

Vitamin B6 Supplementation and Premenstrual Syndrome in Adolescents

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ABSTRACT

Background: Many women experience physical discomfort during menstrual periods with symptoms of menstrual disorders, such as abdominal pain and emotional instability, including mood swings and depression. PMS decreases adolescent creativity and productivity. Vitamin B6 induces the production of serotonin, which is assumed to reduce PMS symptoms. *Objective:* To find out the effectiveness of vitamin B6 supplementation in reducing PMS symptoms and which symptoms are most responsive to Vitamin B6. *Methods:* We conducted quasi-experimental, randomised, blinded, and controlled trials. The intervention and control groups each consisted of 20 adolescent girls aged 15-17 years. Adolescent girls who experienced PMS were randomly divided into two groups: group A was given vitamin B6 supplementation, and group B was given a placebo. where the respondent does not know which group he belongs to. The modified Premenstrual Syndrome Questionnaire and Premenstrual Symptom Questionnaire were used to determine the severity of PMS before and after the intervention. The data was analysed with a T-test. Initially, 154 girls were screened using an initial questionnaire, of which 142 were known to have PMS. 40 adolescent girls were randomly assigned to either a vitamin B6 group or a placebo. *Results:* There was a significant difference in the severity of PMS before and after in the group given vitamin B6 supplementation intervention with a P value of ≤ 0.05 . The change in the severity score was the most in type D PMS. *Conclusion:* Vitamin B6 supplementation has an effect in reducing PMS. The largest score decline was in type D (depression), followed by type A (anxiety). Therefore, vitamin B6 may be recommended as a supplement for adolescent girls who experience PMS.

Keywords:

Premenstrual Syndrome (PMS); Pyridoxine; Depression; Menstruation; Supplementation; Vitamin B6

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1. INTRODUCTION

The *World Health Organization* (WHO) defines adolescence as the age of 10 to 19 years for unmarried people.(WHO, 2024) Adolescence has also been defined as the transitional period between childhood and adulthood. This stage is characterized by physical, behavioral, cognitive, biological, and emotional changes.(Kementerian Kesehatan RI, 2017) Menstruation is a sign that teenagers have reached puberty.(Hagell et al., 2018).During menstruation, many women experience physical discomfort in the abdominal area and emotional instability. (Hofmeister & Bodden, 2016a)

Premenstrual syndrome (PMS) includes psychological and/or somatic symptoms that recur regularly during the luteal phase of the menstrual cycle, ending at the start or during menstruation. The symptoms

can be severe enough to interfere with daily activities and cause weariness.(Dutta & Sharma, 2021) PMS is estimated to affect 40% of women who menstruate, and 2-5% of women experience severe PMS.(Viner et al., 2012) PMS affects millions of women worldwide and has become a daily disturbance for women during the premenstrual dan menstrual period. (Dutta & Sharma, 2021)

In addition to interfering with daily activities, PMS can also hinder the productivity and quality of work of women who experience PMS. According to research by Faremi et al. (2022), the majority of participants experienced premenstrual and menstrual symptoms that affected their quality of life, including overall quality of life, general health, physical health, and psychological domains of quality of life. Self-care was the most commonly used coping strategy during menstrual and premenstrual periods. There was a significant relationship between coping strategies and quality of life. It is recommended that female adolescents be taught how to manage their premenstrual and menstrual symptoms(Funmilola Adenike Faremi et al., 2022).

According to some studies, PMS can be caused by a decrease in estrogen levels before menstruation, which can affect working memory. Estrogen is known to affect memory processes and to improve working memory and brain activity. In addition to the hormone estrogen, serotonin is also linked to working memory, and serotonin deficiency is linked to worsening PMS symptoms called Pre-menstrual Disordic disorder (PMDD). Other studies have also found that a reduction in tryptophan levels impairs working memory and improves PMS symptoms. Therefore, hormonal changes that occur in the luteal phase may be related to the performance of women with PMS/PMDD. These hormonal changes are observed in the difference in memory function between the luteal and follicular phases in the case of PMS/PMDD(Cobanoglu et al., 2021).

