardiovascular disease is the leading cause of death in these patients [1]. Weight gain, obesity, nutrition and low-mobility lifestyle are some of the factors that increase the prevalence of type 2 diabetes [1,2].

Patients with type 2 diabetes face a number of co-morbid problems as a result of their diabetes, including fatigue and anxiety [4–6]. These problems can be extreme - the results of a study conducted in 2016 showed that more than 90% of women and men with type 2 diabetes expressed their anxiety in extreme range [7]. Some factors such as having a chronic disease, blood sugar fluctuations and the inability to control it, the need for hospitalization, complications of diabetes (including cardiovascular disease, nephropathy and retinopathy) and long-term treatment can also lead to further anxiety in diabetics [8–12]. Fatigue may also be more prevalent in diabetics, with the results of another study, which examined fatigue in women with diabetes, showed that the fatigue in this group of women is significantly higher than healthy women [4]. Factors such as having a chronic disease, blood glucose levels and hemoglobin A1C, sleep disorders and decreased activity of daily life can cause fatigue in diabetic patients [13]. Anxiety and fatigue in diabetic patients can also have significant side effects. Disrupted daily functioning and decreased quality of life are often due to fatigue [14] and inconsistency with disease, decreased quality of life, and an increase in the risk of death can be associated

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with anxiety [10,15,16]. Although, in several studies, fatigue and anxiety in patients with type 2 diabetes have been studied and recommendations to screen patients for these conditions have been developed [17], our searches showed very few studies examining strategies for the treatment or reduction of these complications. In many cases, fatigue and anxiety in patients with type 2 diabetes remains untreated and neglected.

Use of complementary and alternative medicine is increasing globally for treatment of numerous conditions [18]. Aromatherapy is one traditional methods of complementary medicine commonly used in Iran [19]. Several studies have determined the positive effects of aromatherapy on the reduction of fatigue and anxiety in patients with diseases other than diabetes. For instance, a study of the effects of aromatherapy treatment, using lavender oil, on the anxiety of patients undergoing gastrointestinal surgery found that aromatherapy, using lavender oil, significantly alleviated the anxiety of these patients [20]. Asazawa et al. studied the effects of aromatherapy treatment on the fatigue in women during childbirth. The results of this study showed that aromatherapy treatment is very effective in reducing fatigue in women during childbirth [21]. Various extracts are used in aromatherapy, with one of the more common extracts being bitter orange extract [19]. Bitter orange extract is originated from a herb [1,11] called *Citrus aurantium*, commonly known as bitter orange. It is produced in the Northern and Southern parts of Iran. Its essence is consisted of 35% of different hydrocarbons, 47% of Terpene alcohols such as Linalool, Terpineol, Geraniol, Nerol, Flavonoid and all their acetates, 6% of Nerolidol and 0.7%–1.1% of Indole [21] (Fig. 1).

Considering that aromatherapy treatment has been effective in reducing the anxiety and fatigue of patients with different diseases, it has been hypothesized that aromatherapy treatment may have effects on reducing the anxiety and fatigue in diabetic patients. However, there have been no studies of aromatherapy for treatment of anxiety and fatigue in diabetic patients. Therefore, the present study was conducted with the aim of studying the effects of aromatherapy treatment, using bitter orange extract, on anxiety and fatigue of patients with type 2 diabetes.

2. Material and methods

2.1. Sample and sampling method

The present clinical trial was conducted during July to October 2016. Subjects were recruited from patients who were referred to Qazvin Velayat and Boali Sina hospitals in Iran. The sample consisted of 60 patients, who were randomly allocated to intervention (aromatherapy) and control groups. Randomization was performed using a simple randomization method.

