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Medical Science**Journal homepage: www.Sjournals.com**Original article****Comparison of effectiveness of ginger and metoclopramide on the treatment of nausea and vomiting in pregnancy****M. Sharief, S.A. Shaker****Department of Gynecology & Obstetrics, College of Medicine, University of Basrah, Basrah, IRAQ.*

*Corresponding author; Department of Gynecology & Obstetrics, College of Medicine, University of Basrah, Basrah, IRAQ.

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ABSTRACT

To determine the effectiveness of ginger in comparison to metoclopramide for the treatment of nausea and vomiting in pregnancy. Patients & Methods, It is a comparative randomized prospective trial which has been done at Basrah Maternity and Child Hospital. Sixty three pregnant women with a gestational age between 8-12 weeks who had nausea and vomiting required antiemetic. They had no medical complication and were not hospitalized. Pregnant women were randomly allocated to receive either capsule of 500 mg of ginger plus 400 mcg of folic acid two times /day or 10 mg of metoclopramide three times/ day for 21 days. The degree of nausea and vomiting were assessed by visual analog scale and Likert scale. These were recorded before treatment for base line and after 1 week, 2 weeks, 3 weeks of treatment. Difference of baseline and post treatment nausea, vomiting scores were calculated for both groups during 21 days. All participants except three remained in the study. The visual analog score of post-therapy minus baseline nausea decreased significantly in both groups (2.57 ± 1.7), (1.39 ± 1.6) respectively with more statistically significant with metoclopramide group ($P < 0.01$). The number of vomiting episodes (base line minus average post therapy) in ginger group was 0.73 ± 0.31 compared with (0.97 ± 0.2) in metoclopramide group although there was no significant difference ($P > 0.24$). Likert scales showed 15 cases out of 30 (50%) ginger women reported that their symptoms had improved compared with 20 out of 30 (66%) in metoclopramide group with significant difference between them

($P > 0.04$). No adverse effect of ginger on pregnancy outcome was detected. **Conclusion**, Ginger is effective for relieving the severity of nausea and vomiting of pregnancy in comparing to the less effective of metoclopramide. Therefore, ginger can be considered as an alternative drug.

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1. Introduction

Nausea and vomiting of pregnancy, is one of the most common complaints of pregnant women with an estimated 50% to 80% of pregnant women experience nausea and/or vomiting (Koch, 2012). Symptoms usually begin between the 4th and 6th week of pregnancy and improve by the 15th to 20th week of gestation. The nausea of pregnancy ranges from mild and disturbing to severe and unremitting, with associated severe vomiting, dehydration, and weight loss, that affects the health of both the pregnant women and her fetus (Koch, 2012).

The most severe manifestations of nausea and vomiting in pregnancy result in hyperemesis gravidarum. Although there is no standard definition of hyperemesis gravidarum, most diagnostic criteria include, persistent vomiting before 9 weeks after the last menstrual cycle, weight loss $>5\%$ of initial body weight, electrolyte imbalance (hypokalemia), and dehydration and/or ketonuria (Fell et al., 2006).

Hyperemesis gravidarum is the most common indication for admission to the hospital in the first half of pregnancy (Zhang et al., 2011).

The goal of treatment is to improve symptoms while minimizing risks to mother and fetus. Treatment modalities range from simple dietary modifications to drug therapy and total parental nutrition (Ebrahimi et al., 2010). Many women turn to non-pharmacologic therapies because of concerns about adverse effects of drugs during embryonic and early fetal development.

Pharmacological treatment must be assessed for both safety and efficacy before being recommended for use in clinical practice. The commended drugs are vitamin B6 (McKeigue et al., 1994), pyridoxine-doxylamine (Koren et al., 2006), Dopamine antagonists (Badell et al., 2006), corticosteroids (National Institutes of Health, 2012) or antihistamines (Klasco, 2000).

Ginger or ginger root is the rhizome of the plant *Zingiber officinale* which has a long history of medicinal use in China and India for conditions such as headaches, nausea, rheumatism, and colds (Grant, 2010). The mechanism underlying ginger's anti-emetic activity is not clearly understood, ginger is suspected to reduce nausea and vomiting by increasing gastrointestinal motility and transport via the 6-gingerol constituent (Jellin et al., 2000). Some evidence suggests that constituents of ginger have central anti-emetic activity (Jellin et al., 2000).

