REVIEW

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The effects of inhaled aromatherapy on complications of hemodialysis patients: a systematic review

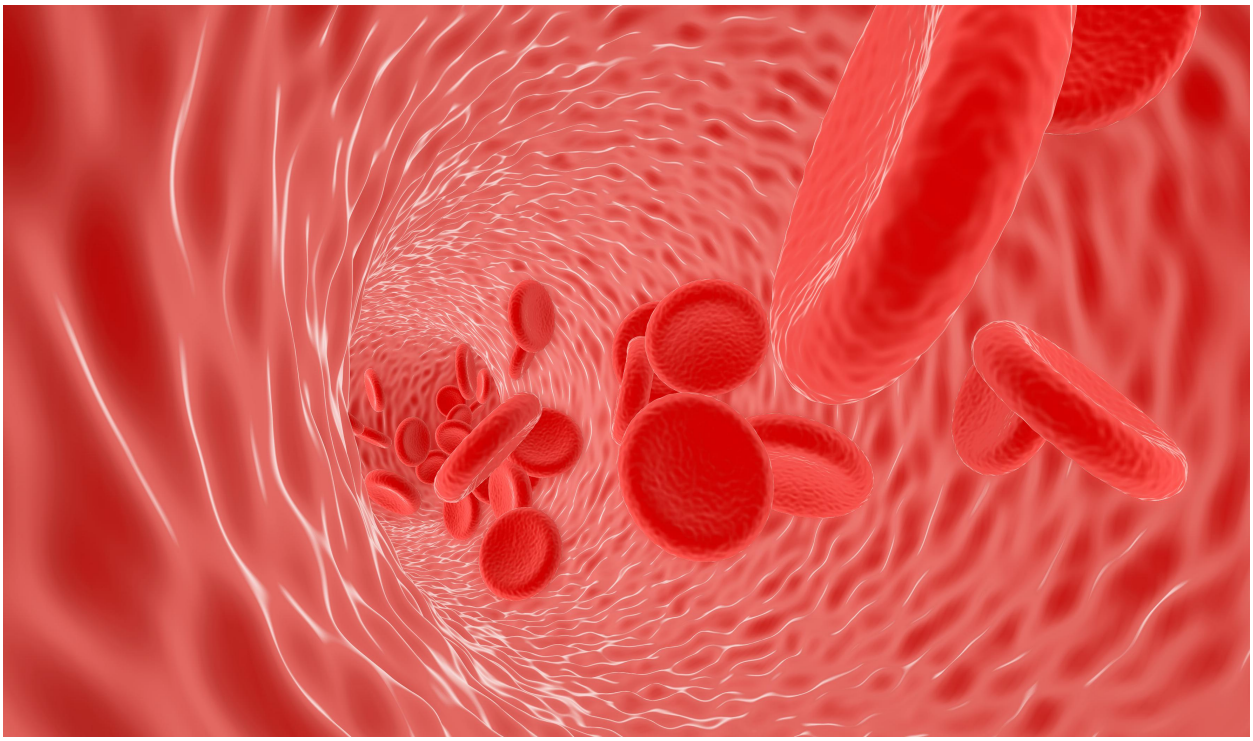
Xiao-Xiao Yang[1], Yuan-Yuan Chen[1], Fan-Jie Meng[2*]

[1]Graduate college, Tianjin University of Traditional Chinese Medicine, Tianjin 301617, China. [2]College of Health Engineering, Tianjin University of Traditional Chinese Medicine, Tianjin 301617, China.

*Corresponding to: Fan-Jie Meng, College of Health Engineering, Tianjin University of Traditional Chinese Medicine, No. 10, Poyanghu Road, West Area, Tuanbo New Town, Jinghai District, Tianjin 301617, China. E-mail: mfj127@tjutcm.edu.cn.

Highlights

This review systematically evaluated the efficacy of inhalation aromatherapy in patients undergoing hemodialysis. The results showed that inhaled aromatherapy can reduce stress, depression, arteriovenous fistula puncture pain, anxiety and fatigue, and improve the perceived well-being and quality of sleep in hemodialysis patients.



Abstract

Objective: To evaluate the effect of inhaled aromatherapy on complications in patients undergoing hemodialysis. **Methods:** We search the PubMed, Web of Science, Cochrane Library, Embase and China Biomedical Literature Database from their inception to December, 2019 to collect randomized controlled trials about the effects of inhaled aromatherapy on hemodialysis complications. Literatures screening, data extraction and risk of bias assessment for the included studies were conducted by two reviewers independently. We summarized all findings with qualitative analysis. **Results:** A total of 15 studies with 967 participants were included in the systematic review. Inhaled aromatherapy can reduce anxiety, depression, arteriovenous fistula puncture pain, stress and fatigue, and improve the quality of sleep and perceived well-being in hemodialysis patients. **Conclusion:** Inhaled aromatherapy had certain effects on complications in hemodialysis patients, which can be used as a simple and convenient treatment, but further research was needed to determine standardized implementation procedures and standards.
Keywords: Inhalation aromatherapy, Randomized controlled trial, Systematic review, Hemodialysis patients

***Abbreviations*:**

CKD, chronic kidney disease; MHD, maintenance hemodialysis; RCT, randomized controlled trial; HAM-A, Hamilton Anxiety Assessment Scale; VAS, Visual Analogue Scale; PSQI, Pittsburgh Sleep Quality Index; FSS, Fatigue Severity Scale; STAI, State-Trait Anxiety Inventory; BFI, Brief Fatigue Inventory; BAI, Beck Anxiety Inventory; PFS, Piper Fatigue Scale; HADS, Hospital Anxiety and Depression Scale; DASS-21, Depression Anxiety Stress Scales.

***Competing interests*:**

The authors declare that there is no conflict of interest.

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Background

Chronic kidney disease (CKD) has become a major public health problem in the world [1]. Maintenance hemodialysis (MHD) is the main treatment for patients with chronic kidney disease, as more than 80% of patients with CKD [2]. The number of maintenance hemodialysis patients in China has up to 553,000 [3]. However, MHD can cause severe complications, which seriously affect the quality of life of patients. Research shows that 20% to 60% MHD patients have anxiety, stress and depression, 60% to 97% patients have fatigue and 45% to 85%patients suffered from sleep disorder [4–7].

