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Effects of Complementary Alternative Medicine on Hyperemesis Gravidarum: A Systematic Review

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ABSTRACT

Background: Nausea and vomiting of pregnancy (NVP) is a common problem for pregnant women. Many pregnant women are worried about the side effects of pharmacological therapy, thus encouraging them to use non-pharmacological therapy. Researchers have recently paid particular attention to complementary medicine methods for the treatment of NVP. With regard to the high prevalence of NVP as well as the adverse effects of chemicals on the mother and fetus of the drug, this study focused on assessing the safety and efficacy of different non-pharmacological methods in eliminating NVP. This systematic review was carried out to assess the safety and efficacy of different non-pharmacological methods in eliminating NVP. **Methods:** This study used a systematic review method by conducting a literature search through the PubMed database, Cochrane library, Science direct, Proquest, and Google Scholar with publication years starting January 2011 and January 2021. **Results:** A total of ten articles were selected as part of the final sample according to the inclusion criteria. Of the 10 articles, 2 were about the use of ginger, 3 were about Acupuncture-moxibustion, 2 were about psychotherapy, one was about Progressive muscle relaxation, and 2 were about psychoeducation. Studies have shown a positive effect on NVP reduction; however, no side effects were reported. **Conclusion:** According to the results of this review, most of the methods used are effective in reducing the incidence of NVP, among which ginger and P6 acupressure can be recommended more reliably.

1. Introduction

Nausea and vomiting is a common problem that often occurs in pregnancy (Boelig et al., 2016), with different levels of severity ranging from mild to severe and this is called hyperemesis gravidarum (Safajou et al., 2020).

The number of cases of nausea and vomiting in pregnancy is up to 80% according to reports from several studies (Burke et al., 2019). Nausea and vomiting in pregnancy is often referred to as "morning sickness" which in fact often occurs throughout the day of pregnancy, not just in the morning (Bazarganipour et al., 2015; Safajou et al., 2020).

Biological and psychological factors can cause this condition although the exact cause is unclear (Abbas et al., 2015; Faramarzi et al., 2015). The incidence of nausea and vomiting in pregnancy that leads to hospitalization is around 10.8% - 60.8% in pregnancy and this depends on the severity of the

nausea and vomiting (Boelig et al., 2016). Hyperemesis gravidarum can be considered as a type of negative emotion response from pregnant women to the underlying condition of anxiety (Nikibakhsh et al., 2016).

Many pregnant women are worried about the side effects of pharmacological therapy and encourage them to use non-pharmacological therapies to relieve symptoms (Martins & Pinto E Silva, 2014). Some of the therapies used to treat nausea and vomiting are supportive therapies such as replacing lost fluids, administering anti-nausea drugs, lifestyle changes (Hamdiah et al., 2017; Joulaeerad et al., 2018). Complementary and alternative medicine (CAM) is widely used in treating nausea and vomiting problems during pregnancy such as acupuncture (Lu et al., 2021; O'Donnell et al., 2016; Tara, Bahrami-Taghanaki, Ghalandarabad, et al., 2020), acupressure (Tabatabaeichehr & Mortazavi, 2020), herbal medicine containing ginger (Dyna & Febriani, 2020) and psychological interventions, such as hypnosis (Wegrzyniak et al., 2012), behavioral therapy (Levac et al., 2016) and mindfulness-based cognitive therapy (MBCT) (Faramarzi et al., 2015).

Therapy for hyperemesis gravidarum has differing efficacy (Matthews et al., 2015). A systematic review has been devoted to various pharmacological and non-pharmacological interventions (Boelig et al., 2017; O'Donnell et al., 2016). However, there has not been a comprehensive systematic review conducted specifically on studies that show the benefits of complementary and alternative medicine for treating nausea and vomiting during pregnancy (López-Morales et al., 2020; Saberi et al., 2014).

2. Methods

The main steps in a systematic review are: formulating research questions, identifying search keywords, searching relevant databases, extracting articles according to selection criteria, and reviewing paper quality on a checklist basis.

