ISSN: 0974-2115
www.jchps.com Journal of Chemical and Pharmaceutical Science

Effects of vitamin B6 on premenstrual syndrome: A systematic review and meta-analysis

samieipoor Soheila[1], Kiani Faezeh[2], Sayehmiri Kourosh[3*], Sayehmiri Fatemeh [4], Naghdi Nasrollah[5], Ghafari Mahin [6], Majid Asadi-Samani[7], Mahmoud Bahmani[8]

[1]Faculty of Alleid Medical Sciences Ilam university of medical sciences, Ilam, Iran.
[2]Student Research Committee, Ilam University of Medical Science, Ilam, Iran.
[3] Faculty of Alleid Medical Sciences Ilam university of medical sciences, Ilam, Iran.
[4]Student Research Committee, Ilam University of Medical Science, Ilam, Iran.
[5]Clinical Microbiology Reaserch Center Ilam University of Medical Sciences, Ilam, Iran
[6] Department of Public Health, School of Health, Shahrekord University of Medical Sciences, Shahrekord, Iran
[7]Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran
[8] Razi Herbal Medicines Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran

***Corresponding author: E.Mail:sayehmiri@razi.tums.ac.ir**

ABSTRACT

Background and Objective: Premenstrual syndrome (PMS) refers to a range of physical and psychological symptoms which regularly occur during the luteal phase of a menstrual cycle and disappear short after menstruation starts. Considering the negative effects of PMS on women's daily life, various treatments have been developed to alleviate its symptoms. Vitamin B6 is one of the complementary therapies used to treat PMS. The present meta-analysis aimed to investigate the effects of vitamin B6 on PMS.

Methodology: Different databases including PubMed, ISI, Scopus, SID, Magiran, Science Direct, and Medlib were searched to identify studies addressing the effects of vitamin B6 on PMS. The relevant data obtained from these papers were analyzed by a random-effects model. Data were analyzed using R Ver. 3.2.3 Software and STATA.

Results: There were significant reductions in the mean scores of PMS after treatment with vitamin B6 compare to control groups. Moreover, the mean PMS scores of the two groups were also significantly different after the treatment. The mean difference between the two groups was -1.19 [95% CI: -1.94,-0.44; P = 0.002]. Significant reductions were also observed in physical symptoms (P = 0.006) and psychological symptoms (P < 0.001) of PMS after the intervention.

Conclusion: The results of our meta-analysis confirmed vitamin B6 as a beneficial, inexpensive, and effective treatment for PMS symptoms. Therefore, the administration of this treatment option will enable midwives to achieve the important goal of reducing PMS symptoms.

KEY WORDS: premenstrual syndrome, physical symptoms, psychological symptoms, vitamin B6, female

INTRODUCTION

Premenstrual syndrome (PMS) refers to a range of physical and psychological (emotional and behavioral) symptoms which can negatively affect the daily lives of women of the reproductive age during the luteal phase of their menstrual cycle. The symptoms of PMS may vary in different women but generally include depression, stress, mood swings, crying spells, irritability, anger, confusion, sleep disorders, clumsiness, social withdrawal, fatigue, abdominal cramping, breast tenderness, headache, stomachache, back pain, food cravings, bloating, and changes in libido. Such symptoms may occur in 10%-98% of women. In addition to the assessment tool used, the ethnicity, socioeconomic status, education level, lifestyle, and menstrual cycle characteristics of the studied population, as well as the use of hormonal contraceptives by the evaluated women, may affect the incidence of PMS. The high prevalence of PMS and its negative effects on women's daily activities highlight the need for effective treatment. Therefore, a variety of treatment options, including antidepressants, anxiolytics, hormonal agents, serotonin reuptake inhibitors (SSRIs) such as fluoxetine, nutritional supplements (e.g. calcium, magnesium, and vitamins), and herbal medicines, have been suggested to reduce the symptoms of PMS.

Pyridoxine (vitamin B6) is also commonly used in thetreatment of PMS. Although this vitamin was initially believed to treat PMS by correcting impaired estrogen metabolism, its role in regulating brain monoamine production has been recently discussed. As an immediate precursor of serotonin and dopamine, vitamin B6 can alleviate PMS symptoms through its role in the production of prostaglandin and fatty acids. Moreover, vitamin B6 deficiency will reduce dopamine levels in kidneys. The consequent increment in sodium excretion will result in water retention and cause various symptoms such as swelling in extremities, edema, and abdominal and chest discomfort. Since a meta-analysis is warranted to clarify the role of vitamin B6 in the treatment of PMS, the present study provided a systematic review and meta-analysis of the effectiveness of vitamin B6 in reducing PMS symptoms.

