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Original article

The therapeutic use of essential oils in the care of cancer patients in chemotherapy: A systematic review

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Abstract

Introduction: Chemotherapy is an important therapy in the treatment of cancer. Nausea, vomiting and worsening quality are some adverse effects of chemotherapy. Aromatherapy is an ancient technique that uses essential oils for physical and psychological/emotional improvement and is able to reduce the symptoms of chemotherapy and can be an excellent complementary technique. Objective: The aim of this systematic review was to determine the effects of aromatherapy on the adverse effects of chemotherapy in patients diagnosed with cancer. Methods: A search in three database PubMed, EMBASE and SCOPUS. Five studies that analyzed the use of aromatherapy to evaluate the reduction of the adverse effects of chemotherapy in a cancer patient, published only in English were included. Two reviewers, which independently examined titles and abstracts, identified records through database search and reference screening and irrelevant studies were excluded based in eligibility criteria. Relevant full texts were analyzed for eligibility, and all selected studies were included in this systematic review. Results: Five studies were included in this systematic review. This review suggests that aromatherapy reduces nausea, frequency of vomiting and improves quality of sleep. Conclusion: Aromatherapy is an effective technique to reduce nausea, the frequency of vomiting and improves the quality of sleep of patients diagnosed with cancer and undergoing chemotherapy. However, more randomized clinical trials with a good methodological quality are necessary to confirm the preliminary findings of this systematic review.

Keywords: Aromatherapy, Cancer, Chemotherapy, Integrative and Complementary Practices.

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Introduction

According to the Pan American Health Organization (PAHO),[1] the cancer arises from the transformation of normal cells into tumor cells, in a multi-stage process, and can be influenced by several factors, including genetics, ultraviolet radiation, carcinogenic chemicals, infections by certain viruses, bacteria or parasites and also by population aging. The term cancer is used generically for a large group of diseases that can affect any part of the body, with the main characteristic of the rapid creation of abnormal cells that grow beyond their usual limits and invade adjacent parts of the body, known as metastasis.

According to data from the Instituto Nacional de Câncer (INCA) José Alencar Gomes da Silva,[2] the cancer is the main public health problem in the world and is already among the top four causes of premature death (before the age of 70) years of age) in most countries. A worldwide estimate for the year 2018 shows that 18 million new cases of cancer occurred worldwide, accounting for approximately 9.6 million deaths in 2018.[1] It already counts among the four main causes of premature death (before the age of 70). Cancer incidence and mortality are increasing worldwide, partly due to aging and population growth.[2] There is also a transition of the main types of cancer observed in developing countries, with a decline in the types of cancer associated with infections and an increase in those associated with the improvement of socioeconomic conditions with the incorporation of habits and attitudes associated with urbanization (sedentary lifestyle, inadequate nutrition, among others).

Antineoplastic chemotherapy is still the most frequent treatment of choice for the treatment of malignant neoplasms, which can be associated with

radiotherapy, surgery, among others.[3] Chemotherapeutics are drugs considered cytotoxic (toxic to cells) or cytostatic (inhibit cell division and consequently their reproduction). Although one of the most common forms of treatment for cancer, due to the toxicity of the drugs administered and the accumulation of toxicity due to repeated administrations, chemotherapy can have several concomitant adverse effects on the patient, including fatigue, nausea and depression, and some form of adverse health impact.[4]

Symptoms of nausea and vomiting induced by chemotherapy (SNVC) are the most common and poorly controlled, and can result in multiple physiological consequences, in addition to impacting quality of life (QOL) and patient compliance with treatment.[5]

Lima et.al.[6] reported that the World Health Organization (WHO) has been encouraging, since the 1980s, the use of complementary therapy practices, as well as encouraging the integration of Traditional Chinese Medicine (TCM) into national health systems. Together with this, from 2006 onwards Brazil became part of the group of countries that have national tradicional medicine policies, with the approval of the National Policy of Integrative and Complementary Practices in Health (NPICPH) in Sistema Único de Saúde (SUS). According to the Ministry of Health, Integrative and Complementary Practices (ICP) are treatments that use therapeutic resources based on traditional knowledge, aimed at preventing various diseases such as depression and hypertension.[7] In some cases, they can also be used as palliative treatments in some chronic diseases, in which cancer can be included. Cancer is often considered a chronic disease and is treated palliative, with no therapeutic possibility of cure. Scientific evidence has shown the benefits of integrated treatment between conventional medicine and ICP. Brazil is a world reference in the use of ICP in primary care, investing in prevention and health promotion in order to prevent people from becoming ill. In addition, when necessary, ICP can also be used to relieve symptoms and treat people who already have some type of illness. As ICP can be considered: TCM; Apitherapy; Aromatherapy; Art Therapy; Ayurveda; Biodanza; Bioenergetics; Family constellation; Chromotherapy; Circular dance; Geotherapy; Hypnotherapy; Homeopathy; Laying on of hands; Anthroposophical medicine/anthroposophy applied to health; Meditation; Naturopathy ; Osteopathy; Ozone therapy; Medicinal plants - phytotherapy; Chiropractic; Reflexotherapy; Reiki; Shantala; Integrative Community Therapy; Flower therapy; Social thermalism/crenotherapy; Yoga.

