



## Effect of Combined Use of Calcium and Vitamin B6 on Premenstrual Syndrome Symptoms: a Randomized Clinical Trial

Seyedeh Zahra Masoumi<sup>1</sup>, Maryam Ataollahi<sup>2\*</sup>, Khodayar Oshvandi<sup>3</sup>

<sup>1</sup>Mother and Child Care Research Center, Department of Midwifery, Faculty of Nursing and Midwifery, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>2</sup>Department of Midwifery, Faculty of Nursing and Midwifery, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>3</sup>Mother and Child Care Research Center, Department of Nursing, Faculty of Nursing and Midwifery, Hamadan University of Medical Sciences, Hamadan, Iran

### ARTICLE INFO

#### Article Type:

Original Article

#### Article History:

Received: 17 Jun. 2015

Accepted: 18 Dec. 2015

ePublished: 1 Mar. 2016

#### Keywords:

Premenstrual syndrome

Calcium

Vitamin B6

Menstrual cycle

### ABSTRACT

**Introduction:** Premenstrual syndrome is one of the most common disorders in women, which includes a group of psychological and physical symptoms. The aim of this study was to examine the impact of combined use of calcium and vitamin B6 on premenstrual syndrome symptoms.

**Methods:** This double blind randomized controlled was carried out on 76 students of Hamadan University of Medical Sciences. Students were randomly allocated to two groups. (38 people in each group). Student in intervention groups received calcium tablet (500mg) and vitamin B6 (40 mg) and student in intervention groups received only vitamin B6 twice a day for two consecutive months.

The symptoms were assessed by Beck depression inventory (BDI) and daily symptom records (DSR) questionnaires. Analyses were carried out by test-retest method, Chi-square, Mann-Whitney, Independent t-test, and paired t-test using SPSS software ver.13.

**Results:** The result showed that although the severity of symptoms decreased in both groups, but this reduction was more significant in the combined calcium and vitamin B6 group.

**Conclusion:** According to the result, using of combination of calcium and vitamin B6 leads to better controlling of the premenstrual syndrome symptoms. Therefore it is recommended for women who suffer from these syndromes.

**Please cite this paper as:** Masoumi SZ, Ataollahi M, Oshvandi Kh. Effect of combined use of calcium and vitamin b6 on premenstrual syndrome symptoms. J Caring Sci 2016; 5 (1): 67-73. doi:10.15171/jcs.2016.007.

### Introduction

Premenstrual syndrome (PMS) is characterized by the presence of physical and psychological symptoms occurring during the late luteal phase of the menstrual cycle and associated with substantial impairment in social relationships, lifestyle, and school performance.<sup>1-2</sup> It includes numerous psychological symptoms such as tension, anxiety, crying, irritability, depression, hypersensitivity, poor concentration, fatigue, mood swings, and anger. There are also physical symptoms including breast tenderness, abdominal

cramps, bloating, swelling, acne, increased appetite, headache, backache, and sleep disturbance.<sup>3</sup> Although the pathophysiology of PMS is not well known, the interactions between ovarian hormones and neurotransmitters, mineral and vitamin (vitamins B6 and calcium) deficiency, and reduced serotonin level are likely to play a role in the etiology of the disorder.<sup>4,5</sup> The exact prevalence of this syndrome is unknown<sup>6</sup>, but epidemiological surveys have estimated that as many as 85% of women at their reproductive age experience at least one symptom of premenstrual

\* Corresponding Author: Maryam Ataollahi (MSc), email: maryam.ataollahi@gmail.com. This clinical trial is registered on the site plan



No: IRCT2014070313405N3.

