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Comparing ginger and vitamin B6 for the treatment of nausea and vomiting in pregnancy: a randomised controlled trial

Jenabi Ensiyeh (MSCa, Faculty member of Azad University)[a,*], Mohammad-Alizadeh C. Sakineh (Ph.D Student, Faculty member of Tabriz University)[b]

[a]*Department of Midwifery, Touyserkan University of Islamic Azad, Hamedan, Iran*
[b]*Department of Midwifery, Tabriz University of Medical Sciences, Iran*
*Corresponding author. *E-mail address:* enciehjenabi@yahoo.ca (J. Ensiyeh).

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Abstract
Objective: to compare the effectiveness of ginger and vitamin B6 for the treatment of nausea and vomiting in early pregnancy.
Methods: double-blind randomised controlled trial. Pregnant women with nausea, who first attended the antenatal clinic at or before 17 weeks gestation, were invited to participate in the study. Over a 3-month period, 70 women were randomised to receive either ginger 1 g/day or vitamin B6 40 mg/day for 4 days. Subjects graded the severity of their nausea using a visual analogue scale, and recorded the number of vomiting episodes in the 24 hours before treatment and during 4 consecutive days while taking treatment. At 7-day follow-up, women reported any changes in the severity of their symptoms.
Results: compared with baseline, the decrease in the visual analogue scores of post-therapy nausea in the ginger group was significantly greater than that for the vitamin B6 group ($p = 0.024$). The number of vomiting episodes decreased in both groups, and there was no significant difference between the groups. In the ginger group, 29/35 women reported an improvement in nausea symptoms, compared with 23/34 women in the vitamin B6 group ($p = 0.52$).
Conclusion: ginger is more effective than vitamin B6 for relieving the severity of nausea, and is equally effective for decreasing the number of vomiting episodes in early pregnancy.

Keywords Ginger; Vitamin B6; Nausea; Vomiting; Pregnancy

Introduction

Nausea and vomiting are the most common symptoms experienced in early pregnancy. Approximately 70–85% of pregnant women experience nausea, and half will also experience vomiting episodes (Hollyer et al., 2002; Jewell and Young, 2003). One-quarter of employed nauseous pregnant women will require time off work because of their symptoms (Vatyavanich et al., 2001). The cause of nausea and vomiting in pregnancy is still unknown (Vatyavanich et al., 2001).

There are limited data on the extent of women's use of herbal medicines during pregnancy (Ben-arye

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and Benoari, 2006). In Australia, it has been reported that 36% of pregnant women take at least one herbal medicine supplement, mainly raspberry leaf, ginger, chamomile, cranberry juice and echinacea (Forster et al., 2006).

The use of herbal supplements during pregnancy may be to relieve pregnancy related symptoms, e.g. nausea and vomiting, reflux, Candida, nutrition or to prepare for labour, or may be for unrelated health issues such as colds, respiratory illnesses or skin problems (Henry and Crowther, 2000; Nordeng and Havnen, 2004).

Despite the high use of herbal medicines, knowledge of the potential benefits or harms of many of these products is scanty, particularly with respect to their use in pregnancy (Forster et al., 2006).

Ginger, known scientifically as *Zingiber officinale*, is a perennial native to many Asian countries (Borrolli et al., 2005). Information on the effectiveness of ginger for the relief of nausea and vomiting during pregnancy is limited (Ben-arye and Benoari, 2006), although one study from Thailand, reported that ginger was effective for relieving the severity of nausea and vomiting in pregnancy (Sripramote and Lekhyananda, 2003).

Vitamin B6 is often used for the treatment of nausea and vomiting in pregnancy (Aikins, 1998). The purpose of the present study was to compare ginger and vitamin B6 for the treatment of nausea and vomiting in pregnancy.

Materials and methods

Women were recruited consecutively from the antenatal clinic at Fatemieh Hospital, Hamedan, Iran. They were included in the study if it was their first attendance at the clinic, were 17 weeks of gestation or less, and had experienced nausea, with or without vomiting. Women were excluded if they: (1) had other medical disorders such as hepatitis or gastrointestinal diseases that might manifest with nausea or vomiting; (2) had mental health problems; (3) had taken other medication in the previous week that might aggravate or alleviate nausea or vomiting, such as iron tablets or antiemetics; (4) refused to participate in the trial; or (5) were unable to return for a follow-up visit 1 week later.