Methods

Search method: National and international databases, including Iranmedex, SID, Magiran, Irandoc, and Medlib in Persian and PubMed/Medline, Scopus, and ISI Web of Knowledge in English, were systematically searched using a number of keywords. The selected keywords were premenstrual syndrome, physical symptoms, psychological

symptoms, treatments, pyridoxine (vitamin B6), and their equivalents in Persian. All papers with the selected keywords in their titles or abstracts were included in the initial list and other unrelated articles were eliminated. We also searched bibliographies of retrieved articles for additional references. In addition, the references from selected articles were examined as a further search tool. Relevant trials noted in the reference lists of each selected article were also evaluated for inclusion.

Inclusion and exclusion criteria: All original articles presenting case-control studies on the effects of vitamin B6 on the severity of PMS symptoms were considered. When necessary, authors were contacted for additional information. Meta-analyses and systematic reviews were not included. Studies were excluded if they were in languages other than English or Persian, provided insufficient data, used a design other than the case-control design, and were a duplicate publication of another study.

Data extraction: For all studies, the following data were extracted: first author, year of publication, location, sample size, sample age, and PMS scores, as well as physical and psychological symptoms, before and after the intervention in the vitamin b6 and placebo groups. Two of the authors independently reviewed the abstracts and full articles and resolved the cases of disagreement in a joint meeting. The data were entered into data collection forms and entered into Microsoft Excel.

Data synthesis and analysis: Studies were combined based on the sample size, mean, and standard deviation. The difference between the PMS score in case and control groups divided to standard erroe of two groups was difened as standard mean difference(SMD). The Cochran's Q, meta-regression and I^2 were used as measures of heterogeneity of the studies. Considering the significant heterogeneity of the studies, the random effects model was applied. The additive method was used to poolded P-values of physical and psychological symptoms in that respect.

Funnel plots and Egger test were used to examine publication bias. P-values less than 0.05 were considered as significant in heterogeneity tests. Sensitivity analyses were pre-specified. Statistical analyses were performed using R Software (version 3.2.1) and STATA (version 10).

Results

A total of 45 potentially suitable articles were identified during the initial search. In a secondary screening, six papers were excluded based on title and abstract evaluation and four others were excluded since they were duplicates of other research. Therefore, 35 articles were retained for detailed full-text evaluation. After full-text evaluation, we excluded another 23 articles (Of these, six were excluded because they did not include a placebo group, five were retrospective and review studies, twelve presented qualitative and defective quantitative data that could not be analyzed); all of these papers were withdrawn (Figure 1). Finally, 12 relevant papers were identified. The characteristics of the 12 studies included in this meta-analysis are summarized in Table 1.

Considering all the included studies, the total number of people in the intervention (vitamin B6) and placebo groups was 586 and 602, respectively. The mean age of the intervention and placebo groups was 27.77 ± 2.3 and 27.21 ± 2.1 years, respectively and there was no significance differences between the two groups in this respect. The mean difference in age was 0.14 [95% CI: - 0.04,0.33; P =0.119 (Table 1).

Table 2 presents the mean scores of PMS before and after the intervention in each group. As seen, the intervention and control groups had no significant differences in the mean scores of PMS symptoms before treatment. The SMD in the scores of the two groups was -0.13 [95% CI: -0.34,0.09; P = 0.254] (Figure 2). However, there was a significant difference in the SMD of PMS before and after treatment in each group. The SMD was -0.85 [95% CI: -1.48,-0.23; P = 0.008] in the control group and -1.76 [95% CI: -2.48,-1.04; P < 0.001] in intervention group. Moreover, a significant difference in PMS scores was observed between the intervention and control groups after the treatment. The SMD was -1.19 [95% CI: -1.94,-0.44; P = 0.002] (Figure 3).