Premenstrual syndrome can reduce work productivity, causing physical discomfort that interferes with activities; (Sulistiyani et al., 2019) even housewives can affect the work of household activities(Al-Shahrani et al., 2021) Pre-menstrual which can reduce the quality of life of a woman, including general well-being, smooth learning and work, stress and control at work, and working on daily household activities(Al-Shahrani et al., 2021). Severe Premenstrual syndrome disorder results in decreased performance at work, a tendency to reduce working hours, arrive late, miss work, or come home early. Meanwhile, moderate symptoms result in a decline in general health, sleep quality, and coping skills, increased anxiety, depression, work-life balance, and psychological resilience(Hardy & Hunter, 2021). Because of this, a woman who is lost and disturbed every month, every time before menstruation, has to experience Premenstrual syndrome and has not overcome her symptoms. Because of the various types of premenstrual syndrome symptoms that exist, each type of symptom should be identified to determine how to treat it. Therefore, this study is important.

PMS is a constellation of symptoms that occur in the weeks of the luteal phase (premenstrual phase), 710 days before the onset of menstruation. Women of reproductive age are diagnosed with PMS if they have one or more of the following symptoms during the luteal phase: depression, anxiety, sadness, irritability, decreased interest in daily activities, difficulty concentrating, fatigue, changes in appetite, hypersomnia or insomnia, or feeling overwhelmed. Other physical symptoms included swollen breasts, dizziness, bloating, and muscle pain. (Buddhabunyakan et al., 2017; Hofmeister & Bodden, 2016b; Takeda et al., 2020)

PMS symptoms are divided into four types: type A (anxiety), type C (craving), type D (depression), and type H (hyperhydration/fluid accumulation). Type A symptoms included anxiety, sensitivity, tense nerves, and feelings of liability. Some women experience mild-to-moderate depression before they experience it. Type C symptoms include edema; flatulence; pain in the chest, hands, and feet; and increased body weight. Type D symptoms include crying easily, weakness, sleep disturbance, forgetfulness, confusion, and difficulty in verbalization. Usually, type D PMS coincides with type A PMS; only approximately 3% of all PMS types are pure type D. Type H symptoms include dizziness, abdominal pain, bloating, fluid retention, weight gain, swollen extremities, and tense breasts.(Freeman et al., 2011; Sammon et al., 2016; Thazhath Pullayikudi & Supriya Preman et al., 2025)

Although many symptoms of Premenstrual Syndrome are often experienced by women and greatly interfere with the quality of life, attention to the management of Premenstrual Syndrome is not prioritized, especially Premenstrual Syndrome, which is in the form of psychological or neurological symptoms. Some of the interventions that have been developed thus far are related to the reduction of physical symptoms, such as abdominal pain, dizziness, and tight breasts.

Worldwide, 13.0-98.2% of girls and women of reproductive age experience Premenstrual symptoms.⁵ In Indonesia, a previous study stated that the number of adolescents experiencing PMS reaches a relatively Int Jou of PHE

large number, 260 adolescent women were found to be 95% have at least one PMS symptom, with the level of moderate to severe PMS being 3.9%.¹² In a study conducted in Universitas Indonesia, 36.9% of students had mild PMS, 13.8% had moderate PMS, and 48.1% had severe PMS,¹³ which may become a social issue if such a large number of experiences hindered creativity and productivity. Therefore, the symptoms arising from PMS must be overcome immediately because premenstrual syndrome can affect women's productivity and quality of life.¹⁴

Many studies have been conducted to overcome or reducing Premenstrual symptoms. However, the majority of PMS symptoms that are amenable to treatment are dysmenorrhea and other physical symptoms, while research on psychological symptoms, such as depression, anxiety, and mood changes, is limited.(Agarwal & Agarwal, 2010; Wagito et al., 2011)

Vitamin B6 is known to help the body produce calming neurotransmitters, including serotonin and gamma-aminobutyric acid (GABA). Thus, vitamin B6 may reduce depressive symptoms during PMS. PMS depression is caused by changes in luteinizing hormones, abnormal thyroid hormone levels, cortisol, prolactin, glucose, prostaglandins, β -endorphins, and vitamins, leading to abnormalities in the gonadal hypophyseal-pituitary gland (HPG) and mood swings.(Abdi et al., 2019; Soheila et al., 2016) Specific neurotransmitters, neuroendocrine abnormalities, and neurosteroid abnormalities are unknown mechanisms that cause PMS. 5HT, noradrenaline, gamma amino butyric acid (GABA), allopregnanolone (ALLO), and endorphins may be involved in the developments of symptoms (5). Imaging research reports the presence of changes in serotonin function and GABA levels in women with PMS when compared to healthy control subjects(Abdi et al., 2019; Zaka & Mahmood, 2012).