The inclusion criteria were: diagnosed as T2D, aged 30–65 years, and having anxiety and fatigue based on patients' reports. Exclusion criteria were: any health crisis in the subjects during the intervention, history of asthma and

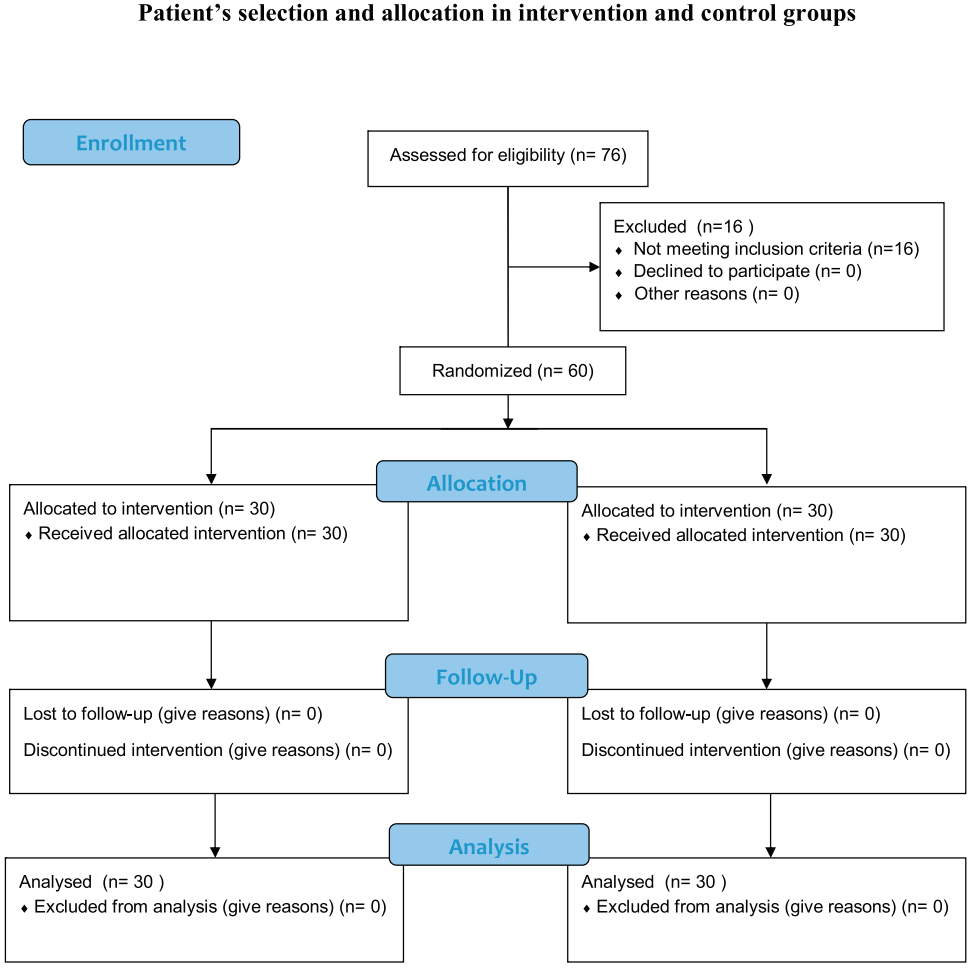

Fig. 1. Patient's selection and allocation in intervention and control groups.

allergies, history of psychiatric disorders, taking anti-anxiety and hypnotic drugs.

The sample size was determined using the following sample size formula. In order to determine the sample size, significance level (α(of 0.05 and statistical power (β-1) of 0.80 were considered from previous studies. After considering the failure rate, the sample size was calculated as 30 subjects in each group [22].

$$N = 1/1\text{-}f \times 2\,(Z_{1-\alpha/2} + Z_{1-\beta})^{2}\,S^{2} / (\mu_1 - \mu_2)^{2}$$

2.2. Instruments

1) A structured demographic checklist. This checklist included patient's age, sex, level of education, marital status and disease duration.
2) Visual Analogue Scale (VAS) for assessing anxiety and fatigue: VAS used in present study was 0 mm–100 mm scale is a10 cm line, 10 cm long. The subjects were asked to mark a point on the line that represented how they feel anxiety and fatigue at the time. VAS is a valid and reliable measure for assessing the intensity of anxiety and fatigue [23]. Patients' anxiety and fatigue was assessed by VAS before and after intervention.

