A Randomized Comparison of Ginger and Dimenhydrinate in the Treatment of Nausea and Vomiting in Pregnancy

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Objective: *To study the efficacy of ginger and dimenhydrinate in the treatment of nausea and vomiting in pregnancy.*
Study design: *Double blind randomized controlled trial.*
Setting: *Department of Obstetrics and Gynecology, Thammasat Hospital, Faculty of Medicine, Thammasat University.*
Material and Method: *Between January 2005 and December 2005, 170 pregnant women who attended at antenatal clinic Thammasat University Hospital with the symptoms of nausea and vomiting in pregnancy were randomly allocated into group A (n = 85) and group B (n = 85). The patients in group A received one capsule of ginger twice daily (one capsule contained 0.5 gm of ginger powder) while the patients in group B received the identical capsule of 50 mg dimenhydrinate twice daily. The visual analogue nausea scores (VANS) and vomiting times were evaluated at day 0-7 of the treatment.*
Results: *There was no significant difference in the visual analogue nausea scores (VANS) between group A and group B in day 1-7 of the treatment.The vomiting episodes of group A were greater than group B during the first and second day of the treatment with statistically significant difference. No difference in vomiting episodes during the day 3-7 of treatment was found in both groups. There was a statistically significant difference in the side effect of drowsiness after treatment in group B greater (77.64%) than group A (5.88%) ($p < 0.01$).*
Conclusion: *From the presented data, ginger is as effective as dimenhydrinate in the treatment of nausea and vomiting during pregnancy and has fewer side effects.*

Keywords: *Ginger, Dimenhydrinate, Nausea, Vomiting*

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Nausea and vomiting are common symptoms experienced by women in early pregnancy and affect 50-90% of pregnant women[1,2]. Although there are a number of medications available for the treatment of nausea and vomiting in pregnancy, many women hesitate to take them due to fear of harming the fetus. No anti-emetics for nausea and vomiting in pregnancy have been approved by the United States Food and Drug Administration (FDA). Evidences on the efficacy of ginger have been evaluated in many randomized controlled trials[3-5].These three randomized controlled trials found ginger to be better than placebo. The studies of Smith C[6] and Sripramote M[7] revealed that ginger was as effective as vitamin B6 in the treatment of nausea and vomiting in pregnancy.

Ginger (*Zingiber officinale*) is used as a broad-spectrum anti-emetic. The pharmacological activity is thought to lie in the pungent principles (gigerols and shagaols) and volatile oils (sequiterpenes and mono-terpenes)[8]. Ginger acts within the gastrointestinal tract by increasing tone and peristalsis due to anti-cholinergic and anti-serotonin action. Ginger avoids the central nervous system side effects caused by most onions and garlic, extracts of ginger can inhibit blood coagulation *in vitro*[9-11]. Ginger has few recorded side effects. In large doses, ginger may increase gastric

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exfoliation and anti-prostaglandin activity *in vitro*[9,10]. However, the clinical significance of these observations is yet to be determined. There are no known reports of toxicity in humans from ginger ingestion in normal amount. Many studies about ginger and pregnancy revealed no adverse effects to the fetus and pregnancy outcome[3-7].

In Thailand, most pregnant women who had nausea and vomiting in first trimester were given dimenhydrinate for the treatment. The undesirable side effect of dimenhydrinate is drowsiness. There were studies that compared ginger and dimenhydrinate only in motion sickness[12,13]. The authors would like to evaluate the efficacy of ginger and dimenhydrinate in the treatment of nausea and vomiting in pregnancy.

Material and Method

The present study was approved by the ethical committee of the Faculty of Medicine, Thammasat University, Pathumthani, Thailand. The trial took place at the antenatal clinic Thammasat University Hospital between January - December 2005. Pregnant women with nausea and vomiting were eligible for the trial if they were less than 16 weeks of gestation. Women were excluded if they 1) had any signs of clinical dehydration, 2) had other gastrointestinal diseases, 3) unable to take oral capsule, 4) unable to return for one week follow up, 5) had known allergy to ginger or dimenhydrinate, 6) had taken other medication in the past week that might aggravate or alleviate nausea and vomiting, 7) refused to participate in the trial.

