

## Selections from Current Literature

# Complementary therapies for nausea and vomiting in early pregnancy

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Nausea and vomiting are uncomfortable and common complaints encountered in early pregnancy. Seventy per cent of women report nausea and 30–50% experience vomiting.<sup>1</sup> Most cases are mild and resolve by the twentieth week of gestation. At the other end of the spectrum is hyperemesis gravidarum, characterized by persistent nausea and vomiting that results in dehydration, ketosis, electrolyte imbalances and weight loss.

Morning sickness is a misnamed descriptive term describing nausea and vomiting of pregnancy. In 1993, Gadsby *et al.* published a comprehensive review of the timing, duration and onset of nausea and vomiting in pregnancy and demonstrated that, although the symptoms were more prevalent between 6 a.m. and noon, many pregnant patients reported nausea and vomiting throughout the day.<sup>2</sup> Studies of nausea and vomiting in pregnancy are often made more challenging because of the subjective nature of the symptom of nausea versus the objective sign of vomiting.

The pathophysiology of nausea and vomiting in early pregnancy and hyperemesis gravidarum is poorly understood. Various hormonal, biochemical, mechanical and psychological factors have been implicated. The aetiology of nausea and vomiting in pregnancy and hyperemesis gravidarum probably encompasses several factors. While the diagnosis may seem straightforward, it is important for primary care physicians never to overlook the other obstetrical and non-obstetrical causes in the differential diagnosis of nausea and vomiting.

The treatment of nausea and vomiting in pregnancy has traditionally been supportive, with dietary modification for mild cases. Such dietary advice consists of eating small portions of foods at frequent intervals, ingesting dry toast or crackers upon arising, and eating bland low-fat foods. Pharmacological treatments, including antihistamines, anti-nauseants, antiemetics and promotility

agents have been employed in more symptomatic patients. Concerns about the potential teratogenic effects of medications often limit their use.<sup>3</sup> A number of trials have found various antihistamines to be safe during pregnancy, although there have been no major epidemiological studies to look for teratogenic effects. Neither the efficacy nor the safety of phenothiazines or metoclopramide have been firmly established despite continued usage.<sup>4</sup> For those women who are not getting complete relief of symptoms with dietary modification and for those women concerned about the safety of medications, many are turning to complementary and alternative therapies to treat nausea and vomiting in early pregnancy.

The landmark study of Eisenberg *et al.*<sup>5</sup> demonstrated the widespread interest and growing use of alternative therapies. Physicians and patients alike may turn to complementary therapies to gain therapeutic benefits with hopes or beliefs of avoiding toxicities. Others may take this route because of a philosophical preference for natural over synthetic remedies. In this instalment of 'Selections from current literature', three different complementary remedies for the treatment of nausea and vomiting in early pregnancy will be evaluated: pyridoxine (vitamin B6), ginger and acupuncture.

**Vutyavanich T, Wongtrangan S, Ruangsri R. Pyridoxine for nausea and vomiting of pregnancy: a randomized, double-blind, placebo-controlled trial. *Am J Obstet Gynecol* 1995; **173**: 881–884.**

Pyridoxine (vitamin B6) has been studied alone or in combination with other drugs for many years as a treatment for nausea and vomiting in pregnancy. In this double-blind study, 342 pregnant women with nausea with or without vomiting were randomized to receive 30 mg pyridoxine daily or a placebo. The pyridoxine (10 mg) or placebo pills were to be taken three times a day for a total of 5 days. Patients were excluded from this study if they were taking any other medications, including iron pills. Dietary advice included a recommendation to divide food intake into small frequent meals rich in carbohydrates and low in fat. The subjects

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were then instructed to grade the severity of nausea on a visual analogue scale twice daily and to record the number of episodes of vomiting. The patients' recall of their symptoms on the day before entering the study served as a baseline. The two groups had similar pre-entry characteristics, pre-treatment nausea scores and frequency of vomiting. There was a significant decrease in nausea in the pyridoxine group compared with the placebo group. After 5 days of treatment, there was a reduction in the number of episodes of vomiting in both treated and placebo groups. There was a greater reduction in the number of vomiting episodes in the treated patients, but this difference was not statistically significant. Pyridoxine also significantly reduced the mean number of vomiting episodes during the first 3 days of treatment, but this beneficial effect appeared to diminish over the course of the study.