The Research Ethics Committee of the University of Touyserkan approved the study protocol, and all women provided informed consent. After obtaining verbal informed consent, women underwent general physical examinations and routine obstetric evaluations. They were subsequently randomised into two groups using a table of random numbers. Women in the ginger group received 1 g/day and those in the vitamin B6 group received 40 mg/day (two capsules daily, after breakfast and dinner, for both ginger and vitamin B6) for 4 days. All women were advised to divide their food intake into frequent small meals, rich in carbohydrates and low in fat, and not to take any other medications outside the trial. The women were asked to return after 1 week for assessment of their responses to the treatment. Those who did not return were contacted by telephone. Compliance was assessed by pill count and by asking women whether the drugs were taken.

The ginger and vitamin B6 capsules were prepared by a pharmacist from Fatemieh Hospital. Briefly, fresh ginger root was chopped into small pieces, baked at 60 °C for 24 hours, and then ground into powder. Ginger powder and vitamin B6 were weighed and packed into 500 and 20 mg capsules, respectively. Excess powder was wiped off the capsule surface with a clean dry cloth. Both vitamin B6 and ginger capsules were packed in an envelope containing eight capsules.

Two independent measurement scales were used to quantify the changes in severity of nausea: a visual analogue scale and a Likert scale. For the visual analogue scale, women were asked on their first visit to grade the severity of their nausea over the past 24 hours (baseline score) by marking an asterisk corresponding to their perceived state on a 10-cm vertical line, ranging from 0 (no nausea) to 10 (nausea as bad as it could be). Over the following 4 days of treatment, the severity of nausea was recorded three times daily at morning, noon and bed time. To obtain an objective measurement, the markings on the visual analogue scales were measured in centimetres. The average daily nausea scores and the mean nausea scores over the 4 days of treatment for each subject were then calculated.

At 1-week follow-up, a five-point Likert scale (much worse, worse, same, better, much better) was used to assess treatment response. Women were also asked to record the number of vomiting episodes in the past 24 hours at their first visit before treatment, and then on each subsequent day of treatment.

The median change in the severity of nausea and the number of vomiting episodes in the two groups was compared using Wilcoxon's rank-sum test.

Other secondary outcome measures included the occurrence of side effects and adverse effects on pregnancy outcomes such as abortion, preterm birth, congenital anomaly, perinatal death and mode of birth. Data collection and follow-up took 12 weeks.

Power analysis was used to determine the sample size. A sample of 31 women per group was needed to achieve a power of 0.80 with an alpha of 0.05. Therefore, 35 women were randomised to each group, which allowed for a 10% attrition rate.

The Statistical Package for the Social Sciences Version 10.0 was used for analyses and a p-value <0.05 was considered to be significant. Analysis was undertaken by intention to treat.

Results

Between 5 April and 5 July 2006, 1200 women attended the antenatal clinic at Fattemieh University Hospital. Of these, 80 women met the study's eligibility criteria and 70 women agreed to participate (Fig. 1). Thirty-five women were randomised to the vitamin B6 group and 35 to the ginger group. One woman randomised to the vitamin B6 group (2.8%) did not return to the clinic and as no data were collected on her, she was excluded from the study. Differences in baseline characteristics of the two groups were not statistically significant (Table 1).

The median change in nausea score (baseline minus average post-therapy nausea score) in the ginger group was significantly greater ($p = 0.024$) than that in the vitamin B6 group (Table 2). Table 2 presents data by intention to treat, and after excluding the missing woman.

When the average number of vomiting episodes over the 4 days of treatment was subtracted from the corresponding baseline value for each woman, and the overall change in the number of vomiting episodes for women in the two groups was compared, there was no significant difference between the groups (Table 3).

At the follow-up visit, a five-point Likert scale was used to assess women's subjective responses to treatment. In the ginger group, 29/35 (82.8%) women reported an improvement in their symptoms, compared with 23/34 (67.6%) women in the

Table 1 Characteristics of participants by treatment groups.

Characteristics	Ginger n = 35	Vitamin B6 n = 34
Age (years)	25.0±4.2	24.2±3.9
Parity		
Nulliparous	25 (71.4%)	17 (51.5%)
Multiparous	10 (28.6%)	16 (48.5%)
Education		
Less than high school	16 (45.7%)	13 (38.3%)
High school or more	19 (54.3%)	21 (61.7%)
Baseline nausea scores (cm)	5.4±2.6	4.6±2.3
Episodes of vomiting in previous 24 hours (median, range)	2 (0–5)	1(0–5)
Occupation		
Housewife	34 (97.1%)	33 (97.1%)
Employee	1 (2.9%)	1 (2.9%)

Data are presented as mean±standard deviation or n (%).