2.3. Ethical considerations

This study was approved by the Ethical Committee of Medical Research at Iran University of Medical Sciences. Data were collected after the informed consent was obtained from the subjects. This research project is taken from a thesis with the ethical code of IR.IUMS.REC 1395.9311686017. Protocol of present study was also assessed and approved by Iranian registry of clinical trial (IRCT 2017011520145 N4).

2.4. Procedure

Patients in the intervention group, in addition to usual care, received aromatherapy using bitter orange extract 20% concentration (*Citrus aurantium* 20%) inhalation. Patients inhaled eight drops of bitter orange extract 20% before sleeping, and the cotton was placed on the collar of their shirt until morning. The intervention was conducted from 10 PM to 6 A M on three consecutive days. The Bitter orange essence, produced by the Hegrat Essence Company (Kashan, Iran), was used in present study. Patients in control group received usual care.

2.5. Data analysis

The data were analyzed using the SPSS software version 22. Demographic variables were analyzed using descriptive statistics (mean, standard deviation and percentage). The homogeneity tests of demographic variables in the aromatherapy and control groups were performed using Chi-square test. Given not normal distribution of anxiety and fatigue, Mann-Whitney U test was used to analyse the anxiety and fatigue level before and after the intervention. P-value of less than 0.05 considered significant in all test.

3. Results

The mean age of patients in the intervention group was 58.30 ± 7.62 year, 46.7% of them were male, and 83.3% were married. The mean age of patients in control group was 59.23 ± 6.73, 26.7% of them were male, and 76.6% were married.

Table 1
Participants demographics characteristics.

Categories	Aromatherapy n (%)	Control group n (%)	$\chi 2$[a]	p
Gender			4.44	0.108
Male	14 (46.7%)	8 (26.7%)		
Female	16 (53.3%)	22 (73.3%)		
Age (year)			1.329	0.514
30–49	5 (16.7%)	4 (13.3%)		
50–59	7 (23.3%)	4 (13.3%)		
60–65	18 (60%)	22 (73.3%)		
Marital Status			0.483	0.785
Single	1 (3.3%)	1(3.3%)		
Married	25 (83.3%)	23(76.6%)		
Widower	4 (13.3%)	6(20%)		
Divorced	0 (0%)	0(0%)		
Education			2.20	0.698
Lower than middle school	27(90%)	28(93.3%)		
High School	2(6.7%)	2(6.7%)		
More than College	1(3.3%)	0(0%)		
Disease duration (year)			0.737	0.864
1–3	7(23.3%)	7(23.3%)		
3–5	3(10%)	2(6.66%)		
5–10	6(20%)	9(30%)		
>10	14(46.6%)	12(40%)		
Occupation			5.535	0.237
Full time job	1(3.3%)	3(10%)		
Part time job	2(6.7%)	1(3.3%)		
House wife	14(46.7%)	20(66.7%)		
Unemployed	4(13.3%)	3(10%)		
Retired	9(30%)	3(10%)		

[a] Chi-square.

There was no significant difference between the two groups in terms of demographics characteristics ($p > 0.05$). Table ... showed the patients demographics characteristics in details (Table 1).

The mean score of anxiety in patients in intervention group before and after intervention were 63.13 ± 40.42 and 52.9 ± 3.57, respectively. This decrease in anxiety level before and after intervention was statistically significant ($P < 0.001$). The mean score of anxiety in patients in control group before and after intervention were 56.73 ± 39.52 and 56.6 ± 3.93, respectively ($P = 0.468$) (Table 2). The mean score of fatigue in patients in intervention group before and after intervention were 65.7 ± 39.63 and 63 ± 3.93, respectively. This decrease in fatigue level before and after intervention was statistically significant ($P < 0.014$). The mean score of fatigue in patients in control group before and after intervention were 56.5 ± 43.15 and 56.26 ± 4.28, respectively ($P = 0.436$) (Table 2).

4. Discussion

To our knowledge, this is the first study that has examined the effect of inhalation aromatherapy on anxiety and fatigue in patients with type 2 diabetes. The results of present study revealed that inhalation aromatherapy with bitter orange extract as a complementary and alternative therapy significantly reduced the level of anxiety and fatigue in type 2 diabetic patients.

