

## Effects of Magnesium and Vitamin B6 on the Severity of Premenstrual Syndrome Symptoms

Elham Ebrahimi<sup>1\*</sup>, Shiva Khayati Motlagh<sup>1</sup>, Sima Nemati<sup>1</sup>, Zohreh Tavakoli<sup>1</sup>

<sup>1</sup> Islamic Azad University, Maragheh, Iran

### ARTICLE INFO

**Article type:**  
Original Article

**Article History:**

Received: 10 Jun. 2011  
Accepted: 15 Apr. 2012  
ePublished: 22 Nov.2012

**Keywords:**

Premenstrual syndrome  
Premenstrual tension  
Magnesium  
Vitamin B6  
Placebo

### ABSTRACT

**Introduction:** The importance of resolving the problem of premenstrual syndrome for patients has been emphasized due to its direct and indirect economical effects on the society. The aim of the current study was to evaluate the effects of magnesium and vitamin B6 on the severity of premenstrual syndrome in patients referring to health centers affiliated to Isfahan University of Medical Sciences, Iran, during 2009-10. **Methods:** This two-stage double-blind clinical trial was conducted on 126 women who were randomly allocated into 3 groups to receive magnesium, vitamin B6, or placebo. The study was performed in 10 selected health centers in Isfahan and lasted for 4 months. To confirm premenstrual syndrome, the participants were asked to complete a menstrual diary for 2 months at home. Drug interventions were continued for two cycles and the results of before and after the intervention were compared. **Results:** The findings of this study showed that the mean scores of premenstrual syndrome significantly decreased after the intervention in all groups ( $p < 0.05$ ). **Conclusion:** According to our findings, vitamin B6 and placebo had the most and least efficiency in improving the mean premenstrual syndrome score.

## Introduction

Premenstrual syndrome affects millions of women and is known as the most important disorder in women.<sup>1</sup> It has been estimated that 80-90% of women of reproductive age experience the symptoms of this syndrome and 3-8% of these women have severe symptoms.<sup>2</sup> In Iran, Bakhshani et al. studied the students of Zahedan University of Medical Sciences and calculated the prevalence of this syndrome to be 16%.<sup>3</sup> Moreover, Tamjidi reported the prevalence of premenstrual syndrome among 15-49 year-old women of Tehran, Iran as 62.4%.<sup>4</sup> Likewise, Soltan Ahmadi suggested the rate as 66.5% in female senior students of high school in Kerman, Iran.<sup>5</sup> A study by Sheikh Al Eslami on 100 patients with major depression in two centers in Tehran revealed

the prevalence of this syndrome to be 76%.<sup>6</sup>

According to the diagnostic criteria of the American Psychiatric Association (APA), premenstrual syndrome is confirmed by keeping a menstrual diary. Recording a minimum of 5 symptoms which persist during the last week of luteal phase until the first 4 days of the next cycle for at least 2 consecutive cycles and that interfere with work or daily activities and communication but are not due to mental disorders would suggest premenstrual syndrome.<sup>7</sup>

Hitherto, numerous etiologies have been proposed to explain this disorder, and consequently various treatment methods have been suggested for controlling its clinical symptoms. This is largely due to the multifactorial nature of the disorder and the role of different biological, psychological, and social factors in its occurrence. In addition, the

\* **Corresponding Author:** Elham Ebrahimi (MSc), E-mail: ebrahimi\_308@yahoo.com  
This research is registered in Iranian Registry of Clinical Trials by IRCT201106216854N1 code.

overlapping of its symptoms with many psychiatric disorders and women's diseases might also be responsible.<sup>8</sup> One of the proposed treatments for this syndrome is magnesium. Abraham was the first person to propose magnesium deficiency as one of the factors causing and intensifying premenstrual syndrome symptoms. He justified this relation through the calming effect of magnesium in controlling neuromuscular stimulation.<sup>9</sup> The magnesium content of erythrocytes and leukocytes of women with premenstrual syndrome has been found to be lower than other women.<sup>10</sup>