Studies indicate that selective serotonin reuptake inhibitors such as citalopram, benzodiazepines, tricyclic antidepressants can improve complications in hemodialysis patients but may accompanied with high protein-binding, aggravated nausea, increased bleeding tendency, QT syndrome, tip torsional ventricular tachycardia [8–10]. Non-pharmacological methods, such as cognitive behavior therapy, humor therapy, aromatherapy, melodiotherapy, exercise therapy, can effectively reduce the complications of hemodialysis patients with the advantage of safety and cheapness [11]. Aromatherapy is an important non-pharmacological method to reduce, prevent or treat some diseases using natural plant spices or aromatic essential oils extracted from them. Studies have shown that aromatherapy can reduce complications in hemodialysis patients such as anxiety, fatigue, itching, arteriovenous fistula puncture pain, sleep quality, depression, stress and headache [12]. Inhalation pathway is the main way of aromatherapy, which refers to the method of treating, alleviating or preventing various diseases through natural volatile inhalation and heating release inhalation of aromatic essential oil, acting on the two target organs of human brain and lung. The common used aromatic essential oils are lavender, rosemary, bergamot, rose, perilla, neroli oil and compound essential oils mixed in a certain proportion [13]. Some studies have shown that inhaled aromatherapy can improve the complications of hemodialysis patients, such as fatigue, anxiety, stress, depression and so on, but results of existing studies on aromatherapy in the treatment of hemodialysis complications are inconsistent [14–16]. The type, dose, inhalation mode and frequency of available essential oils also have not been summarized. To the best of the researchers' knowledge, there is no systematic review to assess the effects of inhaled aromatherapy on complications in hemodialysis patients. The purpose of this systematic review was to evaluate the effects of inhaled aromatherapy with different essential oils, doses, inhalation modes and frequencies on complications in hemodialysis patients and provide guidance for the application of inhaled aromatherapy in the adjuvant therapy of hemodialysis patients in China.

Methods

Search strategy

The published literatures in Cochrane Library, PubMed, Embase, Web of Science and China Biomedical Literature Database were searched, and the references included in the literatures were also searched. The time of literature retrieval was from the establishment of the database to December 2019. The search terms were as follows: (dialysis OR hemodialysis OR dialyses, renal OR h*emodialysis OR end stage kidney failure) AND (aromatherapies OR aroma therapy OR essential oil OR aroma* OR essence OR lavender OR sweet orange OR rose OR bergamot OR rosemary) AND (clinical trials OR randomized trials OR randomized clinical controlled OR RCT). Mesh search terms were used. For example, the search strategy of PubMed is (dialysis OR hemodialysis OR exracorporeal blood cleansing OR hemodialyse OR hemorenodialysis OR dialyses, renal OR dialysis, extracorporeal OR extracorporeal dialyses OR h*emodialysis OR hemodiafiltration[Mesh] OR renal dialysis[Mesh] OR end stage kidney disease OR end stage kidney failure OR end stage renal dysfunction OR end stage renal failure OR end-stage kidney failure OR end-stage renal disease OR stage 5 kidney disease OR ESRD OR renal insufficiency[Mesh]) AND (aromatherapies OR aroma therapy OR aroma therapies OR essential oil OR aroma* OR essence OR lavender OR sweet orange OR rose OR bergamot OR rosemary OR aromatherapy[Mesh]) AND (clinical trials OR randomized trials OR clinical trials, randomized OR randomized clinical controlled OR random allocation OR double-blind method OR single-blind method OR cross-over studies OR multicenter studies OR placebo* OR RCT OR randomly OR randomed OR randomized controlled trials as topic[Mesh]) search terms have been modified and adjusted in other different databases. The two persons searched independently according to the specified admission and exclusion criteria at the same time, and used EndNote X9 software for document management, and in case of differences, the third party intervened to discuss and decide.

Inclusion and exclusion criteria

Type of study. Randomized controlled trial (RCT) published at home and abroad.

Subjects. Patients over 18 years old with end-stage renal disease who received hemodialysis for more than 3 months.

Intervention measures. The experimental group was given inhaled aromatherapy, and the type, concentration, inhalation mode and frequency of essential oil were not limited and the control group was given distilled water, placebo or no intervention.

Outcome. Hamilton Anxiety Assessment Scale (HAM-A) were used to evaluate anxiery score. The Hospital Anxiety and Depression Scale (HADS) and Depression Anxiety Stress Scale (DASS-21) scale were used to assess the depression stress and anxiety level. Arteriovenous fistula puncture pain, quality of sleep and perceived well-being were assessed by Visual Analogue Scale (VAS) and Pittsburgh Sleep Quality Index (PSQI).

Exclusion criteria. ① Full-text literature is not available; ② literature with full text but missing or unavailable important data; ③ literature published repeatedly in the same study; ④ in the experimental group, aromatherapy combined with other adjuvant therapy was used for intervention.

Literature screening and data extraction

Literature screening and data extraction according to the purpose and inclusion and exclusion criteria of this study, the literature was screened independently by two researchers, and the preliminary screening was carried out by reading the title and abstract, and the literature after screening needs to be read in full text. Remove the full-text literature and exclude the Chinese and English literature that do not meet the inclusion criteria. A third party was invited to participate in the discussion on the literature screening criteria with different opinions and decide whether to include the literature or not. The researchers extracted the data according to the unified data extraction table, including the basic information of the literature, sample size, intervention time, inhaled aromatherapy intervention methods, routine nursing group intervention methods, outcome indicators.

