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Comparing the Effects of Ginger and Metoclopramide on the Treatment of Pregnancy Nausea

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Abstract: This study assesses the effects of ginger on nausea and vomiting caused by pregnancy and compares it with metoclopramide medicine. This study was a randomized double-blind controlled trial. Metoclopramide, Ginger and placebo were putted in similar capsules. The medicines were administered three times a day. Then the Rhodes questionnaire was completed and its score were calculated. Data were analyzed by Chi square test, ANOVA and Repeated measurement. The intensity of changes in nausea, vomiting and Rhodes during study were statistically different in two groups of ginger and metoclopramide compared with placebo ($p<0.05$), but it was not statistically significant between two groups of ginger and metoclopramide. According to our study, ginger is less effective than metoclopramide in reducing nausea and vomiting but it could be a good alternative for metoclopramide.

Key words: Nausea and vomiting in pregnancy, rhodes' index, ginger

INTRODUCTION

Nausea and vomiting are common complications at the beginning of pregnancy, which occur among 50 to 90% of pregnant women, though 28% of pregnant women only experience nausea (Gadsby *et al*., 1993; Vikanes *et al*., 2010). This complication has a wide range of symptoms from early-morning nausea to constant nausea (Jueckstock *et al*., 2010).

Though the cause of nausea and vomiting is not clearly known, different influencing factors are suggested including multifetal pregnancy, dysfunction of digestive system, hormonal changes, disorder in vestibular system and Helicobacter pylori infection (Quinlan and Hill, 2003; Jamal *et al*., 2004; Fejzo *et al*., 2008; Goodwin *et al*., 2008; Vikanes *et al*., 2010). Hyperemesis gravidarum could be hereditary and it is common among girls whose mothers experienced the same complication during pregnancy (Vikanes *et al*., 2010).

As taking chemical drugs during pregnancy could be risky, decreasing of symptoms through non-medicinal actions like taking rest, eating small pieces of bread during the day, having small but frequent meals and avoiding tasty, oily and fried foods, is more suggested (Jueckstock *et al*., 2010; Mylonas *et al*., 2007). Antihistamine, Vitamin B6 and metoclopramide are the other suggested medicines, however taking most of these drugs during pregnancy may have side effects and they are not among Group A drugs (Jueckstock *et al*., 2010; Quinlan and Hill, 2003; King and Murphy, 2009). Herbal medicine may have good effects (Karim *et al*., 2011). Ginger is used as a common herbal medicine in different countries and it could be effective in curing this complication (Jewell, 2003; Quinlan and Hill, 2003; Willetts *et al*., 2003). Willetts *et al*. (2003) demonstrated that ginger can reduce nausea and it does not affect embryo. Nevertheless, the effect of this herbal medicine is still controversial and needs further researches (Borrelli *et al*., 2005).

There is no study comparing the effects of using ginger and metoclopramide on treatment of pregnancy nausea. This study assesses the effects of ginger on nausea and vomiting caused by pregnancy and compares it with metoclopramide medicine.

MATERIALS AND METHODS

This study was a randomized double-blind controlled trial, which conducted after verification by ethical committee of Kurdistan's University of Medical sciences. All women who passed less than 20 weeks of pregnancy, referred to B'esat Hospital, were assessed. Main outcome was vomiting and nausea severity that assessed by Rhodes Index. Considering $\delta = 3.5$, $\alpha = 5\%$, $\beta = 10\%$ and

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d = 3, the population size was calculated as 28 participants in each group; considering a down flow of 20%, 34 participants were included in each group.

Patients were visited by gynecologists and medical examination and test were taken to find other diseases and to rule out twin pregnancy pregnancies and pregnancy complications. The tests included blood glucose, hepatic and pancreatic enzyme. After diagnosing vomiting and nausea and fulfilling inclusion criteria, participants were entered in the study. Inclusion criteria were: a single pregnancy and inefficacy of food regimens in controlling vomiting and nausea. Exclusion criteria were: suffering from other diseases that need drugs for treatment, hepatitis, gastritis, rise of intra cranial pressure and pancreatitis, side effects caused by ginger intolerance, metoclopramide side effects (extra pyramidal side effects) and pregnancy side effects like abortion risk, bleeding and pyelonephritis. After signing informed consent form, patients were divided into three groups based on random block allocation (Fig. 1).

The main tools of data collection were two questionnaires; a questionnaire for demographic and background data and Rhodes Index questionnaire for assessment of nausea, vomiting and retching. The questionnaire was translated into Persian and face validity of translated form was confirmed by a group of gynecologists. Its reliability and validity was assessed using 30 patients and its Cronbach's alpha was calculated as 0.87.