The pregnant women underwent a physical examination and routine obstetrics evaluation. Ultrasonography was performed for evaluating gestational age and fetal heart motion. Then, the pregnant women were randomly allocated to receive either a 0.5 gm capsule of ginger (group A) or 50 mg capsule of dimenhydrinate (group B) orally twice daily for one week. Both capsules were identical in size, color, and odor. They were asked to return in one week and gave back the capsule envelope and the record forms. The women who were lost to follow up were excluded from the trial.

The primary outcome in the present study was the improvement in nausea and vomiting symptoms. The degree of nausea was measured using the visual analogue scale (VAS).The patients were asked on their first visit to grade the severity of their nausea over the past 24 hours (baseline score) by marking on "X" corresponding to their perceived station a 10 cm. vertical line ranging from 0 = no nausea to 10 = nausea as bad as it could be. On the following 7 days of the treatment, recordings of the severity of nausea were made twice daily in the morning and evening. The average daily nausea scores were calculated. The frequency of vomiting was recorded daily. The change in nausea score and frequency of vomiting in both group were compared. The secondary outcome was the occurrence of the side effect for example drowsiness, heartburn, palpitation, and mouth dryness.

The data was analyzed by using statistics program SPSS version 14.0. Data were analyzed using Chi-square test or Fisher's exact test and general linear model in the form of repeated measurement adjust for the co-variate by controlling the variation of the difference nausea score and vomiting times before the treatment in both groups (day 0). Student t-test was used to test the coefficient of independent variable (B). A p-value of less than 0.05 was considered significance different.

Results

There were 85 women randomized to ginger (group A) and 85 women to dimenhydrinate (group B). There were 8 women in group A and 11 women in group B who were lost to follow up. The baseline characteristics were similar in both groups (Table 1). After adjusting the variation of the difference nausea score and vomiting times before the treatment in both groups (day 0), the mean of nausea score in day 1-7 of the treatment were decreased in both groups (Fig. 1). The daily mean nausea scores between both groups were not statistically different ($p > 0.05$) (Table 2). The frequency of vomiting times in day 1-7 of the treatment was decreased in both groups (Fig. 2). The daily mean vomiting times in the dimenhydrinate group in day 1-2 of the treatment were less than the ginger group with statistical significance ($p < 0.05$). After day 3-7 post treatment, the daily mean vomiting times in both groups were not statistically different ($p > 0.05$). The occurrence of drowsiness in the ginger group and dimenhydrinate group were 5/85 (5.88%) versus 66/85 (77.64%) ($p < 0.01$). The occurrence of heart burn was 13/85 (15.2%) versus 9/85 (10.58%) ($p = 0.403$), respectively. No other adverse effect was observed in both groups during the one-week follow up.

Discussion

Ginger (*Zingiber officinale*) has traditionally been used for gastrointestinal symptoms such as nausea and vomiting[14].Recent evidences suggest that its anti-emetic activities may be derived from its anti-serotonin-3 effects on both the central nervous and

Table 1. Dermographic data of the patients in both groups. (Group A = Ginger, Group B = Dimenhydrinate)

Group		A (n = 85)		B (n = 85)	
Age (year)		27.85	(±5.3)	26.38	(±5.8)
Weight (kg)		53.22	(±6.9)	52.18	(±6.2)
BMI		21.38	(±3.4)	20.87	(±2.9)
GA (week)		10.25	(±2.8)	9.3	(±3.1)
Nullipara (n)		49	57.65%	56	65.88%
Occupation					
	Employee	39	45.88%	43	50.59%
	Government Officer	6	7.06%	6	7.06%
	Trader	18	21.16%	6	7.06%
	Housewife	22	25.88%	30	35.29%
Education					
	Elementary	30	35.29%	24	28.24%
	Junior high school	29	34.12%	32	37.65%
	High school	15	17.65%	16	18.22%
	Bachelor	11	12.94%	13	15.29%

