

## Efficacy of Acupressure on Nausea and Vomiting in Children Undergoing Chemotherapy: A Systematic Review

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### Abstract

**Background:** Chemotherapy is the main component of systemic cancer treatment; however, the effective application is restricted due to nausea and vomiting. We aimed to assess the effect of acupressure on nausea and vomiting in children undergoing chemotherapy.

**Materials and Methods:** An extensive search was done in databases of Medline, Embase, Scopus, Cochrane, and Web of Science until February 2018. Two independent researchers screened articles, in the next step, full texts of probably relevant articles were summarized and categorized based on the evaluated outcomes and overall effect size was presented.

**Results:** Four studies were included in the systematic review (including 223 children and adolescents aged 5 to 19 years). The first study assessed the effect of acupressure wrist bands and placebo bands; the results showed the feasibility of well tolerated acupressure, but not more effective than placebo. In the second study, researchers concluded that the acupressure bands compared to sham bands could not improve nausea and vomiting, neither in the acute nor the delayed phase. In addition, daily vomiting was not improved via acupressure bands in either the acute, or the delayed phases in chemotherapy. In the third study, a significant difference was observed between the two groups auricular acupressure intervention+ standard care (AAP), and auricular acupressure using sham auricular points (SAP) + standard care regarding occurrence, and severity of both nausea and vomiting. The results of fourth study showed that acupressure has a significant role in the reduction of nausea, vomiting and retching associated with chemotherapy among adolescents with cancer.

**Conclusion:** The patients considered the acupressure as a safe, effective and well-received strategy though objective criteria exhibited no statistically significant improvements compared to conventional care.

**Key Words:** Acupressure, Chemotherapy, Leukemia, Nausea, Pediatric, Vomiting.

\*Please cite this article as: Khakpour M, Dabbaghi B, Noorkhomami S, Javid A, Sezavar M, Ghazanfarpour M. Efficacy of Acupressure on Nausea and Vomiting in Children Undergoing Chemotherapy: A Systematic Review. Int J Pediatr 2019; 7(6): 9601-10. DOI: **10.22038/ijp.2019.39206.3338**

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Received date: Jan.19, 2019; Accepted date: Mar.22, 2019

## 1- INTRODUCTION

Cancer is a group of diseases characterized by uncontrolled cell growth, local tissue invasion and systemic metastases (1, 2). There are several strategies to treat cancer, among which surgery, radiotherapy and chemotherapy are the most commonly used methods. Chemotherapy is the main component of systemic cancer treatment (1, 3). The chemotherapy is an important and systemic therapeutic approach, which is increasingly used in the treatment of cancer (4, 5). However, the effective application of chemotherapy is restricted due to the resulting toxic effects, including nausea, vomiting, diarrhea, mucositis and bone marrow suppression (6, 7). The major causes of these complications during chemotherapy can be attributed to the stimulation of chemically sensitive centers in the brain, autonomic nervous system and psychological factors (1).

The pathophysiology of chemotherapy-induced nausea and vomiting is related to the stimulation of chemo-receptor trigger zone (CTZ), autonomic nervous system, peripheral, and atrial mechanisms and psychosocial factors (1, 8). This complication occurs frequently during the first 24 hours (acute phase) after chemotherapy and can have devastating effects on the personal and occupational life of patients. These problems are still persistent despite the widespread use of chemical antiemetic drugs, such as serotonin type 3 (5-HT<sub>3</sub>) receptor antagonists (also called serotonin receptor antagonists or serotonin blockers), and Neurokinin-1 (NK1) receptor antagonists. The extensive use of antiemetic drugs is associated with complications, such as extrapyramidal adverse effects of hypotension and headache. Hence, the tendency and eagerness to increase the use of herbal medicines has been increasing (9). There are multiple non-

pharmacological methods to reduce chemotherapy-induced nausea and vomiting, such as acupuncture, acupressure, relaxation, self-hypnosis, biofeedback, thought aversion technique, guided imagery, systematic desensitization, music therapy, and aromatherapy using ginger (10, 11). In the perspective of traditional medicine and Chinese medicine, the occurrence of nausea and vomiting is due to energy imbalance in one of the body circuits known as pericardium. This circuit has nine pressure points, each with a specific application. The sixth point of the circuit is known as the Nei Guan (Chinese: 内关), and is shown with acupressure point P6 (pericardium 6). This point is located at a distance of 5 cm from the distal wrist line, and between the two tendons of flexor carpi radialis and palmaris longus (12).