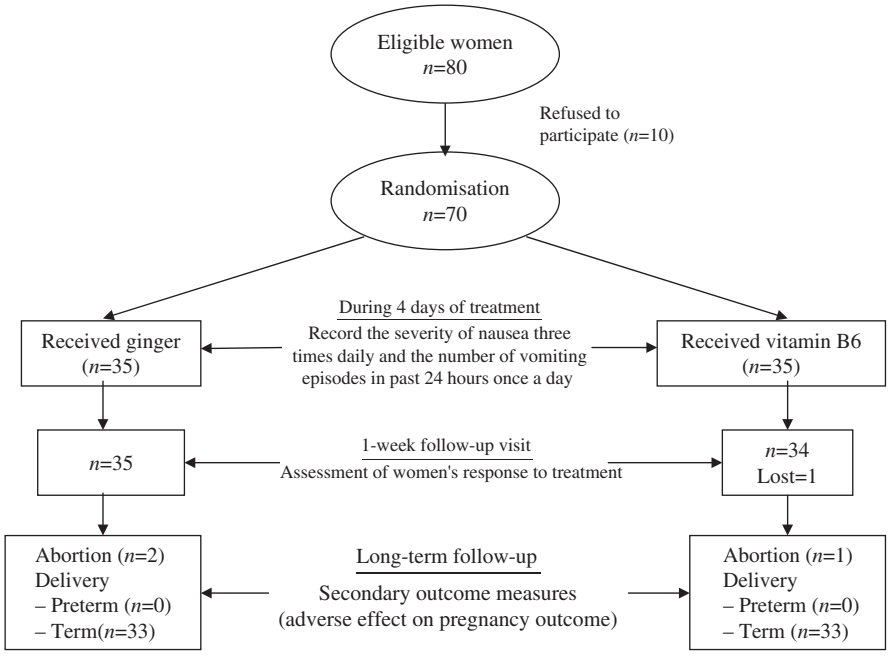

Fig. 1 Trial profile summarising recruitment and randomisation, interventions and delivery outcome.

Table 2 Change in nausea scores by treatment groups.

	From Day 0 to Day 1	From Day 0 to Day 2	From Day 0 to Day 3	From Day 0 to Day 4	From Day 0 to Days 1–4
Type of treatment					
Ginger (n = 35)	1.2±1.6*	1.6±1.9	2.4±2.2	3.3±2.5	2.2±1.9
Vitamin B6 (n = 34)	0.6±1.5	0.9±1.8	1.1±1.9	1.3±2.2	0.9±1.7
p-value†	0.098	0.067	0.019	0.004	0.024
Intent-to-treat analyses					
Ginger (n = 35)	1.2±1.6*	1.6±1.9	2.4±2.2	3.3±2.5	2.2±1.9
Vitamin B6 (n = 35)	0.7±1.6	1.1±2.1	1.3±2.3	1.5±2.6	1.4±2.1
p-value†	0.179	0.149	0.047	0.013	0.046

*Mean±standard deviation of the difference (baseline minus post-therapy).
†Wilcoxon's rank-sum test.

Table 3 Change in the number of vomiting episodes by treatment groups.

	From Day 0 to Day 1	From Day 0 to Day 2	From Day 0 to Day 3	From Day 0 to Day 4	From Day 0 to Days 1–4
Type of treatment					
Ginger (n = 35)	0.3±0.8*	0.5±0.9	0.6±0.8	0.8±1.0	0.6±0.7
Vitamin B6 (n = 34)	0.4±1.0	0.6±1.1	0.5±1.1	0.6±1.1	0.5±1.1
p-value†	0.593	0.537	0.552	0.241	0.809
Intent-to-treat analyses					
Ginger (n = 35)	0.3±0.8*	0.5±0.9	0.6±0.8	0.8±1.0	0.6±0.7
Vitamin B6 (n = 35)	0.5±1.7	0.7±1.4	0.6±1.3	0.7±1.3	0.6±1.4
p-value†	0.713	0.811	0.831	0.432	1.101

*Mean±standard deviation of the difference (baseline minus post-therapy).
†Wilcoxon's rank-sum test.

Table 4 Frequency of reported change in symptoms by treatment groups.

Change in symptoms	Ginger	Vitamin B6
Much worse	0 (0.0%)	0 (0.0%)
Worse	1 (2.9%)	0 (0.0%)
Same	5 (14.3%)	11 (32.4%)
Better	14 (40.0%)	17 (50.0%)
Much better	15 (42.9%)	6 (17.6%)
n	35	34

Fisher's exact test, $p>0.05$.

vitamin B6 group (Fisher's exact test, $p=0.52$) (Table 4).