BMI: Body Mass Index
GA: Gestational age
(Group A = Ginger, Group B = Dimenhydrinate)

Table 2. Mean of nausea score post treatment

Dependent variable	Parameter	B	Std. error	t	Sig.	95% confidence interval	
						Lower bound	Upper bound
N day 1	Intercept	0.2898	0.3004	0.9648	0.3361	-0.3032	0.8828
	N_DAY_0	0.8215	0.0443	18.5295	0.0000	0.7340	0.9090
	[GROUP B]	-0.1991	0.1333	-1.4941	0.1370	-0.4623	0.0640
	[GROUP A]	0.0000	.	.	.	.	.
N day 2	Intercept	-0.1124	0.5112	-0.2200	0.8262	-1.1216	0.8967
	N_DAY_0	0.6847	0.0755	9.0753	0.0000	0.5358	0.8337
	[GROUP B]	-0.0463	0.2268	-0.2041	0.8385	-0.4941	0.4015
	[GROUP A]	0.0000	.	.	.	.	.
N day 3	Intercept	-0.3182	0.5406	-0.5885	0.5570	-1.3855	0.7492
	N_DAY_0	0.6198	0.0798	7.7675	0.0000	0.4623	0.7774
	[GROUP B]	-0.0513	0.2399	-0.2140	0.8308	-0.5249	0.4223
	[GROUP A]	0.0000	.	.	.	.	.
N day 4	Intercept	0.0870	0.4770	0.1824	0.8555	-0.8548	1.0288
	N_DAY_0	0.4984	0.0704	7.0778	0.0000	0.3594	0.6374
	[GROUP B]	-0.2240	0.2117	-1.0580	0.2916	-0.6419	0.1940
	[GROUP A]	0.0000	.	.	.	.	.
N day 5	Intercept	0.3762	0.4722	0.7968	0.4267	-0.5560	1.3084
	N_DAY_0	0.3821	0.0697	5.4827	0.0000	0.2445	0.5197
	[GROUP B]	-0.2423	0.2095	-1.1563	0.2492	-0.6559	0.1714
	[GROUP A]	0.0000	.	.	.	.	.
N day 6	Intercept	0.1688	0.4716	0.3578	0.7209	-0.7624	1.0999
	N_DAY_0	0.3485	0.0696	5.0066	0.0000	0.2111	0.4860
	[GROUP B]	-0.0627	0.2093	-0.2997	0.7648	-0.4759	0.3505
	[GROUP A]	0.0000	.	.	.	.	.
N day 7	Intercept	0.5712	0.4803	1.1893	0.2360	-0.3770	1.5193
	N_DAY_0	0.2293	0.0709	3.2352	0.0015	0.0894	0.3693
	[GROUP B]	-0.1995	0.2131	-0.9360	0.3506	-0.6202	0.2213
	[GROUP A]	0.0000	.	.	.	.	.

(Group A = Ginger, Group B = Dimenhydrinate)