Vitamin B6 is another proposed treatment for this syndrome. On the one hand vitamin B6 increases serotonin and dopamine levels and improves premenstrual syndrome symptoms, and on the other, it has an essential role in the synthesis of prostaglandin and fatty acids, which are reduced in etiologies causing premenstrual syndrome.<sup>11</sup> Moreover, researchers believe that vitamin B6 deficiency decreases dopamine in the kidneys and therefore increase sodium excretion, which in turn causes water accumulation in the body and induces symptoms such as swelling in extremities, edema, and abdominal and chest discomfort. The administration of vitamin B6 can thus decrease these symptoms and improve premenstrual acne.<sup>12</sup> Numerous studies on the effectiveness of these compounds on premenstrual syndrome have reported indefinite findings. Therefore, proving the effectiveness of these drugs on treatment of premenstrual syndrome requires further research. Considering the importance of this syndrome in individual and social issues, and the fact that magnesium and vitamin B6 are low-priced, accessible, and safe, this study aimed to determine the effects of these compounds on premenstrual syndrome.

## Materials and methods

This study was a double-blind clinical trial with placebo. To ensure the double-blind design, the drug boxes were coded by the researcher's coworker. The boxes were then

distributed by the researcher. The participants and researchers were thus unaware of the coding until the end of the study and after decoding. The study was confirmed by ethics committee of Isfahan University of Medical Sciences, Isfahan, Iran.

After evaluating the inclusion and exclusion criteria, a questionnaire was completed to assess the symptoms for temporary diagnosis of premenstrual syndrome. Depression and stress were also studied using the Beck depression inventory and the Holmes and Rahe stress scale, respectively. The participants without proved depression and anxiety were provided with menstrual diary forms. They were asked to complete the forms for 2 months. The menstrual diary form is a standardized tool for confirming the existence and determining the severity of premenstrual syndrome symptoms. It can be easily used by patients and interpreted by physicians.<sup>13</sup> This form has been used in different books and articles with a correlation coefficient of 92%.<sup>14</sup> Moreover, Pakgohar *et al.* collaborated with teachers and faculty members of Tehran University of Medical Sciences and confirmed the validity of the questionnaire used in this study using content validity in 2004. They also reported a Pearson's correlation coefficient of  $r = 0.92$  for the reliability of this questionnaire.<sup>15</sup>

The participants in the current study were 15-45 year-old women who referred to selected health centers and suffered from premenstrual syndrome according to the American Psychiatric Association criteria. Women were included if they had a regular menstrual cycle, did not suffer from depression, anxiety, or acute or chronic illnesses, did not use any drugs or supplements, and did not exercise regularly. The exclusion criteria of the current study were pregnancy, using hormonal methods of contraception or any other hormonal drugs, lack of commitment to correct usage of medications and regular completion of the forms, and unwillingness to continue the treatment.

In order to perform sampling, 10 centers

were randomly selected (drawing method) from the health centers affiliated to Isfahan University of Medical Sciences. The number of subjects from each center was determined according to the population covered by the center using quota method. The participants were then randomly selected from patients who referred to the centers and had the inclusion criteria.

This study was conducted in two stages. In the first stage, 150 patients were entered into the study to complete the menstrual diary. Although 138 subjects returned their forms, analyzing the forms revealed 126 women to have premenstrual syndrome. These participants were randomly (according to their order of referring) placed into 3 groups of 42. Patients in the magnesium, vitamin B6, and control groups received one 250 mg magnesium tablet, vitamin B6 tablets, and placebo, respectively. All tablets looked similar and were provided by the Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran. In the second stage, the participants were asked to complete the menstrual diary and use the drugs from the first day of their menstrual cycle to the beginning of the next cycle. Finally, 36 patients from the vitamin B6 group, 38 from the magnesium group, and 37 from the control group cooperated with the researcher until the end of the study.

The severity of symptoms was determined based on the menstrual diary and rating of symptoms. Participants rated the severity of symptoms as 0-3 in their forms. While absence of the symptom was scored as 0, scores of 1 to 3 indicated mild symptoms which did not interfere with daily activities such as education and work, moderate symptoms which affected daily activities to some extent, and severe symptoms which prevented the

patient from daily activities, respectively.

## Results

In the current study, the mean age of participants in the two intervention groups and the control group was 28.71 and 28.03 years, respectively. The three groups were similar in terms of marital status, education level, method of contraception, job, weight, height, number of children, age of menarche, the time between bleedings, and duration of bleeding ( $p > 0.05$ ).

