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Effectiveness of Ginger in Treating Nausea and Vomiting of Pregnancy

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ABSTRACT

Nausea and vomiting in pregnancy (NVP) is one of the common main complaints in pregnancy. NVP can be a significant burden to the patient, make a decrease in quality of life, pregnancy threatening or even worse can lead to nutritional loss and death. NVP diagnosed when in first trimester of pregnancy and the other possible cause of NVP is excluded. Management of NVP is included maintaining hydration, nutrition, and lifestyle modification. Also avoiding the smells, food, or activity that can cause nause are necessary. There are some methods to treat NVP including pharmacological or nonpharmacological. The non-pharmalogical approach is to change nutritional habits, lifestyle and medications. Several pharmalogical agents that can be used to relief the symptoms of NVP are pyridoxine, pyridoxine/doxylamine, anti-histamines, metoclopramide, promethazine and metoclopramide. Some patients also want to try more "natural" medications for NVP like ginger. The pharmacological activity is thought to stand in the pungent principles (gingerols and shogaols) and volatile oils (sesquiterpenes and monoterpenes). The true mechanism of action of ginger is probable to be a gastric effect, to increase tone and peristaltic due to anticholinergic and anti serotonin act. Ginger acts straight to the digestive tract and avoids the CNS side effects common to centrally acting antiemetics. Ginger is available in capsule or syrup form or in candy, cookies, beer, tinctures, teas, sodas, and jam. Nowadays, true dosing is available only if one uses standardized extracts; however, women may choose to use another form of ginger.

1. Introduction

Nausea and vomiting or NVP (often referred to as morning sickness) are common symptoms in pregnant women approx. 70 – 85% and 40 –50% of pregnant women, respectively. Nausea and vomiting can be a significant obstacle to the patient, resulting in decreased quality of life, furthermore make wide medical complications, malnutrition, and in some conditions, may result in management disruption and stoppage. Nausea and vomiting in pregnant women are diagnosed when the first onset of symptoms is in the first trimester of pregnancy and the other possibilities of causes of NVP have been excluded. There are also risks of recurrence in a future pregnancy (15%–81%). It typically affects pregnant

women between the fourth and the seventh gestational week and usually resolves by the $20 \, \text{th}$ week.³

Management of hyperemesis gravidarum includes maintaining appropriate hydration, electrolytes, and dietary and lifestyle modifications.⁴ Women are commonly offered advice about the (usually) self-limiting nature of the condition and advised to avoid foods, smells, activities, or situations that they find nauseating and to eat small frequent meals of dry, bland foodstuffs. Many remedies are suggested for nausea and vomiting in early pregnancy, including pharmaceutical and non-pharmaceutical interventions.⁵

The non-pharmacological therapy for Nausea and

Vomiting in Pregnancy (NVP) during pregnancy is underpinned by a change in nutritional habits, lifestyle, and medications, which have received scant attention in the literature. The drugs widely used to treat the mild to moderate cases of NVP are pyridoxine, antihistamines, metoclopramide, pyridoxine /doxylamine, promethazine, and metoclopramide. In the event of more severe symptoms, ondansetron and corticosteroids can be prescribed. However, there is little on the efficacy of these drugs. Many mothers feel helpless in dealing with this condition, especially out of concern for the side effects of these drugs on the unborn fetus.⁷

Medication options for nausea and vomiting during pregnancy are limited because of concerns about safety. Initially, treatment consists of identifying and avoiding nausea triggers, avoidance of spicy and fatty foods, and cessation of iron supplements. If these nonpharmacologic approaches do not alleviate symptoms, other options, including multivitamins, vitamin B6, doxylamine, ginger, antihistamines, anticholinergics, and corticosteroids, may be tried. Many patients prefer to avoid "drugs" during pregnancy, choosing instead "natural" alternatives. One of these popular options is ginger. The efficacy and safety of this product are still in question, and it is classified as pregnancy category C. Ginger root is commonly used as a flavoring agent in food and beverages and as a fragrance additive in cosmetic products. The antiemetic constituents of ginger exert their effects on the gastrointestinal tract, but the specific mechanism is unknown. In vitro, it shows that to have some ability to antagonize serotonin 5- HT3 receptors.8