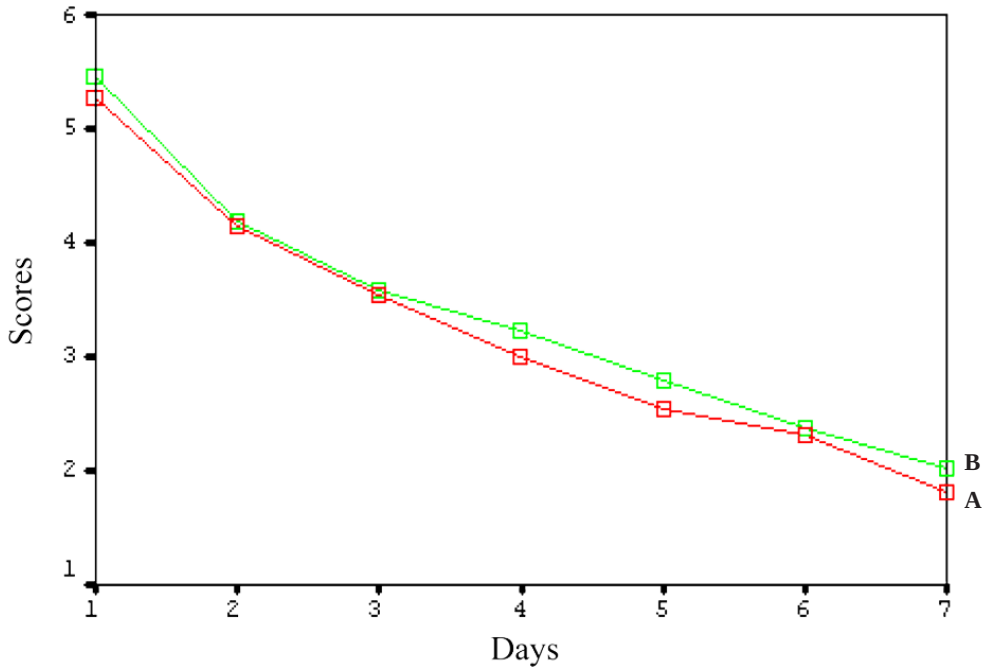

Fig. 1 Comparative means of nausea score between both groups (Group A = Ginger, Group B = Dimenhydrinate)

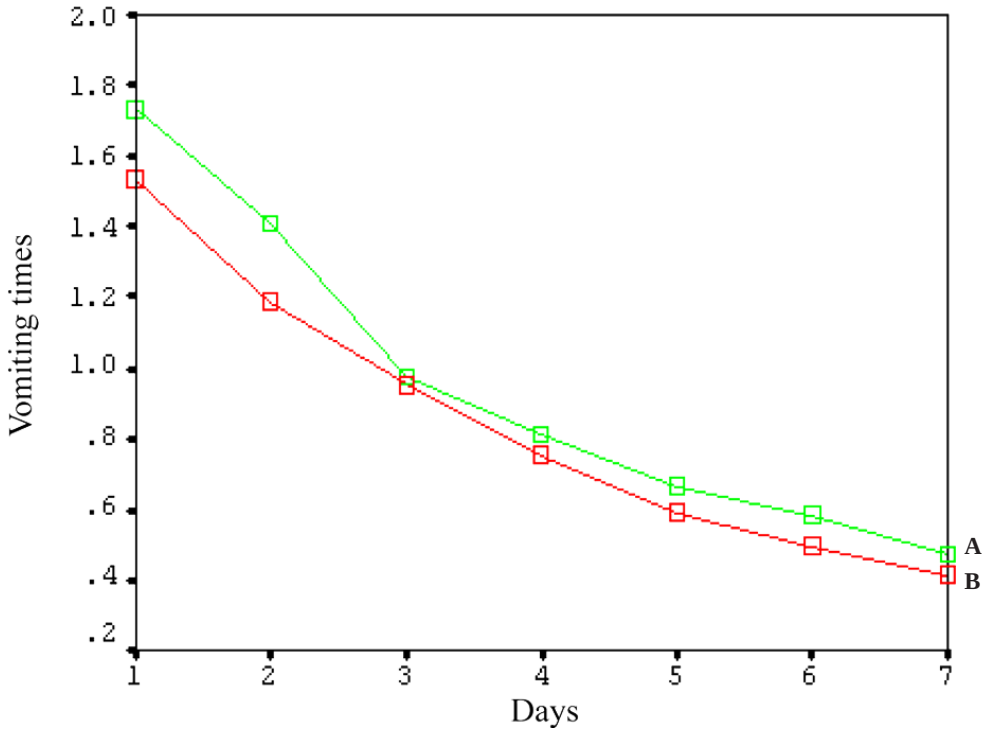

Fig. 2 Comparative means of vomiting times between both groups (Group A = Ginger, Group B = Dimenhydrinate)

