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Effects of Vitamin B6 and St. John's Wort on Maternal Premenstrual Syndrome Symptoms and Children's School Activities: A Secondary Study

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Abstract

Background: Premenstrual syndrome (PMS) is characterized by physical, emotional, and behavioral symptoms occurring before menstruation. This secondary analysis compared the effectiveness of vitamin B6 (pyridoxine) and *Hypericum perforatum* (St. John's Wort) in reducing PMS symptoms and evaluated impacts on participants' daughters' school activities.

Materials and Methods: In this randomized, double-blind, controlled clinical trial (secondary analysis), 251 women diagnosed with PMS were assigned to receive *Hypericum perforatum* (550 mg/day), vitamin B6 (80 mg/day), or placebo for two menstrual cycles. PMS symptom severity was assessed using the Daily Symptom Record (DSR) questionnaire before and after treatment. Additionally, 150 daughters of participants completed a six-point scale evaluating the impact of their mothers' treatment on their school activities during the same period. Data were analyzed using ANOVA and repeated measures tests.

Results: A total of 251 women with premenstrual syndrome (PMS) and 150 of their daughters participated in this study. Repeated measures analysis revealed that all three groups—Hypericum perforatum, vitamin B6, and placebo—showed reductions in PMS symptom severity over the study period. Although the Hypericum perforatum group exhibited the largest decrease, the differences among the groups were not statistically significant ($p = 0.202$). Similarly, while there was a general trend toward improved school activities among the daughters, these changes were not statistically significant between groups ($p = 0.363$). Overall, improvements in maternal PMS symptoms did not translate into significant differences in the school activities of their daughters.

Conclusion: Vitamin B6 and Hypericum perforatum may be effective, accessible, and low-risk options for reducing PMS symptoms. However, improvements in maternal symptoms did not significantly influence the school activities of their daughters.

Key Words: Premenstrual syndrome, Vitamin B6, Hypericum perforatum, School activities.

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1- INTRODUCTION

Premenstrual syndrome (PMS) is a common clinical condition characterized by a range of somatic, psychological, and behavioral symptoms that occur cyclically during the luteal phase of the menstrual cycle and typically resolve with the onset of menstruation. Symptoms often include mood swings, irritability, anxiety, depression, breast tenderness, abdominal bloating, headaches, and fatigue, which can vary in intensity and interfere with daily functioning. The global prevalence of PMS is estimated to be between 20% and 50% among women of reproductive age, with severe symptoms affecting approximately 3–8%. A more disabling form, known as premenstrual dysphoric disorder (PMDD), also exists (1, 2). Among medical science staff and healthcare professionals—especially nurses and female medical personnel—the prevalence is notably high, ranging from approximately 42.5% to over 52%, with a substantial proportion experiencing moderate to severe symptoms (3–5).

The etiology of PMS is multifactorial and not fully understood, but it is believed to involve hormonal fluctuations—particularly in estrogen and progesterone—and neurotransmitter dysregulation, especially in the serotonin and gamma- aminobutyric acid (GABA)ergic systems (6). Emerging evidence also suggests that inflammatory processes and oxidative stress may contribute to symptom severity (7–9). Diagnosis is clinical, often based on prospective symptom recording during the luteal phase and exclusion of other medical or psychiatric disorders (10).

Female healthcare workers are particularly vulnerable to PMS due to occupational stressors such as high emotional and quantitative job demands, shift work, and irregular schedules. For example, a cross-sectional study among Iranian nurses found that moderate to severe PMS was significantly associated with emotional and quantitative job demands, monthly COVID-19 shifts, and irregular menstrual cycles (3). Similarly, a comparative study in Egypt reported that 45.8% of medical workers suffered from severe PMS, a rate significantly higher than that among non-medical staff, and PMS was negatively correlated with work-related quality of life (4). These findings suggest that occupational stress and working conditions exacerbate PMS symptoms, leading to reduced work productivity and quality of life.

In addition to its impact on individual well-being, PMS can have broader psychosocial effects on family life and children. The mood and behavioral changes associated with PMS may increase family tensions, reduce marital satisfaction, and disrupt parent–child relationships, potentially exposing children to emotional instability and stress (5, 9, 11). As a result, the psychological well-being and academic performance of children may be indirectly affected. Despite the importance of these effects, research specifically addressing the consequences of PMS on children and family dynamics remains limited and warrants further investigation (1, 5).

