Original Article

A randomized comparison of vitamin B6 and dimenhydrinate in the treatment of nausea and vomiting in early pregnancy

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Abstract

Background: Nausea and vomiting are the common symptoms of early pregnancy. Without treatment, vomiting can complicate the pregnancy, so it must be reduced. Wide varieties of treatment have been used for nausea and vomiting in pregnancy. This study compared the effectiveness of vitamin B6 and dimenhydrinate for gestational nausea and vomiting.

Materials and Methods: One hundred and forty pregnant women with a gestational age of <16 weeks who had symptoms of nausea and vomiting were selected. They were randomly allocated into group A (n = 70) and group B (n = 70). The patients in group A received a vitamin B6 tablet, while the patients in group B received a dimenhydrinate tablet daily; the tablets were identical in appearance. The degree of nausea and vomiting was assessed by physical symptoms of Rhodes score.

Results: One hundred and thirty-five women returned to follow-up. Dimenhydrinate and vitamin B6 significantly reduced nausea and vomiting scores from 8.3 (7.4) to 2.8 (2.0) and from 8.6 (2.9) to 3.8 (2.3), respectively. The mean score change after treatment with dimenhydrinate was greater than with vitamin B6.

Conclusion: Both dimenhydrinate and vitamin B6 were effective in the treatment of nausea and vomiting in early pregnancy. Dimenhydrinate was more effective than vitamin B6.

Key words: Dimenhydrinate, Iran, nausea, pregnancy, vitamin B6

Introduction

Nausea and vomiting are the common symptoms experienced by women during early pregnancy and affect 50-90% of pregnant women.[1,2] Complications of vomiting include fluid and electrolyte disturbances (dehydration), pulmonary aspiration, gastroesophageal mucosal tearing, malnutrition, and rupture of the esophagus.[3] The cause of nausea and vomiting during pregnancy is still unknown. Therefore, wide varieties of treatment have been used.[4]

There are a number of medications for the treatment of nausea and vomiting during pregnancy. The American College of Obstetrics and Gynecology recommends that first-line treatment of nausea and vomiting of pregnancy be started with pyridoxine (vitamin B6).[5]

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Pyridoxine (vitamin B6), a water-soluble vitamin and an essential coenzyme in the folate metabolism pathway, was first referenced for use in treating nausea and vomiting during pregnancy. The pyridoxine mechanism of affecting nausea is unknown. No teratogenic risks have been associated with the use of pyridoxine, and it belongs to Food and Drug Administration (FDA) Pregnancy Category A (adequate, well-controlled studies in pregnant women have not shown an increased risk of abnormalities to the fetus in any trimester of pregnancy).[6] A randomized clinical trial (RCT) has found that regular use of pyridoxine is effective in decreasing the severity of nausea, but has no effect on the frequency of vomiting episodes.[7] However, Sripramote and Lekhyananda showed that vitamin B6 significantly reduced the degree of nausea and the number of vomiting episodes.[8]

Another drug that is used in nausea and vomiting is dimenhydrinate. It is an antihistamine and anticholinergic that acts in the brain to decrease nausea and vomiting. Dimenhydrinate belongs to FDA Pregnancy Category B (animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester).[9]

The efficacy of dimenhydrinate in the treatment of nausea and vomiting during pregnancy has been evaluated in many RCTs.[5,9] In Thailand, most pregnant women who had nausea and vomiting in the first trimester were given treatment with dimenhydrinate.[9]

Thus, considering the above-mentioned points, and the importance of treatment of nausea and vomiting during pregnancy, the safety of dimenhydrinate and vitamin B6, and a more effective administration of these drugs, the present study was conducted with an aim to compare the effectiveness of 50 mg of dimenhydrinate daily and the recommended dose of 50 mg of vitamin B6 daily to treat nausea and vomiting during early pregnancy.

Materials and Methods

This study was a double-blind, randomized, controlled clinical trial performed at two antenatal clinics of the referral hospitals affiliated to Shiraz University of Medical Sciences, Shiraz, southern Iran. The study was approved by the ethics committee of Shiraz University of Medical Sciences.

The sample size was calculated using data from a pilot study of 20 cases treated with vitamin B6 and dimenhydrinate. Researchers calculated that if the score change of 30% was clinically important, a sample size of 63 subjects per group would be able to detect this difference with probability of two-tailed type I error of 5% and type II error of 20%. To allow for a 10% dropout rate, a sample size of a total of 70 subjects per group was calculated.