2.1 Formulating research questions

The research question formulation for a systematic review is: is complementary and alternative medicine effective in dealing with nausea and vomiting during pregnancy?

2.2 Extract keywords

The following keywords and their English equivalents to search for articles: nausea AND vomiting AND pregnancy" OR "hyperemesis gravidarum" AND [hypnotherapy OR hypnosis) AND acupuncture OR acupressure AND mindfulness AND "psychological intervention"; complementary alternative medicine AND nausea AND vomiting pregnancy.

2.3 Search database

Relevant papers published electronically from January 2011 and January 2021 searched in international databases (PubMed, Cochrane library, Science direct, proquest, Google Scholar)

2.4 Extract articles based on selection criteria

All relevant related articles will be extracted during systematic and follow-up search. Examines non-conforming articles by identifying the title, abstract, and full text. The results of all studies were reviewed to determine and remove duplicate studies.

2.5 Inclusion and exclusion criteria

The study is a clinical trial published in English, full text and examining the effects of complementary and alternative medicine on nausea and vomiting during pregnancy for review. Non-specific studies with complementary and alternative medicine in treating nausea and vomiting were excluded.

2.6 Extract, classify and report data

After reading the full text of the eligible articles, the data needed to conduct the review was extracted. Furthermore, the data extracted from the articles were then classified and reported in the review.

