The Effect of Ginger Biscuit on Nausea and Vomiting in Early Pregnancy

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Abstract: Nausea and vomiting of pregnancy (NVP) are often alleviated by eating dried biscuits or foods. Natural products such as ginger have been suggested as herbal remedies for its treatment. The purpose of this study was to determine the effectiveness of ginger in biscuit form for the treatment. Sixty-five women with NVP at or before 17 weeks of gestation, who attended the antenatal clinic of Yahyanejad hospital in Babol town, Northern Iran, during 2005-2006 were included in the study. The subjects were randomized in a double-blind design and divided into two groups to take biscuits. 0.5g of ginger as fine powder was incorporated in each biscuit. Subjects received 5 ginger biscuits per day or an identical placebo biscuit for 4 days. They graded their severity of nausea using visual analog scales (VAS) and recorded the number of vomiting episodes in the previous 24 hours and again during 4 consecutive days. Five-item Likert scales were used to assess the severity of their symptoms. The average VAS scores of day 1 to 4 of post-therapy minus baseline nausea was decreased significantly in ginger (2.6±1.77) compared with the placebo group (1.4±1.62) (P=0.01). The number of vomiting episodes was also decreased in ginger (0.96±0.21) and placebo (0.62±0.19), the difference being insignificant. A significant difference was seen in inter-group variations per day in both groups. Likert scale showed an improvement in symptoms in both groups (P=0.43). Therefore, ginger in biscuit form is effective for relieving the severity of nausea and, to some extent, of vomiting in pregnancy.

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Introduction

Nausea and vomiting during pregnancy (NVP) have a pervasive impact on women's family, social and professional life (1). Vomiting affects more than 50% of women early in pregnancy and nausea is present in 70-80% (2). 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 resulting in dehydration, ketosis, electrolyte imbalances and weight loss (3).

The pathophysiology of NVP is poorly understood. Various hormonal, biochemical, mechanical and psychological factors have been implicated.[3] Treatment of NVP has traditionally been supportive, with dietary modification consisting of eating small portions of food at frequent intervals, ingesting dry toast or crackers initiation, and eating bland low-fat foods.[3] Pharmacological approaches for the treatment of NVP have been based on the pathophysiology of nausea and vomiting and on treatments found to be successful for non-pregnant subjects as well (4). Some pregnant women prefer natural, non-pharamacological therapies, such as life-style and nutritional habit changes, pyridoxine and ginger. Herbal medication for NVP is common. Ginger, chamomile, peppermint, Echinacea, cranberry and raspberry are among the herbs used for this purpose (4, 5).

Ginger (*Zingiber officinale*) has been used for medicinal purposes since ancient times. One of its indications has always been the treatment of nausea and vomiting. The aromatic, spasmolytic, carminative and absorbent properties of ginger suggest that it has direct effects on the gastrointestinal tract (6). Ginger has been shown to have anti-inflammatory effects. It is also known to have beneficial effects on motion sickness, anorexia, dyspepsia, and common cold (7, 8).

It has been used as an anti-nausea and anti-vomiting agent in pregnancy. Researchers showed no side effect

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of ginger when used during pregnancy (9-11). Ginger-containing products at hand include drop form with regard to its taste and probable not incompliance of some patients . Therefore, this study was conducted to determine the effect of ginger in a biscuit form on NVP.

Patients and Methods

A randomized double-blind clinical trial was conducted on 65 pregnant women with nausea and vomiting of pregnancy, who attended an antenatal clinic of Yahyanejad hospital in Babol town, Northern Iran, during 2005-2006. The study was approved by the ethical committee.

Subjects of the age of 19-35 years, weighing within 20% of normal weight at the beginning of pregnancy and being in 7 and 17 weeks of gestation were included. The exclusion criteria were: coexistence of other disease that cause vomiting such as thyroid disease, history of gastroenteritis, or gastrointestinal disease, infections, multiple pregnancy, hyperemesis gravidarum, trophoblastic disease and psychological disorders.[12] This also applied to women who received antiemetic agents such as vitamin B6, metoclopromide or drugs enhancing the condition such as iron tablets during last week.

After getting informed consent, the subjects were randomly entered into a double-blind design to receive either ginger (n=35) or non-ginger containing (placebo) (n=30) biscuits.