Ginger rhizome (Zingiber officinale), used worldwide as a spice and an herbal remedy, has a long history as a digestive aid and antinausea remedy. It is the herb most commonly used to treat nausea and vomiting during pregnancy, either recommended by providers or used as self-treatment by women. The pharmacological activity is thought to stand in the pungent principles (gingerols and shogaols) and volatile oils (sesquiterpenes and monoterpenes). The

true mechanism of action of ginger is thought to be a gastric effect, to increase tone and peristaltic due to anticholinergic and anti serotonin action. Ginger acts straight to the digestive tract and avoids the CNS side effects common to centrally acting antiemetics. Ginger is available in capsule or syrup form or in candy, cookies, beer, tinctures, teas, sodas, and jam. Currently, true dosing is available only if one uses standardized extracts; however, women may choose to use another form of ginger.⁹

The recommendation of the daily dose of ginger for the medication of PNV is 1000 mg. In addition to concerns about dosage, ginger also has the potential to interact with other medications. It is recommended that ginger not be combined with medications such as dimenhydrinate (Dramamine) since the possible interactions are currently unknown. Ginger should also be avoided in patients prescribed oral hypoglycaemic agents or insulin, as some of the constituents of ginger could theoretically potentiate the hypoglycaemic effect of these medications. ¹⁰

2. Methods

The researcher searched for all studies published between 01 January 2000 and 01 August 2021, using the following databases: PubMed. The following keywords were used in the databases during the literature search: "((ginger) AND (morning sickness)) AND (pregnancy)". The research was limited to a human study published in the English language. More studies were identified through a manual search of the bibliographic references of the relevant articles and existing reviews. The inclusion criteria were studies that describe the pharmacology of ginger. The exclusion criteria were studies that include other conditions (e.g. comorbid conditions (anxiety, socioeconomic status, nutrition level, and the number endocrine problems, of previous pregnancies), neurovascular problems, immunopathological problems, hematological problems, and oncology problems that could play an important role in nausea and vomiting in pregnancy. Moreover, because these confounding factors are difficult to account for in this

study, the adjusted results were used and discussed in this article when available. In the first step, the researcher assesses the titles and abstracts of the studies to exclude articles based on the criteria. In the second step, the researcher read and evaluated the full-text studies that met the criteria.

3. Results

The PubMed search results identified 62 potential studies, with 50 potential studies remaining after duplicates were removed. After a quick review of the titles and abstracts of all 50 studies, 20 studies were identified for potential inclusion in the review. After a deep examination of the full text of the 20 studies against the inclusion criteria, a total of 10 trials were excluded Reasons for exclusion were: studies that include other conditions (e.g. comorbid conditions (anxiety, socioeconomic status, nutrition level, and a number of previous pregnancies), endocrine problems, neurovascular problems, immunopathological problems, hematological problems, oncology problems. See Figure 1 for the study selection and inclusion process.

4. Discussion

Six double-blind RCTs with a total of 675 participants and a prospective observational cohort study (n = 187) met all inclusion criteria. The methodology quality of 4 of 5 RCTs was high. Four of the 6 RCTs (n = 246) showed the superiority of ginger over placebo; the other 2 RCTs (n = 429) showed that ginger was as effective as the reference drug (vitamin B6) in relieving the severity of NVP episodes. The observational study obtained and RCTs (including follow-up periods) show the absence of significant side effects or adverse effects on pregnancy outcomes. There are no spontaneous or case reports of adverse events during ginger treatment in pregnancy.

This article identifies nine studies and seven reviews that investigated ginger for morning sickness, postoperative NVP, chemotherapy-induced, and antiretroviral-induced NVP. All studies reported that ginger provides a significant reduction in NVP;

however, the clinical relevance of some studies is less certain. Common obstacles within the literature include the lack of standardized extracts, not very good controlled or blinded studies, and limited sample size. Respectively, recent evidence has provided further support for 5-HT3 receptor antagonism as a mechanism by which ginger may show its potentially beneficial effect on nausea and vomiting.

Several differences were shown in the different guidelines for the management of NVP. Frequent snacks and avoidance of iron supplements in NVP are recommended for prevention. The intake of ginger, dopamine acustimulations, antihistamines, phenothiazines, and serotonin 5-hydroxytryptamine type 3 receptor antagonists is a routine recommendation for use in the community as treatment.