Therefore, the aim of the study is to determine the effectiveness of ginger for the treatment of nausea and vomiting of pregnancy and to determine the adverse effect of ginger on the pregnancy outcome.

2. Materials and methods

It is randomized comparative prospective trial which was conducted in Basrah Maternity and Child Hospital between April 2012 till September 2013. The study was approved by the Ethical Committee of the College of Medicine, Basrah, Iraq and all women gave written informed consent before enrolling in the trial.

Women with nausea and mild vomiting that not interfere with her daily work who attended antenatal clinic and private clinic were eligible in the trial. They were between 8-12 weeks pregnant and periods were confirmed by ultrasound.

The inclusion criteria was a single pregnancy.

The exclusion criteria were,

1. Patients were hospitalized for hyperemesis gravidarum
2. Medical disorder like diabetes mellitus, hepatic, gastric, pancreatic, pylonephritis, thyroid and psychological disorder.

Sixty three women were randomly allocated to receive either ginger in form of capsule named as MOM's PRENATAL PLUS (the ingredient is 500 mg ginger plus 400 mcg of folic acid manufactured by DaVinci Laboratories of Vermont USA) taken orally twice daily and regarded as group 1 and metoclopramide tablets in a dosage of 10 mg three times daily as group 2 for 21 days. Both groups then continued the pregnancy on tonics.

The subject underwent physical examination and routine obstetric evaluation.

Demographic information, history of nausea, vomiting, assessment of sign of dehydration, vital sign examination include pulse rate, temperature and blood pressure were undertaken. Liver function test, renal function test, general urine examination was performed to all subjects before randomization.

Because nausea is subjective symptom independent measure scales were used to qualify the change in severity.

3. Visual analog scale

The patients were asked on their first visit to grade the severity of their nausea over 24 hrs. (base line score) by marking an (X) corresponding to their perceived station at 10 cm vertical line ranging from 0= no nausea to 10 = nausea as bad as it could be. on the following 7 days the treatment recordings of the severity and after 14 days, 21 days.

To obtain an objective measurement, we measured the markings on each of the scales in centimeters. The average daily nausea scores and the mean nausea scores over the 21 days of treatment for each subject were then calculated. We compared the median change in the severity of nausea (Post-therapy minus base line scores) in the ginger and the metoclopramide by rank sum test (Streiner and Norman, 1989).

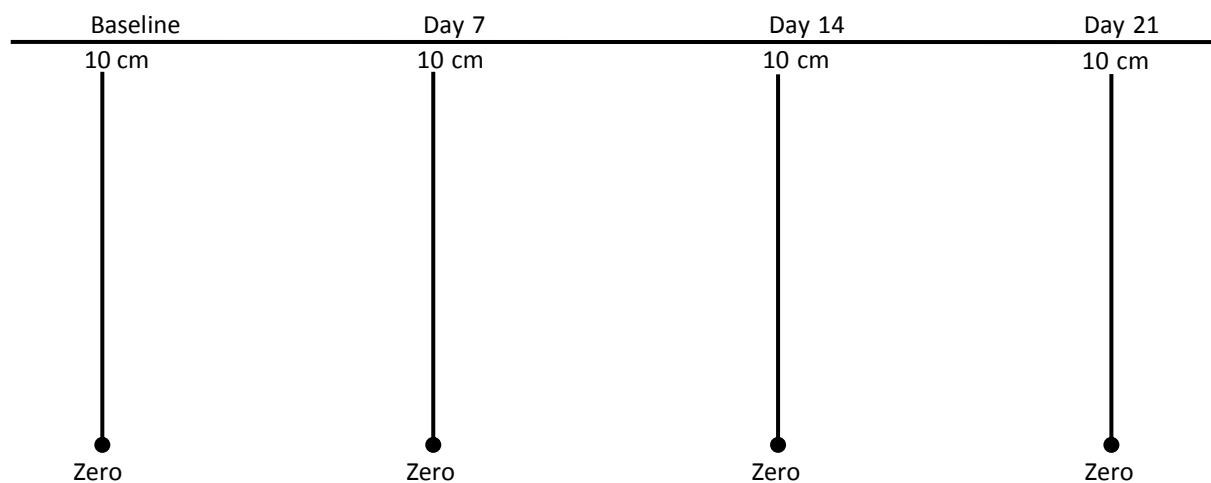
3.1. Assessment of vomiting

Patients were asked to record the number of vomiting episodes in the 24 hours before treatment and then on each subsequent visit the change in the number of vomiting episodes in the two groups was compared by rank sum test and the proportion of subjects with vomiting before and after treatment were compared by X2 testes (Streiner and Norman, 1989)..