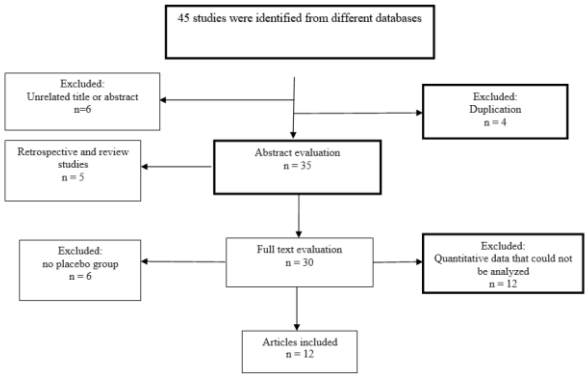

Figure.1.The flowchart of article selection for final analysis

Table.1.The characteristics of the selected studies

N-Vitamin B6	N-Placebo	Mean age		SMD(95% CI)		SMD	Dose
		Vitamin B6	Placebo	Lower	Upper		
42	42	28.71 ± 5.37	28.03 ± 5.02	-0.30	0.56	0.13	250 mg daily over 2 menstrual cycles
20	20	28.01 ±5.08	28 ± 5.17	-0.62	0.62	0.00	100 mg daily over 3 menstrual cycles
16	16	-	-	-	-	-	50 mg daily over 3 menstrual cycles
29	26	28.1 ± 6.5	27.7 ± 6.6	-0.47	0.59	0.06	150 mg daily over 2 menstrual cycles
46	48	-	-	-	-	-	80 mg daily over 2 menstrual cycles
30	30	-	-	-	-	-	300 mg daily over 3 menstrual cycles
31	31	21.1 ± 0.6	20.7 ± 0.5	0.21	1.24	0.72	40 mg daily over 2 menstrual cycles
204	230	33.4 ± 7.9	33.3 ± 7.4	-0.18	0.20	0.01	100 mg daily over 3 menstrual cycles
31	31	23.19 ± 2.1	22.4 ± 1.9	-0.11	0.90	0.39	40 mg daily over 3 menstrual cycles
40	40	32 ± 6.5	32 ± 6.1	-0.44	0.44	0.00	50 mg daily over 1 menstrual cycles
52	40	24.5 ± 2.3	23 ± 2.1	0.25	1.10	0.68	200 mg daily over 2 menstrual cycles
46	48	31.4 ± 6.2	30.2 ± 5.5	-0.20	0.61	0.21	80 mg daily over3 menstrual cycles
SMD: standard mean difference, CI: confidence interval							

Table.2.Scores of premenstrual syndrome before and after the intervention in vitamin B6 and placebo groups

Scores of PMS Before the intervention		SMD (95% CI)		SMD	Scores of PMS after the intervention		SMD (95% CI)		SMD
Vitamin B6	Placebo	Lower	upper		Vitamin B6	Placebo	Lower	Upper	
36.51 ± 7.06	35.80 ± 6.76	-0.33	0.53	-0.10	22.84 ± 6.76	28.41 ± 4.33	-1.43	-0.53	-0.98
30.15 ± 10.71	31.35 ± 7.67	-0.75	0.49	-0.13	10.1 ± 4.79	29.2 ± 10.31	-3.19	-1.56	-2.38
-	-	-	-	-	10.39 ± 1.91	17.74 ± 1.89	-2.79	-1.09	-1.94
18.74 ± 4.90	21.35 ± 6.85	-0.89	0.09	-0.44	16.67 ± 4.37	17.79 ± 5.13	-0.77	0.30	-0.24
40 ± 8.10	40.3 ± 7.91	-0.54	0.47	-0.04	21.90 ± 12.60	21.6 ± 11	-0.48	0.53	0.03
41.23 ± 9.03	43.18 ± 10.05	-0.61	0.20	-0.20	21.25 ± 8.15	40.63 ± 12.18	-2.35	-1.38	-1.86
SMD: standard mean difference, CI: confidence interval									