The target population was pregnant women at or before 16 weeks of gestation who had nausea with or without vomiting and required treatment. Subjects were excluded if they: (1) were hospitalized for severe vomiting; (2) had taken other medications in the past week that might aggravate or alleviate nausea and vomiting, such as iron tablets or antiemetic; (3) were unable to take the medication as prescribed; (4) had other medical disorders such as hepatitis or gastrointestinal diseases that might manifest with nausea and vomiting; (5) were unable to return for 1-week follow-up; and (6) refused to participate in the trial.

All patients gave written informed consent before enrolling in the trial. They underwent a physical examination and routine obstetrics evaluation. Ultrasonography was performed for evaluating gestational age and fetal heart motion. Then, the 140 participating women in this trial were randomly assigned into two groups: 70 women received a 50 mg tablet of vitamin 6 (group A) and the other 70 received a 50 mg dimenhydrinate tablet (group B) orally every morning for 1 week. Both tablets were identical in size, color, and odor. They were asked to return in 1 week and give back the tablet envelope and the record forms. The women who were lost to follow-up were excluded from the trial.

Researchers recommended the patients to swallow the tablets. The pregnant women were requested to record their symptoms at first enrollment (24 h before treatment) for the baseline score, and then at noon of each day of treatment. Patients were requested to return on the day after completing their medication to assess their responses to treatment.

The primary outcome was the change in nausea and vomiting scores (mean of post-treatment scores minus baseline scores). Nausea and vomiting scores were assessed by three physical symptoms (episodes of nausea, duration of nausea, and numbers of vomits) by Rhodes Index. The Index of Nausea and Vomiting (INV), developed by Rhodes *et al*., measures three dimensions of upper gastrointestinal distress [nausea, vomiting, and retching (NVR)]. The revised version of this index (INV2) has been tested with a variety of high-risk populations and found to be a valid measurement tool.[10,11]

In this study, the drug side effects (such as drowsiness or dizziness) were the secondary outcome.

Data were analyzed by SPSS for Windows (version 14.0; SPSS Inc., Chicago, IL, USA). The differences of quantitative data were analyzed by analysis of variance (ANOVA). *P* value of less than 0.05 was considered significant. Descriptive statistics were summarized as mean with standard deviation and percentage.

Results

Seventy pregnant women were placed in the vitamin B6 group (group A) and another 70 pregnant women in the dimenhydrinate group (group B). Three cases (4.2%) in the vitamin B6 group and two cases (2.7%) in the dimenhydrinate group did not return to follow-up. Group A consisted of 67 cases, and group B 68 cases. The demographic characteristics (age, gestational age, weight, height, body mass index, parity, education, and occupation) were similar in both groups [Tables 1 and 2].

The baseline nausea vomiting scores [8.6 (2.9) in group A and 8.3 (7.4) in group B] and post-treatment scores are shown in Table 3.

Comparison of the baseline scores and post-treatment scores in the two groups showed that both vitamin B6 and

dimenhydrinate decreased nausea and vomiting scores from baseline values. The average score change in the vitamin B6 group was less than that in the dimenhydrinate group [4.4 (1.6) vs. 5.7 (5.5)] and was statistically significant ($P < 0.05$). Each day, there were significant differences in the score change of the vitamin B6 group compared to the dimenhydrinate group.

On comparing the side effects of both groups, we found that the occurrence of drowsiness in the vitamin B6 group was 5 (4.46%) versus 36 (52.94%) in the dimenhydrinate group ($P < 0.01$). No other adverse effect was observed in the two groups during the 1-week follow-up.

Table 1: The mean scores of age, gestational age, weight, height, and BMI of vitamin B6 and dimenhydrinate groups

Groups characteristics	Vitamin B6		Dimenhydrinate	
	Mean	SD	Mean	SD
Age (years)	24.8	2.1	25.4	3.3
Gestational age (weeks)	10	7	11	3
Weight (kg)	52.6	5.4	53.2	1.1
Height (cm)	161.7	5.3	159.1	5.5
BMI	19.42	3.2	20.11	1.7

BMI: Body mass index

Table 2: Percentages of scores in parity, education, and occupation of vitamin B6 and dimenhydrinate groups

Groups characteristics	Vitamin B6 (%)	Dimenhydrinate (%)
Parity		
Nulliparous	55.4	57.1
Multipara	44.6	42.9
Education		
Under diploma	35.29	38.24
Diploma	45.12	47.65
University	19.59	14.11
Occupation		
Housewife	65.1	68.3
Employed	34.9	31.7

Discussion

Nausea and vomiting during early pregnancy is a significant public health problem that has physiological, emotional, social, and economic consequences for pregnant women, their families, and society. Many medications and alternative therapies are currently available for the treatment of nausea and vomiting.