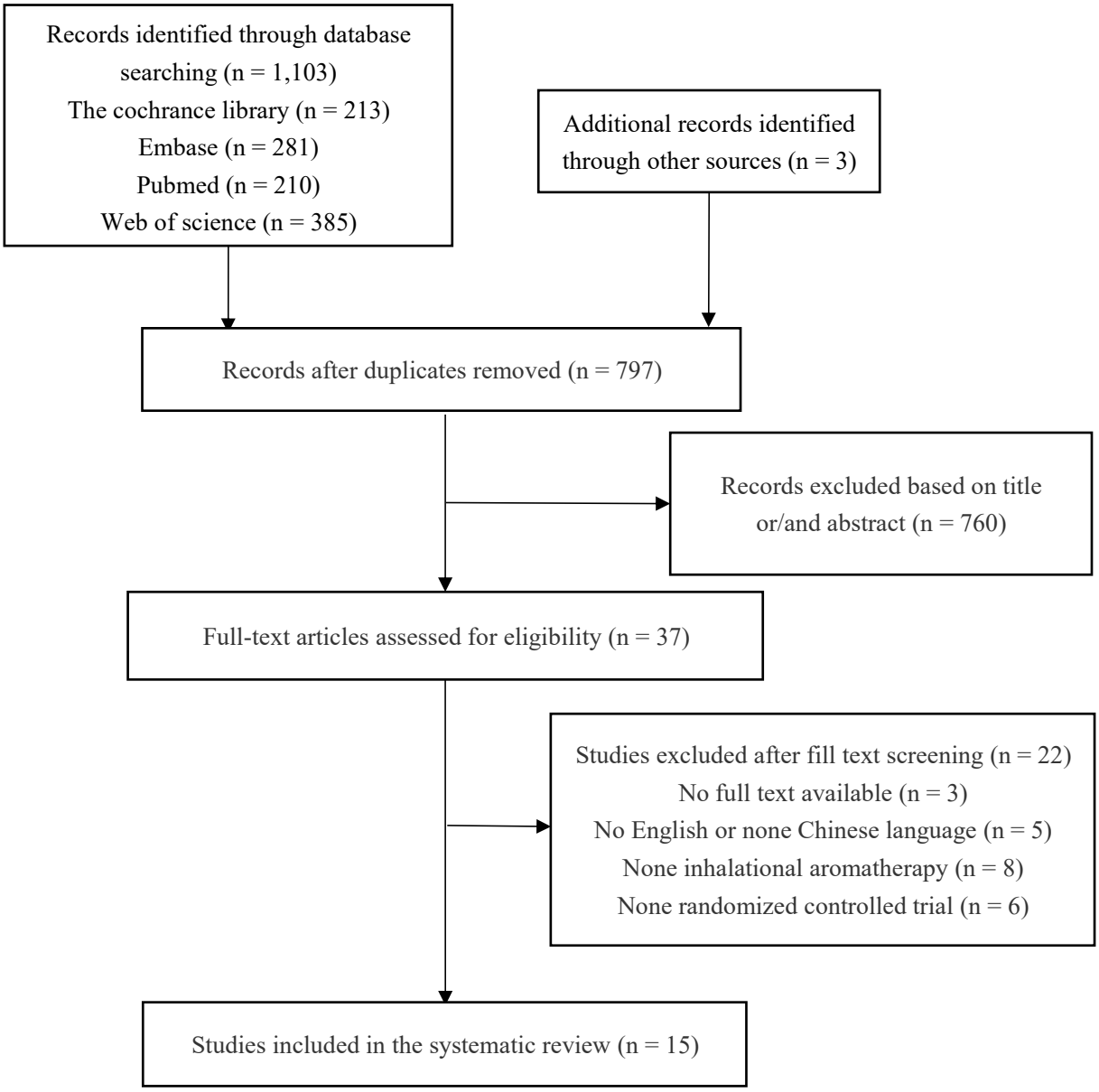

Figure 1 Study selection flow chart.

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Risk of bias assessment

It was independently completed by two researchers to evaluate the quality of the literature, and there were different opinions to seek a third party to participate in the discussion, and finally reached an agreement. The researchers used the quality evaluation method recommended by the Cochrane System Evaluation Manual 5.1.0 to evaluate the quality of RCT from seven aspects: ① random sequence generation; ② allocation concealment; ③ blinding of participants and personnel; ④ blinding of outcome assessment; ⑤ incomplete outcome data; ⑥ selective reporting; ⑦ other sources of bias. The evaluator made a low-risk, high-risk and unclear judgment on each research.

Search results

According to the pre-set retrieval strategy, 1,105 articles were initially detected, and 37 articles were initially included by reading topics and abstracts, excluding reviews, animal experiments and irrelevant studies. Further reading excluded 23 articles that did not meet the criteria and could not extract data, of which 5 were non-Chinese and English articles, 6 were non-RCT articles, 8 were non-inhaled aromatherapy, and 4 were unable to obtain the full text. Finally, 14 English articles [14–27] and 1 Chinese article [28] were included. The flow chart of study selection was shown in Figure 1.

Description of the subjects and quality assessment

The basic characteristics of the literature included are shown in Table 1. The total number of subjects in all studies was 967, with 478 females (49.4%) and 489 males (50.6%). The included studies are mainly in Iran (n = 9) [14, 15, 17–19, 21, 24–26], Turkey (n = 5) [16, 20, 22, 23, 27], China (n = 1) [28]. The quality of the methodology included in the study is detailed in Table 2.

Intervention

Intervention group. All the interventions evaluated in this system are inhaled aromatherapy, but there are some differences in the frequency, dose, duration of aromatherapy, and the distance between the source of aromatherapy and the subject's nose. The dose of inhaled aromatherapy is 2 to 5 drops, and the most commonly used doses are 2 drops and 3 drops. In most studies, the diluted essential oil was poured onto a cotton ball, gauze, or handkerchief and placed at an appropriate distance (5–30 cm) next to the patient's collar or pillow. Then the patient was asked to take a deep breath or breathe normally. Unlike other studies, Huang et al. [24] poured diluted essential oil into an electrically heated aromatherapy light and asked patients to lie 0.5 meters away from the light and breathe calmly. According to different research purposes, inhaled aromatherapy is mostly used in patients during hemodialysis, before going to bed or getting up in the morning, each time lasts from 5 minutes to the whole night, but 15–20 min is the most, the frequency of intervention is 2 times/week to 2 times/day, mostly 3 times/week, the total intervention time is 1 week to 2 months, mostly one month.

Control group. In the study, the main intervention measures in the control group were placebo and usual care.

Type of essential oils

The essential oils used in inhalation aromatherapy are generally pure essential oils, diluted essential oils or two or more essential oils mixed in a certain proportion. The concentrations of essential oils used in the study ranged from 1% to 25%. The type of essential oil is lavender essential oil diluted with sweet almond oil according to a certain proportion (n = 7) [14–18, 21, 25], lavender essential oil (n = 3) [20, 23, 26], lavender essential oil diluted with distilled water (n = 1) [28], Damask rose essential oil (n = 1) [19], Rose essential oil (n = 1) [24], Sweet orange essential oil (n = 1) [26], Lavender essential oil mixed with rosemary essential oil (n = 1) [27], Lavender essential oil mixed with sweet orange essential oil (n = 1) [22].