© 2016 The Author(s). This work is published by Journal of Caring Sciences as an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited.

syndrome<sup>7,8</sup> and 2.5–3% of women suffer from the severe form of PMS, known as premenstrual dysphonic disorder (PMDD).<sup>9</sup>

Therapeutic interventions for the premenstrual syndrome range from nonpharmacological management to psychotropic medications and hormonal therapy, oral contraceptives, selective serotonin reuptake inhibitors (SSRIs), and SNRIs as well as GnRH agonists.<sup>10-13</sup> There is no research directly addressing the effect of combined use of calcium and vitamin B6 on PMS symptoms. But, various studies have been conducted on the positive effect of vitamin B6 or calcium on reducing PMS symptoms. In this regard, Alexander confirmed the effectiveness of vitamin B6 on PMS.<sup>14</sup> Also, Panay Moayyed showed the positive effect of vitamin B6 on reducing PMS symptoms.<sup>4</sup> In other studies, positive effects of vitamin B6 for PMS symptoms have been shown.<sup>15-16</sup>

Pourmohsen *et al.*, demonstrated the positive effect of calcium and vitamin E on reducing PMS symptoms.<sup>17</sup> Sutariya *et al.*, reported the positive effect of the intake of calcium on reducing PMS symptom.<sup>18</sup>

Ghanbari *et al.*, indicated the positive effect of calcium on mitigating the physical and psychological symptoms.<sup>5</sup> Since separately taking calcium and vitamin B6 reduces the severity of PMS, it seems that using the combination of calcium and vitamin B6 might be more effective in reducing the symptoms of premenstrual syndrome. Therefore, this study was aimed to examine the impact of combined use of calcium and vitamin B6 on premenstrual syndrome symptoms.

## Materials and methods

This study was a double blind randomized controlled clinical trial carried out in Hamadan University of Medical Sciences in 2015. The sample size was estimated using the following formula:  $N = (Z_{\alpha/2} + Z_{\beta})^2 \sigma^2 / \epsilon^2$ . With 95% confidence interval, the minimum sample size of 76 participants was determined. Out of 312 students who

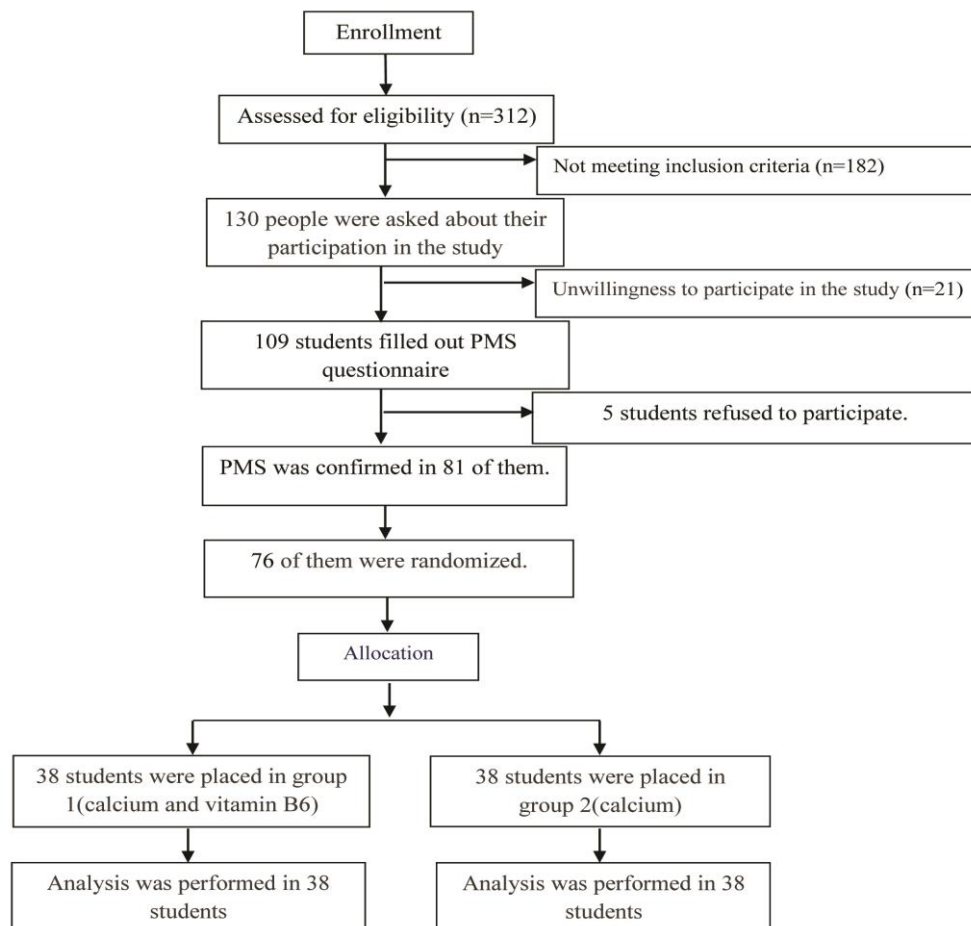
were assessed, 130 people meet the following inclusion criteria: 20-30 years of age; regular menstrual periods with 21-35 days of cycles and 3-10 days of bleeding period; no known mental illnesses; no physical illnesses such as diabetes, seizure disorders, hypothyroidism, and so on; no death of close relatives; divorce or other adverse events during the last three months; no surgery in the three months before entering the study; and no use of antidepressants, hormonal contraceptives, medroxy progesterone acetate, and vitamins in the past three months. The students were excluded from the research in the case of pregnancy, incidents like death of close relatives, divorce, and other adverse events. Data collection tools included demographic data, Beck depression inventory (BDI), and daily symptom records (DSR). At the first stage, the participants filled out Beck depression inventory. If they got the score of 1-10, they entered the study.