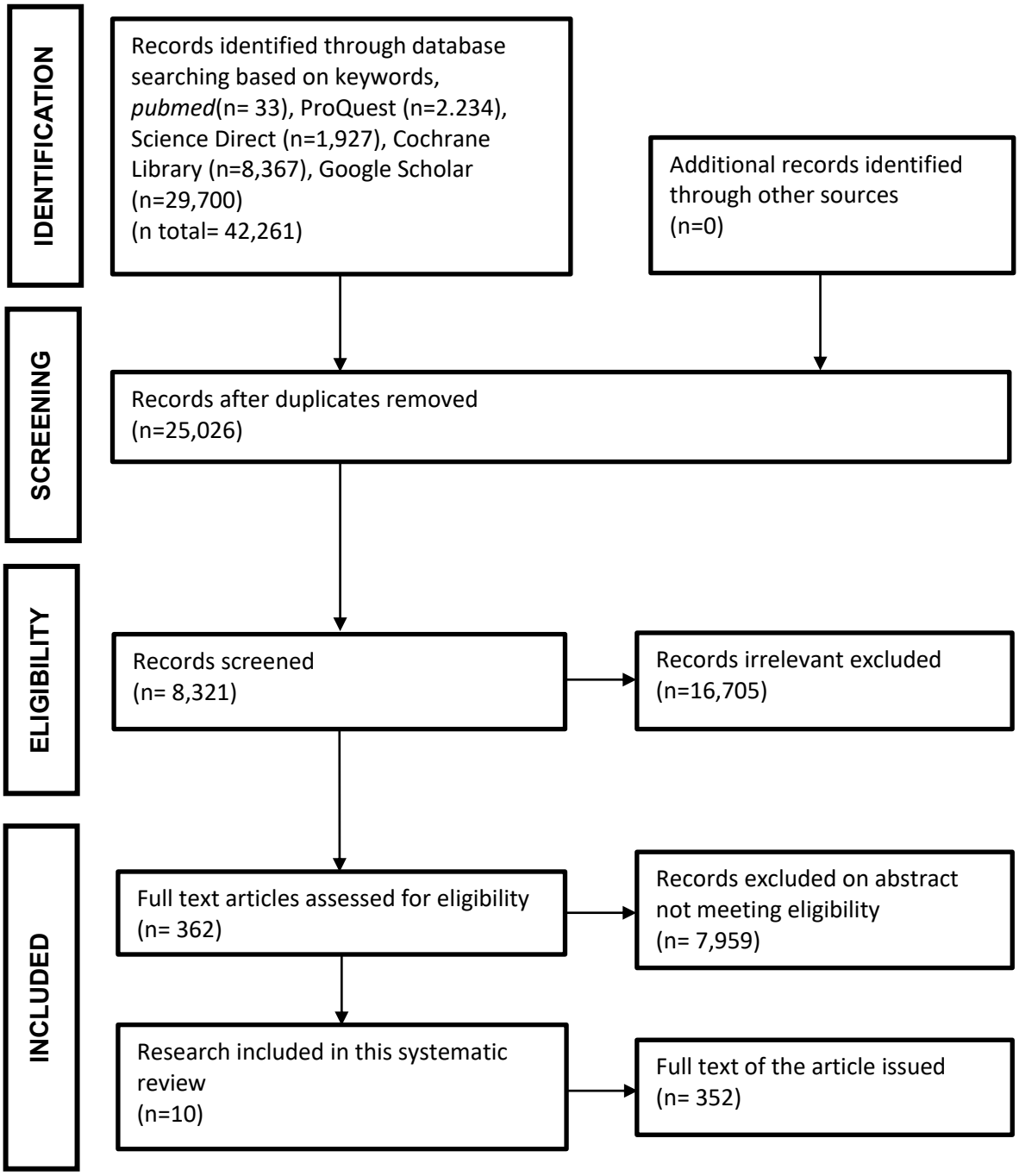

Fig. 1. Prism Flowchart

3. Results/Findings

There are 42,261 preliminary studies were identified as relevant reviews. After deletion of similar and unrelated studies for the purpose of the review, abstracts from 8,321 papers and full text of 362 papers evaluated. From this study, 10 were selected as part of the final sample (Fig. 1).

Psychoeducation and guided imagination

Psychoeducation based on relaxation methods gave positive results to reduce nausea and vomiting in pregnant women with hyperemesis gravidarum. One of the complements of non-pharmacological treatment is relaxation such as progressive muscle relaxation (PMR) and guided imagery are considered as complementary alternative treatments and as cognitive behavioral strategies (Charalambous et al., 2015; Evertsz et al., 2017). Strategies such as stress reduction and guided imagery have been used to control nausea and vomiting in patients undergoing chemotherapy (Charalambous et al., 2015).

Progressive muscle relaxation (PMR) is a treatment intervention defined as a procedure to facilitate successive contraction and relaxation of a group of muscles, simultaneously leading to the recognition of different sensations. This method is proven to be effective in dealing with nausea and vomiting (Mobarakabadi et al., 2020). Because of the relationship that exists between the severity of HG and the level of stress women feel (Nan et al., 2020), integrating the PMR stress reduction method and guided imagery in a general pregnancy training program could be effective in controlling nausea and vomiting. In most cases, women who suffer from nausea and vomiting in pregnancy do not receive the proper care and necessary medical attention. Nausea and vomiting may be a common complication during pregnancy and will gradually go away on their own. However, this condition causes a lot of problems for women and their families. Psychological factors involved in this condition such as anxiety, emotion, adaptation, acceptance of pregnancy (Raza et al., 2018). Therefore, it is necessary to design an intervention that integrates relaxation methods and conventional training to deal with the symptoms of pregnancy while considering the psychological stress of pregnant women (Rahman, A.E., Perkins, J., Islam, S., 2018; Segal et al., 2013).