Complications and measurement tools

The complication included in the literature study was fatigue (n = 6) [18, 22, 23, 25–27], anxiety (n = 7) [14, 15, 19, 20, 23, 24, 28], depression (n = 2) [14, 19], sleep quality (n = 2) [20, 22], stress (n = 1) [19], pain of arteriovenous fistula puncture (n = 3) [16, 17, 28], perceived sense of well-being (n = 1) [21]. The most commonly used measurement tools were VAS (n = 7) [16, 17, 20–22, 27, 28], Fatigue Severity Scale (FSS, n = 3) [18, 23, 26], State-Trait Anxiety Inventory (STAI, n = 3) [15, 24, 28] and Brief Fatigue Inventory (BFI, n = 2) [25, 27]. Other measurement tools were Beck Anxiety Inventory (BAI) [23], PSQI [22], Piper Fatigue Scale (PFS) [22], HAM-A [20], Hospital Anxiety and Depression Scale (HADS) [14] and Depression Anxiety Stress Scales (DASS-21) [19].

Effect of inhalation aromatherapy on complications of hemodialysis

Fatigue. Six studies [18, 22, 23, 25–27] evaluated the effect of inhaled aromatherapy on fatigue in hemodialysis patients. The results of meta-analysis showed excessive heterogeneity, so only descriptive analysis was conducted in this paper. Four studies [18, 23, 25, 26] intervened with lavender essential oils, three of which [23, 25, 26] showed that inhaling lavender essential oils could reduce the fatigue of hemodialysis patients ($P < 0.05$). Ahmady S. et.al. [26] reported that the mean of fatigue before and after the intervention in lavender essential oil group was (47.83 ± 14.8) and (30.27 ± 13.9), respectively ($P = 0.01$). However no significant difference in the control group,

Table 1 Characteristics of the participants included in the selected studies

First author (year)	Study characteristics 1. Design 2. Sample 3. Country	Intervention 1. Essential oil type and dose 2. Administration method 3. Duration of per session/ frequency/total duration of intervention	Comparison	Outcome and measure
Ahmady S 2019 [26]	RCT 90 Iran	Group 1: lavender essential oil (5 drops). Group 2: orange essential oil (5 drops). Each essence was poured on a cotton ball and pinned to the patient's collar. 30 min/seven times a week/ two weeks. 3 times per week at hospital (the first 30 min of hemodialysis). 4 times per week at home (half an hour before the nighttime sleep).	Five drops of distilled water were used similarly.	1. Fatigue 2. FSS
Hassanzadeh M 2018 [25]	RCT 70 Iran	5% lavender essential oil (2 drops). Lavender essential oil inoculated in sweet almond oil was added on a cotton ball and pinned to the subjects' collar and the patients were asked to breathe as normal. 15-20 min/twice a day/ four weeks (in the morning after waking and before bed at night).	Routine care	1. Fatigue 2. BFI
Bagheri-Nesami M 2016 [18]	RCT 59 Iran	5% lavender essential oil (3 drops). A cotton ball soaked in lavender essential oil (diluted1: 20 with sweet almond oil) was attached to each patient's collar and they were then asked to breathe slowly. 10 min/three times a week/4 weeks.	Routine care	1. Fatigue 2. FSS
Muz G 2017 [22]	RCT 62 Turkiye	Sweet orange and lavender oil (1:1) (one drop Sweet orange and one drop lavender). Put oils almost 5 cm under nose before bed. 2 min/every day/1 month.	Routine care	1. Sleep quality and fatigue 2. PSQI, VAS and PFS

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Table 1 Characteristics of the participants included in the selected studies (*continued*)

First author	Study characteristics 1. Design 2. Sample 3. Country	Intervention 1. Essential oil type and dose 2. Administration method 3. Duration of per session/ frequency/total duration of intervention	Comparison	Outcome and measure
Bicer S 2017 [27]	RCT 50 Turkey	Lavender and rosemary (3 drops). Lavender and rosemary oils were dripped in it and the patients were inhaled from an approximately 30 cm distance at the last hour of every dialysis session. 5 min/three times a week/one week.	Sunflower oil (no therapeutic value) were used similarly	1. Fatigue 2. BFI/VAS
Karadag E 2019 [23]	RCT 60 Turkey	2% lavender oil (2 drops). Before hemodialysis when they came to hemodialysis of lavender oil were dropped on a 2×2 cm gauze dressing, placed on the chest area of the patients' clothes (about 10 cm distance to the nose). 20 minutes/2 or 3 times a week /30 days.	Routine care	1. Fatigue and Anxiety 2. FSS and BAI
Dehkordi AK 2017 [19]	RCT 60 Iran	2% Damask rose oil (3 drops). Piece of cloth smeared the damask rose oil with a constant density of was attached to the patient's collar and the patient was asked to breathe normally. One hour/three times a week/two months.	Usual care	1. Depression, anxiety and stress 2. DASS-21
Kiani F 2016 [15]	RCT 70 Iran	5% lavender (2 drops). Lavender essence combined with sweet almond oil was poured by dropper on cotton and was attached by pin to patients' collar in addition to common cares of hemodialysis ward and then they were asked to breathe normally. 15–20min/two times a week/Four weeks.	Usual care	1. Anxiety 2. STAI

Table 1 Characteristics of the participants included in the selected studies (*continued*)

First author	Study characteristics 1. Design 2. Sample 3. Country	Intervention 1. Essential oil type and dose 2. Administration method 3. Duration of per session/ frequency/total duration of intervention	Comparison	Outcome and measure
Senturk A 2018 [20]	RCT 34 Turkey	Lavender oil (2 drops). Drip lavender oil into the box and to place it 15 to 20 cm away from the pillow. One night/every day/1 week (30 min before go to bed).	Usual care	1. Sleep quality and anxiety 2. VAS and HAM-A
Barati F 2016 [24]	RCT 46 Iran	25% rose water (3drops). Put three drops of rose water on a clean absorbent cotton handkerchief using a dropper each night before sleeping. 15–20 min/ever night/four weeks.	Usual care	1. Anxiety 2. STAI
Bagheri-Nesami M 2014 [17]	RCT 92 Iran	Lavender essence (3 drops). The essence was diluted 1:10 with sweet almond oil. A cotton ball soaked in diluted lavender essence was kept at a 10 cm distance from the patients' nose and they were asked to breathe slowly. 5 min/three times a week/one week.	The smell of lavender without its properties essence used similarly.	1. Pain of arteriovenous fistula puncture. 2. VAS
Taşan E 2019 [16]	RCT 60 Turkey	1:10 ratio of lavender and sweet almond oil (3 drops). The mixture oil was dripped on the sterile sponge and place data distance of 10 cm away from patient's nose, whereupon the patient was told to inhale it prior to inserting the fistula needle. 3 to 5 min/-/three consecutive HD sessions.	Usual care	1. Pain of arteriovenous fistula puncture 2. VAS