Every subject was handed 20 biscuits. They took five biscuits daily for four days. Time of consumption was based on patient's demand, especially when they experienced nausea. The ginger and identical-looking placebo biscuits were prepared by an expert confectionary under researcher's supervision. 0.5-g of ginger as fine powder was incorporated in each ginger biscuit. Placebo biscuit was similarly prepared. Both ginger and placebo biscuits were similarly packed in an envelope containing 20 biscuits in it. Before the trial, a research nurse who was not responsible for patient care was asked to use a table of random numbers to prepare the treatment assignment. The treatment codes were kept in sequence in a sealed black envelope that could not be read through. As each subjects entered the trial, she received the next envelope in the sequence which determined her assignment. Neither the physician nor the patients knew the composition of the biscuits administered.

Subjects graded the severity of their nausea and recorded the number of vomiting episodes in the last 24 hours before treatment and again during 4 consecutive days while taking biscuits. Because nausea is a subjective symptom, two independent measurement scales were used to quantify the changes in severity, namely a visual analog and a Likert scale.

For the visual analog scales (VAS), patients were asked on their first visit to grade the severity of their nausea over the past 24 hours (baseline scores) by marking an "X" corresponding to their perceived states on a 10cm vertical line, ranging from 0=no nausea to 10=severe nausea as bad as it could be. On the following 4 days, recording of the severity of nausea were made daily at bed time.

At a follow-up visit 7 days later, the nausea score and the number of vomiting episodes before and in different days of treatment were used to assess the severity of their symptoms. The average daily nausea scores and total scores over 4 days for each subject were calculated. Then, we compared the average change in the severity of nausea (post- therapy minus baseline) in the ginger with the placebo groups using the Mann-Whitney U test.

Subjects also recorded the number of vomiting episodes in the 24 hours before the study, and then during 4 days. The change in the score of nausea and number of vomiting episodes in the two groups were compared by student T-test as well. Inter- and intra-group daily variations of data were analyzed by repeated measure analysis.

Also, we assessed the general idea of the patients to treatment with five-item Likert scales (much worse, worse, same, better, much better). Chi-square test was used to compare these findings.

Results

In this study, sixty-five women consented to participate. Thirty subjects were assigned to placebo and 35 to ginger biscuits. Three subjects in ginger group did not consume the ginger biscuit due to its hot spicy taste and they were excluded from the study. Women were matched in relation to age, body mass index, gestational age and parity in both groups. Differences in baseline characteristics of the two groups were not statistically significant.

The average change in nausea scores (baseline minus average post-therapy nausea scores of day 1-4 for all subjects) in the ginger group was significantly greater (P=0.01) than that in placebo group (Table 1). The nausea score of day 4 in the placebo and ginger group was decreased to 3.03±2.47 from 4.67±1.97 and 3.03±2.19 from baseline score of 5.88±1.83, respectively.

Intra-group analysis of variations by repeated measurement showed a significant difference in placebo (P<0.001) and ginger (P<0.001) groups (Figure 1).

Table 1. The Average changes of nausea score in different days to the baseline of two group of study

	Baseline (day0)	Day 0-day 1	Day 0-day 2	Day 0-day 3	Day 0-day 4	average 1- 4	day0-avarage 1-4
Placebo(n=30)	4.67±1.97	1.03±0.999	1.43±1.38	1.47±2.25	1.63±2.51	3.27±1.84	1.39±1.62
Ginger(n=32)	5.88±1.83	2.03±1.93	2.34±2.08	3.06±1.74	2.84±2.09	3.30±1.80	2.57±1.77
*P value	0.008	0.021	0.048	0.003	0.023	0.99	0.010

* Mann –Whitney U test

† Data are presented as mean± SD of the difference (baseline minus post therapy) in nausea scores.

But repeated measurement could not detect significant differences in a inter-group variation analysis (*P*=0.543).

All subjects in two groups of the study had one or more vomiting episodes during 24 hour before treament.

The average change (±SEM) in the number of vomiting episodes (baseline minus average post therapy vomiting number of day 1-4) in ginger biscuit group was (0.96±0.21) compared with (0.62±0.19) in the placebo biscuit group, although there was no significant difference (P=0.243, Table 2).