Acupressure is a skill that is easy to learn, and can be used in routine nursing and midwifery care, and is considered to be low-cost and non-invasive strategies for future interventional studies (2). Acupuncture is the insertion of needles into specific points for therapeutic purposes. Previous clinical trials reported the controversial results on the effects of acupressure on nausea and vomiting in children undergoing chemotherapy (13-16). The aim of this study was to assess the effect of acupressure on nausea and vomiting in children undergoing chemotherapy.

## 2- MATERIALS AND METHODS

### 2-1. Strategy search

The present study was conducted based on the Cochran's guidelines. An extensive search was performed on the Medline, Embase, Scopus, Cochrane, and Web of Science until February 2018. The search query in Medline (via PubMed) is shown in **Table.1**. In addition, a manual search was conducted in Google motor engine,

Google Scholar, and bibliography of related articles and reviews.

**Table-1:** Search strategy for Medline (via PubMed).

Search terms
((("acupressure"[MeSH Terms] OR "acupressure"[All Fields]) AND ("drug therapy"[Subheading] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapy"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "chemotherapy"[All Fields])) AND (("nausea"[MeSH Terms] OR "nausea"[All Fields]) OR ("vomiting"[MeSH Terms] OR "vomiting"[All Fields])) AND (("child"[MeSH Terms] OR "child"[All Fields]) OR ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields])) AND (Efficacy[All Fields] OR ("treatment outcome"[MeSH Terms] OR ("treatment"[All Fields] AND "outcome"[All Fields]) OR "treatment outcome"[All Fields])).

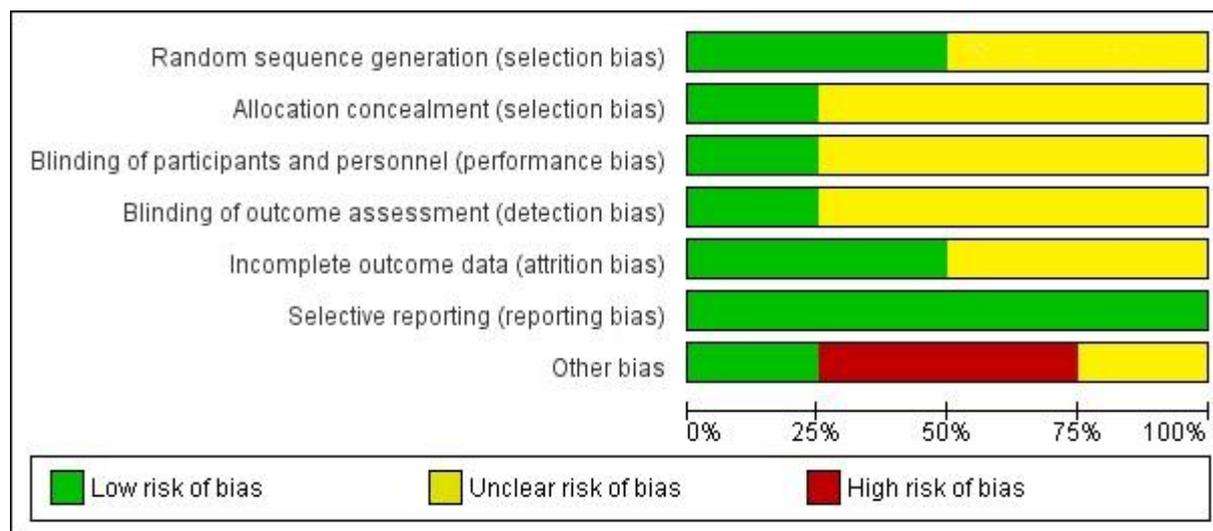
### 2-2. Selection criteria

We included all clinical trials evaluating the influence of acupressure on nausea and vomiting. No time and language limitations were applied.