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Table 1 Characteristics of the participants included in the selected studies (*continued*)

First author	Study characteristics 1. Design 2. Sample 3. Country	Intervention 1. Essential oil type and dose 2. Administration method 3. Duration of per session/ frequency/total duration of intervention	Comparison	Outcome and measure
Bagheri-Nesami M 2018 [21]	RCT 60 Iran	Lavender essence (2 drops). Five cotton balls were prepared using lavender essence diluted with sweet almond oil. Lavender was used at five concentrations of 10%, 20%, 30%, 40%, and 50%, administered through pinning the soaked cotton ball on the patients' collar on the first, second, third, fourth, and fifth weeks of the intervention, respectively. The patients were asked to breathe normally in a semi-sitting position during the first hour of dialysis. 20 min/three times a week/five week.	Usual care	1. Perceived sense of well-being 2. VAS
Huang YX 2015 [28]	RCT 82 China	1% lavender essential oil. The lavender essential oil diluted with distilled water was poured into the electric heating aromatherapy lamp. The subjects lay in the most comfortable position, 0.5 m away from the aromatherapy lamp, and asked to breathe peacefully prior to inserting the fistula needle. 5 min/-/-.	Distilled water were used similarly.	1. Pain of arteriovenous fistula puncture and anxiety 2. VAS and STAI
Bagheri-Nesami M 2017 [14]	RCT 72 Iran	5% lavender essential oil (3 drops) A cotton ball infused with lavender essential oil (diluted 1:20 with sweet almond oil) was attached to the patients' collar and they were then asked to breathe normally. 10 min/3 times a week/four weeks.	Routine care	1. Anxiety, Depression 2. HADS

Note: RCT, randomized controlled trial; VAS, Visual Analogue Scale; HADS, Hospital Anxiety and Depression Scale; FSS, Fatigue Severity Scale; STAI, State-Trait Anxiety Inventory; PSQI, Pittsburgh Sleep Quality Index; DASS-21, Depression Anxiety Stress Scales; PFS, Piper Fatigue Scale; BFI, Brief Fatigue Inventory; HAM-A, Hamilton Anxiety Assessment Scale; BAI, Beck Anxiety Inventory.

Table 2 Quality assessment of studies included

Reference	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Ahmady S 2019 [26]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Hassanzadeh M 2018 [25]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Bagheri-Nesami M 2016 [18]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Muz G 2017 [22]	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Bicer S 2017 [27]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Karadag E 2019 [23]	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Dehkordi AK 2017 [19]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Kiani F 2016 [15]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Senturk A 2018 [20]	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Barati F 2016 [24]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Bagheri-Nesami M 2014 [17]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Taşan E 2019 [16]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Bagheri-Nesami M 2018 [21]	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Huang YX 2015 [28]	Low risk	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear
Bagheri-Nesami M 2017 [14]	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear

the mean of fatigue before and after the intervention was (37.57 ± 16.42) and (34.7 ± 15.09), respectively. Hassanzadeh, Hassanzadeh Met al.'s [25] results showed that the mean of fatigue before and after the intervention in lavender essential oil group was (6.49 ± 1.11) and (3.64 ± 0.79) , respectively (P = 0.01), however, the control group was (6.44 ± 1.27) and (6.21 ± 1.29), respectively (P = 0.392). Karadag E et.al. [23] founded that in the intervention group the difference of FSS before and after test was statistically significant (t = 7.177, P = 0.001), but in the control group there was no significant difference in FSS scores between pre-test and post-test (t =−1.289, P = 0.208).

While one study [18] showed that inhaling lavender

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Table 3 The effect of inhaled aromatherapy on fatigue

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Ahmady S 2019 [26]	FSS	1. Lavender essential oil vs. distilled water. 2. Orange essential oil vs. distilled water.	1. Statistics (mean ± SD): I = 30.27 ± 13.88, C = 34.7 ± 15.09. 2. Statistics (mean ± SD]: I = 33.06 ± 14.55, C = 34.7 ± 15.09. Interpretation: fatigue levels in the intervention group improved significant compared with the control group. ($P < 0.001$).
Hassanzadeh M 2018 [25]	BFI	Lavender essential oil vs. routine care.	Statistics (mean ± SD): I = 3.64 ± 0.79, C = 6.21 ± 1.29. Interpretation: There was a significant difference in the mean score of fatigue before and after the intervention between aromatherapy group, but this difference was insignificant in the control group ($P = 0.001$).
Bagheri-Nesami M 2016 [18]	FSS	Lavender essential oil vs. routine care.	Statistics (mean ± SD): I = 42.61 ± 3.45, C = 41.70 ± 3.39. Interpretation: no statistically significant differences were observed between the two groups in terms of the fatigue scores before, and after the last intervention ($P > 0.05$).
Muz G 2017 [22]	VAS and PFS	Sweet orange and lavender oil vs. routine care.	Statistics: VAS (median (%25p–%75p)]: I = 2.00 (1.00-4.20), C = 8.00 (7.00-9.60). Statistics: PFS behavioral/severity (mean ± SD): I = 3.19 ± 2.10, C = 7.40 ± 1.50. Statistics: PFS affective meaning (mean ± SD): I = 3.10 ± 1.95, C = 7.44 ± 1.40. Statistics: PFS sensory (mean ± SD): I = 3.17 ± 2.12, C = 7.65 ± 1.32. Statistics: PFS cognitive/mood (mean ± SD): I = 2.93 ± 1.93, C = 7.09 ± 1.28. Statistics: PFS total fatigue scale (mean ± SD): I = 3.09 ± 2.01, C = 7.38 ± 1.33. Interpretation: statistically significant differences were observed between the two groups in terms of the fatigue scores ($P < 0.001$).
Bicer S 2017 [27]	BFI and VAS	Lavender and rosemary vs. sunflower oil.	Statistics: VAS (mean ± SD): I = 3.04 ± 1.39, C = 6.60 ± 1.25. Statistics: BFI (mean ± SD): I = 19.52 ± 6.7, C = 45.08 ± 11.88. Interpretation: statistically significant differences were observed between the two groups in terms of the fatigue scores ($P < 0.05$).

Table 3 The effect of inhaled aromatherapy on fatigue (*continued*)

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Karadag E 2019 [23]	FSS	Lavender oil vs. routine care.	Statistics: (mean ± SD): I = 35.23 ± 5.21, C = 38.46 ± 9.12. Interpretation: statistically significant differences were observed between the two groups in terms of the fatigue scores ($P < 0.05$).