Aromatherapy comes from the Greek "arôma" (aroma, odor) and "therapia" (therapy, cure). In this practice essences are used essential oils (EO) from aromatic parts of medicinal plants. The term aromatherapy was created by the chemical engineer and researcher from Lyon, France - René Maurice Gattefossé in 1935, he was the first to establish the relationship between the activities and structures of EO.

Aromatherapy is a secular therapeutic practice that consists of the intentional use of volatile concentrates extracted from vegetables, EO - in order to promote or improve health, well-being and hygiene. In the 1930s, France and England started to adopt and research the therapeutic use of EO. Aromatherapy is recognized by the US National Institutes of Health as a complementary and alternative medicine, and is considered very safe, in addition to a cheap practice.[8] In Brazil, aromatherapy is recognized as an integrative and complementary practice with wide individual and/or collective use, being practiced in a multidisciplinary way, which include health professionals such as nurses, psychologists, physiotherapists, doctors, veterinarians, holistic therapists, naturists, and others. It is used in different sectors of the area to assist in a complementary way to establish the individual's physical and/or emotional balance.[9]

Considering that aromatherapy uses EO extracted from the flowers, leaves, or roots of several natural plants, it is important to note that this PICS is a safe, non-invasive approach, and can be easily self-administered.[10] The absorption of oils into the skin by massage is effective in reducing anxiety and depression due to muscle and psychological relaxation caused in patients, including patients undergoing cancer treatment.[11]

Aromatherapy massage is an effective intervention in cases of neuropathic pain, also one of the most common effects related to the use of chemotherapy.[12] Several existing studies have combined aromatherapy with reflexology to improve treatment and effectiveness.[13]

According to a controlled pilot study carried out by the Oncology Nursing Society, which evaluated the viability and preliminary effects of massage and inhalation aromatherapies on evidence-based practices in the prevention, management and treatment of acute nausea/vomiting induced by chemotherapy, the severity of nausea was significantly lower in the aromatherapy groups for massage and inhalation than in the control group. The incidence of nausea was also reduced in the aromatherapy groups. Which implies

in practice that non-pharmacological approaches are recommended for the management of CINV.[14]

Methods

The methods of this review were prespecified in a protocol that was registered under number CRD42020206485, with the PROSPERO International Prospective Register of Systematic Reviews (PROSPERO)[15] and was followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[16]

Eligibility Criteria.

Inclusion criteria: To be included in this review, publications must meet the research criteria and investigate the effects of EO on patients diagnosed with cancer and under chemotherapy, only randomized clinical trial (RCT), regardless of the year of publication. A flowchart (Figure 1), based on the PRISMA analysis, shows the steps in the selection of the complete articles analyzed in this review 16.

Exclusion criteria: Exclusion criteria allowed the elimination of unnecessary publications. Papers were excluded if: (i) published in a language other than English; (ii) with findings not related to cancer patient under chemotherapy; (iii) did not use essential oils; (iv) replies, cohort, editorials, short communications, letters book, abstracts or reviews (v) be conducted with animal.

Search methods for the identification of relevant studies.

The searches were carried out in the following electronic databases: Pubmed, EMBASE and SCOPUS on July 7, 2020 and the search string was ((aromatherapy) AND (chemotherapy) AND (cancer)).

The keywords used in the search were defined based on the PICOS strategy,[17] focus on cancer patients under chemotherapy (Participants) receiving essential oil (Intervention), control group, placebo or any type of comparison (Comparison), all reported outcomes (Outcomes) and only RCT (Study desing). This strategy allowed to consider all the relevant publications to the studied population.