Then, the demographic questionnaire was presented to them. Daily symptom records were completed by the students to confirm PMS diagnosis and they were informed about how to complete the questionnaires. The participants recorded daily symptoms score with numbers 0 (no), 1 (mild), 2 (moderate), and 3 (severe). The mean score of the symptoms was calculated from 1 week prior to the menstrual period to 5 days afterwards. Total score of the symptoms of headache, breast tenderness, acne, swelling, bloating, and palpitations demonstrated the severity of physical symptoms and total score of the symptoms of irritability, tension, sleep problems, mood swings, food cravings, wish to be alone, depression, forgetfulness, anxiety, poor concentration, crying, suicide, decreased libido, and fatigue showed the severity of psychological symptoms. The questionnaires were collected after two months. Totally, 109 students filled out and returned the questionnaire, based on which the diagnosis of premenstrual syndrome

was confirmed in 81 students. Out of these 81 students, 5 refused to participate and 76 entered the study. They were then divided into two groups using the table of random numbers; 38 in the intervention and 38 in the control groups (Figure 1). Student in intervention groups received calcium tablet (500 mg) and vitamin B6 (40 mg) and student in intervention groups received only vitamin B6 twice a day in the, between the 16<sup>th</sup> days of the menstrual cycle to the 5<sup>th</sup> day of the next menstrual period for two consecutive months. Validity of BDI and DSR questionnaires was confirmed through content validity and test-retest method was used to assess their reliability ( $r = 0.89, 0.82$  respectively). DSR questionnaire has been standardized worldwide and its validity

and reliability has been confirmed in previous studies.<sup>19-21</sup> BDI is also a global standard questionnaire which its validity and reliability has been confirmed in various studies.<sup>20,22-23</sup> The data was analyzed using SPSS software ver.13 by following tests: test-retest method, Chi-square, Mann-Whitney, Independent t-test, paired t-test. The significance level was assumed to be  $P < 0.05$ .

This double blind clinical trial was approved by Ethics Committee of Hamadan University of Medical Sciences. Also, a written consent form was taken from the students. We also assured the confidentiality of all participants.



**Figure 1.** Consort flow chart

## Results

In this clinical trial, 132 students were eligible and finally 76 students were included in the study (Figure 1). The results showed that the two groups were similar in terms of demographic characteristics. The mean (SD) age of study samples in the intervention (calcium and vitamin B6) and control (vitamin B6 alone) groups was 20.78 (1.23) and 21.23 (2.89) respectively. The mean (SD) of BMI in intervention and control group was 20.46 (2.76) and 21.58 (2.20), respectively (Table 1). The history of premenstrual syndrome in the intervention and control group was 71.05% and 60.52%, respectively. The mean score of physical symptoms were significantly reduced in

intervention group compared to control group 0.25 (0.15) vs. 0.42 (0.46) ( $P=0.03$ ) (Table 2). As well as the mean score of psychological symptoms was decreased in intervention group compared to control group 0.26 (0.21) vs. 0.47 (0.37) with significant differences ( $P=0.003$ ) (Table 3). Also, the mean score of general symptoms were decreased in intervention group compared to control group 0.25 (0.17) vs. 0.44 (0.32) ( $P=0.002$ ) (Table 4). The mean score of physical, psychological and general symptoms in intervention group were significantly reduced, but within control group just psychological and general symptoms were significantly reduced after receiving drugs.