Note: SD, standard deviation; VAS, Visual Analogue Scale; FSS, Fatigue Severity Scale; PFS, Piper Fatigue Scale; BFI, Brief Fatigue Inventory.

essential oils had no effect on reducing fatigue in hemodialysis patients ($P > 0.05$). Bagheri-Nesami M et.al. [18] reported that no significant differences in two groups. The mean of fatigue before and after the intervention in lavender essential oil group was (45.24 ± 3.22) and (40.58 ± 3.55), respectively ($P > 0.05$), in control group was (41.50 ± 3.17) and (41.70 ± 3.39) ($P > 0.05$).

Three other studies [22, 26, 27] used orange essential oil, lavender essential oil mixed with sweet orange essential oil and lavender essential oil mixed with rosemary essential oil, respectively. Ahmady S et.al.'s [26] findings showed that the mean of fatigue before and after the intervention was (48.8 ± 12.8) and (33.06 ± 14.55), respectively ($P = 0.01$), but no significant difference were observed in the control group before and after the intervention ($P > 0.05$). Muz G et.al. [22] reported that the VAS fatigue scores and PFS scores in the intervention group were significantly lower than the control group ($P < 0.001$). Bicer S et.al.'s [27] result showed that in the intervention group, the average BFI score decreased from (42.92 ± 13.23) to (19.52 ± 6.7), and the average VAS fatigue score decreased from (7.16 ± 1.54) to (3.04 ± 1.39) ($P < 0.05$), while no statistically significant differences were observed in the placebo group ($P > 0.05$). The results indicate that inhaled aromatherapy can relieve the fatigue in patients undergoing hemodialysis. Detailed result information is shown in Table 3.

Anxiety. Seven studies [14, 15, 19, 20, 23, 24, 28] assessed the effect of inhaled aromatherapy on anxiety in hemodialysis patients. The results of meta-analysis showed excessive heterogeneity, so only descriptive analysis was conducted. Five studies [14, 15, 20, 23, 28] used lavender essential oil, four of them [15, 20, 23, 28] showed that inhaled lavender essential oil could reduce the anxiety level of hemodialysis patients ($P \leq 0.05$). Karadag E et.al. [23] founded that the mean of BAI before and after the intervention in lavender essential oil group was (49.43 ±10.9) and (33.2 ± 9.45), respectively ($t = 10.371$, $P = 0.001$), in control group the mean of BAI was (48.26 ± 12.29) and (49.76 ± 10.68) ($t = -3.829$, $P = 0.001$). Senturk A et.al.'s [20] findings showed that the total mean score of the HAS decreased from (11.11 ± 3.85) to (5.29 ± 2.59) in the intervention group, whereas it increased from (15.35 ± 5.55) to (18.05 ± 5.42) in the control group ($P < 0.01$). Huang YX et.al. [28] reported that the State anxiety (S-AI) score in fumigation group were significantly lower than those in control group ($P < 0.05$). However, one study [14] showed that inhaled lavender essential oil had no significant effect on the anxiety level of hemodialysis patients ($P = 0.738$). Bagheri-Nesami M et.al.'s [14] results showed that the mean anxiety score was changed from (4.42 ± 4.04) to (3.77 ± 4.10) in the experimental group, in the control group the mean anxiety score was changed from (4.75 ± 4.39) to (3.69 ± 4.14), the differences between the two groups in their level of anxiety were no statistically significant ($P > 0.05$).

The other two studies used rose water [24] and Damask rose essential oil [19] respectively. Kiani F et.al. [15] founded that state and trait anxiety decreased than before the intervention by (13.86 ±6.91) and (-6.04 ± 5.35) respectively. Dehkordi AK et.al. [19] reported that in the intervention group the average anxiety score decreased from (6.2 ± 4.5) to (3.1 ± 3.8) and in the control group the average anxiety score decreased from (8.1 ± 6.2) to (7.5 ± 6.5).

The results showed that inhaled aromatherapy had a positive effect on the anxiety level of hemodialysis patients. Detailed result information is shown in Table 4.

Pain. Total of three studies [16, 17, 28] explored the effects of inhaled aromatherapy on arteriovenous fistula puncture pain in hemodialysis patients. All three studies used lavender essential oil, and the results showed that aromatherapy inhaled lavender essential oil could effectively relieve the pain of arteriovenous fistula puncture ($P < 0.05$). Huang YX et.al. [28] reported that the arteriovenous fistula puncture pain in fumigation group were significantly lower than those

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Table 4 The effect of inhaled aromatherapy on anxiety

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Karadag E 2019 [23]	BAI	Lavender oil vs. routine care.	Statistics: (mean ± SD): I = 33.2 ± 9.45, C =49.76.46 ± 10.68. Interpretation: statistically significant differences were observed between the two groups ($P < 0.05$).
Dehkordi AK 2017 [19]	DASS-21	Damask rose oil vs. usual care.	Statistics: DASS Anxiety (mean ± SD): I = 3.1 ± 3.8, C = 7.5 ± 6.5. Interpretation: statistically significant differences were observed between the two groups ($P = 0.004$).
Kiani F 2016 [15]	STAI	Lavender oil vs. usual care.	Statistics: STAI obvious anxiety mark changes (mean ± SD): I = 33.06 ± 3.27, C = 41.80 ± 43.80. Statistics: STAI trait anxiety mark changes (mean ± SD): I = 47.28 ± 4.36, C = 49.96 ± 6.36. Statistics: STAI total anxiety mark changes (mean ± SD): I = 81.8 ± 7.17, C = 91.9 ± 13.3. Interpretation: there is a significant difference between state and trait anxiety marks in the two groups ($P < 0.05$).
Senturk A 2018 [20]	HAM-A	Lavender oil vs. usual care.	Statistics: HAM-A Psychological (mean ± SD): I = 1.29 ± 1.15, C = 7.17 ± 2.09. Statistics: HAM-A Somatic (mean ± SD): I = 4.00 ± 2.03, C = 10.88 ± 4.25. Statistics: HAM-A Total score (mean ± SD): I = 5.29 ± 2.59, C = 18.05 ± 5.42. Interpretation: statistically significant differences were observed between the two groups in terms of the mean score of total and sub-dimensions of Hamilton Anxiety Assessment Scale ($P < 0.01$).
Barati F 2016 [24]	STAI	Rose water vs. usual care.	Statistics: Mean State Anxiety (mean ± SD): I = 6.5 ± 37.1, C = 9.4 ± 49.5. Statistics: Mean Trait Anxiety (mean ± SD): I = 10.1 ± 42.9, C = 12.4 ± 52.8. Interpretation: statistically significant differences were observed between the two groups in terms of mean scores of state and trait anxiety.