All duplicates references were removed. The review was conducted following four phases: (i) records were identified through database search and reference screening (Identification), (ii) two reviewers (B, AC) independently examined titles and abstracts and irrelevant studies were excluded based in eligibility criteria (Screening), (iii) relevant full texts were analyzed for eligibility (Eligibility), and all relevant studies were included in the systematic review and (iv) the disagreement was resolved by a third reviewer (PD). The same researchers were responsible for data extraction from the included studies. Data regarding study information (author, year and country), population (sample size, age and sex), study design, protocol, prescription, EO and results were extracted.

To assess the level of evidence for each publication was used the National Health and Medical Research Council (NHMRC)[18] as showed in the Figure 2.

To assess the risk of bias in the articles included, the Cochrane Collaboration tool was used.[19] Two reviewers used the tool to assess the risk of bias (B, AC) and the third researcher was used to resolve disagreements (PD) (Figure3).

Results

A total of 165 studies were identified through a database search and, after the removal of 73 duplicates, 92 studies were identified. During the screening process, 61 publications were excluded for not being related to the research question, and the full text of 31 studies was reviewed in detail. After careful analysis, 26 studies were excluded (24 review articles, 2 published in a language other than English). Finally, 5 studies were included in the systematic review. The figure 1 shows the process summarized.

The objectives, the characteristics of the participants, the results and the level of evidence of the selected articles are in Table 1. The level of evidence [18] of the five studies included in the current review were considered LE II.

Some variables included in the RCT selected were assesed by relevant instruments such as: (i) pain and nausea score, by the Visual-Analog Scale (VAS),[5] the Rhodes Index of Nausea and Vomiting[22] and the Pediatric Nausea Assessment Tool (PeNAT);[8] (ii) frequency of vomiting, by the Visual-Analog Scale (VAS),[5] (iii) quality of life , by the Health-related quality of life (HRQoL) profile and The European Organisation for Research and Treatment of Cancer Quality of Life Group (EORTC QLQ-C30 scores),[5] (iv) Nutritional status,[20] (v) General perception on aromatherapy,[20] (vi) sleep quality, by the Pittsburgh Sleep Quality Index,[21] (vii) different symptoms, by the Edmonton Symptom Assessment Scale-Revised,[21] (viii) Final evaluation of aromatherapy.[21]

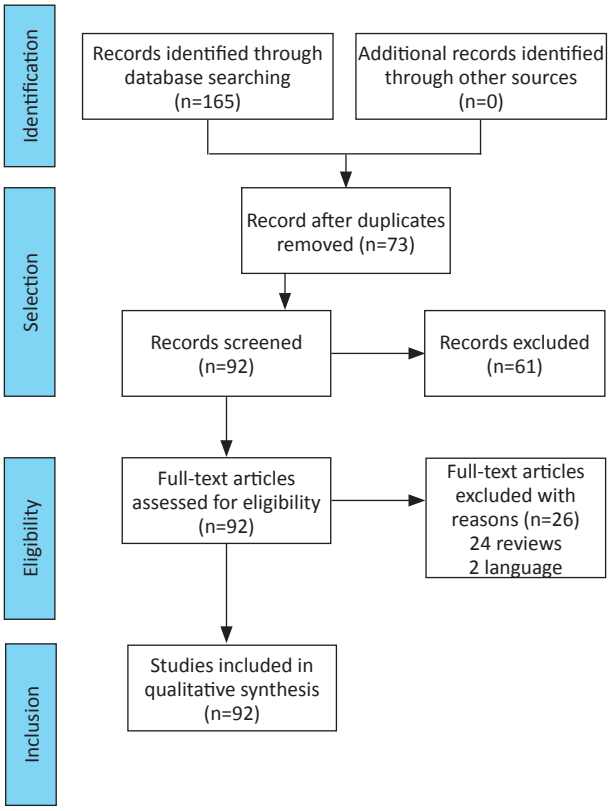

Figure 1. PRISMA flow diagram of the literature selection process
Authorship: Bessa, BMO (2020).

Considering the use of EO , three works[5,8,20] reported the effects of ginger oil, and this was the most used, one work[21] reported the use of EO in synergy, the authors used peppermint, lavender and chamomile oils and one work[22] reported the effects of peppermint oil.

Two works[5,20] reported the used of aromatherapy necklace, one work[21] reported the use of diffusor at night in patient's room at hospital, one work reported[22] the use of tissue paper attached to the collar of patient's clothes by a pin and one work[8] reported the use of EO in a cotton ball for each patient in a capped urine sample with three deep breaths of the cup essence.