Moreover, no significant differences in the mean scores of premenstrual syndrome symptoms were found between the two intervention groups and the control group before treatment ( $p = 0.76$ ). However, a significant difference was observed between the 3 groups after treatment ( $p < 0.05$ ). Table 1 presents the mean scores of premenstrual syndrome before and after intervention in each group. As it is seen, the mean scores of premenstrual syndrome symptoms were similar in the 3 groups (range: 35-37) before the intervention. One-way analysis of variance (ANOVA) showed no significant difference between the groups in this respect ( $p > 0.05$ ). The table shows that the subjects were randomly allocated into the 3 groups since the mean scores of premenstrual syndrome in all groups are in the same range before the intervention. Paired t-test showed that the mean scores of premenstrual syndrome in all groups decreased significantly after the intervention in comparison to before the intervention ( $p < 0.05$ ). On the other hand, Tukey's test revealed a significant statistical difference between B6 and magnesium groups and magnesium and placebo groups ( $p < 0.05$  for both).

**Table 1.** Scores of premenstrual syndrome before and after the intervention in the three groups

	<b>Magnesium</b>	<b>Vitamin B6</b>	<b>Placebo</b>
Before the intervention	36.89 (7.27)	36.51 (7.06)	35.8 (6.76)
After the intervention	22.22 (4.69)	22.84 (6.76)	28.41 (4.33)
p	< 0.001	< 0.001	< 0.001

Values are expressed as mean (SD)

To simplify the comparisons between groups in terms of effectiveness on reducing each symptom, 30 symptoms of the menstrual diary were divided into 5 subgroups according to the Abraham's classification.<sup>9</sup> The effectiveness of each compound on the symptoms was then evaluated in detail. The subgroups were as follows:

- **Craving:** Craving for sweets, palpitation, feeling weak, decreased energy, increased appetite, and fatigue;

- **Depression:** Depression and seclusion, social inactivity, crying, impatience, the desire to stay at home, anger, forgetfulness, insomnia, and lack of concentration;

- **Anxiety:** Stress, irritability, and anxiety;

- **Water retention:** Pain and breast tenderness, swelling of the legs, and abdominal bloating, pain, and discomfort;

- **Somatic changes:** Feeling cold, nausea, frequent urination, hot flashes, back pain, headaches, acne, oily skin, joint pain, and muscle pain.

The effects of each intervention on the subgroups of syndrome symptoms are summarized in Table 2. According to ANOVA, scores of craving did not decrease significantly after the intervention ( $p = 0.2$ ). However, the differences were significant in other subgroups of syndrome symptoms ( $p < 0.001$  in all cases). Vitamin B6 and magnesium were most effective in the subgroups of depression, water retention, and anxiety. The two interventions were also similar in improving somatic symptoms.

## Discussion

In accordance with previous research, the findings of this study demonstrated the positive effects of magnesium and vitamin B6 on reduction of all premenstrual syndrome symptoms. Facchinetti *et al.* found that compared to placebo, a two-month intervention with magnesium significantly reduced the mean total score of premenstrual syndrome ( $p < 0.04$ ). Magnesium particularly caused significant reductions in the severity of symptoms of water retention ( $p < 0.03$ ) and pain ( $p < 0.04$ ).<sup>16</sup> The higher effectiveness of magnesium on a greater number of symptoms of the syndrome in our study in comparison to the study by Facchinetti *et al.* may be due to the pattern of magnesium usage in the current study. We prescribed a 250 mg magnesium oxide tablet from the first day of menstrual cycle until the beginning of the next cycle while Facchinetti *et al.* used a 360 mg magnesium tablet in the form of pyrrolidone carboxylic acid from day 15 of the cycle to the beginning of the next cycle.<sup>16</sup> On the other hand, the available literature suggests the daily requirement of magnesium in an adult to be 320 mg. In addition, the kidneys of a healthy person excrete excess magnesium into the urine to avoid magnesium poisoning.<sup>17</sup> Therefore, prescribing a higher dosage in a shorter period of time does not reduce the symptoms since the excess magnesium is excreted. In the study by Quaranta *et al.* on the efficacy and safety of a slow-release magnesium 250 mg tablet (Sincromag) for the treatment of premenstrual syndrome on 41 patients, magnesium showed the highest efficacy on