In addition to its individual and family impacts, examining the effects of maternal PMS on daughters is particularly important. Daughters—especially during adolescence—are often emotionally close to their mothers and model their behaviors after them, making them more susceptible than other family members to the emotional and behavioral changes associated with maternal PMS (12). Research has shown that parental mental health and behavior, particularly that of mothers, can play a crucial role in shaping the psychological, social, and academic development of children (13, 14). For instance, maternal mood disorders and stress have been associated with increased

risk of emotional and behavioral problems in children (15). Therefore, assessing whether improvements in maternal PMS symptoms can lead to better academic and psychological outcomes in daughters is of great significance. Such investigations can help identify effective interventions to promote family health and prevent psychological and academic problems in the next generation. Various pharmacological and non-pharmacological treatments have been explored. Selective serotonin reuptake inhibitors (SSRIs) are considered first-line therapy for psychological symptoms but may have limitations due to side effects (16). Complementary therapies such as Hypericum perforatum (St. John's Wort) and vitamin B6 (pyridoxine) have shown promising results in reducing both physical and psychological PMS symptoms, with favorable safety profiles (17, 18).

Given the high prevalence and significant impact of PMS on female healthcare workers and their families, this secondary analysis aims to compare the efficacy of vitamin B6 and Hypericum perforatum in alleviating PMS symptoms in this population and to explore the effects of these treatments on the school activities of their daughters.

2- MATERIALS AND METHODS

2-1. Study Design

This secondary analysis was a randomized, double-blind, placebo-controlled clinical trial designed to evaluate the effectiveness of *Hypericum perforatum* and vitamin B6 on premenstrual syndrome (PMS) symptoms in female administrative staff at Shiraz University of Medical Sciences, Shiraz, Iran. Baseline data for the participating mothers have been published previously (19). In the present study, we re-analyzed data to investigate the effects of these maternal treatments on their children's school performance. The study protocol strictly adhered to ethical guidelines and was approved by the Ethics Committee of Shiraz University of Medical Sciences.

2-2. Inclusion and Exclusion Criteria

Eligible participants were women aged 18 to 45 years who self-reported experiencing PMS symptoms for at least six months and had regular menstrual cycles. Exclusion criteria included: having psychiatric disorders or chronic diseases; use of psychotropic medications or alternative PMS treatments; being pregnant or breastfeeding; not using effective contraception; or having irregular menstrual cycles. All participants provided written informed consent.

2-3. Sample Size Determination and Selection

The sample size was calculated for the original trial based on data from previous interventional studies involving similar populations (20, 21). Assuming a 95% confidence interval (CI), 80% statistical power, and the minimum expected difference between groups, an initial sample size of 78 participants per group was estimated. To account for potential attrition, the sample size was increased to 90 participants per group. A total of 270 women were screened for eligibility, of whom 251 met the inclusion criteria and were randomly assigned to one of three groups: *Hypericum perforatum* (n= 85), vitamin B6 (n = 81), or placebo (n= 85). Participants were selected using convenience sampling and subsequently randomized into the three study groups.

2-4. Study Procedures

Data from the study consisted of three phases: screening, preparation, and treatment. During the screening phase, 270 women were assessed for eligibility, resulting in 251 eligible participants. In the preparation phase, participants recorded their symptoms daily using the Daily Symptom Record (DSR) questionnaire for

two consecutive menstrual cycles without intervention. The DSR questionnaire assessed 17 common PMS symptoms, each rated on a six-point Likert scale, and has demonstrated high validity and reliability (22–25). Throughout this phase, bi-weekly telephone calls were made to participants to ensure accurate completion of the questionnaires and to monitor for any problems or side effects.

After two months of data collection, PMS severity was diagnosed based on the DSR questionnaire scores. Eligible participants were then randomly assigned to one of three groups for the treatment phase, which lasted for two consecutive menstrual cycles (from day 1 to day 30 of each cycle):

- The first group (n = 85) received two tablets of Hypericum perforatum daily, providing a total of 330 μg of hypericin per day.
- The second group (n = 81) received two tablets of vitamin B6 daily, providing a total of 80 mg of vitamin B6 per day.
- The third group (n = 85) received two placebo tablets daily, containing lactose and cellulose.