Discussion

This systematic review aims to assess the effects of use the EO on patients diagnosed with cancer and under chemotherapy. After analyzing the included references, and considering their limitations, the results suggest that EO can be effective in treating cancer patients by helping to reduce the side effects of chemotherapy.

Effects on nausea score and on frequency of vomiting

Authors found improvements in nausea and the frequency of vomiting with the use of EO. The EO most used due to their antiemetics and antispasmodics in

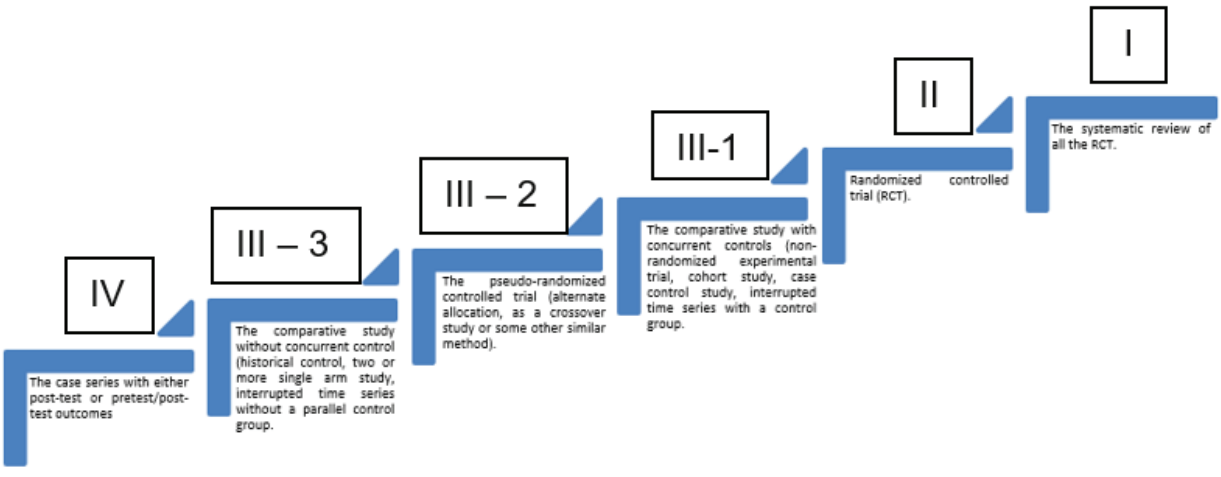

Figure2. Level of evidence (National Health and Medical Research Council Hierarchy of Evidence)
Authorship: Paineiras-Domingos, LL (2021).

the gastric lining and in the colon are mint (Mentha spicata) Ginger (Zingiber officinale), and peppermint (Mentha piperita). Mapp *et al.*,[23] reported significant improvements in nausea, assessed using the Baxter Retching Faces pictorial scale, in a patient undergoing chemotherapy after using peppermint OE compared to the group that used a moist unscented towel. In the review by Awoyama *et al.*,[24] it has been reported that ginger oil was able to reduce the adverse effects of nausea and vomiting from chemotherapy, especially in the acute phase, in adult cancer patients. Lua, *et al.*[5] reported used ginger oil, presented a significant result in relation to the symptoms of nausea and vomiting after inhalation and in the work of Eghbali, *et al.*,[22] which used the essential oil of peppermint, also showed significant results in breaking nausea and vomiting in conjunction with post-chemotherapy medication. Very close results found in the review except for the work of Evans *et al.*,[8] also used Ginger oil, however, unlike the other studies, it did not show significant results in relation to reducing the nausea of the participants.

Effects on quality of life

The effects of aromatherapy to improve quality of life on adverse chemotherapy symptoms in patients diagnosed with cancer are limited, but some studies have reported improvements in quality of life in cancer patients when aromatherapy is combined with massage or another relaxation technique. Stringer J *et al.*[25] applied a single massage therapy session (using EO and without) reported the increase in physiological and psychological well-being of patients undergoing intensive chemotherapy safely in both groups compared to the control group. Ovayolu O *et al.*[26] reported improvements in quality of life in a patient diagnosed with cancer after treatment with massage with and without aromatherapy and the improvement was most notable in the group that received aromatherapy massage. Ho SSM[27] reported that all individuals had a positive experience with aromatherapy massage and had the following benefits: general comfort, relaxation, pain reduction, muscle tension, lymphedema and numbness, improved sleep, energy level, appetite, mood in addition to physical dimensions and psychological.