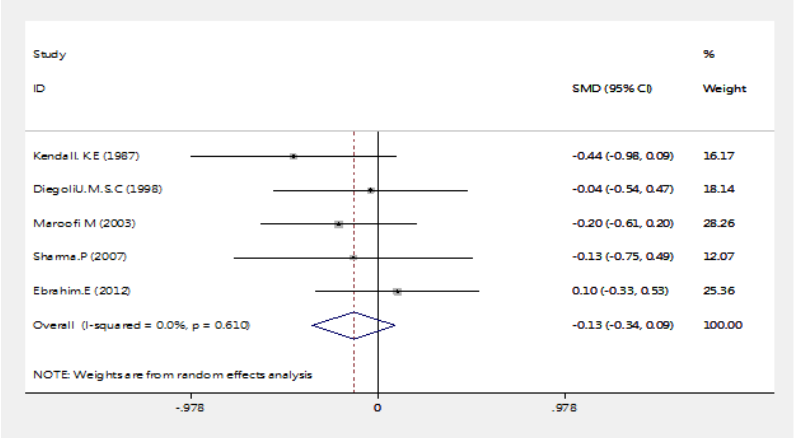

Figure.2.The results of meta-analysis of mean premenstrual syndrome scores before the intervention in vitamin B6 and placebo groups. The squares represent the effect estimates and their 95% confidence intervals indicated by individual studies. Square sizes are proportional to the weight assigned to the study in the meta-analysis. Diamond shows poold results of studies. In this chart, studies are displayed in the order of the year of publication and authors' names based on a random effects model

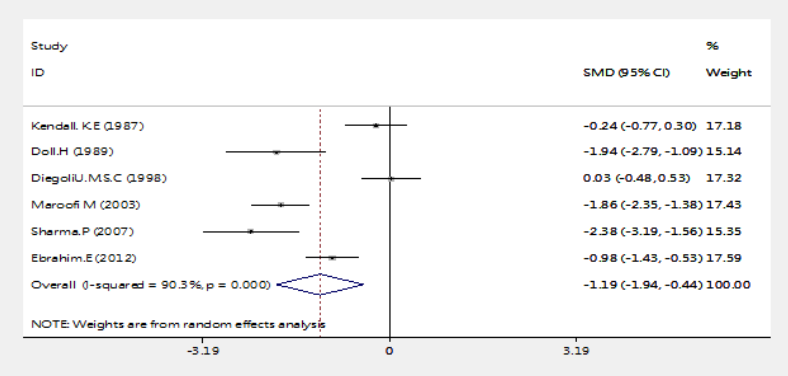

Figure.3.The results of meta-analysis of mean premenstrual syndrome scores after the intervention in vitamin B6 and placebo groups. The squares represent the effect estimates and their 95% confidence intervals indicated by individual studies. Square sizes are proportional to the weight assigned to the study in the meta-analysis. Diamond shows poold results of studies .In this chart, studies are displayed in the order of the year of publication and authors' names based on a random effects model

Tables 3 and 4 show the mean scores of physical and psychological symptoms of PMS before and after the intervention in each group. As seen, vitamin B6 and placebo groups had a significant difference in physical symptoms of PMS after the intervention (P = 0.006; Figure 4). A similar significant difference was also observed between the two groups in terms of psychological symptoms of PMS after the intervention (P < 0.001; Figure 5).

The results of meta-analysis of physical symptoms of premenstrual syndrome after the intervention in vitamin B6 and placebo groups accoding to combine p-vale of 11 studies using edgington additive models show that, there was significance difference between two groups(P=.0069).

Table.3.Physical symptoms of premenopausal syndrome before and after the intervention in vitamin B6 and placebo groups

Physical symptoms	Scores of physical symptoms		SMD (95% CI)		SMD	P value
	Vitamin B6	Placebo	Lower	Upper		
Mean changes before and after the intervention	-12.8± 19.25	-2.5± 16.97	-01.00	-0.13	-0.56	0.011
	-0.54± 0.63	-0.33± 0.7	-0.72	0.09	-0.31	0.129
Mean scores after the intervention	8.69± 1.24	8.97± 1.08	-0.94	0.45	-0.24	0.497
	2.7± 0.74	2.97± 0.95	-0.85	0.21	-0.32	0.24
	6.16± 1.71	7.35± 1.6	-1.23	-0.20	-0.72	0.006
	18.7± 5.9	19.3± 6.3	-0.54	0.34	-0.10	0.6
	98.91±26.14	96.18±19.7	-0.29	0.52	0.12	0.567
Number of cases after the intervention	14/30	13/30	0.62	1.98	1.08	0.795
	14/31	6/31	1.03	5.28	2.33	0.042
	105/204	105/230	0.93	1.37	1.13	0.226
	12/52	20/40	0.26	0.83	0.46	0.010

Table.4.Psychological symptoms of premenstrual syndrome before and after the intervention in vitamin B6 and placebo groups