Table 4 The effect of inhaled aromatherapy on anxiety (*continued*)

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Huang YX 2015 [28]	STAI	Lavender essential oil vs. distilled water.	Statistics: Mean State Anxiety (mean ± SD): I = 46.35 ± 9.74, C = 57.18 ± 12.33. Interpretation: statistically significant differences were observed between the two groups.
Bagheri-Nesami M 2017 [14]	HADS	Lavender essential oil vs. routine care.	Statistics: HADS anxiety (mean ± SD): I = 3.77 ± 4.10, C = 3.69 ± 4.14. Interpretation: no significant difference between the two groups in terms of the severity of anxiety.

Note: SD, standard deviation; HADS, Hospital Anxiety and Depression Scale; FSS, Fatigue Severity Scale; STAI, State-Trait Anxiety Inventory; DASS-21, Depression Anxiety Stress Scales; HAM-A, Hamilton Anxiety Assessment Scale; BAI, Beck Anxiety Inventory.

in control group ($P < 0.05$). Bagheri-Nesami M et.al.'s [17] results showed that in the intervention group the mean VAS pain intensity score decreased from (3.78 ± 0.24) to (2.36 ± 0.25) and in the control group the average anxiety score decreased from (4.16 ± 0.32) to (3.43 ± 0.31) ($P = 0.09$). Taşan E [16] found that the pain mean score of the intervention group was (3.8 ± 0.3) points before and (3.0 ± 0.2) points after lavender oil inhalation. In the control group, the average pain score increased from (5.4 ± 0.3) to (5.6 ± 0.6). Detailed result information is shown in Table 5.

Sleep quality. Two studies [20, 22] evaluated the effects of inhaled aromatherapy on sleep quality. Both studies used lavender essential oils, and the results showed that inhaled aromatherapy had a positive effect on sleep quality in hemodialysis patients ($P \leq 0.05$). Senturk A et.al.'s findings [20] showed that in the intervention group the VAS mean sleep score was decreased from (6.00 ± 1.45) to (3.82 ± 1.70) ($P < 0.05$), the mean sleeping time score was changed from (5.96 ± 2.31) to (7.07 ± 1.59) ($P < 0.01$) while no statistically significant differences were observed in the control group in terms of mean VAS daytime sleepiness score and mean score of sleep duration. However, there was no significant difference in the mean score of time for falling asleep between two groups ($P > 0.05$), as the mean score of duration of falling asleep decreased from (94.41 ± 47.06) to (58.52 ± 63.56) at the last follow-up in the intervention group, whereas in the control group was changed from (69.70 ± 42.07) to (69.70 ± 52.21). Muz G et.al. [22] reported that all subscales of PSQI in the study group were lower than the scores of the control group, and this decrease was statistically significant ($P > 0.001$). Detailed result information is shown in Table 6.

Depression. A total of two studies [14, 19] assessed the effects of inhaled aromatherapy on depression. One study used Damask rose essential oil and another used lavender essential oil, both of which showed that inhaled aromatherapy could reduce depression in hemodialysis patients ($P \leq 0.05$). Dehkordi AK et.al. [19] founded that in the intervention group the average depression score decreased from (8.2 ± 6.6) to (5.1 ± 4.5) and in the control group the average depression score changed from (7.4 ± 6.9) to (7.4 ± 7.3). Bagheri-Nesami M et.al.'s [14] results showed that the mean anxiety score was changed from (4.54 ± 4.11) to (3.82 ± 4.07) in the experimental group, and in the control group the mean anxiety score was changed from (4.05 ± 4.48) to (4.27 ± 5.04), the differences between the two groups in their level of anxiety were statistically significant ($P = 0.005$). Detailed result information is shown in Table 7.

Stress. Only one study [19] assessed the effect of inhaled aromatherapy on stress. The study used Damascus rose essential oil and the results showed that aromatherapy inhaled Damascus rose essential oil can reduce anxiety in hemodialysis patients ($P \leq 0.05$). Dehkordi AK et.al. [19] founded that in the intervention group the average stress score decreased from (11.2 ± 5.9) to (5.5 ± 4.6) and in the control group the average stress score changed from (9.6 ± 6.5) to (9.6 ± 6.4). Detailed result information is shown in Table 8.

Perceived sense of well-being. Only one study [21] evaluated the effects of inhaled aromatherapy on perceived well-being. The study, which used different concentrations of lavender essential oils, showed that

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Table 5 The effect of inhaled aromatherapy on pain

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Bagheri-Nesami M 2014 [17]	VAS	Lavender essence vs. the smell of lavender without its properties essence.	Statistics: (mean ± SD): I = 2.36 ± 0.25, C = 3.43 ± 0.31. Statistically significant differences were observed between the two groups in terms of the pain of arteriovenous fistula puncture (P = 0.09).
Taşan E 2019 [16]	VAS	Lavender and sweet almond oil vs. usual care.	Statistics: (mean ± SD): I = 3.0 ± 0.2, C = 5.6 ± 0.6. Statistically significant differences were observed between the two groups in terms of the pain of arteriovenous fistula puncture.
Huang YX 2015 [28]	VAS	Lavender essential oil vs. distilled water.	Statistics: VAS (mean ± SD): I = 3.06 ± 0.22, C = 4.11 ± 0.53. Statistically significant differences were observed between the two groups in terms of the pain of arteriovenous fistula puncture (P < 0.05).

Note: SD, standard deviation; VAS, Visual Analogue Scale.

aromatherapy inhaled 40% and 50% lavender essence can improve the perceived well-being in hemodialysis patients (P < 0.05), while 10%, 20% and 30% low concentrations had no similar effect (P > 0.05) [21]. Detailed result information is shown in Table 9.

Discussion

This is the first systematic review of inhaled aromatherapy for complications in hemodialysis patients. This study determined the effects of inhaled aromatherapy on blood patients from the establishment of the database to December 2019. A total of 15 related randomized controlled trials were included in 967 hemodialysis patients.