Table 3. Mean of vomiting times post treatment

Dependent variable	Parameter	B	Std. error	t	Sig.	95% confidence interval	
						Lower bound	Upper bound
Frequency of vomiting at day 1	Intercept	-0.0831	0.0733	-1.1329	0.2589	-0.2279	0.0617
	B_DAY_0	0.8730	0.0274	31.8715	0.0000	0.8189	0.9271
	[GROUP B]	-0.1991	0.0762	-2.6126	0.0098	-0.3495	-0.0486
	[GROUP A]	0.0000	.	.	.	.	.
Frequency of vomiting at day 2	Intercept	-0.1595	0.1003	-1.5899	0.1138	-0.3575	0.0386
	B_DAY_0	0.7551	0.0375	20.1597	0.0000	0.6812	0.8291
	[GROUP B]	-0.2259	0.1042	-2.1685	0.0315	-0.4316	-0.0202
	[GROUP A]	0.0000	.	.	.	.	.
Frequency of vomiting at day 3	Intercept	-0.1810	0.1078	-1.6785	0.0951	-0.3938	0.0319
	B_DAY_0	0.5566	0.0403	13.8230	0.0000	0.4771	0.6361
	[GROUP B]	-0.0266	0.1120	-0.2377	0.8124	-0.2477	0.1945
	[GROUP A]	0.0000	.	.	.	.	.
Frequency of vomiting at day 4	Intercept	-0.2225	0.1176	-1.8912	0.0603	-0.4547	0.0098
	B_DAY_0	0.4962	0.0439	11.2956	0.0000	0.4095	0.5830
	[GROUP B]	-0.0571	0.1222	-0.4669	0.6412	-0.2983	0.1842
	[GROUP A]	0.0000	.	.	.	.	.
Frequency of vomiting at day 5	Intercept	-0.2425	0.1135	-2.1356	0.0342	-0.4667	-0.0183
	B_DAY_0	0.4370	0.0424	10.3055	0.0000	0.3533	0.5207
	[GROUP B]	-0.0762	0.1180	-0.6464	0.5189	-0.3091	0.1566
	[GROUP A]	0.0000	.	.	.	.	.
Frequency of vomiting at day 6	Intercept	-0.2318	0.1078	-2.1498	0.0330	-0.4447	-0.0189
	B_DAY_0	0.3930	0.0403	9.7601	0.0000	0.3135	0.4725
	[GROUP B]	-0.0908	0.1120	-0.8109	0.4186	-0.3120	0.1303
	[GROUP A]	0.0000	.	.	.	.	.
Frequency of vomiting at day 7	Intercept	-0.2692	0.1017	-2.6473	0.0089	-0.4700	-0.0685
	B_DAY_0	0.3560	0.0380	9.3716	0.0000	0.2810	0.4309
	[GROUP B]	-0.0616	0.1057	-0.5833	0.5605	-0.2702	0.1470
	[GROUP A]	0.0000	.	.	.	.	.

(Group A = Ginger, Group B = Dimenhydrinate)

Table 4. Side effects

Group	A	%	B	%	p-value
Drowsiness	5	5.88	66	77.64	<0.001
Heart burn	13	15.29	9	10.58	0.493

(Group A = Ginger, Group B = Dimenhydrinate)

gastrointestinal system[11-14]. Four confirmatory studies, two vs. placebo[4,5] and two vs. vitamin B6[6,7], demonstrated that the 0.5 gm or 1 gm of ginger powder or extract was effective in treating nausea and/or vomiting during pregnancy. These exploratory studies back this result.

In the present study, the duration of ginger treatment was very short and the dosage used was very low. The authors used 0.5 gm of ginger powder twice daily for one week. In the study of Smith C et al[6], the dosage of ginger was 1.05 gm daily compared with 75 mg of vitamin B6 for three weeks. Sripramote M[7]

used 0.5 gm of ginger compared with vitamin B6 10 mg three times daily for one week (total 1.5 gm ginger per day). The authors usually use dimenhydrinate 50 mg one to three times per day for treating nausea and vomiting in pregnancy. Because the undesirable effect is drowsiness, in this study the authors used 500 mg of ginger compared with 50 mg of dimenhydrinate twice daily to minimize this adverse effect that might result in the higher rate of patient non-compliance and loss to follow up.