Psychological symptoms	Scores of psychological symptoms		SMD (95% CI)		SMD	P value
	Vitamin B6	Placebo	Lower	Upper		
Mean changes before and after the intervention	-16.32± 17.2	-8.2±18.8	-0.94	-0.07	-0.50	0.023
	-1.26± 1.91	-0.6± 1.78	-0.77	0.05	-0.36	0.085
Mean scores after the intervention	3.96± 0.9	7.06± 1.29	-3.78	-1.80	-2.79	0.000
	2.1±0.47	2.45±0.8	-1.08	-0.00	-0.54	0.049
	11.97± 2.33	10.47± 1.67	0.22	1.26	0.74	0.005
	21.2± 6.7	17.6± 5.1	0.16	1.05	0.60	0.008
	12.16±24.96	136.8±21.14	-6.28	-4.52	-5.40	0.000
Number of cases after the intervention	14/30	14/30	0.58	1.72	1.00	1.00
	21/31	10/31	1.19	3.69	2.10	0.010
	115/204	119/230	0.92	1.30	1.09	0.333
	7/52	13/40	0.18	0.94	0.41	0.035

The results of meta-analysis of psychological symptoms of premenstrual syndrome after the intervention in vitamin B6 and placebo groups, accoding to pooled p-vale of 11 studies using edgington normal models show that, there was significance difference between two groups(P=.000)

Figure 4 presents the funnel plot of the included trials. Regression analysis of this plot indicated no significant asymmetry(P=.389) and thus no evidence of bias. In fact, most studies were located inside the funnel plot, i.e. the results of most relevant studies performed were included in the analysis (Figure 6).

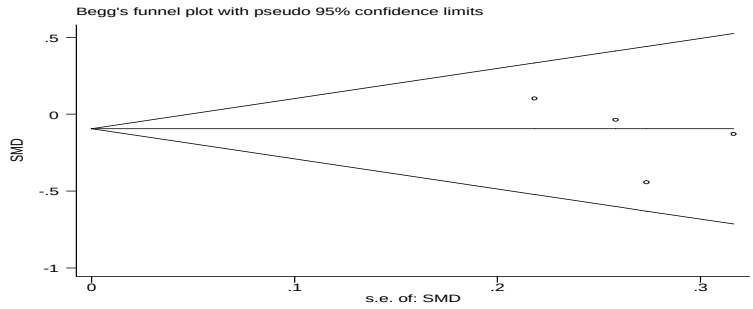

Figure.4.Funnel plot for publication bias in the risk difference (RD) analysis

Discussion

Pyridoxine, or vitamin B6, is one of the most widely used and probably the most controversial treatment for PMS. In a survey of 658 women with PMS, Corney and Stanton found that vitamin B6 was the most common treatment for PMS. According to the National Association for Premenstrual Syndrome in UK, 68% of general practitioners prescribed vitamin B6 for premenstrual symptoms. In a review study, Wyatt et al. confirmed vitamin B6 as the first choice over-the-counter treatment for many women with PMS. The UK Department of Health then offered some plans to restrict the dosage available because of potential neurotoxic effects at very high doses. As a result, vitamin B6 prescriptions dropped markedly from 22% in 1993 to 11% in 1997 and 1998. Wyatt et al. concluded that the most effective management method for PMS symptoms cannot be identified unless evidence for all possible treatments are assessed by critical appraisal and meta-analysis. Therefore, we conducted a systematic review and meta-analysis to evaluate the effects of vitamin B6 on PMS symptoms. We selected studies which had compared the mean changes in PMS scores following the use of vitamin B6 and placebo. The obtained statistical results suggested the significant positive effect of vitamin B6 on reducing PMS symptoms. In a review study in 2002, The low quality of studies included in the meta-analysis and enormous inhomogeneity in their results might have been responsible for the inconsistency between our findings and the results of the mentioned studies. Furthermore, the difference in selection criteria of studies, analysis methods, and results could also justify the observed discrepancies.

Our findings highlighted the positive effects of vitamin B6 on reducing the psychological symptoms of PMS. Likewise, a meta-analysis conducted by Wyatt et al. demonstrated the beneficial effects of vitamin B6 in the treatment of depression. Similarly, Salehi et al. indicated the efficacy of daily consumption of pyridoxine (200 mg) in controlling the psychological symptoms of PMS, e.g. depression, anxiety, unrest, and sleepiness. Another study documented reductions in frustration, anger, mental pressure, social avoidance, increased appetite, and tachycardia following the daily consumption of vitamin B6 (40 mg). Maroufi et al. also confirmed the significant effects of vitamin B6 on alleviating the temperamental and behavioral symptoms of PMS. Ebrahimi et al. suggested vitamin B6 to effectively treat the psychological symptoms associated with depression and anxiety. Other studies have also reported similar results. Therefore, previous studies and the current meta-analysis support this the positive effects of pyridoxine, even in small doses, on reducing the psychological symptoms of PMS.