At present, it is believed that the mechanism of inhaled aromatherapy is that the aromatic gas enters the olfactory cells and mucosa of the nasal epithelium, transmits from the olfactory nerve to the cerebral cortex, and then adjusts the physical and mental sensation through the individual's own perception. On the other hand, some aromatic molecules enter the respiratory system and enter the circulatory system after oxygen exchange [13]. At present, a large number of studies have proved that inhaled aromatherapy can improve physique, mood and mental well-being. [29–31].

This study shows that inhaled aromatherapy can reduce anxiety, depression, arteriovenous fistula puncture pain, stress and fatigue, and improve the quality of sleep and perceived well-being in hemodialysis patients. Lavender is the most commonly used essential oil. It contains camphor, terpinene-4-ol, linalool, linalool, linaloyl acetate, β-basil and 1meme 8-cineole. These ingredients can inhibit the central nervous system, have sedative and anesthetic effects, reduce anxiety and sleep difficulties, improve well-being, etc. [32, 33] can also reduce the body's physiological arousal level and reduce sensitivity to pain by passivating the autonomic system. This may explain why inhaled aromatherapy can improve the complications of hemodialysis patients. Other studies have similar results to this study. Wang Yuan Yunzi et al. [29] showed that inhaled aromatherapy can relieve anxiety and pain in perioperative patients. Abdelhakim MA et al. [34] showed that inhaled aromatherapy can reduce pain and anxiety in patients undergoing cardiac surgery. Hawkins J et al. [35] showed that inhaled aromatherapy can reduce fatigue in women with hypothyroidism. Mi-kyoung L et al. [36] showed that inhaled aromatherapy can improve sleep quality and reduce stress.

Table 6 The effect of inhaled aromatherapy on sleep quality

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Muz G 2017 [22]	PSQI	Sweet orange and lavender oil vs. routine care.	Statistics: subjective sleep quality: (mean ± SD): I = 0.85 ± 0.90, C = 2.60 ± 0.65. Statistics: PSQI sleep latency: (mean ± SD): I = 0.81 ± 1.00, C = 2.94 ± 0.23. Statistics: PSQI sleep duration: (mean ± SD): I = 0.22 ± 0.42, C = 2.74 ± 0.50. Statistics: PSQI habitual sleep efficiency: (mean ± SD): I = 0.62 ± 0.63, C = 2.68 ± 0.79. Statistics: PSQI sleep disturbance: (mean ± SD): I = 1.11 ± 0.50, C = 2.02 ± 0.38. Statistics: PSQI daytime dysfunction: (mean ± SD): I = 1.03 ± 0.97, C = 2.62 ± 0.49. Statistics: PSQI global sleep quality: (mean ± SD): I = 4.66 ± 3.66, C = 15.62 ± 1.81. Statistically significant differences were observed between the two groups in terms of the sleep quality ($P < 0.05$).
Senturk A 2018 [20]	VAS	Lavender oil vs. usual care.	Statistics: VAS daytime sleepiness-level: (mean ± SD): I = 3.82 ± 1.70, C = 5.52 ± 1.69. Statistics: time taken to fall asleep: (mean ± SD): I = 58.52 ± 63.56, C = 69.70 ± 52.21. Statistics: mean sleeping time: (mean ± SD): I = 7.07 ± 1.59, C = 4.58 ± 1.37. Statistically significant differences were observed between the two groups in terms of the daytime sleepiness score, mean score of sleep duration and mean score of total and sub-dimensions of Hamilton Anxiety Assessment Scale. However, the differences of mean score of time for falling asleep between the two groups were not different ($P < 0.05$).

Note: SD, standard deviation; VAS, Visual Analogue Scale; PSQI, Pittsburgh Sleep Quality Index.

However, Masoumeh Bagheri-Nesami1 et al. [14, 18] in the study showed that aromatherapy inhaled lavender essential oil had no significant effect on fatigue and anxiety in hemodialysis patients. The reason for the analysis may be due to the differences in the concentration of essential oils used in their research, intervention time and methods, which need to be further studied.

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Table 7 The effect of inhaled aromatherapy on depression

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Dehkordi AK 2017 [19]	DASS-21	Damask rose oil vs. usual care.	Statistics: DASS depression (mean ± SD): I = 5.1 ± 4.5, C = 7.4 ± 7.3. There was a significant difference in the DASS-21 scale scores before and after the intervention between aromatherapy groups, but this difference was insignificant in the control group (P = 0.05).
Bagheri-Nesami M 2017 [14]	HADS	Lavender essential oil vs. routine care.	Statistics: HADS depression (mean ± SD): I = 3.82 ± 4.07, C = 4.27 ± 5.04. Statistically significant differences were observed between the two groups in terms of depression (P < 0.05).

Note: SD, standard deviation; HADS, Hospital Anxiety and Depression Scale; DASS-21, Depression Anxiety Stress Scales.

Table 8 The effect of inhaled aromatherapy on stress

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Dehkordi AK 2017 [19]	DASS-21	Damask rose oil vs. usual care.	Statistics: DASS stress (mean ± SD): I = 5.5 ± 4.6, C = 9.6 ± 7.4. There was a significant difference in the DASS-21 scale scores before and after the intervention between aromatherapy groups, but this difference was insignificant in the control group ($P \leq 0.05$).

Note: SD, standard deviation; DASS-21, Depression Anxiety Stress Scales.

Table 9 The effect of inhaled aromatherapy on perceived sense of well-being

Study	Fatigue outcome	Comparisons	Description of the intervention's therapeutic effects
Bagheri-Nesami M 2018 [21]	VAS	Lavender essence vs. usual care.	Statistics: (mean ± SD): I = 8.3 ± 1.17, C = 6.43 ± 1.81. Statistically significant differences were observed between the two groups in terms of the mean level of well-being.

Note: SD, standard deviation; DASS-21, Depression Anxiety Stress Scales.

Our limitations include that most of the samples included in the literature are small, and the blind method is not used, and there are differences in the type, concentration, dose, exposure time and intervention frequency of essential oils included in the study. some studies also failed to provide details of intervention measures.

Conclusion

This study concluded that inhaled aromatherapy can reduce anxiety, depression, arteriovenous fistula puncture pain, stress and fatigue, and improve their sleep quality and perceived well-being. The aromatic essential oils analyzed include lavender essential oil, sweet orange oil, rosemary, rose and so on. For hemodialysis patients with different complications, clinical nurses can choose appropriate aromatic essential oils for inhalation aromatherapy according to specific conditions. The method is effective, convenient and easy to implement. However, the specific implementation process and standards, look forward to a higher level, high-quality research, to provide evidence support.

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