After 4 days of treatment, the proportion of women who had no vomiting in the ginger group (11 out of 32 patients, 34%) was greater than that in the placebo group (6 out of 30, 18%). When the average number of vomiting episodes over the 4 days of treatment was subtracted from the corresponding baseline value for each patient, and the overall change in the number of vomiting episodes for subjects in the two groups was compared, a greater reduction in the number of vomiting episodes was found in the ginger group, but no significant difference was seen (Table 2). The comparison between the variation of number of vomiting before, during and after 4 days in a within group analysis by repeated measurement showed a significant decrease in placebo (*P*<0.001) and ginger group (*P*<0.001; Figure 2). However, there was no significant differences in a inter-group variation (*P*=0.969).

On follow-up visits, five-item Likert scales were recruited to assess patient's subjective response to treatment. Twenty-eight of 32 (87.5%) ginger-treated women reported that their symptoms had improved, compared with 21 out of 30 (70%) in placebo group. Ginger-treated women felt much better and chi-square test found a significant difference between these findings of two groups (*P*=0.043, Table 3).

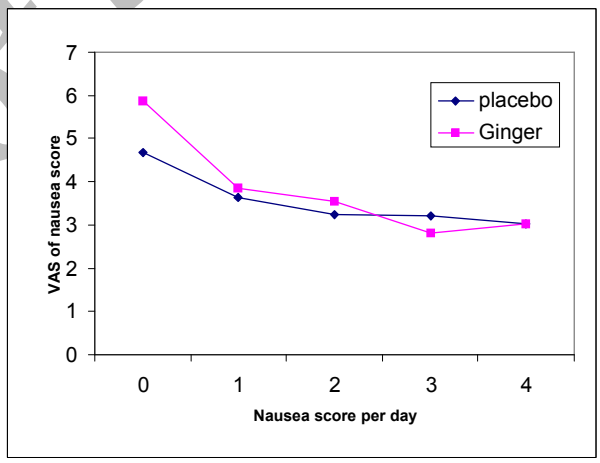

Figure 1. Trend lines of the nausea scores in days of study in two groups. Number of patients in placebo and ginger groups were 30 and 32, respectively.

Table 2. The average changes of the number of vomiting episodes in different days to the baseline of two groups of study

	Baseline (day0)	Day 0-day1	Day 0-day 2	Day 0-day 3	Day 0-day 4	average day 1-4	Day 0- average 1-4
Placebo (n=30)	1.3±1.3	0.33±0.175	0.67±0.18	0.77±0.28	0.73±0.31	0.74±0.21	0.62±0.19
Ginger (n=32)	1.63±1.18	0.84±0.216	0.94±0.24	1.09±0.22	0.97±0.25	0.66±0.17	0.96±0.21
*P-value	0.426	0.073	0.384	0.367	0.556	0.78	0.243

* Student T-test

† Data are presented as mean ± SEM of the differences (baseline minus post therapy) in number of vomiting scores.

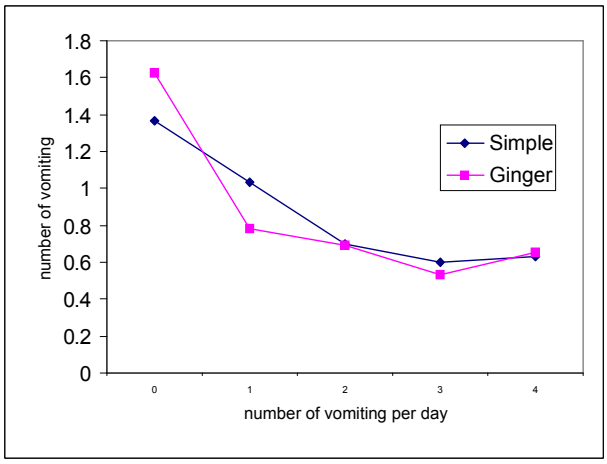

Figure 2. Trend lines of the vomiting scores in days of study in two groups. Number of the patients in placebo and ginger groups were 30 and 32, respectively.

Table 3. Symptoms assessed by likert scales

Symptom rating	Placebo (n=30)	Ginger (n=32)
Same	9(30%)	4(13%)
Better	4(13%)	1(3%)
Much better	17(57%)	27(84%)

Data are presented as frequency (%); chi-square test, p=0.043.
* because of no data of much worse and worse items of likert scales, they were not included.

Compliance as assessed by biscuit count. The result showed that all women finished the study in the placebo and ginger group received 5 biscuit daily.