Herbal medicine

Consuming 1 g of ginger per day can reduce nausea and vomiting compared to the placebo group. In addition, ginger was observed to have an effect comparable to that of vitamin B6 (Javadi et al., 2015). Experimental data in animal models show that ginger in doses below 1000 mg/kg does not cause toxicity but doses of 1000 mg/kg or 2000 mg/kg do cause maternal toxicity (ElMazoudy & Attia, 2018). Data on pregnant women also do not report an increased frequency of side effects from using ginger in doses below 1000 mg. Therefore, its use during pregnancy appears to be safe both for the mother-to-be and for the developing fetus. Data regarding other herbs are most often heterogeneous and give conflicting results without clear conclusions. Of these, the intake of garlic during pregnancy can significantly reduce the risk of early and late spontaneous preterm birth (Myhre et al., 2013). Some data also report a beneficial effect of inhalation with peppermint oil to relieve nausea and vomiting (Joulaeerad et al., 2018; Safajou et al., 2020). However, there is still not enough evidence to prove the effectiveness of cranberry, Echinacea, Ginkgo biloba, chamomile, or peppermint in pregnant women (Chowdhury & Chakraborty, 2019). All herbal products should be used with caution in pregnancy, because safe consumption limits have not been studied. Further studies in larger groups of pregnant women are needed to confirm safe doses of herbal products, which can be used by pregnant women (Dong et al., 2020; Lu et al., 2019).

Acupuncture

As a complementary therapy, acupuncture is used to treat hyperemesis gravidarum. Through stimulation of the meridians and acupuncture points, acupuncture can regulate blood qi and yin-yang and improve visceral function (Chen & Yu, 2020). Although similar treatments, such as acupressure and hydro-acupuncture, are commonly used in hyperemsis gravidarum, acupuncture still has its own advantages. Puncture acupuncture outperforms acupressure in onset and duration of treatment. Acupressure takes a long time (at least 8-12 hours). Acupuncture can relieve vomiting in the treatment of hyperemsis gravidarum within minutes, which may be related to some neural substrates. In addition, acupressure is often performed on the Neiguan point (PC6), the acupuncture point commonly used in treating hyperemesis gravidarum, while acupuncture is more flexible, choosing acupuncture points dialectically according to individual and holistic conditions. Acupuncture is superior to acupressure

in treating hyperemesis gravidarum, probably due to the lighter and faster stimulation of acupressure while the intense neurophysiological effects produced by acupuncture are more (Foster, Bishop, Bartlam, Ogollah, Barlas, Holden, Ismail, Owett, et al., 2016; Yang, Yun, et al., 2021). In addition, acupuncture is often referred to as mind body therapy. which has a beneficial effect on mental and gastrointestinal psychosomatic disorders through regulation of the autonomic nervous system (Yang, Yang, et al., 2021).

Acupuncture can reduce anxiety and depression scores in patients with nausea during pregnancy (Ball et al., 2016; Foster, Bishop, Bartlam, Ogollah, Barlas, Holden, Ismail, Jowett, et al., 2016). The mechanisms of acupuncture in the treatment of hyperemesis gravidarum are gradually being explored and are currently focusing on its antiemetic and gastrointestinal functions. Many trials have demonstrated the effect of acupuncture on the endogenous opioid system (Zakarija-Grkovic & Stewart, 2020), as well as 5-transmission hydroxytryptamine (Olapour et al., 2013) by activating 5-hy droxytryptamine and noradrenergic fibers, thereby affecting afferent stimulation from the central nervous system to the vomiting center and reducing nausea and vomiting. In addition, it can regulate gastrointestinal motility by stimulating vagus and sympathetic nerve reflexes (Liu M., 2019) and affects gastric emptying via visceral somatic reflexes. Recent studies have found that the use of acupuncture during pregnancy is a safe treatment modality to reduce discomfort (Foster, Bishop, Bartlam, Ogollah, Barlas, Holden, Ismail, Jowett, et al., 2016).

MBCT

Mindfulness based cognitive therapy (MBCT) intervention for pregnant women with nausea and vomiting with gestational age of 6-12 weeks was conducted for eight sessions and implemented for three weeks (each session lasted 50 minutes) (Kianpour et al., 2018). This program is designed to help pregnant women manage stress, recognize their reality, accept their thoughts and feelings in a systematic way. Intensive MBCT for pregnant women with moderate nausea and vomiting, including integration of elements of mindfulness-based stress reduction and cognitive behavioral therapy. Each session involves training on labeling thoughts, feelings, and behaviors, meditation practice, yoga, mindful eating, and diaphragmatic breathing. The participants are also given homework after each session (Faramarzi et al., 2015).