2. METHOD

This Research is Umbrella Research about Premenstrual Syndrome, led by Siti Nurunniyah, and received a grant from the High Education Minister as Research Funding for Beginner lecturers. This research used a pre-post quasi-experimental study with a control group conducted at Gamping 1 Senior High School. The research sample included grade X and XI students who experienced PMS symptoms, as assessed using a questionnaire. The inclusion criteria were Indonesian female adolescents aged 15 to 18 years who had moderate to severe PMS, regular menstrual cycles, and were present at the time of sampling. The exclusion criteria were girls of similar age with chronic diseases and those who were not willing to participate. There were 142 respondents who met the inclusion criteria and 40 respondents were randomly selected as samples in this study. The Research was approved by the ethics committee of Alma Ata University (No. 007/EC/UAA/VI/2017).

The study sample from the preliminary study, 154 adolescent girls, were organized by distributing questionnaires to determine whether they have premenstrual syndrome or not. Respondents who experienced premenstrual syndrome they are 142 adolescent girls, from this number then taken randomly 40 respondent divided in two groups, each groups consist of 20 students, -the vitamin B6 group (1x 100 mg/day for one week before menstruation to 1 week after the first day of menstruation) or the control group (placebo 1x per day for one week before menstruation until one week after the first day of menstruation).

The questionnaire was translated and modified from standardised premenstrual PMS questionnaires and premenstrual symptoms questionnaires. The questionnaire was translated by the author and co-authors, reviewed by a language expert, and tested for validity and reliability. Validity and reliability tests with a T-value of Pearson product-moment and Cronbach's alpha result test greater than the T-table value at a significance level of 0.05. The subjects completed the questionnaire pre- and post-intervention. Bivariate analysis with a paired-sample t-test was used to compare pre- and post-intervention results. In addition, univariate analysis was performed to determine the intensity of PMS symptoms in subjects pre- and post-intervention, using a ratio scale of the total questionnaire score. The scores were determined based on the results of the questionnaire. The higher the score, the more severe the PMS (**Table 1**).

Table 1. Questionnaire Grid

Number of question	Item	Score
-	Identity of respondent	-
1-4	Symptoms of PMS type A	1-5
5-9	Symptoms of PMS type C	1-5
10-14	Symptoms of PMS type H	1-5
15-19	Symptoms of PMS type D	1-5

Symptoms were divided into four subgroups according to Abraham Classification (Dewi et al., 2020a): type A (anxiety), type C (craving), type D (depression), and type H (hyperhydration). The PMS symptom types were defined as follows: type A, stress, irritability, and anxiety; type C, craving sweets, palpitations, feeling weak, as well as having reduced energy, increased appetite, and fatigue; type D, depression, seclusion, social inactivity, crying, impatience, desire to stay at home, anger, forgetfulness, insomnia, and lack of concentration; type H, hyperhydration/water retention, breast pain, leg swelling, flatulence, pain, and discomfort; somatic changes of type H were feeling cold, nausea, frequent urination, back pain, headaches, acne, oily skin, joint pain, and muscle pain.

3. RESULTS AND DISCUSSION

The subjects had a median age of 16 years, with a range of 15-18 years; the age distribution is shown in Table 2. Most participants were aged 16 years (52.1%), and the preliminary study showed that most respondents experienced PMS in the severe category at 45.55%, followed by the moderate category at 30.35%, and the mild category at 24.10%.

Table 2. Characteristics of respondents

Characteristics	N=142
Age, n (%)	
15 years	24 (16.9)
16 years	74 (52.1)
17 years	42 (29.6)
18 years	2 (1.4)
PMS category, n (%)	
Light	42 (24.10)
Moderate	49 (30.35)
Severe	51 (45.55)

The results of the analysis of the pre-intervention and post-intervention scores are shown in table 3.

Table 3. Analysis of pre- and post-intervention PMS scores

Group	Mean score		Mean difference	P value
	Pre	Post		
B6	53.40	44.05	9.35	0.00
Control	53.00	53.00	0.00	1.00

From table 5, we can see that the PMS score in the intervention group after the intervention decreased by approximately 9 points; in the control group, there was no decrease in score. The mean post-intervention PMS score was significantly decreased in the vitamin B6 group, but not in the placebo group, compared to the pre-intervention scores (Table 3). The mean score of the intervention group at pre intervention 53.40 became 44.05 for post intervention, with a mean core difference of 9.35 and a p-value <0,05. Therefore, there was a significant difference between the pre-and post-intervention.

The distribution of the frequency of pre-and post-intervention scores if differentiated according to each PMS symptom experienced, the average difference is as follows: in the symptoms of depression there is a mean difference of 3.16, then in the symptoms of anxiety there is a mean difference of 2.42 points, followed by craving symptoms of 2 points and hyperhydration of 1.82 points.