Pyridoxine is a cofactor in the synthesis of neurotransmitters and an immediate precursor of serotonin and dopamine. It is also involved in gamma-aminobutyric acid (GABA) synthesis and enzymatic steps of tryptophan and tyrosine metabolism. Its deficiency may, hence, lead to reduced concentrations of noradrenaline and serotonin. Vitamin B6 is claimed to be associated with psychological symptoms of PMS. Low levels of vitamin B6 increase prolactin levels and results in more psychological symptoms during the premenstrual period. These symptoms may also be a consequence of a reduction in the metabolism of tryptophan to 5-hydroxytryptamine (5HT). On the other hand, imbalances in the levels of steroid hormones may cause a relative pyridoxine deficiency. The mentioned mechanisms can justify the findings of previous research and the present study regarding the role of vitamin B6 in alleviating the psychological symptoms of PMS.

The results of the present study showed that daily consumption of vitamin B6 was significantly more effective than placebo in improving the physical signs and symptoms of PMS. Dolatian et al. compared a daily dose of 40 mg of vitamin B6 with placebo and reported vitamin B6 to significantly reduce the physical symptoms of PMS, e.g. abdominal pain, backache, muscular pain, chest pain, and allergy. Likewise, Salehi et al. highlighted the beneficial effects of daily intake of pyridoxine (200 mg) on reducing breast sensitivity (a somatic sign of PMS).

Some other case-control studies have also confirmed considerable reductions in physical symptoms of PMS following the consumption of vitamin B6. In contrast, a number of studies have rejected the role of vitamin B6 in improving physical symptoms of PMS.

Researchers believe that vitamin B6 deficiency decreases dopamine in the kidneys. The consequent increase in sodium excretion will in turn cause water retention and lead to the physical symptoms of PMS such as swelling in extremities, edema, and abdominal and chest discomfort. Therefore, vitamin B6 consumption should be able to alleviate the physical and psychological symptoms of PMS. Studies have also suggested reductions in red blood cell counts to cause PMS through decreasing brain dopamine and increasing aldosterone. As mentioned earlier, these problems can be treated by using pyridoxine. Considering the role of pyridoxine in water metabolism, regulation of adrenal hormones, and synthesis of some amino acids, as cofactors, consuming vitamin B6 during the whole menstrual cycle can reduce the general symptoms of PMS.

Another finding of the present study was the effect of placebo on reducing PMS symptoms. Although this reduction was significantly lower compared to the intervention group, placebo could exert some positive effects. Similarly, many studies on PMS have observed reductions in PMS symptoms in control groups (with or without the use of placebo). Apparently, receiving attention could positively affect the mental status of the participants and facilitate the treatment of PMS .

Previous research on the dosage of vitamin B6 has reported contradictory results. While some studies have emphasized the need for high doses of vitamin B6 over a long period of time (during the whole menstrual cycle), some others did not detect any significant effects on PMS symptoms even with high doses of vitamin B6. Low doses of vitamin B6 have also been reported ineffective by some studies. In a study on Iranian women, Ebrahimi et al. showed that consuming 250 mg of vitamin B6 per day for two months significantly reduced the general symptoms of PMS as compared to placebo. In India, Sharma et al. compared vitamin B6 and placebo and concluded that daily consumption of 100 mg of vitamin B6 for three months significantly improved PMS symptoms. In the US, Doll et al. highlighted the beneficial effects of daily consumption of vitamin B6 (100 mg) for three months. A meta-analysis by Wyatt et al. confirmed the mentioned positive effects. However, based on the analysis of previous studies in the current meta-analysis, the efficiency of vitamin B6 does not depend on its dosage. No evidence has been reported about the toxicity or side effects of vitamin B6. This might have been due to the low dosage of vitamin B6 in most studies evaluated by the present meta-analysis.