### 2-3. Quality Assessment and Data Extraction

After conducting the search and eliminating duplicated reports, two independent researchers screened the titles and abstracts of the studies, and then potentially relevant studies were selected. Any disagreement was solved by discussion. Data related to the design of the study, the name of the first author, the year of publication, age of participants, study design, number of participants intervention/control, type of intervention, and assessment tool were recorded (**Table.2**) (*please see the table at the end of paper*).

The quality of the studies was assessed using Cochrane's proposed guidelines (17). The risk of bias of the included studies was assessed by two authors independently using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions (Tarsilla, 2008) that evaluated: (a) random sequence generation; (b) allocation concealment; (c) blinding of participants and personnel; (d) blinding of outcome assessment; (e) incomplete outcome data; (f) selective reporting; and (g) other bias. In this assessment, each item was graded as 'low', 'high' or 'unclear' risk of bias (**Figure.1**).



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Abusaad & Ali, 2016	?	?	?	?	?	+	?
Dupuis et al. 2018	+	+	+	+	+	+	+
Jones et al. 2008	?	?	?	?	+	+	-
Yeh et al. 2012	+	?	?	?	?	+	-

Fig.1: Assessment of risk of bias through eligible studies.

### 3- RESULTS

#### 3-1. Summary of included studies

Systematic and manual search led to achieving 106 non-repetitive records. After the screening, four articles were entered (13-16) (**Figure.2**).

#### 3-2. Acupressure wrist bands and placebo bands

In a prospective, randomized and crossover trial, Jones et al., evaluated the effect of acupressure on chemotherapy-induced nausea and vomiting (CINV), among 18 pediatrics randomly divided into two groups of acupressure wrist bands and placebo bands. The treatment procedure was to administrate standard antiemetic therapy for all patients. A questionnaire was used to measure the outcomes of nausea and vomiting. At last, their results showed the feasibility of well tolerated acupressure but not more effective than placebo (13).