No. of children:
Patient's name:
Abortion:
Age:

Primary outcome:

1. Visual analog:



2. Vomiting assement

1 st day 7 th day 14 day 21 day
 N,- N,- N,- N,-

3.2. Likert scale

At the end of 21 days assessment the response of the patients to treatment by five item (1) much worse (2) worse (3) same (4) better (5) much better, chi-square test was used to compare these findings.

The primary outcome assessed by change in women experience from nausea, drug retching, vomiting from base line and after 7 days, 14 days, 21 days (Streiner and Norman, 1989)..

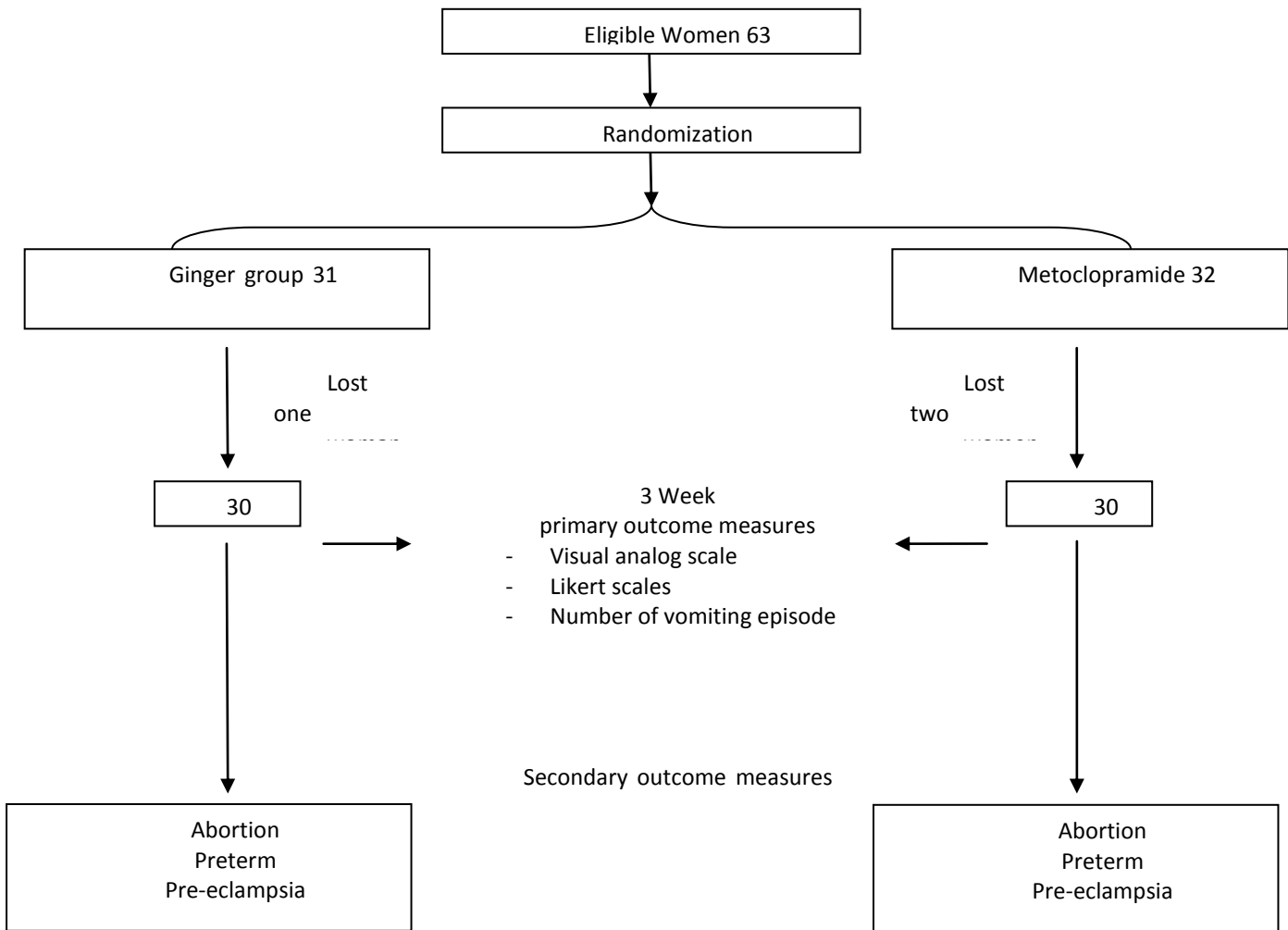
Secondary out comes included the occurrence of complications during pregnancy like antepartum haemorrhage, pre-eclampsia, preterm delivery, perinatal outcome like stillbirth, neonatal complication during follow up the patients throughout the pregnancy.