A person who assisted the study conducted the randomization; she gave medicines to the patients for five days. Medicines were putted in similar capsules made by Gol Daroo Company (Iran). Metoclopramide group had 10 mg of metoclopramide and ginger group had 200 mg of ginger essence. Placebo was 200 mg of flour the medicines were administered three times a day. Patients were called everyday in order to ensure taking medicine and to fill the questionnaire. The first questionnaire was filled up by researcher at the beginning of the study and 10 standard Rhodes Index questionnaires (with two extra questionnaire) were given to the patient in order to be filled up twice a day at 9 AM and 5 PM. Then the questionnaire point and the vomiting and nausea points were calculated.

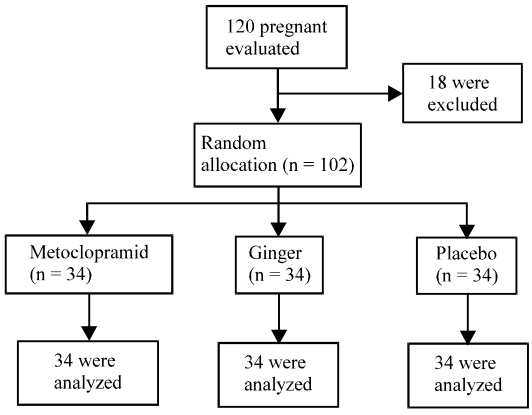

Fig. 1: NTS profile in metoclopramide, ginger and placebo groups during study. Nobody were excluded from analysis during study

Data were entered in SPSS11.5 software; Chi square test was used for comparing qualitative characteristics in three groups; ANOVA test was used for comparing quantitative data in three groups and Repeated Measurement was used for comparing trend of questionnaire points during different days in each group. Within-subject contrasts test was used to assess the main effect and interactions. In these tests, the effects of metoclopramide and ginger were compared with placebo as referent group. The sphericity assumption was assessed via Mauchly-test. The assessment showed that this assumption is rejected for variables of vomiting, nausea and Rhodes Index ($p<0.05$), which after adjusting the degree of freedom through Greenhouse-Geisser, Huynh-Feldt correction coefficients, their average of p-value was reported.

RESULTS

In this study, there was no significant statistical difference among these three groups regarding age, duration of pregnancy and gravidity (Table 1). From the first day, the trend of changes in nausea severity was decreasing in all three groups but it had a little increase in metoclopramide group at the fourth day. The observed difference between nausea severities at the second to fifth days of intervention compared with the first day was statistically significant ($p = 0.006$); so the trend of changes between two groups of ginger ($p = 0.046$) and metoclopramide ($p = 0.018$) had a significant statistical

Table 1: Demographic characteristic of metoclopramide, ginger and placebo groups

Variables	Metoclopramide (N=34)	Ginger (N=34)	Placebo (N=34)	p-value
Age (years)	27.88±3.21	26.94±3.94	26.97±4.22	0.514 †
Length of pregnancy (weeks)	10.03±1.99	9.5±2.02	10.32±2.25	0.261††
Gravid number Mean (median)	1.88 (2)	1.61 (1)	1.64 (1)	0.464††
Partum number; Mean (median)	0.82 (1)	0.45 (0)	0.56 (0)	0.157††

†ANOVA, ††Kruscal-Wallis test

Table 2: Mean and standard deviation of nausea, vomiting severity and Rhodes Index in day 1 to 5 in metoclopramide, ginger and placebo groups

Indicator	Day	Metoclopramide (N = 34)	Ginger (N = 34)	Placebo (N = 34)	p-value†	Statistical significant different groups††
Vomiting (Mean±SD)	1	10.56±2.98	10.82±1.98	10.56±1.78	0.006	AC, BC
	2	9.09±2.23	8.85±1.54	9.68±1.27		
	3	7.29±2.28	7.62±1.99	8.76±1.13		
	4	8.06±1.70	7.44±1.28	8.12±1.12		
	5	6.53±1.81	6.18±1.25	7.59±1.35		
Nausea (Mean±SD)	1	16.53±4.89	16.59±3.12	17.03±2.53	<0.0001	AC, BC
	2	16.47±3.65	17.56±2.86	17.68±2.36		
	3	13.06±4.19	14.62±3.24	16.00±2.35		
	4	22.76±4.24	20.94±3.80	23.68±2.58		
	5	11.21±3.37	11.50±1.81	14.26±2.68		
Rhodes index (Mean±SD)	1	30.00±8.29	31.68±5.32	30.53±4.64	<0.0001	AC, BC
	2	25.56±5.51	26.41±4.12	27.35±3.36		
	3	20.35±6.14	22.24±5.02	24.76±3.06		
	4	22.76±4.24	20.94±3.80	23.68±2.58		
	5	18.53±5.18	18.71±2.81	23.15±4.03		

†Repeated measurement, ††A: Metoclopramide, B: Ginger, C: Placebo; significant at 0.05 level

difference with placebo group. However this difference was not statistically significant between ginger group and metoclopramide group (p = 0.718) (Table 2).