2-5. Blinding

The Hypericum perforatum, vitamin B6, and placebo tablets were manufactured by Barij Essence Pharmaceutical Company to be identical in shape, color, and packaging, ensuring the double-blind nature of the study. Neither the participants nor the researchers were aware of the treatment assignments. The coded medication packages were prepared and distributed by an individual who was not involved in the research team.

2-6. Data Collection Tools

2-6-1. Daily Symptom Record (DSR) Questionnaire: The Daily Symptom Record (DSR) questionnaire, developed by Allen et al. in 1991, consists of 17 common symptoms of premenstrual syndrome (PMS), including anger, mood swings, anxiety, depression, sleep disturbances, and fatigue. Each symptom is rated on a six-point Likert scale (1 = not at all to 6 = extreme), resulting in a total daily score ranging from 17 to 102. This tool is widely recognized for its high validity and reliability, with Cronbach's alpha coefficients typically above 0.80 (22, 23). The Persian version has also demonstrated good psychometric properties among Iranian women (24). Higher scores indicate more severe symptoms, while lower scores reflect improvement in participants' clinical status.

2-6-2. Assessment of Student School Activities: To assess the indirect effects of maternal treatments on children's school activities, the daughters of participating mothers completed a researcher-developed, five-item questionnaire that evaluated changes in their school activities during the two menstrual cycles before and after the intervention. Each item was rated on a six-point Likert scale and addressed key areas such as classroom participation, academic achievement, timely completion of homework and assignments, relationships with classmates, and overall engagement in school activities. The validity of the questionnaire was established by a panel of five faculty experts in statistics, general psychology, midwifery, nursing and health education, while its reliability was confirmed by a strong Cronbach's alpha coefficient of 0.87, indicating a high level of internal consistency.

2-7. Data Collection Training and Monitoring

At the beginning of the study, all participants received training on how to accurately complete the DSR questionnaire, both in person and through a written guide. The researchers emphasized the importance of consistent

and precise symptom recording and instructed participants to rate the severity of each of the 17 symptoms daily using the six-point scale (1 to 6). Throughout the data collection period, participants received bi-weekly telephone calls to ensure regular completion of the questionnaires, clarify any ambiguities, and address any questions or issues. Participants were also provided with the researchers' contact information to report adverse events, specific incidents, or any difficulties in completing the forms promptly.

2-8. Monitoring and Safety

Continuous oversight was maintained by an independent monitoring team to ensure accurate protocol implementation and the protection of participants' rights. All potential adverse events were systematically recorded and analyzed. After study completion, the medications used in the intervention were made available to the control group, allowing them to access treatment for premenstrual syndrome if desired.

2-9. Ethical Considerations

This secondary analysis of a randomized, double-blind, placebo-controlled clinical trial was conducted in full compliance with ethical principles for human research. The original research protocol was reviewed and approved by the Ethics Committee of Shiraz University of Medical Sciences prior to initiation (IR.SUMS.REC.1388.4713). All participants received detailed information about the study objectives, procedures, potential benefits, and possible risks, and subsequently provided written informed consent. Participation was entirely voluntary, and participants were assured that they could withdraw from the study at any time without any consequences or loss of benefits (25). All participant data were coded and kept confidential, accessible only to authorized members of the research team. Throughout the study, participants were closely monitored for adverse events or unexpected outcomes and were provided with the research team's contact information to promptly report any concerns or incidents. All reported adverse events were documented and managed according to ethical guidelines and clinical trial standards (25, 26). The correct implementation of the protocol and the protection of participants' rights were continuously monitored by an independent oversight team. Upon completion of the study, participants in the control group were offered the opportunity to receive the intervention if they wished. All procedures were conducted in accordance with the Declaration of Helsinki (25).