Our meta-analysis had several limitations. First, insufficient information about vitamin B6 toxicity and side effects prevented us from the evaluation of such cases. Moreover, some included studies did not enjoy acceptable quality or presented defective quantitative data that could not be included in meta-analysis. Furthermore, since the selected studies were quite heterogeneous in terms of their inclusion and exclusion criteria, the dose and duration of treatment, and the outcome measures examined, the interpretation of the findings was difficult. Finally, some studies associated with PMS were not accessible.

CONCLUSION

Considering the importance of PMS and the numerous effects it has on women's lives (and thus the society), the diagnosis and treatment of this syndrome should be prioritized. Optimal management of PMS requires a systematic approach to find the most effective drug with the least side effects to prevent the occurrence of the syndrome. The results of our meta-analysis revealed that using vitamin B6 could reduce the overall symptoms of PMS. No conclusive evidence of vitamin B6 toxicity was reported and there seems to be no dose-related response to treatment. In conclusion, vitamin B6 is a beneficial, inexpensive, and effective treatment for the symptoms of PMS. Although women with PMS can be encouraged to take pyridoxine, further studies are warranted to confirm vitamin B6 as a safe and effective treatment for PMS.

Acknowledgements

The authors are grateful to the Student Research Committee, Ilam University of Medical Sciences for their support.

REFERENCES

Abdollahi FS, Dolatian M, Heshmat R, Alavimajd H. The effect of foot reflexology on premenstrual syndrome. Archives Des Sciences Journal. 2013; 65: 140-149. (Persian).

Abraham GE, Rumley RE. Role of nutrition in managing the premenstrual tension syndromes. J Reprod Med. 1987; 32(6): 405-22.

Abraham GE. Schwartz UB, Lubran MM . Effect of vitamin B6 on plasma and red blood cell magnesium levels in premenopausal women. Ann Cling Lab Sci 1981; 11: 333-336.

Allais G, Acuto G, Benedetto C, Andrea G, grazzi L, Manzoni Gc, et al. Evolution of migarine - association symptoms in menstrually related migrine following symptomatic treatment with almotriptan. Neurol Sci. 2010; 31: 115-119.

American College of Obstetrics and Gynecology Practice Bulletin. Clinical management guidelines for obstetricians-gynecologists. Obstet Gynecol. 2000; 95:1–9.

Bendich A. The potential for dietary supplements to reduce premenstrual syndrome symptoms. Journal of American College of Nutrition. 2000; 19(1):3-12.
Bendich, Adrianne. The potential for dietary supplements to reduce premenstrual syndrome (PMS) symptoms. JOA Nutrition. 2000; 19(1): 3-12.
Biggs W, Demuth R. Premenstrual syndrome and premenstrual dysphoric disorder. Am Fam Physician. 2011; 84(8):918-24.
Biskind MS, Biskind GR. Effect of vitamin B complex deficiency on inactivation of estrone in liver. Endocrinology. 1942; 31: 109-114.
Brown RR, Rose DP, Price JM, Wolf H. Tryptophan metabolism as affected by anovulatory agents. Ann NYAcad Sci 1969; 166: 44-56.
Chakmakjian ZH. A critical assessment of therapy for the premenstrual tension syndrome. J Reprod Med. 1983; 28: 532-538.
Coppen A, Brooksbank BWL, Peet M. Tryptophan concentration in the cerebrospinal fluid of depressive patients. Lancet. 1972; 1: 1393.
Corney RH, Stanton R. A survey of 658 women who report symptoms of premenstrual syndrome. J Psychosom Res. 1991; 35(4/5):471-482.
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.
Diegoli M.S.C, da Fonseca A.M, Diegoli C.A, Pinotti J.A. A double-blind trial of four medications to treat severe premenstrual syndrome. International Journal of Gynecology & Obstetrics.1998; 62:63-67.
Direkvand-Moghadam A, Sayehmiri K, Delpisheh A, Kaikhavandi Sattar. Epidemiology of premenstrual syndrome (PMS) – a systematic review and meta-analysis study. J Clin Diagn Res. 2014; 8:106–109.
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).
Doll H, Brown S, Thurston A, Vessey M. Pyridoxine (vitamin B6) and the premenstrual syndrome: a randomized crossover trial. J R Coll Gen Pract. 1989; 39(326): 364–368.
Douglas S. Premenstrual syndrome, Evidence-based treatment in family practice. Can Fam Physician. 2002; 48:1789-1797.
E.Kendel K, P.Schurr P. The effects of vitamin B6 supplementation on premenstrual Syndrome. Obstet Gynecol. 1987; 70(2):145-149.
Ebrahimi E, Khayati Motlagh Sh, Nemati S, Tavakoli Z. Effects of Magnesium and Vitamin B6 on the Severity of Premenstrual Syndrome Symptoms. Journal of Caring Sciences.2012; 1(4): 183-189.
Freeman EW, Osborn TH, Maclean AB. Premenstrual syndrome new treatments that early work. Contemporary ob/gyn. 1996; 21(25): 25-45.
Freidrich W. Vitamin B6. In: Vitamins. New York, NY: De Gruyter; 1988. p. 543-618.
Hagen I, Nesheim BI, Tuntland T. No effect of vitamin B6 against premenstrual tension: A controlled clinical study. Acta Obestet Gynecol Scand. 1985; 64: 667-669.
Hartlage SA, Freels S, gotman N, Yonkeres K. Criteria for premenstrual dysphoric disorder. Arch Gen Psychiatry. 2012; 69(3):300-5.
Iasco SM, Castro AA, Atallah AN. Vitamin B6 in premenstrual syndrome (Protocol for a Cochrane review). In: The Cochrane Library. Oxford, Engl: Update Software; 1999. Issue 4.
J WilIiams M, I Harris R, C Dean B. Controlled Trial of Pyridoxine in the Premenstrual Syndrome. J Int Med Res.1985; 13: 174-179.
Kashanian M, R Mazinani R, Jalalmanesh S. Pyridoxine (vitamin B6) therapy for premenstrual Syndrome. Khajeh Nasir Toosi Ave. 2006; 83.
Lapin IP, Oxenkrug GF. Intensification of the central serotoninergic processes as a possible determinant of the thymoleptic effect. Lancet 1969; 1: 132-136.
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.
Marcus R and Coulston AM. Water Soluble Vitamins. In Hardman JG, Limbird LE eds. Goodman Oilman's The Pharmacological Basis of Therapeutics. New York, Me Graw-Hill. 2001; 1761.
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).
Mutti Tacani P, de Oliveira Ribeiro D, Evelyn Barros Guimarães B, Fernanda Perez Machado A, Eduardo Tacani R. Characterization of symptoms and edema distribution in premenstrual syndrome. International Journal of Women's Health. 2015:7 297–303.