Effects of quality of sleep

Hamzeh S *et al.*, 2020[28] reported significant improvements after using lavender and peppermint EO in the sleep quality of patients, assessed by PSQI) with cancer after 7 days of treatment compared to the control group. Three drops of the EO were used on a cotton ball and fixed on the patient's collar for 20 minutes. In the study by Ozkaraman *et al.*[29] reported that the use of lavender oil reduced the PSQI score before and

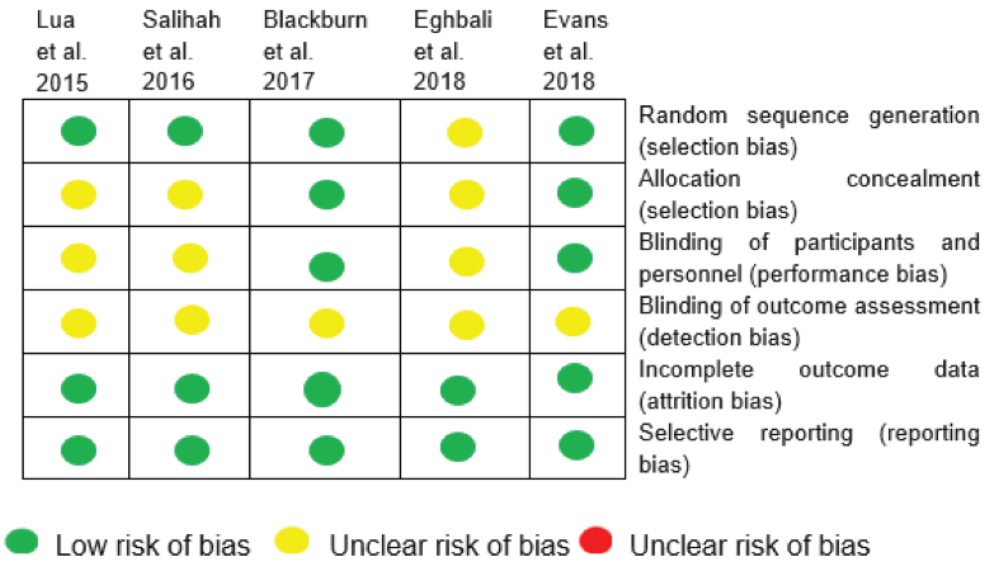

Figure2. Risk of bias summary: authors assessment for each risk of bias criterion
Authorship: Paineiras-Domingos, LL (2021).

Table 1. Description of the characteristics of the selected studies

Reference / Country	Population (n)	Study design	Protocol	Prescription	Essential oil	Variables Evaluated	Results	L.E
Lua, P. L., *et al*. 2015 Malaysia	N= 60 Group 1 = 30 ginger fragrance oil (placebo) Females = 30 Age 45.9 ± 9.5 years Group 2 = 30 Ginger essential oil Females = 30 Age 48.7 ± 8.9 years	Single-blind, controlled, randomized cross-over study	The study was divided into two phases, with the use of the necklace, for 5 days each and a wash-out period of 2 weeks, after which the groups were crossed.	An aromatherapy necklace was given to the patients to wear it for five days during day and night. The necklace was hang around their neck, and placed approximately 20 cm from their nose. On each day, patients were asked to hold the necklace just under their nose and breathe in deeply at least three times a day for at least three periods of two minutes duration, even if they did not have symptoms. This aromatherapy necklace was filled with either two drops of ginger essential oil or ginger fragrance oil (placebo)	Ginger	VAS nausea score, Frequency of vomiting HRQoL profile (EORTC QLQ-C30 scores)	The VAS nausea score was significantly lower after ginger essential oil inhalation compared to placebo during acute phase but not sustained for overall treatment effect. There was no significant effect of aromatherapy on vomiting. A statistically significant change from baseline for global health status was detected after ginger essential oil inhalation.	II
Salihah, N., *et al.* 2016 Malaysia	N = 60 Group 1 = 30 Ginger FO (placebo) Females = 30 Age 45.9 ± 9.5 years Group 2 = 30 Ginger EO Females = 30 Age 48.7 ± 8.9 years	A single-blind, randomized, placebo-controlled, crossover study	The study was divided into two phases, with the use of the necklace, for 5 days each and a wash-out period of 2 weeks, after which the groups were crossed	Patients were asked to wear an aromatherapy necklace containing either two drops of ginger or ginger fragrance oil fragrance-matched placebo.	Ginger	Nutritional status General perception on aromatherapy	Energy intakes were significantly higher after patients were treated with ginger EO than ginger FO at day 3 and day 5. Significant improvements in energy intake were also observed over time reaching almost 90% of the energy requirement 5 days' post-chemotherapy. Inhaled aromatherapy using ginger EO was rated marginally more helpful than the ginger FO.	II