Twenty studies were included in the systematic review and eight teens in the meta-analysis. Acupuncture (OR: 18.9; 95% CI: 2.1, 168), acupressure (OR: 26.7; 95% CI: 2.5, 283.1) and methylprednisolone (OR: 6.7; 95% CI: 1.1, 38.8) was associated with better control of HG symptoms than the standard of care. Acupressure decreases the requirement of rescue anti-emetics (OR: 0.06; 95% CI: 0.01, 0.44); ondansetron with reduced hospital stay (WMD: -0.2; 95% CI: -0.31, -0.01) and diazepam with reduced risk of hospital admission (OR: 0.11; 95% CI: 0.01, 0.95). The quality of evidence is very low.

Thirty-seven trials involving 5049 women, met the inclusion criteria. These trials covered many interventions, including acupressure, mint oil, acustimulation, acupuncture, ginger, chamomile, lemon oil, vitamin B6 and several antiemetic drugs. We identified no studies of dietary or other lifestyle interventions. Evidence-based on the effectiveness of P6 acupressure, auricular (ear) acupressure, and acustimulation of the P6 point was limited. Acupuncture (P6 or traditional) showed no significant plus for women during pregnancy. The use of ginger products may be helpful to women, but the evidence of effectiveness was low and not consistent, though two recent studies support ginger over placebo. There

was only a little evidence from trials to support the use of pharmacological agents including vitamin B6, and anti-emetic drugs to relieve mild or moderate NVP. There was little information on maternal and fetal adverse outcomes and on psychological, economic, or social outcomes. We were unable to pool findings from studies for most results due to heterogeneity in study participants, interventions, comparison groups, and outcomes measured or reported. The methodologic quality of the included study was mixed.

In a study of 27 women, 250 mg powdered ginger root appeared to be superior to placebo in reducing NVP. The placebo was an equivalent dose of lactose, which may not be an inert ingredient for some subjects. Ginger root, however, is reported to contain a thromboxane synthetase inhibitor, which may affect testosterone receptor binding in the fetus. Whether powdered ginger root in quantities of 250 mg might adversely affect fetal development is not known.

All studies showed that ginger had a positive effect on nausea in pregnant women. Unlike other studies, one study reported that ginger was not beneficial to the treatment of vomiting. Herbal medicines such as Matricaria chamomilla, Elettaria cardamomum, pomegranate and spearmint syrup, and lemon provide safe and effective medical alternatives for treating pregnant women with mild to moderate NVP. The results suggested that ginger was more effective than vitamin B, but at the dose of 35-500 mg ginger, vitamin B6 and ginger had an identical effect. However, over a longer treatment period (60 days), vitamin B6 was proven to be more effective than ginger. The same effect was shown in the comparison of quince and vitamin B6 as well as ginger and doxylamine plus pyridoxine. Mentha did not generate a positive effect on NVP. However, this finding should be considered in light of the above limitations.

There is evidence suggesting that ginger is effective in reducing nausea and vomiting experienced during pregnancy. The studies used divided doses ranging between 500 and 1500 mg/day, with no higher incidence of birth defects, miscarriages, or deformities than in the general population. While most of the

studies concluded that there was no increased risk of birth defects in women taking gin-ger, the inclusion of those >12 weeks' gestation means that their data are, in reality, inconclusive.

In all 4 studies reviewed here, no rationale was offered for the choice of dose and length of treatment. As with all herbal, prescription, and over-the-counter medications, it is important to know the maximum safe dose and length of treatment with the fewest side effects, the consequences of overdose, and potential drug/herb interactions. In no study was the safety of ginger consumption during pregnancy explicitly addressed, nor was any study powered well enough to get statistically significant results concerning safety. The studies were time-limited, yet nausea and vomiting of pregnancy can last for weeks. Animal reported both mutagenic have antimutagenic effects of isolated components of ginger, and human studies have conflicting results regarding the potential inhibition of platelet aggregation when ginger is consumed at high doses. One recent study examines pregnancy outcomes of 187 women known to have consumed ginger during the first trimester and found no statistically significant difference in major malformations, spontaneous abortion, and stillbirth rates among the ginger and the comparison group. Four RCTs met the inclusion criteria. All trials found orally taken ginger to be significantly more effective than placebo in reducing the frequency of vomiting and intensity of nausea. Side events were generally mild and infrequent.

5. Conclusion

Gingers may be an effective treatment for nausea and vomiting in pregnancy. However, more observational studies, with larger sample size, are needed to confirm the encouraging preliminary data on ginger safety. The results of a study in this article suggest that ginger is a promising treatment for nausea and vomiting in a variety of clinical settings and possesses a clinically relevant mechanism. However, further studies are required to address the limitations in the current clinical literature before firm

recommendations for its use can be made.

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