**Table 2.** Comparison of changes in mean premenstrual syndrome scores before and after the intervention in each group

	Magnesium	Vitamin B6	Placebo	f	p
<b>Craving</b>	-23.04 (19.49)	-19.37 (16.62)	-14.09 (18.97)	1.56	0.20
<b>Depression</b>	-17.3 (18.26)	-23.43 (17.26)	-13.33 (18.38)	6.4	< 0.001
<b>Water retention</b>	-15.39 (16.39)	-11.28 (15.74)	-5.2 (17.30)	6.81	< 0.001
<b>Anxiety</b>	-12.14 (26.14)	-11.19 (19)	0.000 (20.41)	6.34	< 0.001
<b>Somatic changes</b>	-12.73 (16.87)	-12.8 (19.52)	-2.5 (16.97)	4.55	0.005

Values are expressed as mean (SD)

The mean changes are negative due to the reduction of syndrome symptoms after the intervention in comparison to before the intervention

reducing depression, craving, and anxiety. The effectiveness of magnesium was also higher than placebo in improving other symptoms.<sup>14</sup> Walker et al. reported magnesium to cause a significant decrease in the severity of symptoms related to water retention after 2 months of prescription ( $p = 0.009$ ).<sup>18</sup> Although, magnesium improved all symptoms of premenstrual syndrome in this study, this improvement was not significant. The difference between the findings of Walker et al. and the current study might have been due to the younger age of their participants (15-25 vs. 28-30 years). In fact, younger age could have been associated with consuming more chocolate, sweets, and caffeine and thus more severe symptoms which reduced the effects of the drugs.

Sharma et al. evaluated the efficiency of vitamin B6 on 60 patients suffering from premenstrual syndrome in India. They found the mean score of premenstrual syndrome to decrease from 30.15 to 14.7 (16 points) in the second month of using 100 mg vitamin B6 daily.<sup>17</sup> We however, could not establish such a reduction which might have been caused by the higher severity of the syndrome in our participants (36.51, i.e. in the moderate intensity range of premenstrual syndrome) compared to the subjects in the study by Sharma et al. (30.15, i.e. in the mild intensity range of premenstrual syndrome). Reviewing scientific literature on vitamin B6 shows that its effectiveness does not depend on its dosage.

Table 2 would be helpful in comparing the efficacy of vitamin B6 and other compounds on each symptom of premenstrual syndrome. The table shows that vitamin B6 most efficiently reduced depression-related symptoms of premenstrual syndrome. Maroofi et al. assessed the effectiveness of vitamin B6 on premenstrual syndrome in 94 patients in Isfahan. They found that using 40 mg vitamin B6, in comparison to placebo, will cause a significant reduction in the mood symptoms of premenstrual syndrome ( $p = 0.001$ ). They thus suggested vitamin B6 as an effective drug in reducing mood

symptoms of premenstrual syndrome.<sup>19</sup> In a study on 93 patients with premenstrual syndrome, Dolatian et al. reported that compared to placebo and vitamin E, the daily usage of 40 mg of vitamin B6 would significantly improve somatic changes of premenstrual syndrome, such as pain, abdominal discomfort, back pain, oily skin, muscle pain, and breast pain and tenderness after 2 months ( $p < 0.03$ ).<sup>20</sup> These symptoms fall in the subgroup of water retention of physical symptoms in the current study. On the contrary, vitamin B6 was less effective than vitamin E in reducing mood symptoms of premenstrual syndrome.<sup>20</sup> In a study by Salehi and Salehi on 92 patients, a daily dosage of 200 mg of vitamin B6 significantly decreased depression, anxiety, drowsiness, and breast tenderness in comparison to placebo ( $p < 0.05$ ).<sup>21</sup>