Table 1. Description of the characteristics of the selected studies (continued)

Blackburn, L., *et al.* 2017 USA	N = 50 Female= 22 Male= 28	Randomized, crossover, washout trial	The patients were given a choice of three different essential oils: lavender, chamomile, or peppermint. Rose water was used as the placebo. The essential oil has been changed every week.	A diffuser with an essential oil or the placebo was placed in a predetermined, measured place within the patient room to ensure that diffusion was standardized for each patient. All bottles were used only by a single patient and were offered to the patient at the completion of the trial. Diffusion began during 9 pm rounds, with eight drops of the essential oil or placebo used and continued until the solution ran dry and the diffuser automatically turned off about eight hours later. Doors were kept closed during diffusion except when staff were entering and exiting the room.	Lavender Peppermint Chamomile	Pittsburgh Sleep Quality Index ESASr Final evaluation of aromatherapy	Aromatherapy decreased the overall PSQI. PSQI subscale scores, aromatherapy significantly increased sleep duration and sleep quality and decreased sleep disturbances. Aromatherapy reduced the weekly average ESASr score points. All subscales demonstrated a reduction in ESASr score with six symptom score changes showing a statistically significant benefit from aromatherapy: tiredness, drowsiness, lack of appetite, depression, anxiety, and well-being.	II
Eghbali, M., *et al.* (2018).	N = 100 Females = 100 Intervention group N = 50 Age 47.89±9.5 2years Control group N= 50 Age 45.74±9.92 years	RCT		Each participant was given a package containing 20 ml dropper bottle (containing normal saline or 100% peppermint EO), a tissue paper and pin. The intervention group used two drops of 100% peppermint essential oil were poured over the tissue paper and it was attached to the collar of the patient's clothes by a pin. They were then asked to breathe normally for 20 minutes, and this procedure was performed three times a day (morning, noon, and night). Patients in the control group used a placebo instead of inhaling the peppermint oil during this specified period.	Peppermint	Rhodes Index of Nausea and Vomiting	The study showed that the use of aromatherapy with peppermint essential oil, along with the use of routine anti-nausea/vomiting drugs, can reduce nausea and vomiting in the acute phase of chemotherapy.	II

Table 1. Description of the characteristics of the selected studies (continued)

Evans, Anna *et al.* 2018. USA	N = 49 3 groups: CG [water] N=10; Females = 5 Men = 5 Placebo group (inhalation of Johnson's® baby shampoo N=19 Females = 5 Men = 14 The intervention group (inhalation of EO of ginger N=20 Females = 9 Men = 11	Randomized, double-blind, placebo-controlled study	Control group - no treatment control group (inhalation of the aroma of a non-fragrant substance [water] The no treatment placebo group (inhalation of the aroma of a nontherapeutic fragrant substance [Johnson's® baby shampoo The intervention group (inhalation of the aroma of essential oil of ginger.	Four drops of one EO in a cotton ball for each patient in a capped urine sample with three deep breaths of the cup essence. It was performed before the infusion of chemotherapy and antiemetics were administered.	Ginger	PeNAT	Did not significantly decrease nausea in patients.	II

Authorship: The authors (2020).

after chemotherapy and reduced anxiety values after compared to tea tree and placebo. Three drops of EO (lavender or tea tree) were placed on a piece of cotton that was positioned about 25 centimeters below each patient's nose. Some authors have reported improvements in sleep quality after combining aromatherapy and massage. In the work Soden *et al.*[30] reported significant improvements in the group that received lavender oil massage that received thirty minute back massage weekly for four weeks and in a more recent study, Blackburn *et al.*[21] reported that aromatherapy improves sleep quality assessed by PSQI in a patient with a recent diagnosis of acute leukemia.

Conclusion

In conclusion, the work evaluated the effect of aromatherapy on the adverse effects of chemotherapy in cancer patients and the treatment was efficient in reducing nausea and the frequency of vomiting and improving the quality of sleep in this population.

The strength of this review is to demonstrate the effectiveness and beneficial and positive effects that patients diagnosed with cancer and undergoing chemotherapy can have with the use of aromatherapy.

Conflict of interest

The authors have no conflicts of interest to declare.

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