#### 3-3. Acupressure versus sham bands

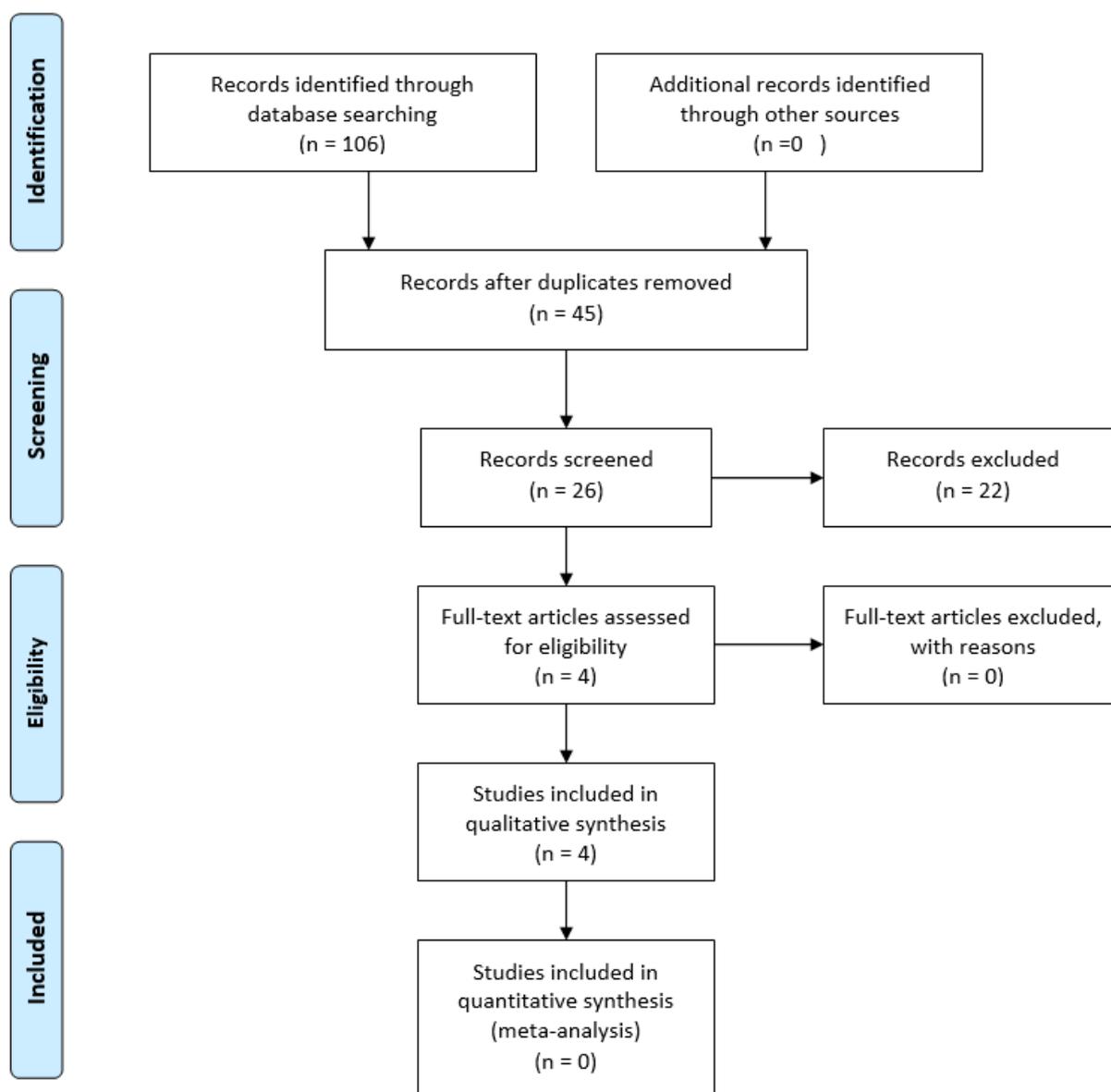
Dupuis et al., conducted a multicenter, prospective, randomized, single-blind, sham-controlled trial on the patients aged between 4 and 18 years. The research units received highly standard antiemetic chemotherapy and were assigned into two groups of acupressure and sham bands. The results showed no attenuation in the chemotherapy-induced nausea intensity using acupressure bands either in the acute (odds ratio [OR]: 1.33; 95% confidence interval [CI]: 0.89-2.00), or the delayed (OR: 1.23; 95% CI: 0.75-2.01) phases. In addition, daily vomiting was not improved via acupressure bands in either the acute (OR: 1.57; 95% CI: 0.95-2.59), or the delayed (OR: 0.84; 95% CI: 0.45-1.58) phases (14).

#### 3-4. Auricular acupressure intervention + standard care (AAP), and auricular acupressure using sham auricular points (SAP) + standard care

Yeh et al. in a randomized crossover trial evaluated CINV among 10 patients before and seven days after three rounds of chemotherapy drugs (CTX). The subjects were divided into two groups of Auricular acupressure intervention + standard care (AAP), and auricular acupressure using sham auricular points (SAP) + standard care. Occurrence ( $p=0.0289$ ) and severity ( $p=0.0310$ ) during chemotherapy-induced nausea in pediatric patients were significantly lower in the AAP group compared to the standard care (SC) group ( $p<0.05$ ). Occurrence ( $p=0.0024$ ) and severity ( $p=0.0007$ ) during chemotherapy-induced nausea in pediatric patients were significantly lower in the AAP group compared to the SC group. However, duration of nausea ( $p=0.6193$ ) and ( $p=0.7154$ ) vomiting did not show any significant difference between two groups. Moreover, no significant difference was observed in CINV between the two groups of AAP and SAP (15).