The trend of changes in nausea severity in all three studied groups was decreasing from the first day to the third day but it became increasing at the fourth day and it became decreasing again in the fifth day in a way that it was less severe than the first day. The observed difference in nausea severity between second to fifth day compared with the first day was statistically significant (p<0.0001). The trend of changes in nausea severity was the same in all three groups however the intensity of changes were statistically different. These differences were existed in two groups of ginger (p = 0.003) and metoclopramide (p = 0.011) compared with placebo but it was not statistically significant between two groups of ginger and metoclopramide (p = 0.683) (Table 2).

The trend of changes in Rhodes Index in two groups of placebo and ginger was decreasing from the first day. It was decreasing in metoclopramide as well but it represents a small increase in the fourth day. The observed difference of Rhodes Index in the second and fifth day compared with the first day of intervention was statistically significant (p<0.0001). Though the trends of changes in Rhodes Index was decreasing in all three groups, the intensity of changes were statistically different in ginger (p = 0.004) and metoclopramide (p = 0.025) compared with placebo but it was not statistically significant between two groups of ginger and metoclopramide (p = 0.509) (Table 2).

DISCUSSION

Previous studies has shown the positive effects of ginger in reducing nausea and vomiting during pregnancy, however it was suggested to do more studies with higher qualities (Borrelli *et al*., 2005). In this study the three groups were similar in background factors including age, pregnancy and childbirth etc., so these factors may did not affect the results. Based on the results, the observed trends in nausea severity, vomiting severity and Rhodes indexes were decreasing in all three groups during the study, which showed that all three medicines may improve the symptoms in pregnant women. But this effect was higher in metoclopramide and ginger groups, compared with Placebo group and there was a significant statistical difference. However, this difference was not seen between metoclopramide and ginger group. Hence, it can be said however ginger is less effective than metoclopramide in reducing nausea and vomiting but it could be a good alternative for metoclopramide. There was a small increase, with an unknown reason, in nausea and vomiting in fourth day in both groups of metoclopramide and ginger. There was no special happening, which for example, affects patients reporting. Thus, it is probable some physiologic compensatory mechanisms involve and these mechanisms cause temporary increase in symptoms.

Though the main reason of nausea and vomiting during pregnancy is not clearly known, ginger could be effective in condensing this etiology. Some studies compared the effects of ginger, with the effects of vitamin B6, dimenhydrinate and placebo (Portnoi *et al*., 2003; Chittumma *et al*., 2007; Pongrojpaw *et al*., 2007; Ozgoli *et al*., 2009), but there is no study comparing ginger with metoclopramide. In addition, in our study Rhodes index questionnaire was used for assessing nausea and vomiting which can evaluate both frequency and severity of symptoms.

Chittumma *et al*. (2007) study had similar results. In our study a smaller dose of ginger was used however it was effective in nausea and vomiting. Willetts *et al*. (2003) showed that a dose of 125 mg ginger taken four times a day for 4 days, compared with placebo, could significantly decrease nausea and retching. But it was not significant for vomiting. No side effect related to mother and child

was seen in this study. Other studies as well confirmed ginger as a harmless medicine (Portnoi *et al*., 2003). Ozgoli *et al*. (2009) a dose of 250 mg ginger taken four times a day for 4 days, decreased vomiting time up to 50% and this reduction was only 9% in placebo group. In other study, ginger was as effective as dimenhydrinate in decreasing nausea and vomiting (Pongrojpaw *et al*., 2007).

As a whole, the results of the studies were somehow similar. The prescribed dose was from 500 mg to 2000 mg in different studies (Willetts *et al*., 2003; Chittumma *et al*., 2007). Because of its decreasing effect on nausea and vomiting and as it is harmless, ginger could be a good alternative for chemical medicines. A biscuit form ginger was used in a study and it was as well effective in reduction of nausea and vomiting (Basirat *et al*., 2009). The mechanism of effect maybe is stimulating the motility of the gastrointestinal tract; reduce stimuli to the chemoreceptor zone and blocking the gastrointestinal reactions and the subsequent nausea feedback (Mowrey and Clayson, 1982).

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