Hypnosis

Brief hypnosis was performed on four women who experienced persistent nausea and vomiting. Before the hypnosis started, the therapist asked pregnant women about the cause of their nausea, but none of the participants mentioned the cause. Therapists hypnotize pregnant women to help them identify the real cause of their nausea by accessing their unconscious and resolving conflicts they are hiding unconsciously (Chen & Yu, 2020).

Progressive muscle relaxation

The role of progressive muscle relaxation in the treatment of pregnant women with hyperemesis gravidarum performed by a psychiatrist individually and every day in a room with dim light and suitable ventilation for 20 minutes for two weeks (Chowdhury & Chakraborty, 2019; ElMazoudy & Attia, 2018; Emami-Sahebi et al., 2020). After the patient is placed in a supine position and after the technique the patient is asked to tense and relax the calf muscles, thigh muscles, gluteal muscles, abdominal muscles, chest muscles, hand muscles, forearms, shoulders, neck muscles, facial muscles, and forehead muscles in sequence. which has been specified (Yang, Yang, et al, 2021).

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Table 1. Characteristics of the research reviewed

Author, Year	Design	Population	Intervention	Measured variables	Results
Shakiba M et al, 2019	Quasi experiment	Pregnant women with hyperemesis gravidarum (n=100)	Providing psychoeducational interventions and progressive muscle relaxation	Frequency of nausea and vomiting	Psychoeducation based on the relaxation method in this study has a positive and significant effect on reducing the intensity of hyperemesis gravidarum
Sarecka-Hujar and Szulc-Musioł, 2021	*literature review*	Pregnant mother	Pregnant women who drink cranberry, chamomile, Echinacea purpurea, garlic, ginger, Ginkgo biloba, and peppermint herbs	Frequency of nausea and vomiting	Ginger doses below 1000 mg per day can help relieve hyperemesis gravidarum, the amount of ginger does not increase the frequency of side effects for either the woman or the developing fetus
ZN Mao and CE Liang, 2009	Quasi experiment	100 and 50 cases *hyperemesis gravidarum* divided into 3 groups, acupunture-moxibustion, Chinese medicine and western medicine, 50 cases in each group	The acupuncture-moxibustion group was given acupuncture at the Zhongwan (CV 12), Neiguan (PC 6), Zusanli (ST 36) and Yinlingquan (SP 9) points, and mild moxibustion for 10-15 minutes.	Frequency of nausea and vomiting	*Acupuncture-moxibustion*is the best method for hyperemesis gravidarum
Faramarzi M et al, 2015	*Prospective, open-label, randomized, controlled, parallel-group study*	86 pregnant women aged 18-40 years, between 6-12 weeks of gestation with moderate nausea and vomiting, Education more than 5 years and not practicing relaxation techniques or under psychotherapy	MBCT program given for 8 weeks	nausea, vomiting, anxiety, depression, for PDQ; birth concerns, relationship concerns and total PDQ	These findings indicate that 3 weeks of psychological intervention for medical therapy showed positive therapeutic results after treatment was completed, and 1 month after treatment. This suggests that psychotherapy should be considered as an additional treatment option for women with nausea vomiting pregnancy
Madrid et al, 2014	Qualitative	4 pregnant women with hyperemesis gravidarum	Provide hypnotic intervention	Frequency of nausea and vomiting	Psychodynamic investigation of the causes of nausea and finding solutions
Gawande S et al, 2011	a prospective, randomized, observer blind and comparative study	30 pregnant women	Received pharmacotherapy and progressive muscle relaxation every day for 2 weeks in the intervention group while the control group only received pharmacotherapy	*Number of Drugs, Complete Response, Recurrence, Clinical Global Improvement*	*Progressive muscle relaxation* effective in hyperemesis gravidarum and in combination with antiemetics, can reduce the amount of antiemetic given in hyperemesis gravidarum. The patient also showed an early response, reduced recurrence of nausea and vomiting and improved progress when combined with antiemetics
Saberi et al, 2014	*A Randomized, Placebo-Controlled Trial*	120 eligible pregnant women with mild to moderate nausea	Giving ginger capsules to the ginger group and giving lactose capsules with a similar form to the placebo	Subtractionsymptoms of nausea and vomiting using Rhodes Index scores	There was a significant difference in the mean reduction of the Rhodes Index score on nausea and vomiting in the three groups