#### 3-5. Antiemetic drugs+ acupressure Point 6 (P6), and the control group

In a study by Abusaad and Ali, the acupressure was applied to attenuate CINV in 60 adolescents with cancer who were selected by convenience sampling method within two equal groups of case and control. The intervention group received the antiemetic drugs+ acupressure Point 6 (P6), and the control group was administered by mere antiemetic drugs. In the first week, the intervention group exhibited a reduction in the total mean score of vomiting frequency ( $p=0.01$ ), and retching experience ( $p=0.31$ ), nausea duration ( $p=0.003$ ), vomiting severity ( $p=0.05$ ), nausea frequency ( $p=0.02$ ), compared to the control group. In the second week, the intervention group exhibited a reduction in the total mean score of vomiting frequency ( $p=0.01$ ), and retching frequency ( $p=0.02$ ), and retching frequency ( $p=0.42$ ), compared to the control group (16).



**Fig.2:** PRISMA flowchart of present study.

#### 4- DISCUSSION

This is the first systematic review to address the effect of acupressure on nausea and vomiting in children undergoing chemotherapy. In developed countries, leukemia accounts for 30% of all cancers among children below 15 years of age, and is considered the most common childhood malignancy, where acute lymphoblastic leukemia (ALL) is the most predominant type representing 80% of all cases of

leukemia (18, 19). Chemotherapy is considered the standard therapy for patients with acute leukemia and other cancers with the aim of controlling these diseases via suppressing the growth and spread of cancer cells (20). Chemotherapy-induced nausea and vomiting are the most common side effects of chemotherapy with a prevalence of 54 to 96%, in addition to a list of other chemotherapy-related side effects in the pediatric oncology (21). CINV may have negative effects on the

overall quality of life and represents a bad experience during cancer treatment (22). So that, alternative and complementary medicine (CAM) has attracted the attention of the healthcare providers and assumed significant importance in cancer therapy for reasons varying from accessibility to cost (23-27). Acupressure is a non-pharmacological method that was reported to play a role in reducing the incidence or controlling the severity of CINV. Chemotherapy-induced nausea-vomiting is a prevalent and detrimental side effect of cancer chemotherapy treatments, however, studies suggest that the clinical uptake of antiemetic guidelines is often suboptimal, and CINV is a persistent problem for patients receiving chemotherapy, even with current advances in pharmaceutical technologies, approximately 60% of patients under chemotherapy despite receiving antiemetic medications have experience nausea and vomiting and may be dispirited from completing their chemotherapy regimen (28). Moreover, insufficient management of these side effects may result in metabolic imbalance, fatigue, distress, and lowered quality of life (29, 30).

Jones et al., assessed the effect of acupressure wrist bands and placebo bands. Their results showed the feasibility of well tolerated acupressure but it was not more effective than placebo (13). In a study by Abusaad and Ali, there was statistically significant difference in the total mean score of nausea, vomiting and retching of CINV between the Antiemetic drugs+ acupressure Point P6, and the control group. At last, the acupressure had a significant function to ameliorate the CINV, suggesting the efficacy of using this non-pharmacologic approach by oncology nurses. There was statistically significant difference in frequency, severity and duration of CINV between Antiemetic drugs+ acupressure Point P6, and the control group (16).

In Yeh et al., no significant difference was observed in CINV between the two groups. The subjects were divided into two groups of auricular acupressure intervention + standard care (AAP) and auricular acupressure using sham auricular points (SAP) + standard care (15). In Dupuis et al.'s study, the research units received highly standard antiemetic chemotherapy assigned into two groups of acupressure and sham bands. The results showed no attenuation in the chemotherapy-induced nausea intensity of acute or the delayed phases. Using acupressure bands, daily vomiting was not improved via acupressure bands in either the acute or the delayed phases (14).

There are some positive outcomes reported for acupuncture regarding the attenuation of nausea and vomiting. However, this technique has several risks, and it needs certain education and sometimes certification for special areas. Moreover, the needles used for the treatment is accompanied with fear and problems among children. Accordingly, the present study aimed to evaluate the effects of acupressure on reducing nausea and vomiting. In comparison with the acupuncture, the acupressure is cheaper and more available. One of the leading factors in the success of numerous therapeutic strategies, including acupressure, is the expectations. The bias in previous studies could affect the reported effectiveness (31).