2-10. Statistical Analysis

Descriptive statistics—including mean, standard deviation, frequency, and percentage—were calculated to summarize demographic characteristics and primary study variables. Group differences at baseline were assessed using analysis of variance (ANOVA). To evaluate changes over time and the effects of interventions, repeated measures ANOVA was conducted, enabling analysis of main effects for time, treatment, and their interaction. All statistical analyses were performed using SPSS version 15, with statistical significance defined as $p < 0.05$

3- RESULTS

The study comprised 251 female participants with an overall mean age of 31.57 ± 6.91 years. These participants were randomly assigned to three groups: 85 women received Hypericum perforatum, 81 received vitamin B6, and 85 received a placebo. There were no statistically significant differences among the groups regarding mean age, weight, or height. Additionally, 150 daughters of these women were included, with a mean age of 12.34 ± 2.1 years and no significant age difference between groups (**Table 1**).

Table-1: Demographic Characteristics of the Study Groups (n=251 mothers and 150 daughters).

Variables	H. perforatum, n = 85	Vitamin B6, n = 81	(Placebo, n = 85)	*P-value
Age of mothers (years)	31.01 (6.98)	32.16 (6.65)	31.62 (7.12)	0.580
Weight of mothers (kg)	59.87 (9.20)	59.79 (9.47)	59.08 (0.83)	0.834
Height of mothers (cm)	162.29 (6.31)	160.41 (6.30)	161.10 (7.89)	0.364
Age of daughters (years)	12.29 (2.19)	12.38 (2.04)	12.36 (2.13)	0.964

* Repeated measures ANOVA test.

No statistically significant difference was observed in the severity of premenstrual syndrome (PMS) among the three groups before and after treatment, as determined by repeated measures ANOVA (P= 0.202). The results are summarized in **Tables 1 and 2** and illustrated in **Figure 1**.

Figure 1 displays the mean changes in PMS severity from two months prior to the intervention through two months after the intervention across the study groups. The largest reduction in PMS severity was observed in the Hypericum perforatum group (14.01), followed by the vitamin B6 group (12.57), while the placebo group showed the smallest reduction (9.72). However, these differences did not reach statistical significance (P=0.202; **Table 2**), indicating that the improvements in the intervention groups were not significantly greater than those in the placebo group.

Table-2: PMS Severity Scores Before and After Treatment and Reduction in Severity by Group.

Groups	PMS Severity Before Treatment	PMS Severity at Month 2	Reduction in PMS Severity	*P-value
Hypericum perforatum	33.28	19.54	14.01 (Highest)	0.202
Vitamin B6	33.30	20.89	12.57 (Moderate)	
Placebo	32.50	23.32	9.72 (Lowest)	

* Repeated measures ANOVA test. PMS: Premenstrual syndrome.

While both the Hypericum perforatum and vitamin B6 groups demonstrated greater reductions in PMS severity compared to placebo, these differences were not statistically significant within the study period. This secondary analysis suggests that, although some improvement was observed with the active treatments, the evidence from this analysis does not support a significant advantage over placebo.