Table 4. Pre-and post-intervention PMS scores of each PMS type

Type of PMS	Mean score		Mean difference	P value
	Pre	Post		
Anxiety	13.67	11.25	2.42	0.42
Hyperhydration	11.16	9.34	1.82	0.08
Craving	13.4	11.40	2.00	0.19
Depression	15.16	12.00	3.16	0.01

Table 4 shows that the greatest score reduction was in type D symptoms, followed by type A then Type C and the last is type H.

4. DISCUSSION

The characteristics of the respondents in this study were based on the age of having an age between 16-19 years, this condition is not the same as in the research conducted by Syafila et al., who conducted research on dysmenhorea in adolescent girls aged 14-17 years (Syafila et al., 2024). In addition, this is not the same as the research conducted by Cahyaningsih et al. with the majority of respondents aged 19-22 years(Cahyaningsih et al., n.d.). This allowed for the difference between the results of the study and this study because there was an age difference. According to research conducted by Pedro et al. in 2025, there is a tendency to increase the prevalence and severity of Premenstrual Syndrome with increasing age (Pedro et al., 2024).

The results of this study showed that the majority of adolescents experienced a combined type of premenstrual syndrome. The single type of PMS that the majority of respondents suffer from is type A (anxiety), followed by Type C then Type H and Type D with the same prevalence. The results of this study support the previous research conducted by Dewi et al., who found that the prevalence of type Premenstrual syndrome suffered by adolescents in the study was type A, similar to the results of this study, but for the second prevalence is type D, then type C and the least is type H(Dewi et al., 2020b).

The vitamin B6 treatment group had significantly lower mean total PMS scores post-intervention than pre-intervention ($P=0.00$). The mean pre- and post-intervention PMS scores of the control group were not significantly different ($P=1.00$). These results suggest that vitamin B6 can reduce the general symptoms of PMS. Nutritional deficiencies such as vitamin B6 can aggravate PMS symptoms.(Sammon et al., 2016) . Vitamin B6 supplementation administered at a dosage of 50-100 mg per day can reduce PMS symptoms.(Masoumi et al., 2016; Setianingsih & Kartasurya, 2013) Vitamin B6 can be found in three forms, namely pyridoxine, pyridoxal, and pyridoxamine, one of which can be used as therapy (synthetic form); vitamin B6 hydrochloride,(Hellmann & Mooney, 2010) our vitamin B6 group was given this form at a dose of 100 mg daily, as was used in the Yogyakarta study.

PMS therapy focuses on alleviating symptoms and improving the quality of life. Supplements were considered non-pharmacological treatments. Severe PMS symptoms may require pharmacological treatment with selective serotonin reuptake inhibitors (SSRIs), oral contraceptive pills (OCPs), gonadotropin-releasing hormone (GnRH) agonists, and/or non-contraceptive estrogen formulations.(Littell et al., 2008) Vitamin B6 induces serotonin production, thereby potentially reducing PMS symptoms by neurotransmitter synthesis in the brain Thus, PMS symptoms such as depression, headaches, and anxiety might decrease as serotonin levels increase.(Hellmann & Mooney, 2010; Setianingsih & Kartasurya, 2013) A previous study also showed that the administration of vitamin B6 supplementation can be recommended by health care workers to reduce the incidence of Pre-menstrual Syndrome with a P value (0.000) between the intervention group treated with vitamin B6 and the control group with placebo.(Anityo & Giri K, 2014)

We found the most significant decrease in type D PMS symptoms in the vitamin B6 group, followed by type A. Subjects had noted reductions in anxiety, irritability, and depression. Estrogen fluctuations during the pms can reduce serotonin levels. Since vitamin b6 has been theorized to act as an anti-depressant by inducing serotonin production, which can affect emotions, it may be useful in overcoming mood swings.

Vitamin B6 has also been shown to significantly reduce premenstrual symptoms. Vitamin B6 also plays a role in growth and development of the nervous system (Calderón-Ospina & Nava-Mesa, 2020). Vitamin B6 is also essential for the hormonal balance in the human body. Vitamin B6 helps the body to produce serotonin, a chemical that affects mood. Low serotonin levels are associated with depression, and some antidepressant medications increase serotonin levels. A study found that 40 mg of vitamin B6 significantly reduced emotional swings compared with placebo.(Ebrahimi et al., 2012)