#### *Comment*

Pyridoxine (vitamin B6) is a water-soluble B complex vitamin and essential co-enzyme that aids in the metabolism of lipids, carbohydrates and proteins. There have been few studies evaluating pyridoxine alone for treatment of nausea and vomiting in pregnancy. The only other randomized, double-blind, placebo-controlled study reported improvement in nausea scores in treated patients with severe symptoms, but not in those with mild to moderate nausea.<sup>6</sup> However, this study, while carefully designed, had a small sample size and evaluated only 3 days of treatment.

There is little evidence in support of teratogenicity associated with vitamin B6 supplementation at these dosages during pregnancy.<sup>4</sup> One example of the gap between public perception of teratogenic risk and evidence-based proof of safety involves Bendectin. Bendectin, a combination of an antihistamine, doxylamine and pyridoxine, was an effective and common treatment for morning sickness until it was removed by the manufacturer from the American market in 1983 because of fear of continued litigation.<sup>7</sup> Subsequent studies failed to establish teratogenicity associated with Bendectin, which is available in some countries and often used to treat nausea and vomiting of pregnancy.

Although no correlation has been found between pyridoxine levels and nausea and vomiting in pregnancy,<sup>6</sup> the study by Vutyavanich *et al.* seems to support the efficacy of vitamin B6 in relieving nausea and vomiting in some pregnant patients. Perhaps, prescribing vitamin B6 intermittently rather than every 8 hours would have a more efficacious effect in reducing nausea and vomiting in early pregnancy by eliminating any risk of tolerance.

**Fischer-Rasmussen W, Kjaer SK, Dahl C, Asping U. Ginger treatment of hyperemesis gravidarum. *Eur J Obstet Gynecol Reprod Biol* 1990; 38: 19–24.**

Supplementation with ginger root was studied for its effectiveness in reducing the symptoms of hyperemesis

gravidarum. In this double-blind, placebo-controlled study, 27 hospitalized pregnant patients were randomized to receive 250 mg of powdered ginger root or placebo four times a day for the 4 day study period. After a 2 day washout period, patients were crossed over to the other group for 4 days. Although intravenous fluids were allowed, all other antiemetic medication was withdrawn. Seventy per cent of women stated a preference for the ginger treatment while four women (14.8%) had no preference. A numerical scoring system evaluating the relief of symptoms (nausea, vomiting, change in body weight, and overall relief) presented a less subjective assessment. There was a significant reduction in the symptoms of hyperemesis associated with the ginger treatment. The severity of nausea and the number of episodes of vomiting were reduced in the treated group. The preference for the ginger management period was statistically significant. No side effects were reported. There was one spontaneous miscarriage at 12 weeks' gestational age and one elective termination. The remaining 25 women in the study delivered healthy infants near or at term.

#### *Comment*

Ginger (*Zingiber officinale*) is a medicinal herb that has been used since ancient times as an antiemetic. The characteristic odour and flavour of ginger root come from its volatile oil.<sup>8</sup> The efficacy of ginger rhizome for prevention of symptoms of motion sickness as well as for post-operative vomiting has been well documented and demonstrated in many clinical studies.<sup>9,10</sup> This particular study was limited to those pregnant patients suffering from the most severe form of nausea and vomiting in pregnancy. Although the question remains whether it can be concluded that ginger is efficacious in reducing mild to moderate nausea and vomiting in pregnancy, it may be a reasonable alternative treatment to try. It is inexpensive, readily obtainable and available in a variety of different preparations.

The efficacy of ginger for the treatment of nausea and vomiting may depend on the source and the active ingredients in a particular preparation. Limited information is available regarding any adverse effects ginger root may have on foetal development. The absolute safety of ginger in pregnancy has been recently questioned because of the effect of ginger on foetal brain development and inhibition of thromboxane synthetase activity, which theoretically could increase bleeding in early pregnancy. The principal author of the study refutes these concerns in a follow-up communication.<sup>11</sup> Human consumption of ginger (raw and cooked) has not been demonstrated to affect platelet thromboxane production.<sup>12</sup>

Short-term use of ginger to treat nausea and vomiting during pregnancy is unlikely to pose a safety problem. Certainly, interest and enthusiasm in ginger as an antiemetic have been revived in recent years because of the many clinical trials yielding favourable results.