Regarding the side effects, there was no complaint in placebo group whereas in ginger group one patient (3.12%) complained from dizziness and one (3.12%) from heartburn due to ginger biscuit, which were mild and did not result in stopping consumption. No subjects in this trial took any other medications for nausea or vomiting as rescue dose. The side effects were reported by subjects as minor and didn't preclude them from taking their prescribed medication.

No abnormal pregnancy and delivery outcome ocurred and no infants had any congenital abnormalities recognized and all were discharged in good condition.

Discussions

Ginger, known scientifically as *Zingiber officinale*, is a perennial native to many Asian countries. It can be used as a spice to enhance the flavor of food (e.g. ginger bread, tarts, and cookies) (6). In this study, we used ginger and non-ginger containing (placebo) biscuit for NVP.

Our result showed a reduction in nausea severity score in the group receiving ginger biscuit compared to placebo biscuit (P=0.01). Although the decrease in the number of vomiting was greater in ginger group, the difference was not statistically significant (P=0.24).

There are only few data on the actions of ginger. Gingerols, in particular 6-gingerol, have been identified as the active ingredient of ginger, and are also responsible for its characteristic taste. There are several mechanisms which could explain the possible antiemetic effects of ginger. In an animal model, for instance, it was demonstrated that 6-gingerol enhanced gastrointestinal transport. This and other compounds of ginger have also been shown to have anti-hydroxytryptamine activity in isolated guinea pig ileum. Galanolactone, another constituent of ginger, is a competitive antagonist at ileal 5-HT3 receptors. Thus antiemesis could be brought about by effects on the gastric system through 5-HT3 antagonism. This hypothesis is weakened by the results of a randomized, placebo-controlled crossover study in human volunteers reporting that oral ingestion of powdered ginger root did not affect gastric emptying rate. In contrast, effects on the central nervous system may be involved. This notion is strengthened by the finding that in an animal model, oral 6-gingerol prevented vomiting in response to cyclophosphamide. A central effect is also implicated by studies reporting that ginger partly prevents motion sickness symptoms in healthy human volunteers (6).

We chose a study period of 4 days because a previous study (9, 11) showed that the effect of ginger was evident within a few days of treatment and too long a period would result only in a higher rate of subject incompliance and, thus, fewer individuals to follow-up. We used VAS to quantify nausea severity, because these scales give an objective measure, have construct validity and are reproducible (13-15).

In a small crossover study on 27 women suffering from NVP a significantly greater symptomatic benefit after administration of ginger compared with placebo has been shown (P<0.05) (11).

In a study conducted by Smith C, women with NVP in less than 16 weeks of gestation were randomly allocated to receive either 1.05g of ginger or 75mg of vitamin B6 daily in a blind fashion for 3 weeks. Their results showed that ginger was as effective as vitamin B6 in reducing nausea, dry retching and vomiting (16).

The result of our study showed that ginger is effec-

tive for relieving the severity of nausea of pregnancy, which is consistent with previous studies (9).

Willets et al. performed a study on women with NVP; 120 women underwent treatment with 125mg of ginger extract (equivalent to 1.5 gram of dried ginger) or placebo given four times per day for 4 days. They found the nausea experience score was significantly less for the ginger extract group compared to the placebo group, but no significant effect was observed on vomiting (17). In our study in a intra-group analysis, we showed that biscuits could decrease the number of vomiting episode in placebo (P<0.001) and ginger group (P<0.001), but inter group analysis of change in the number of vomiting episode did not reveal any statistical significant difference (P=0.969). This finding was seen in the nausea score as well, It could be concluded that the biscuit alone can be effective in relieving nausea and vomiting, although the effect of ginger is considerable and statistically greater than placebo (Table 1,2). As the traditional belief of ingesting dry toast or crackers for reliving NVP (3), it can be due to effect of biscuit form.

Regarding the probable adverse effects, in this study one patient (3.12%) reported dizziness and one (3.12%) heartburn after consumption of ginger biscuits which were both mild and did not result in quitting the usage of biscuits. In the previous studies, there were no reports of adverse events during ginger treatment in pregnancy (10, 18).

Betz et al. when considering the ginger effect in different clinical trials, reported mild side effect such as gastrointestinal symptoms and sedation, of which none needed a further treatment (19).

The majority of studies showed that ginger alleviated nausea and vomiting of different origins.

Since dietary modifications including eating small proportions of food at frequent intervals and ingesting dry toast or crackers are advised, we performed this study and concluded that ginger in biscuit form can be recommended to pregnant women.

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