No women in this trial took any other medication for nausea or vomiting. There were two spontaneous abortions in the ginger group and one in the vitamin B6 group (Fisher's exact test, $p>0.05$). Term birth occurred in 29/35 (82.9%) subjects in the ginger group and 28/34 (82.4%) subjects in the vitamin B6 group.

There were four (11.4%) caesarean deliveries in the ginger group and six (17.6%) in the vitamin B6 group (Fisher's exact test, $p>0.05$). No babies had any congenital anomalies and all were discharged in good condition.

Discussion

The efficacy of ginger and vitamin B6 for the treatment of pregnancy-related nausea and vomiting compared with placebo has been investigated previously. This study was a randomised double-blind controlled trial to compare the efficacy of ginger and vitamin B6 for the treatment of pregnancy-related nausea and vomiting.

In this study, the median change in nausea scores in the ginger group was significantly greater than that in the vitamin B6 group, while a study in Thailand (Sripramote and Lekhyananda, 2003) reported that the difference was not significant. This may be related to the higher

dose of ginger used in this study (1 g/day versus 500 mg/day).

In this study, 82.8% of women in the ginger group reported an improvement in nausea symptoms. This rate is similar to the reports of other studies (Fischer-Rasmussem et al., 1990; Sripramote and Lekhyananda, 2003).

In the present study, a treatment period of 4 days was chosen because a previous study (Fischer-Rasmussem et al., 1990) had shown that the effect of ginger was evident within a few days of treatment, and a long treatment period would potentially result in a higher rate of non-compliance and loss to follow-up.

Although this study did not find any adverse effects of ginger on pregnancy outcome, compared with vitamin B6, the number of subjects in this study was not large enough to draw any conclusions about the adverse effects, especially on abortion and congenital anomalies. However, it is reassuring that this trial, involving a cumulative total of 69 women, showed that ginger and vitamin B6 did not have adverse effects on pregnancy outcome. These findings support previous results (Portnoi et al., 2003).

As dietary changes may be associated with both types of treatment and outcomes, this can be considered as a potential confounding factor. As this was not assessed in the present study, it can be considered as a limitation. The effect of dietary changes should be controlled for in future studies.

The present study showed that ginger is more effective than vitamin B6 for relieving the severity of nausea, and is equally effective for decreasing the number of vomiting episodes in early pregnancy.

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References

Aikins, M.P., 1998. Alternative therapies for nausea and vomiting of pregnancy. Obstetrics & Gynecology 91, 149–155.

Ben-arye, A., Benoari, A., 2006. Herbal medicine in women's life cycle. Harefuah 145, 738–742.

Borrolli, F., Capasso, R., Aviello, G., Pittler, M.H., Izzo, A.A., 2005. Effectiveness and safety of ginger in the treatment of pregnancy-induced nausea and vomiting. Obstetrics & Gynecology 105, 849–856.

Fischer-Rasmussem, W., Kjaer, S.K., Dahl, C., Asping, U., 1990. Ginger treatment of hypermesis gravidarum. European Journal of Obstetrics, Gynaecology and Reproductive Biology 38, 19–24.

Forster, D.A., Denning, A., Wills, G., Bolger, M., McCarthy, E., 2006. Herbal medicine use during pregnancy in a group of Australian women. BMC Pregnancy and Childbirth 6, 1–9.

Henry, A., Crowther, C., 2000. Patterns of medication use during and prior to pregnancy: the MAP study. Australian Journal Obstetrics Gynecology 40, 165–172.

Hollyer, T., Boon, H., Georgousis, A., Smith, M., Einarson, A., 2002. The use of CAM by women suffering from nausea and vomiting during pregnancy. BMC Complementary and Alternative Medicine 2, 1–6.

Jewell, D., Young, G., 2003. Interventions for nausea and vomiting in early pregnancy. Cochrane Database Systematic Reviews 4, CD000145.

Nordeng, H., Havnen, G., 2004. Use of herbal drugs in pregnancy: a survey among 400 Norwegian women. Pharmacoepidemiology and Drug Safety 13, 371–380.

Portnoi, G., Chng, L.A., Karimi-Tabesh, L., Koren, G., Tan, M.P., Einarson, A., 2003. Prospective comparative study of the safety and effectiveness of ginger for the treatment of nausea and vomiting in pregnancy. American Journal of Obstetrics and Gynecology 189, 1374–1377.

Sripramote, M., Lekhyananda, N., 2003. A randomized comparison of ginger and vitamin B6 in the treatment of nausea and vomiting of pregnancy. Journal of the Medical Association of Thailand 86, 846–853.

Vatyavanich, T., Kraisarin, T., Ruangsri, R.A., 2001. Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial. Obstetrics & Gynecology 97, 577–582.