3. Likert scales

Much worse	Baseline	Day 21
Worse		
Same		
Better		
Much better		

Secondary outcome

1. Timing of delivery
2. Ante Partum Hemorrhage
3. Birth outcome
4. Preeclampsia



4. Results

In this study, 63 pregnant women who suited the criteria were enrolled. They were randomly allocated to receive ginger tablet in 30 cases and Metoclopramide tablet in 30 cases and 3 cases were lost to follow up. Table (1) showed the baseline characteristics were similar in both groups.

Table 1

Base line characteristic of the women in both groups (group 1= Ginger, group 2 = Metoclopramide).

	Group 1 N=30	Group 2 N=30	P value
Age (year)	29 ± 5	28 ± 4	N/S
BMI (kg/m ²)	25.6 ± 6	24.9 ± 5	N/S
Gestational age week median and range	12.5 (8-15)	11.6 (8-15)	N/S
Parity			
0	17	19	N/S
≥1	13	11	N/S
Education			
Illiterate	5	4	N/S
primary school	6	5	N/S
secondary school	10	13	N/S
high education	9	8	N/S
Occupation			
house wife	11	9	N/S
Employee	19	21	N/S

Table (2) showed nausea was experienced by 60 (100%) women, and 57 women (95%) drug retched, and 36 (60%) vomited before joining the trial.

Table 2

Base line data for pregnancy symptoms including nausea, vomiting, drug retching.

Symptoms	Total	N,60
Nausea	60	100%
Drug retching	57	95%
Vomiting	36	60%

The average change in nausea score (base-line minus average post-therapy) nausea scores from first day till day 21 for all subjects in Metoclopramide was significantly greater ($P < 0.01$) than that in the ginger group (Table 3).

Table 3

The Average changes of nausea score in different days to the baseline of two groups.

	Baseline	0 -7 day	0 -14 day	0 -21 day
Metoclopramide N (30)	5.78 ± 1.8	2.03 ± 1.7	2.84 ± 2	2.57 ± 1.7
Ginger (N 30)	4.45 ± 1.9	1.03 ± 0.9	1.63 ± 2.5	1.39 ± 1.6
P value	0.8	0.021	0.02	0.010

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

All subjects in two groups of the study had one or more vomiting episodes during 24 hour before treatment. Table (4) showed the average change in the number of vomiting episodes (baseline minus average post therapy)

vomiting number of day (0-21 days) in ginger group was 0.73 ± 0.31 compared with (0.97 ± 0.2) in metoclopramide group although there was no significant ($P > 0.24$).

Table 4

The average changes of the number of vomiting episodes in different days to the base line of two groups of study.

	Base line day (0)	0-7 day	0-14 day	0-21 day
Metoclopramide	1.3 ± 1.3	0.82 ± 0.1	1.09 ± 0.2	0.97 ± 0.2
Ginger	1.6 ± 1.18	0.32 ± 0.17	0.77 ± 0.2	0.73 ± 0.31
*P value	0.426	0.07	0.38	0.24

*Student T test.

On follow up visits, five-item Likert scales were recruited to assess patients subjective response to treatment. 15 cases of out of 30 (50%) ginger treated women reported that their symptoms had improved compared with 20 out of 30 (66.5%) in metoclopramide group. Ginger treated women felt less better and chi square test that found a significant difference between these finding of two group ($P=0.04$) (Table 5).

Table 5

Symptoms assessment after the end of treatment by Likert scales.