**Table 1.** Comparison of demographic characteristics in both groups

Variable	Treatment categories		P
	Calcium and vitamin B6	Vitamin B6	
Age* (years)	20.78 (1.23)	21.23 (2.89)	0.34
Age of menarche* (years)	13.31 (1.16)	12.31 (1.29)	0.09
BMI* (kg/m <sup>2</sup> )	20.46 (2.76)	21.58 (2.20)	0.05
Education level**			0.21
<(bachelor)	86.84	78.94	
>(bachelor)	13.15	21.05	
Marital status**			0.23
Single	76.31	86.84	
Married	23.68	13.15	

\*Mean (SD), \*\*Value is Percent

**Table 2.** Comparison of mean score severity of physical symptoms premenstrual syndrome before and after the intervention in both groups

Treatment round groups	Before treatment Mean (SD)	Physical symptoms	P*
		8 Weeks after treatment Mean (SD)	
Calcium and Vitamin B6	0.57 (0.31)	0.25 (0.15)	0.00
Vitamin B6	0.53 (0.33)	0.42 (0.46)	0.21
P**	0.627	0.030	

\*Paired t-test, \*\* t-test

**Table 3.** Comparison of mean score severity of psychological symptoms premenstrual syndrome before and after the intervention in both groups

Treatment round groups	Before treatment Mean (SD)	Psychological symptoms	P*
		8 weeks after treatment Mean (SD)	
Calcium and Vitamin B6	0.74 (0.37)	0.26 (0.21)	0.000
Vitamin B6	0.61 (0.36)	0.47 (0.37)	0.017
P**	0.112	0.003	

\*Paired t-test, \*\* t-test

**Table 4.** Comparison of mean score severity of general symptoms premenstrual syndrome before and after the intervention in both groups

Treatment round groups	Before treatment Mean (SD)	General symptoms	P*
		8 weeks after treatment Mean (SD)	
Calcium and Vitamin B6	0.72 (0.33)	0.25 (0.17)	0.000
Vitamin B6	0.61 (0.35)	0.44 (0.32)	0.007
P**	0.16	0.002	

\*Paired t-test, \*\* t-test

## Discussion

The results showed that although the score of overall symptoms of premenstrual syndrome in the two groups decreased, this reduction was significantly greater in the group taking combined calcium and vitamin B6. In our study physical symptoms of PMS have been decreased by using a combination of vitamin and calcium. In Pourmohsen's study in 2010 in Tehran, combined administration of calcium and vitamin E resulted in 56% reduction of the overall symptoms in premenstrual syndrome.<sup>17</sup> Also, Sutaria demonstrated that daily use of 500 mg calcium led to 75% reduction of overall symptoms of PMS after three months of treatment.<sup>18</sup> In another study daily use of 600 mg calcium resulted in 48% reduction of physical symptoms in the intervention group.<sup>24</sup> other study conducted by Kashanian in 2007 showed that using of vitamin B6 for two consecutive cycles decreased some of the physical symptoms such as edema, bloating, and heart palpitations.<sup>25</sup>

The results of our study indicated that the reduction in psychological symptoms have been reduced in the students treated with combined calcium and vitamin B6. Vitamin B and calcium plays an essential role in the regulation of mood, psychological imbalances, particularly symptoms of depression. This effect is related to the production of serotonin and tryptophan metabolism.<sup>26</sup> In a study there has been 48 percent reduction in psychiatric symptoms with a daily intake of 600 mg of calcium.<sup>17</sup>

In the study by Chou in 2008, the positive effect of B vitamins on reducing

psychological symptoms such as stress, anxiety, crying offense, fatigue, insomnia, and forgetfulness was mentioned.<sup>16</sup>