**O'Brien B, Relyea MJ, Taerum T. Efficacy of P6 acupressure in the treatment of nausea and vomiting during pregnancy. *Am J Obstet Gynecol* 1996; 174: 708–715.**

The efficacy of P6 acupressure in reducing the symptoms of morning sickness was investigated in a 7 day study. In this prospective, randomized, placebo-controlled study, 161 pregnant patients with nausea and vomiting in pregnancy received P6 acupressure, placebo or no therapy (control group). Patients in the treatment group were given acupressure wristbands (Sea-Bands) and instructed to apply the bands three finger-widths up from the wrist crease with the button between the flexor tendons on the medial aspects of both forearms. This was felt to be consistent with the Neiguan or P6 acupressure point. The women in the placebo group were given similar instructions except that they were told to place the button in a different position over the radius of both forearms. Participants began wearing the wristbands as continuously as possible from day 3 to day 6 of the study. Symptoms of nausea, vomiting and retching were recorded on a daily basis by all three groups. A research assistant also provided daily telephone follow-up. The majority of the participants (78.6%) were <12 weeks pregnant and they were allowed to continue any previously prescribed antiemetic medications or comfort measures. The 149 (92.5%) patients completing the study had a significant decrease in nausea, vomiting and retching, regardless of which randomized group they were assigned. This study suggested that the use of P6 acupressure provides no significant medical benefit.

*Comment*

Acupressure is based on the concept of *qi*, an essential life-force flowing through invisible channels in the body known as meridians. According to Chinese medicine, when *qi* flows freely, harmony and good health are possible.<sup>13</sup> Acupressure, in contrast to acupuncture, employs pressure, rather than needles, to specific areas of the body. There are specific places on the skin or acupoints where *qi* may be guided using focused finger pressure. When *qi* circulation improves, a harmonious equilibrium of mind and body is encouraged and the body is able to promote self-healing.

There have been several studies of stimulation of the P6 acupressure point in the treatment of nausea and vomiting of pregnancy.<sup>14,15</sup> Because of the nature of acupressure, it is difficult to perform a true double-blind study that involves no intervention. A 'dummy' or sham acupressure point as utilized in the placebo group of this study may elicit a therapeutic response, as has been noted by Lewith and Machin in their studies of acupuncture and chronic pain.<sup>16</sup> Beyreuther and colleagues performed a crossover study comparing wristbands over the P6 point with a sham position and noted no effect on vomiting, but a significant reduction in nausea.<sup>17</sup> Belluomini *et al.* asked patients to apply manual pressure

on the P6 point or a sham point and also noted that nausea decreased significantly in the treatment group but without a difference in the severity or frequency of vomiting.<sup>18</sup>

This particular experiment was a large randomized study that allowed patients to continue pharmacological measures to help relieve nausea and vomiting. It is conceivable that such measures may have blunted any response to acupressure. Self-application of the wrist bands to a pressure point that was not the precise P6 spot could also explain the unexpected outcome in this study. The authors also acknowledge that daily telephone contact with a research assistant may have had a therapeutic effect on the participants and may have obscured any benefit of acupressure.

## Summary

Nausea and vomiting are uncomfortable and sometimes debilitating symptoms encountered in early pregnancy. Many of the more conventional remedies offer only partial to negligible relief. Some pregnant women also express scepticism regarding the safety of the more traditionally prescribed pharmacological agents used to combat morning sickness. Vitamin B6, ginger root and acupressure are three complementary modalities that may help alleviate these self-limiting discomforts.

Safety is as important as efficacy. Unfortunately, not all alternative therapies have been adequately tested in this regard. Since pyridoxine is believed to be non-teratogenic in the above-described therapeutic doses, it can be judiciously recommended. When nausea predominates over vomiting, acupressure may be a very safe alternative remedy. More rigorous controlled conditions are required before all preparations of ginger can be safely recommended. Short-term use of ginger for nausea and vomiting during pregnancy is probably a safe recommendation based on available data.

Whether one criticizes or advocates their use, it is crucial for healthcare providers to have open discussions on complementary medical therapies with all patients. Such dialogues often expose patients' needs that may not be adequately addressed in the biomedical or biopsychosocial model.

It has been difficult for most practising physicians to keep well informed about complementary treatments since there are few evidence-based guidelines. However, many treatment options embraced as conventional are not based on evidence, but rather handed down from mentor to *protégé* throughout the ages. Physician-patient dialogue about integrating complementary methods with more conventional treatments and sharing the decision making remains critical. The three complementary modalities reviewed here might offer simple, inexpensive, safe and effective strategies to incorporate into managing this common discomfort of pregnancy.

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