		and vomiting before 16 weeks of gestation.	group as many as 12 capsules for 4 days while the control group did not receive anything.		(ginger, placebo, control). Vomiting and nausea in the ginger group decreased by 51% and 46%, respectively. Ginger was more effective in treating nausea and vomiting than the placebo group.Ginger is effective in reducing NVP in pregnant women with mild symptoms before 16 weeks of gestation.
Tara et al, 2020	*Randomized, multi-center clinical trial*	90 pregnant women were randomly divided into 3 groups, namelyacupressure group, medication group, and Sham acupressure group	Pregnant women were randomly divided into three groups, group 1 was given PC6 acupressure (4 times a day, for 10 minutes), group 2 was given*sham acupressure*, and group 3 was given treatment with vitamin B6 and metocloram.	Subtractionsymptoms of nausea and vomiting using Rhodes Index scores	There was a decrease in complaints of nausea and vomiting, and the severity and frequency of nausea and vomiting as well as the frequency of nausea and vomiting in pregnant women in the pre-intervention phase compared to after the PC6 intervention. Giving PC6 acupuncture pressure can reduce the severity of nausea, vomiting, and vomiting in pregnant women.
Sahebi et al, 2020	*quasi-experimental study*	52 pregnant women with moderate to severe Nausea and Vomiting of Pregnancy (NVP).	Participants were divided into 2 groups with 26 people in each group. The intervention group received ICBT in six sessions (in addition to the usual prenatal care), whereas those in the comparison group received the usual prenatal care.	Assessment of the level of nausea and vomiting usingPregnancy-Unique Quantification of Emesis/ Nausea scale. Assessment of anxiety levels using the Spielberger State-Trait Anxiety Inventory and assessment of levels of postnatal depression using the Edinburgh Postnatal Depression Scale	The ICBT group showed a significant reduction in the frequency of vomiting immediately in 1,2,3,4 weeks after the intervention. For duration of nausea and number of vomiting episodes, ICBT and comparison groups showed significant time-group interactions, but generalized estimation equation testing revealed no significant group differences at the aforementioned time.
Mobarakabadi et al, 2019	*randomized, single-blind, placebo-controlled trial*	75 pregnant women with mild to moderate nausea and vomiting in pregnancy <20 weeks' gestation were assigned to the same three groups (n = 25).	Pressure was applied to P6 in the acupressure group using the Sea-Band button for three days; in the placebo group, sea-band was applied to acupressure at point P6; the control group did not receive any intervention.	The severity and frequency of nausea and vomiting of pregnancy usingSea-Band button	There was a significant reduction in the frequency, duration and severity of nausea and also in the frequency of vomiting in the acupressure and placebo groups after three days, but not in the control group. Significant differences were observed between the acupressure and placebo groups in terms of frequency and severity of nausea, but not duration or frequency of vomiting.Acupressure on P6 applied using a wristband for at least three days appears to be effective in relieving nausea and vomiting of pregnancy.

4. Discussion

This review focuses on research with complementary alternative medicine (CAM) interventions on nausea and vomiting during pregnancy. The results can be used by health professionals, especially obstetricians as guidelines and measures to reduce symptoms of nausea and vomiting in pregnant women and improve the quality of pregnancy, although not many studies have used CAM so little evidence has been provided to confirm consistent quality in all CAM interventions. The need for CAM counseling and intervention for patients with severe nausea and vomiting during pregnancy is a unique challenge faced by healthcare professionals. Psychological factors also need to be considered such as stress, anxiety, depression can also affect the frequency of nausea and vomiting during pregnancy.