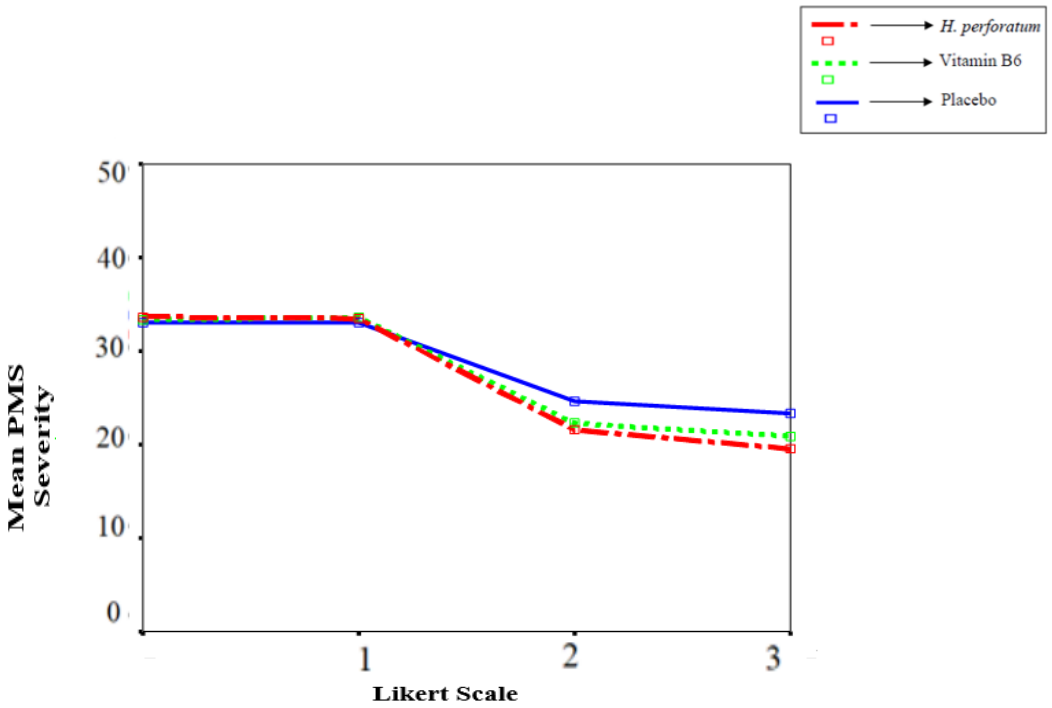

Fig. 1: Mean improvement in premenstrual syndrome (PMS) symptoms before and after the intervention in the three study groups.

In this study, 150 daughters were categorized into three groups according to their mothers' treatment assignment: Hypericum perforatum (48 girls), vitamin B6 (50 girls), and placebo (52 girls). **Table 3** presents the comparison of mean improvements in school activities among these groups. Repeated measures analysis indicated no statistically significant differences in school activity improvements between the groups (p=0.363) (**Table 3**). Although all groups exhibited a positive trend over the intervention period, the pattern of change was similar across groups. Thus, none of the maternal treatments—Hypericum perforatum, vitamin B6, or placebo—proved to be more effective than the others in enhancing the school activities of their daughters.

Table-3: Comparison of School Activity Improvements in Daughters of Mothers with PMS Receiving Hypericum perforatum, Vitamin B6, or Placebo (n = 150).

School Activity Item (Mean (SD)	Hypericum perforatum (n=48)	Vitamin B6 (n=50)	Placebo (n=52)
1. Answering teachers' questions in class	3.60 (0.90)	2.80 (0.85)	3.55 (0.80)
2. Achieving better grades	3.50 (0.80)	2.70 (0.90)	3.45 (0.85)
3. Completing homework and assignments on time	3.55 (0.85)	2.85 (0.80)	3.50 (0.75)
4. Having better relationships with classmates	3.40 (0.75)	2.90 (0.80)	3.35 (0.80)
5. Greater interest and participation in school activities	3.45 (0.80)	2.95 (0.90)	3.40 (0.75)
Overall Mean Improvement (SD)	3.50 (0.82)	2.84 (0.85)	3.45 (0.79)
Minimum	2.1	1.8	2.0
Maximum	5.0	4.2	4.8
P-value (Repeated measures ANOVA)	0.363		

Note: All values are presented as mean (standard deviation) based on a 6-point Likert scale (1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Very Often, 6 = Always). Minimum and maximum represent the lowest and highest scores observed in each group. PMS: Premenstrual Syndrome.

4-DISCUSSION

We conducted a secondary analysis to compare the effectiveness of vitamin B6 (pyridoxine) and Hypericum perforatum (St. John's Wort) in alleviating premenstrual syndrome (PMS) symptoms, and to explore whether improvements in maternal symptoms influenced the academic performance of their daughters. The results showed that both interventions reduced the severity of PMS symptoms, with the greatest improvement observed in the Hypericum perforatum group; however, these differences were not statistically significant compared to the vitamin B6 and placebo groups. Additionally, although there was a trend toward improved school activity among the daughters, these changes were not statistically significant.

4-1. The Role and Necessity of Complementary and Alternative Medicine (CAM) in PMS

The findings of this study reinforce the growing importance of CAM in PMS management. Many women seek alternatives to conventional pharmaceuticals due to concerns about side effects, chronicity of symptoms, and a preference for natural therapies (27, 28). Both vitamin B6 and Hypericum perforatum are among the most widely studied and promising CAM options for PMS, as supported by systematic reviews and clinical trials (27–30).