Moreover, Kashanian in 2007 found that the use of 80 mg vitamin B6 for two consecutive cycles decreased some of the mental symptoms, including irritability, anxiety, crying for no reason, forgetfulness, and tendency to eat sweets.<sup>25</sup> Also, Ghanbari evaluated the effect of calcium supplementation on the symptoms of premenstrual syndrome and demonstrated that the daily use of 500 mg calcium for three consecutive cycles could reduce the psychological symptoms including fatigue, depression, and appetite changes.<sup>5</sup> In another study, combined administration of calcium and vitamin E had positive effect on the reduction of some psychological symptoms including withdrawal from social relationships.<sup>17</sup> The results of the above studies have been consistent with our results. Due to the positive effect of combined use of calcium and vitamin B6 on the symptoms of PMS, the use of this supplement is recommended to reduce the symptoms of this syndrome.

## Conclusion

This study showed that combined use of calcium and vitamin B6 significantly reduced the symptoms of premenstrual syndrome as compared with vitamin B6 alone. It seems that the combination of calcium and vitamin B6 can be used for better controlling of the premenstrual syndrome symptoms. Since few studies have been done in this area, further studies and comparison the effect of these drugs



with other chemical drugs are recommended. Based on the results obtained in this study, midwives and gynecologists can administer the combined use of calcium and vitamin B6 for the patients with premenstrual syndrome.

This study was conducted on the students of Hamadan University of Medical Sciences who might not be the representative of all the women; thus, the results cannot be generalized to all the women at the reproductive age.

### Acknowledgments

The authors would like to thank the Vice-Chancellor of Research and Technology, Hamadan University of Medical Sciences, which approved and financially supported this project. They would also like to thank all the students who participated in this study for their cooperation.

### Ethical issues

None to be declared.

### Conflict of interest

The authors declare no conflict of interest in this study.

### References

- Cheng SH, Shih CC, Yang YK, Chen KT, Chang YH, Yang YC. Factors associated with premenstrual syndrome—A survey of new female university students. *Kaohsiung J Med Sci* 2013; 29 (2): 100-5. doi: [10.1016/j.kjms.2012.08.017](https://doi.org/10.1016/j.kjms.2012.08.017)
- Zaka M, Mahmood KT. Pre-menstrual syndrome-a review. *Journal of Pharmaceutical Sciences & Research* 2012; 4 (1): 1684-91.
- Delaram M, Jafari F. The effect of fennel on the premenstrual syndrome. *Knowledge and Health Journal* 2011; 6 (1): 1-6
- Panay N. Management of premenstrual syndrome. *J Fam Plann Reprod Health Care* 2009; 35 (3): 187-94. doi: [10.1783/147118909788708147](https://doi.org/10.1783/147118909788708147)
- Ghanbari Z, Haghollahi F, Shariat M, Foroshani AR, Ashrafi M. Effects of calcium supplement therapy in women with premenstrual syndrome. *Taiwan J Obstet Gynecol* 2009; 48 (2): 124-29. doi: [10.1016/S1028-4559\(09\)60271-0](https://doi.org/10.1016/S1028-4559(09)60271-0)
- Braverman PK. Premenstrual syndrome and premenstrual dysphoric disorder. *J Pediatr Adolesc Gynecol* 2007; 20 (1): 3-12. doi: [10.1016/j.jpag.2006.10.007](https://doi.org/10.1016/j.jpag.2006.10.007)
- Seedhom AE, Mohammed ES, Mahfouz EM. Life Style Factors Associated with Premenstrual Syndrome among El-Minia University Students, Egypt. *Int Sch Res Notices* 2013; 2013 (2013). doi: [10.1155/2013/617123](https://doi.org/10.1155/2013/617123)
- Kroll AR. Recreational physical activity and premenstrual syndrome in college-aged women. [Master's thesis]. 2010. Massachusetts: University of Massachusetts Amherst.
- Milewicz A, Jedrzejuk D. Premenstrual syndrome: from etiology to treatment. *Maturitas* 2006; 55: S47-S54. doi: [10.1016/j.maturitas.2006.06.016](https://doi.org/10.1016/j.maturitas.2006.06.016)
- Potter J, Bouyer J, Trussell J, Moreau C. Premenstrual syndrome prevalence and fluctuation over time: results from a French population-based survey. *Journal of Women's Health* 2009; 18 (1): 31-9. doi: [10.1089/jwh.2008.0932](https://doi.org/10.1089/jwh.2008.0932)
- Zukov I, Ptáček R, Raboch J, Domlivilová D, Kuzelová H, Fischer S, et al. Premenstrual dysphoric disorder—review of actual findings about mental disorders related to menstrual cycle and possibilities of their therapy. *Prague Med Rep* 2010; 111 (1): 12-24.
- Cunningham J, Yonkers KA, O'Brien S, Eriksson E. Update on research and treatment of premenstrual dysphoric disorder. *Harv Rev Psychiatry* 2009; 17 (2): 120-137. doi: [10.1080/10673220902891836](https://doi.org/10.1080/10673220902891836)