As Table 2 shows, vitamin B6 was more effective than magnesium on symptoms related to depression. However, symptoms of craving, water retention, and anxiety were better controlled by magnesium. Desouza et al. suggested vitamin B6 to be more efficient than magnesium in relieving symptoms related to depression (107% vs. 88%) which is in accordance with the current study. However, in contrast to the present study, they found vitamin B6 to be more effective than magnesium in relieving other symptoms as well.<sup>22</sup> This difference may have resulted from the longer duration of the intervention in the current study since magnesium oxide needs at least 2 months to show its therapeutic properties on premenstrual syndrome. The reason might be the low bioavailability of magnesium oxide which necessitates a longer time for the compound to fill the body's resources and cause therapeutic properties. Walker et al. prescribed 2 months of 200 mg magnesium oxide supplementation for 38 women suffering from premenstrual syndrome. They found that 1 month of supplementation with magnesium oxide had no significant effects on the symptoms of the syndrome. However,

continuing supplementation until the second month significantly affected the symptoms.<sup>18</sup> On the other hand, the difference between the findings of the current study and the study by Desouza *et al.* may be due to higher dosage of magnesium in the current study which increased the bioavailability of magnesium oxide.<sup>22</sup>

Finally, we should review the effect of placebo on premenstrual syndrome. Many studies on this syndrome have found placebo to have significant effects on treatment of this syndrome.<sup>23</sup> The response rate to placebo has been normally reported as 30-40%. It appears that receiving attention could positively affect the mental status of the participants and thus the treatment of premenstrual syndrome.<sup>24</sup> In the study by Desouza *et al.* placebo caused a significant decrease in all symptoms of premenstrual syndrome. This reduction ranged from 16% in symptoms relating to depression to 31% in symptoms relating to water retention.<sup>22</sup>

Overall, compared to chemical medications, magnesium is a beneficial, low cost, and effective treatment for the symptoms of premenstrual syndrome. Therefore, considering the cyclical and chronic nature of premenstrual syndrome, prescription of magnesium seems reasonable.

## Conclusion

Considering the importance of premenstrual syndrome and the numerous effects it has on society and the lives of women, health groups should prioritize the diagnosis and treatment of this syndrome. Since there is no definitive etiology and treatment for this syndrome, many researchers have tried to find the best and most effective drug with the least side effects to prevent the occurrence of the syndrome. Each researcher has thus proposed suggestions for the enhancement of future studies. The current study was also undertaken with the goal of finding an effective compound with no side effects to reduce the symptoms of this syndrome and its direct and indirect economic and social effects. All compounds used in the current

study had no side effects, were effective, non-chemical, and acceptable by most groups of women in the society. Hence, health groups, especially midwives, can compare the effectiveness the compound on their specific patients and select the most appropriate treatment for each individual. Moreover, in cases where the patient is prohibited from using chemical drugs to treat premenstrual syndrome, such as oral contraceptive pills and gonadotropin releasing hormone (GnRH) agonists, the use of these compounds seems effective. However, the prescription of high dosages of every drug should be done with caution.

## Ethical issues

None to be declared.

## Conflict of interest

The authors declare no conflict of interest in this study.

## Acknowledgments

The authors would like to express their appreciation to the Research Deputy of Isfahan University of Medical Sciences who financially supported this study.

## References

1. Shin KR, Ha JY, Park HJ, Heitkemper M. The effect of hand acupuncture therapy and hand moxibustion therapy on premenstrual syndrome among Korean women. *West J Nurs Res* 2009; 31(2): 171-86.
2. Khajehei M, Abdali K, Parsanezhad ME, Tabatabaee HR. Effect of treatment with dydrogesterone or calcium plus vitamin D on the severity of premenstrual syndrome. *Int J Gynaecol Obstet* 2009; 105(2): 158-61.
3. Bakhshani NM, Mousavi MN, Khodabandeh G. Prevalence and severity of premenstrual symptoms among Iranian female university students. *J Pak Med Assoc* 2009; 59(4): 205-8.
4. Tamjidi A. Study of Prevalence and Severity of Premenstrual Syndrome Symptoms in 15-45 Year Old Women in Tehran, Iran [MSc Thesis]. Tehran: School of Nursing and Midwifery, Iran University of Medical Sciences; 1995. p. 12, 18, 19, 95.