There are differences among studies; there was a possibility of non-continuous wearing and improper use of acupressure bands by patients reporting significant effect. However, the patients are unlikely to regularly wear the acupressure bands in clinical practice. The patients are more likely to wear wrist bands simply with no internal stud-exerting pressure, so that an antiemetic or sham effect was found in the sham group. For this reason, three-arm trials were designed to cover three

domains of acupressure, sham acupressure, and no bands (14). The effectiveness of acupressure to prevent the pediatric chemotherapy-induced nausea and vomiting can be evaluated via a larger prospective research.

#### 4-1. Study Limitations

There are some limitations in the current study including small size, high patient heterogeneity (for example age and chemotherapy and antiemetic regimens). In a study, the enrollment study rate was calculated to be 77%. The reasons for refusing to participate were common, including parental time limits and patient's unwillingness to fill self-report questionnaires (14).

#### 5- CONCLUSIONS

The results of the present systematic review show that the patients considered the acupressure as a safe, effective and well-received strategy though objective criteria exhibited no statistically significant improvements compared to conventional care. In addition, educational programs should be provided in order to increase the knowledge and skills of health-care professionals in applying acupressure in their management plans.

**6- CONFLICT OF INTEREST:** None.

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**Table-1:** Characteristics of five studies included in our systematic review.

Author, Year, Country, Reference	Duration, week	Age, year	Measurement tools	Drop out, %	Type of treatment		Number of participants Treatment/ Control	Intention to treat	Basel Comparability of the treatment and control groups	Adverse effect	Major relevant findings
					Intervention group	Control group					
Kianpour et al., 2016, Iran (22)	4	---	21-item Depression, Anxiety, and Stress Scale and the Edinburgh Stress, Anxiety, and Depression Scale	18.1	Aromatherapy consisted of inhaling three drops of lavender essential oil every 8 h for 4 weeks	Received routine care	70/70	No	No	--	The mean stress, anxiety, and depression at time point of 2 weeks ( $p=0.012$ , $p<0.0001$ , and $p=0.003$ , respectively), and stress, anxiety, and depression scores at time points of 1 month ( $p<0.0001$ ) and 3 months after delivery ( $p<0.0001$ ) were significantly lower in the study group compared with the control group.
Chen et al., 2015, Taiwan (19)	4	32	PSQS, Edinburgh Postnatal Depression Scale	11.2	Drink one cup of lavender tea after smelling (appreciating) its aroma 1 hour before bedtime for a period of 2 weeks	Received regular postpartum care only	40/40	No	Yes	--	ANCOVA analysis with educational level as confounding variable showed that depression score was lower in lavender tea group compared to control group at week two after treatment ( $p=0.033$ ).
Tabeshpour et al., 2017, Iran, (23)	8	28	BDI-II	23	Tablet saffron (15 mg/Bid)	Placebo tablets, two tablets to be taken twice daily	30/30	No	Yes	--	The depression score changed significantly from 20.3 to 8.4 ( $p<0.01$ ) in saffron group and 19.8 to 15.1 in placebo group ( $p<0.01$ ). Rate of response to treatment was 6% in placebo group in comparison with 66% in saffron group. Comparison of two groups was significant.
Effati Daryani et al., 2017, Iran, (2)	6	27.7	DASS-21	2.1	Group 1: Received Lavender cream Group 2: Footbath and Lavender cream	Placebo cream	47/47/47	No	Yes	--	ANOVA analysis was followed by post hoc and showed that score of depression was lower in both lavender alone ( $p<0.001$ ), and lavender in combination with footbath compared to control group ( $p<0.001$ ).
Imura et al., 2006, Japan, (21)	30 min	31	Maternity Blues Scale,	--	Aromatherapy-massage	Received regular postpartum care only	16/20	No	Yes	--	The aromatherapy massage group experienced significantly lower Maternity Blues Scale, State-Anxiety Inventory scores after receiving aromatherapy-massage than those of the control group.

PSQS: Postpartum Sleep Quality Scale; BDI-II: Beck Depression Inventory-II; DASS-21: Depression, Anxiety and Stress Scale - 21 Items.