Vitamin B6 (pyridoxine) was discovered in 1934 and has been associated with more than 140 co-enzyme roles. It is widely accepted for its essential function in the formation of neurotransmitters, such as dopamine from L-DOPA, serotonin from 5-HTP, and gamma-aminobutyric acid (GABA) from glutamate. Pyridoxine affects serotonergic, adrenergic, and glutamatergic systems. Pyridoxine can also be attributed to the glutamatergic system, and thus to GABA and glutamate levels. Glutamatergic signaling plays an important role in various brain functions such as learning, memory, and cognition. (Calderón-Ospina & Nava-Mesa, 2020; Kennedy, 2016). Serotonin and endorphins maintain mood stability and create happiness. Decreased estrogen and progesterone levels before menstruation can affect the decrease

in endorphin and serotonin levels, thus affecting a woman's mood before menstruation. Vitamin B6 is known to increase the production of the hormones serotonin and endorphin to improve mood. Vitamin B6 can be obtained through food and vitamin B6 supplements, or a combination of both. The recommended nutritional adequacy rate (FDA) varies according to age, sex, and health conditions. The requirement for adolescent girls was 1.2 mg/day(Abosamak & Gupta, 2023).

Vitamin B6 could not be obtained in the form of 100 mg tablets as used in this study, it can also be obtained through natural sources such as chicken breast, in 100 grams of chicken breast, there is about 0.2 to 0.5 mg of vitamin B6, shrimp and beef contain about 0.3 mg of vitamin B6 per 100 grams, sweet potatoes, contain about 0.3 mg of vitamin B6 per 100 grams, Tuna fish contains about 0.5 mg of vitamin B6 per 100 grams, almonds and beef liver contain about 1 mg of vitamin B6 per 100 grams.

In this study, evidence of the effectiveness of vitamin B6 was demonstrated through the consumption of vitamin B6 100 mg. In 2018, Cahyaningsih et al. showed that a combination of vitamin B6 supplementation (15 mg) with vitamin C and calcium in the form of evervesence could reduce the level of dysmenorrhea pain(Cahyaningsih et al., n.d.). Another study that is also supported by this research was conducted by Dewi et. A cross-sectional study found that vitamin B6 intake was associated with the incidence of premenstrual syndrome. This study has a better level of evidence than previous studies because it used an experimental research design with a pre-post design with a control approach, and has specifically researched the types of premenstrual symptoms, not just pre-menstruation in general.

As shown in table 6, the study also showed a decrease in menstrual complaints in the form of dysmenorrhea, but the decrease in complaint scores was higher in patients with depression. This study supports previous studies; several previous studies have not examined in detail premenstrual syndrome, and several studies have investigated dysmenorrhea as a symptom of Premenstrual syndrome type H. Herviana et al. found a relationship between dysmenorrhea and herbal consumption habits(Herviana & Farapti, 2023), and a study conducted by Primalova found that dysmenorrhea is related to nutritional status and consumption patterns in adolescents(Primalova & Stefani, 2024). Regular vitamin B6 supplementation in women who experience severe premenstrual syndrome may need to be considered to maintain a woman's quality of life. In the UK, some women with severe premenstrual syndrome have been supplemented with vitamin B6 (Sammon et al., n.d.). This study has limitations, namely, it did not control for confounding variables that may have interfered with the results of the study, such as physical activity habits, rest patterns, stress management, and food intake, which may have affected the results. This study also did not compare the dose of vitamin B6, because it only uses a single dose; therefore, so what is the exact and effective dose to overcome premenstrual syndrome can not be determined. In the future, this research can be developed by conducting research with better methods and designs, correcting from previous studies, and developing food ingredients or nutraceuticals that are effective and preferred with the right nutritional content to reduce the symptoms of premenstrual syndrome.

CONCLUSIONS

The mean PMS post-intervention score was significantly lower in the vitamin B6 group than that in the placebo group. The greatest symptom reduction following vitamin B6 supplementation was observed in type D PMS. Further study is needed with a larger sample size and longer duration to assess the effectiveness of vitamin B6 in reducing Pre-Menstrual symptoms in adolescent girls and developing nutraceuticals containing vitamin B6.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

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AUTHOR CONTRIBUTIONS

SR: provides interventions, collecting data, formal analysis, writing the original draft, writing-review

SN: Conceptualization, methodology, supervision, analysis of research results, write-review, and editing.

EN: Methodology, preparation of tools and materials, data collection, and analysis of results.

DPP: formal analysis, writing original draft.

PK: provide interventions, collecting data, and formal analysis;

ASA: formal analysis, writing-review;

AY: formal analysis, writing-review,

W: formal analysis, resources, writing-review

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