Symptom	Group A 30 %	Group B 30 %	P
Much worse	0	0	0
Worse	2 (6.6%)	1 (3.3 %)	N/S
Same	11 (36%)	6 (20%)	0.04
Better	15 (50%)	20 (66.5)	N/S
Much better	2 (6.6%)	3 (10%)	N/S

Table (6) showed there were two spontaneous abortion in the Ginger group (6.6 %). The overall risk of pregnancy complications did not differ in both groups. The mean birth weight for babies in the trial was $3.4 \text{ kg} \pm 1.2$ with no differences in both groups.

Table 6

Pregnancy out come in both groups.

Outcome	Ginger N= 30	Metoclopramide N= 30	P
Spontaneous abortion	2 (6.6%)	1 (3.3%)	N/S
Still birth	0 (0%)	0 (0%)	N/S
Neonatal death	0 (0%)	0 (0%)	N/S
Live birth	28 (93%)	29 (95%)	N/S
APH	0 (0%)	0 (0%)	N/S
PPH	2 (6.6%)	3 (10%)	N/S
Pre eclampsia	0 (0%)	1 (3.3%)	N/S
Birth weight (kg)	3.9 ± 1.2	3.5 ± 1.2	N/S
Gestational age	39 ± 2	38 ± 1	N/S
Congenital abnormalities	0	0	N/S

5. Discussion

Nausea and vomiting in early pregnancy remain a significant public health problem which has physiological, emotional, social and economic consequences to women, their families and society. Many medication and alternative therapies are currently available for the treatment of morning sickness (Fischer-Rasmussen et al., 1991) Ginger has been evaluated in some controlled trials for the treatment of morning sickness (Fischer-Rasmussen et al., 1991; Smith et al., 2004).

Ginger is a perennial native to many Asian countries. It is widely cultivated for its aromatic rhizome which can be used as spice to enhance the flavor of food, beside as herbal medicine for the relief of gastrointestinal distress. The efficacy of ginger is believed to be due to its aromatic, carminative and absorbent properties (Tyler and Foster, 1996).

In the present study, there were no difference among both groups with respective to demographic data.

The observed trends in nausea severity where decrease in both groups which showed that the two medicine may improve the symptoms in pregnant women but this effect was higher in metoclopramide than in ginger group with statistical difference. This finding is in agreement with the Mohammedbeyi & Shangcibi. Although the decrease in the number of vomiting was greater in metoclopramide group than Ginger group, but the difference was statistically insignificant. It has been observed that small dose of ginger was effective in nausea and vomiting (Chittiumma, 2007) while Willettes et al. (2003) showed that a dose of 125 mg ginger taken 4 times a day for 4 days compared with placebo could significantly decrease nausea and retching but not for vomiting.

Though the main reason of nausea and vomiting during pregnancy is not clearly known, ginger could be effective in condensing the etiology by 2 possible mechanisms either by enhanced intestinal or central nervous system activity. Skidmore-Roth (2003) reported that with studies in humans indicating that the latter is more likely while Jednak et al. (1999) suggested that symptoms of nausea and vomiting during pregnancy improved in direct correlation to the improvement in pregnancy included gastric dysrhythmias, they suggested that ginger cause significant decrease in gastric myoelectrical activity.

Most recently Smith and his colleagues (Smith et al., 2004) conducted a randomized controlled equivalence trial to compare the effectiveness of ginger versus vitamin B6 in treating nausea and vomiting in 291 outpatient pregnant women less than 16 weeks. Ginger was found to be equivalent to vitamin B6 in reducing nausea, drug retching and vomiting.

In the present study, the occurrence of side effects from ginger was reported to be minor during short period of treatment. Previous study showed that most of the side effects reported by women were associated with problem swallowing and retching after ingestion (Skidmore-Roth, 2003).

Pregnancy outcome in the present study was not statistically significant in both groups. In clinical trial there was no adverse effects arising from ginger for mother and baby. Recent experimental data in an animal model reported in utero exposure to ginger tea resulted in an increased early embryo loss and increased growth in surviving fetuses in rats, but findings from animals model appear not to be transferable to the human model. In conclusion, ginger is a safe and effective treatment option for nausea and vomiting as alternative for chemical medicines. In addition, Future research needs to address potential risks from high doses during pregnancy although ginger has a long history safety, because it has been used for centuries for medicinal purpose as well as a food substance and spice (Wilkinson, 2000).

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