Some of the CAMs that are useful for reducing nausea and vomiting during pregnancy are:relaxation techniques such as progressive muscle relaxation (PMR) and guided imagery are considered as complementary alternative treatments and as cognitive behavioral strategies (Charalambous et al., 2015). Strategies such as stress reduction and guided imagery have been used to control nausea and vomiting in patients undergoing chemotherapy. Relaxation is a form of behavioral therapy that is simple, practical, useful, and can be applied after a short training session (Seyed Ahmadi Nejad et al., 2015). Compared with pharmacologic therapy alone, progressive muscle relaxation techniques combined with pharmacologic therapy reduced the amount of medication needed to control nausea and vomiting, the number of days it took to complete therapy, and the number of patients who relapsed after treatment. The authors also found improvement in clinical symptoms among pregnant women with hyperemesis gravidarum. Consuming 1 g of ginger per day can reduce nausea and vomiting compared to the placebo group. Ginger is effective in reducing nausea and vomiting in pregnant women with mild symptoms at gestational age before 16 weeks (Saberi et al., 2014).

Hypnosis, a type of psychological intervention, is a transitional state that results from changes in the individual's focus and concentration and includes phenomena such as: changes in consciousness and memory, increased sensitivity to inclusiveness, and the emergence of responses and beliefs. Hypnosis deepens relaxation through the parasympathetic nervous system and helps relieve symptoms of nausea and vomiting (Wegrzyniak et al., 2012). Hypnosis to reduce gastrointestinal symptoms and frequency of persistent nausea and vomiting.

MBCT is a newly developed therapeutic intervention that requires: special and targeted attention. Mindfulness aims to maintain an individual's awareness of the current reality and includes educating people to adopt an attitude of acceptance without judgment, and to recognize emotions, thoughts, and bodily sensations to eliminate negative moods (Segal et al., 2013). MBCT has the effect of reducing nausea and vomiting during pregnancy. Researchers reported a reduction in the frequency of nausea and vomiting at 6 - 12 weeks' gestation. We also found that cognitive and behavioral therapies such as ICBT also showed a significant reduction in the frequency of vomiting immediately within 1,2,3,4 weeks after the intervention (Emami-Sahebi et al., 2020).

Acupuncture is used as the treatment of hyperemesis gravidarum, through stimulation of the meridians and acupuncture points, acupuncture can regulate blood qi as well as yin-yang and improve visceral function (Chen & Yu, 2020; Wu et al., 2020). Acupuncture is superior to acupressure in treating hyperemesis gravidarum, probably due to the lighter and faster stimulation of acupressure while the intense neurophysiological effects produced by acupuncture are more (Lu et al., 2021; Matthews et al., 2015). Giving PC6 acupuncture pressure can reduce the severity of nausea, vomiting, and vomiting in pregnant women (Tara, Bahrami-Taghanaki, Amini Ghalandarabad, et al., 2020). Researchers also found that Acupressure on P6 applied using a sea-band for at least three days appeared to be effective in relieving nausea and vomiting of pregnancy (Mobarakabadi et al., 2020).

Implication And Limitation

Several studies that have been conducted do not use a control group, do not have inclusion and exclusion criteria, and small sample sizes, thus distorting the generalizability of the results to the target population. In addition, maternal conditions such as depression may interfere with the intervention, thereby eliminating the possibility of recognizing the contribution of CAM interventions to the reduction of nausea and vomiting. Note that other factors such as side effects, cost-effectiveness,

additional health care costs, disorders, and accompanying therapies must be considered when selecting an intervention plan.

5. Conclusion

The results of the review of the CAM intervention on nausea and vomiting during pregnancy were less than optimal. Therefore, there is a need for strong evidence and more research on the effectiveness of CAM as a treatment intervention for nausea and vomiting during pregnancy. It also requires high quality research such as randomized control trials, a larger number of respondents and a variety of CAM interventions.

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