Anxiety is common syptom among diabetic patients. Anxiety in this group of patients can cause several complications such as tension, fear, depressed mood, cardiovascular and gastrointestinal symptoms, insomnia, somatic symptoms, autonomic symptoms, respiratory and genitourinary symptoms [24]. Management of anxiety with nonpharmacological methods is important, particularly in groups such as diabetics that may already be on multiple medications. Patients who received aromatherapy in our study reported lower levels of anxiety compared to those who received the usual nursing care. Our literature searches did not show any

Table 2
Level of anxiety and fatigue before and after intervention in intervention and control groups.

Outcome measure	Aromatherapy group(n=30) Mean ± SD	Control group(n=30) Mean ± SD	p	z
Anxiety (VAS) Score Before the intervention			0.468	−0.726
After the intervention	63.13 ± 40.42	56.73±39.52		
	52.9 ± 3.57	56.6±3.93		
Fatigue (VAS) Score before and after the study	65.7±39.63	56.5±43.15	0.436	−0.778
	63±3.93	56.26±4.28		
Differences in Anxiety (VAS) Score before and after aromatherapy	10.23 ± 9.92	3.23 ± 5.48	<0.001	−5.18
Differences in Fatigue(VAS) Score before and after aromatherapy	2.7±5.52	0.23±1.69	0.014	−2.451

*Mann-Whitney Test.

study that examined the effects of inhalation aromatherapy with bitter orange extract on anxiety of type 2 diabetic patients. However, studies on other groups of patients, with other extracts, has shown similar findings. Nagafi et al., examined the effect of aromatherapy on the anxiety of patients with myocardial infarction [25]. Patients in Nagafi et al., study received inhalation aromatherapy with lavender aroma twice a day for two subsequent days. Similar to finding of the present study, results of Nagafi et al., study revealed that aromatherapy is an effective method to relieve patient's anxiety [25]. Barati et al., examined the effect of inhaling rose water aromatherapy on anxiety in hemodialysis patients for 4 weeks. They used the state-trait anxiety inventory of Spielberger to investigate the anxiety level of the patients. Similar to findings of present study, results of Barati et al., study revealed that the aromatherapy using rose water significantly alleviate the anxiety of hemodialysis patients [26].

Fatigue is also common and distressing complaint among diabetics. Fatigue may have a negatie impact on diabetics ability to perform daily diabetes self-management tasks [27]. Management of fatigue is therefore an important issue for improving diabetic' clinical situations. The results of the present study also revealed that using inhalation aromatherapy with bitter orange extract significantly decreased the fatigue of patients with type 2 diabetes. Our literature searches did not show any study that examined the effects of inhalation aromatherapy with bitter orange extract on fatigue of type2 diabetic patients. However, studies on the other groups of patients showed similar findings. Sung-Hee et al. examined the effects of aromatherapy inhalation on fatigue of postpartum women. The results of Sung-Hee et al., study revealed that aromatherapy is an effective intervention for alleviating fatigue [28]. Muz & Taşc examined the effects of inhalation aromatherapy on fatigue level of hemodialysis patients. Patients in Muz & Taşc study received sweet orange and lavender oil aromatherapy before going to bed every day for one month. Similar to finding of present study, the results of Muz & Taşc study revealed that inhalation aromatherapy is effective intervention for reliving fatigue in hemodialysis patients [29].

5. Limitation

Using self-reports to examine the anxiety and fatigue is the limitation of our study. Additionally, this study examined a specific oil (bitter orange extract) and may not be generalisable to other aromatherapy interventions.

6. Conclusion

Aromatherapy is a readily available and low cost intervention. Side effects of this method are alsorare. Findings from this study suggest that aromatherapy may be an effective intervention to decrease the anxiety and fatigue in type 2 diabetic patients. It is recommended that healthcare providers of diabetic patients consider nonpharmacological methods for management of anxiety and fatigue. Further studies are strongly recommended, with time of patients' follow up after intervention increased.

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