Because the variation in nausea score and vomiting times before the treatment (day 0) were significant, in the present study the authors used general linear model in the form of repeated measurement adjust for the co-variate by controlling these variation. The authors found that ginger was as effective as dimenhydrinate in the treatment of nausea and vomiting. Although the vomiting times of the ginger group in day 1-2 of the treatment were greater than the dimenhydrinate group, the effectiveness were similar after day 3-7 post treatment.

According to the safety of ginger in pregnancy, the study of Vutyavanich T et al[4] found that ginger had a similar adverse pregnancy outcome as the control group (abortion, preterm delivery, cesarean section, congenital anomaly). The study of Portnoi G et al[15] confirmed the safety of ginger but they found the rate of low birth weight in the control group greater than the ginger group (6.4% vs. 1.6%).This study explained that they had eight sets of twins in the control group. However, the other adverse pregnancy outcomes were similar.

Nausea and vomiting in early pregnancy remain a significant public health that have physiological, emotional, social, and economic consequences to women, their family, and society. Many medications, for example vitamin B6, metoclopamide etc, are used in the treatment of nausea and vomiting in pregnancy. In spite of its undesirable effect, dimenhydrinate is still commonly used in general practice. Ginger has long been recommended as folklore treatment for nausea and vomiting in pregnancy without significant side effects. The present study support that ginger can be used as an alternative choice for the treatment of nausea and vomiting in pregnancy.

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การศึกษาเปรียบเทียบขิงกับยา dimenhydrinate ในการรักษาภาวะคลื่นไส้อาเจียนในสตรีตั้งครรภ์

เด่นศักดิ์ พงศ์โรจน์เผ่า, จรินทร์ทิพย์ สมประสิทธิ์, อธิตา จันทเสนานนท์

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบประสิทธิภาพของขิงกับยา dimenhydrinate ในการรักษาอาการคลื่นไส้อาเจียนในสตรีตั้งครรภ์

รูปแบบการวิจัย: Double blind randomized controlled trial

สถานที่: ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์

วัสดุและวิธีการ: ศึกษาตั้งแต่ มกราคม พ.ศ. 2548 - ธันวาคม พ.ศ. 2548 สตรีตั้งครรภ์ที่มารับการตรวจครรภ์ ณ โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ ที่มีอาการคลื่นไส้อาเจียนระหว่างตั้งครรภ์ จำนวน 170 ราย ได้ทำการแบ่งกลุ่มแบบสุ่ม เป็น 2 กลุ่ม ๆ ละ 85 ราย กลุ่ม A จะได้รับ ยาขิง 1 แคปซูล วันละ 2 ครั้ง (1 แคปซูลประกอบด้วยขิง 0.5 กรัม) และกลุ่ม B จะได้รับยา dimenhydrinate (50 mg) ประเมิน Visual analogue nausea score (VANS) จำนวนครั้งที่อาเจียน และผลข้างเคียง วันที่ 0-7 ของการรักษา

ผลการศึกษา: ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของคะแนนอาการคลื่นไส้ (VANS) ในการรักษาทั้งสองกลุ่ม ในวันที่ 1 และ 2 ของการรักษา กลุ่มที่ได้รับยาขิงพบว่ามีจำนวนครั้งของการอาเจียนมากกว่ากลุ่มที่ได้รับยา dimenhydrinate อย่างมีนัยสำคัญทางสถิติ แต่ในวันที่ 3-7 ของการรักษา พบว่าจำนวนครั้งของการอาเจียนไม่แตกต่างกันทั้งสองกลุ่ม กลุ่มที่ได้รับยาขิงพบว่ามีอาการง่วงนอนน้อยกว่ากลุ่มที่ได้รับยา dimenhydrinate อย่างมีนัยสำคัญทางสถิติ

สรุป: จากการศึกษา พบว่าขิงมีประสิทธิภาพในการรักษาอาการคลื่นไส้อาเจียนในสตรีตั้งครรภ์ไม่แตกต่างจากยา dimenhydrinate แต่มีอาการข้างเคียงน้อยกว่า