13. Biggs WS, Demuth RH. Premenstrual syndrome and premenstrual dysphoric disorder. *Am Fam Physician* 2011; 84 (8): 918-24.
14. Alexander L. Natural wellness strategies for the menopause years: natural wellness strategies for women (women's wisdom). Scotland: Findhorn Press; 2012.
15. Sabet-Birjandi S, Tadayon-Najafabadi M, Siyahpooshan A, Haghighizadeh M. Comparison the effect of hypericum perforatum and vitamin B6 in the treatment of premenstrual syndrome. *Zahedan Journal of Research in Medical Sciences* 2011; 13 (4): 1-5.
16. Chou PB, Morse CA, Xu H. A controlled trial of Chinese herbal medicine for premenstrual syndrome. *J Psychosom Obstet Gynaecol* 2008; 29 (3): 189-96. doi: [10.1080/01674820801893011](https://doi.org/10.1080/01674820801893011)
17. Pourmohsen M, Zounemat KA, Taavoni S, Hosseini AF. Effect of combined calcium and vitamin E consumption on premenstrual syndrome. *Iran Journal of Nursing* 2010; 23 (65): 8-14. (Persian)
18. Sutariya S, Talsania N, Shah C, Patel M. An interventional study (calcium supplementation and health education) on premenstrual syndrome-effect on premenstrual and menstrual symptoms. *National Journal of Community Medicine* 2011; 2 (1): 100-4.
19. Chocano- Bedoya PO. Micronutrient intake and premenstrual syndrome. [Dissertations]. Massachusetts: University of Massachusetts – Amherst. 2011.
20. Suija K, Rajala U, Jokelainen J, Jokelainen J, Liukkonen T, Härkönen P, et al. Validation of the Whooley questions and the Beck Depression Inventory in older adults. *Scand J Prim Health Care* 2012; 30 (4): 259-264. doi:[10.3109/02813432.2012.732473](https://doi.org/10.3109/02813432.2012.732473)
21. Fritz MA, Speroff L. Clinical gynecologic endocrinology and infertility. 8<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins. 2011.
22. Singh N, Verma P, Pandey B. Therapeutic potential of organic triticum aestivum linn. (Wheat grass) in prevention and treatment of chronic diseases: an overview. *International Journal of Pharmaceutical Sciences and Drug Research* 2012; 4 (1):10-4.
23. Seddigh R, Shariat SV, Gharraee B, Azarnik S. Evaluation of relationship between severity of depression and chess skill in members with international rating scale in chess federation of islamic republic of Iran in 1389. *Razi Journal of Medical Sciences* 2012; 19 (100): 29-36. (Persian)
24. Pearlstein T, Steiner M. Premenstrual dysphoric disorder: burden of illness and treatment update. *Women's Mental Health* 2012; 10 (1): 90-101. doi: [10.1176/appi.focus.10.1.90](https://doi.org/10.1176/appi.focus.10.1.90)
25. Kashanian M, Mazinani R, Jalalmanesh S. Pyridoxine (vitamin B6) therapy for premenstrual syndrome. *Int J Gynaecol Obstet* 2007; 96 (1): 43-44. doi: [10.1016/j.ijgo.2006.09.014](https://doi.org/10.1016/j.ijgo.2006.09.014)
26. Merete C, Falcon LM, Tucker KL. Vitamin B6 is associated with depressive symptomatology in Massachusetts elders. *J Am Coll Nutr* 2008; 27 (3): 421-27.