5. Soltan Ahmadi ZH. Study of Prevalence and Severity of Premenstrual Syndrome in Students in their last Year of High School Students of Kerman, Iran. *Iran Journal of Nursing* 1998; 12(18-19): 95. (Persian).
6. Sheikh Al Eslami SH. A Study of Prevalence of Premenstrual Syndrome in the Two Centers of Shahid Esmaili and Navab Safavi [MSc Thesis]. Tehran: School of Nursing and Midwifery, Iran University of Medical Sciences; 1993.p. 23, 34, 90. (Persian).
7. Gharekhani P, Sadatian SA. Cardinal Manifestations & Management of Diseases (CMMD). 2<sup>nd</sup> ed. Tehran: Noure Danesh Publication; 2005. 125-45 p. (Persian).
8. Jurgens T, Whelan AM. Advising patients on the use of natural health products to treat premenstrual syndrome. *Canadian Pharmacists Journal* 2009; 142(5): 228-33.
9. Abraham G. Premenstrual tension syndrome. *J Reprod Med* 1956; 21(4): 123-27.
10. Salamat S, Ismail KM, Brien OS. Premenstrual syndrome. *Obstetrics, Gynaecology & Reproductive Medicine* 2008; 18(2): 29-32.
11. Abraham GE, Rumley RE. Role of nutrition in managing the premenstrual tension syndromes. *J Reprod Med* 1987; 32(6): 405-22.
12. Freeman EW, Osborn TH, Maclean AB. Premenstrual syndrome new treatments that early work. *Contemporary ob/gyn* 1996; 21(25): 25-45.
13. Shils ME, Shike M. *Modern Nutrition in Health and Disease*. 10<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2006. 567-678 p.
14. Quaranta S, Buscaglia MA, Meroni MG, Colombo E, Cella S. Pilot study of the efficacy and safety of a modified-release magnesium 250 mg tablet (Sincromag) for the treatment of premenstrual syndrome. *Clin Drug Investig* 2007; 27(1): 51-8.
15. Pakgohar M, Mehran A, Salehi Sormaghi M, Akhondzadeh SH, Ahmadi M. Effect of Hypericum Flowers in Treatment of Premenstrual Syndrome in Students Living in Dormitories of Tehran University of Medical Sciences and Tehran University [MSc Thesis]. Tehran: School of Nursing and Midwifery, Tehran University of Medical Sciences; 2003. (Persian).
16. Facchinetti F, Borella P, Sances G, Fioroni L, Nappi RE, Genazzani AR. Oral magnesium successfully relieves premenstrual mood changes. *Obstet Gynecol* 1991; 78(2):177-81.
17. Sharma P, Kulshreshtha S, Singh GM, Bhagoliwal A. Role of bromocriptine and pyridoxine in premenstrual tension syndrome. *Indian J Physiol Pharmacol* 2007; 51(4): 368-74.
18. Walker AF, De Souza MC, Vickers MF, Abeyasekera S, Collins ML, Trinca LA. Magnesium supplementation alleviates premenstrual symptoms of fluid retention. *J Womens Health* 1998; 7(9): 1157-65.
19. Maroofi M, Rezaie Z, Maroofi M. Efficacy of Vitamin B6 in Premenstrual Syndrome. *Journal of Nursing and Midwifery, Kerman* 2003; 3(1): 1-5. (Persian).
20. Dolatian M, Montazeri SH, Velaei N, Ahmadi M. Comparative effects of vitamin B6 and vitamin E on symptoms of premenstrual syndrome. *J Zanjan Univ Med Sci* 2002; 37: 5-10. (Persian).
21. Salehi L, Salehi F. Comparative study of vitamin B6 versus placebo in premenstrual syndrome. *Sci J Kurdistan Univ Med Sci* 2007; 12(3) :42-9. (Persian).
22. De Souza MC, Walker AF, Robinson PA, Bolland K. A synergistic effect of a daily supplement for 1 month of 200 mg magnesium plus 50 mg vitamin B6 for the relief of anxiety-related premenstrual symptoms: a randomized, double-blind, crossover study. *J Womens Health Gend Based Med* 2000; 9(2): 131-9.
23. London RS, Bradley L, Chiamori NY. Effect of a nutritional supplement on premenstrual symptomatology in women with premenstrual syndrome: a double-blind longitudinal study. *J Am Coll Nutr* 1991; 10(5): 494-9.
24. Sharma P, Kulshreshtha S, Singh GM, Bhagoliwal A. Role of bromocriptine and pyridoxine in premenstrual tension syndrome. *Indian J Physiol Pharmacol* 2007; 51(4): 368-74.