N Kues J, Janda C, Kleinstäuber M, Weise C. Internet-based cognitive behavioural self-help for premenstrual syndrome: study protocol for a randomised controlled trial. Trials. 2014; 15:472.
O'Brien P, Bäckström T, Brown C. Towards a consensus on diagnostic criteria, measurement and trial design of the premenstrual disorders: the ISPMD Montreal consensus. Arch Womens Ment Health. 2011; 14(1):13-21.
Rose DP. Oral contraceptives and depression. Lancet 1969; 2: 321.
Salehi L, Salehi F. Effect of Vit B 6 on pms. Scientific Journal of Kordestan Journal of Medical Science. 2007; 12:32-9.
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.
Stewart A: A rational approach to treating premenstrual syndrome. A women's nutritional advisory service publication for the National Association of Premenstrual Syndrome. 1989
Sveindóttir H, Bäckström T. Prevalence of menstrual cycle symptom cyclicity and premenstrual dysphoric disorder in a random sample of women using and not using oral contraceptives. Acta Obstret Gynecol Scand. 2012; 79:405–413.
Tanaka E, Momoeda M, Osuga Y, et al. Burden of menstrual symptoms in Japanese women: an analysis of medical care-seeking behavior from a survey-based study. Int J Womens Health. 2014; 6:11–23.
Vishnupriya R, Rajarajeswaram P. Effects of aerobic exercise at different intensities in premenstrual syndrome. J Obstet Gynaecol India. 2011; 61:675–682.
Wyatt K M, Dimmock P W, Jones P W, O'Brien P M S. Efficacy of vitamin B-6 in the treatment of premenstrual syndrome: systematic review. Brit Med J. 1999; 318: 1375–1381.
Wyatt KM, Dimmock PW, Frischer M, Jones PW, PM O'Brien SH. Prescribing patterns in premenstrual syndrome. BMC Women's Health. 2002; 2: 1-8.
Zafari M, Aghamohammady A.Comparison of the Effect of Vit E, VitB6, Calcium and Omega-3 on the Treatment of Premenstrual Syndrome: A Clinical Randomized Trial. Annual Research & Review in Biology. 2014; 4(7): 1141-1149.