The first-line treatment for nausea and vomiting is vitamin B6 that has been evaluated in many controlled trials for the treatment of morning sickness. Smith found vitamin that B6 reduces nausea and vomiting in early pregnancy.[12]

Chittumma *et al.* concluded that vitamin B6 was effective in the treatment of nausea and vomiting in pregnancy, and the average score change from baseline was 2.6 (1).[4]

Another research in Bangkok showed that the use of vitamin B6 for 3 days significantly reduced the nausea scores from 5.3 to 3.3. The mean score change after treatment with vitamin B6 was 2.0.[8] Our study confirmed the results of this research and showed that vitamin B6 significantly reduced nausea and vomiting. However, in our study, the subjects took vitamin B6 tablets for 7 days in order to resolve nausea and vomiting completely.

Another drug that is used in nausea and vomiting treatment is dimenhydrinate. This substance is an antihistamine, but is used most commonly as an antiemetic because it is an antagonist H receptor.[13]

Dimenhydrinate 50 mg twice daily was evaluated by Pongrojpaw *et al*. for treating nausea and vomiting. They

Table 3: Baseline and post-treatment scores of nausea and vomiting in vitamin B6 and dimenhydrinate groups

Vitamin B6 (n=67)						Dimenhydrinate (n=68)					
Baseline		Post-treatment			P value*	Baseline		Post-treatment			P value*
Mean	SD	Days	Mean	SD		Mean	SD	Days	Mean	SD	
8.6	2.9	1	8.1	2.5	0.080	8.3	7.4	1	7.9	2.8	0.090
		2	7.3	2.3	0.060			2	6.8	7.3	0.060
		3	6.8	2.0	0.050			3	5.6	2.3	0.050
		4	5.4	7.1	0.050			4	4.8	1.4	<0.001
		5	4.7	2.8	<0.001			5	3.4	2.3	<0.001
		6	3.9	4.2	<0.001			6	2.9	1.2	<0.001
		7	3.8	2.3	<0.001			7	2.8	2.9	<0.001

*Paired *t* tests: $P < 0.05$, SD: Standard deviation

found that the mean nausea score, daily mean number of vomiting episodes, and the frequency of vomiting episodes decreased.[9] Our result about dimenhydrinate is consistent with the results of other studies, which showed that it reduced nausea and vomiting. However, pregnant women in our research took dimenhydrinate 50 mg once a day until the side effects were reduced to the least amount.

The authors did not find any report that compared the antiemetic effect of dimenhydrinate and vitamin B6.

This study showed that both vitamin B6 and dimenhydrinate significantly reduced nausea and vomiting. Considering the difference between groups A and B, the average score change in the dimenhydrinate group was 2.3 (3.9), which was significantly higher than the vitamin B6 group ($P < 0.05$).

The present study is consistent with the other trials showing that vitamin B6 or dimenhydrinate is an effective treatment for nausea and vomiting in early pregnancy, but dimenhydrinate was more effective than vitamin B6 as it significantly reduced nausea and vomiting symptoms during the 7 days of treatment.

There were no differences between the groups with respect to age, gestational age, weight, height, BMI, parity, education, and occupation.

In some studies, there were minor side effects for vitamin B6, such as sedation (32.8%) and heartburn (6.3%).[4,8] However, in this research, the occurrence of drowsiness in the vitamin B6 group was 5 (4.46%) versus 36 (52.94%) in the dimenhydrinate group ($P < 0.01$). No other adverse effect was observed in the two groups during the 1-week follow-up.

Further studies can be conducted to compare the effect of vitamin B6 or dimenhydrinate with other antiemetic drugs like metoclopramide that is a category B drug in pregnancy.

Conclusion

Both dimenhydrinate and vitamin B6 were effective in the treatment of nausea and vomiting in early pregnancy. Dimenhydrinate was more effective than vitamin B6.

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