4-2. Efficacy of Hypericum perforatum, Vitamin B6, and Herbal PMS Treatments

Multiple studies have investigated the effectiveness of Hypericum perforatum (St. John's Wort) and vitamin B6 in alleviating symptoms of PMS, with both treatments showing significant reductions in PMS scores and being considered safe and effective options for women suffering from this condition (27, 29, 31). However, the landscape of herbal and dietary interventions for PMS is complex, with some evidence suggesting that other remedies, such as evening primrose oil, may outperform vitamin B6 in certain symptom domains (32).

4-2-1. Efficacy of Hypericum perforatum

Clinical trials have demonstrated that Hypericum perforatum can significantly reduce physical and behavioral symptoms associated with PMS. For example, Stevinson et al. (2000) reported that more than half of participants experienced a significant reduction in PMS symptoms, particularly in behavioral and physical domains (30). The primary mechanism is believed to involve modulation of the serotonergic system, which plays a key role in mood regulation and psychological symptoms of PMS (27, 30). Randomized, double-blind trials have shown Hypericum perforatum to be statistically superior to placebo in improving physical and behavioral symptoms, although its effects on mood and pain symptoms have been less consistent (30). Comparative studies with other herbal remedies, such as Vitex agnus-castus and saffron, suggest that while these alternatives may also be effective, Hypericum perforatum benefits from a relatively stronger and more extensive body of evidence (31). Furthermore, combination therapies, such as Hypericum perforatum with Vitex agnus-castus, have shown promise in specific populations, including perimenopausal women (33).

4-2-2. Role of Vitamin B6

Vitamin B6 is one of the most well-established supplements for PMS, with robust evidence from multiple systematic reviews and meta-analyses confirming its efficacy in reducing both psychological and physical symptoms (27-29). The systematic review by Canning et al. (2006) specifically highlights vitamin B6 as one of the few supplements with substantial

and consistent evidence for benefit in PMS, showing significant reductions in PMS symptom scores in several randomized controlled trials. Its effectiveness appears to be dose- and duration-dependent, and side effects are generally mild and transient (27). Clinical studies have shown that vitamin B6 can significantly decrease PMS symptom scores, and it is often considered a first-line supplement for PMS management (27, 34, 35).

4-3. Comparative Effectiveness and Safety

While both *Hypericum perforatum* and vitamin B6 are effective, some studies suggest that herbal remedies like evening primrose oil may outperform vitamin B6 in specific symptom domains such as breast tenderness and mood symptoms (30, 36, 37). Nevertheless, the overall consensus in systematic reviews supports the use of both *Hypericum perforatum* and vitamin B6 as safe and effective options for PMS management (27, 34, 38). Reported side effects for both treatments are generally mild, including gastrointestinal discomfort and dizziness, which typically resolve upon discontinuation (39, 40). Despite these positive findings, systematic reviews consistently highlight the need for larger, well-controlled trials to establish the comparative and combinational effectiveness of these interventions and to develop standardized treatment protocols (34, 41). Evidence for some herbal treatments, such as evening primrose oil, remains mixed or insufficient, and further research is necessary to clarify their role in PMS management (32, 41).

4-4. Impact of Maternal PMS Symptom Management on Children's Academic Performance

This study examined whether alleviating maternal premenstrual syndrome symptoms could improve the academic performance of their daughters. The findings showed no statistically significant improvement in daughters' school activities ($p = 0.363$), even though the Hypericum perforatum group exhibited the greatest improvement; this difference was not statistically significant. These results indicate that the factors influencing children's academic outcomes are complex and extend beyond maternal symptom management alone.

The broader literature supports these findings. While premenstrual symptoms can negatively affect academic performance—impacting concentration, class attendance, and assignment completion—the relationship is multifactorial and influenced by a range of psychosocial, familial, and individual factors. Recent studies report that up to 90% of female students experience an impact of premenstrual symptoms on their academic performance, particularly in attention, attendance, physical activity, and meeting assignment deadlines. However, the extent of this impact varies with symptom severity and is shaped by individual and contextual factors (27, 42, 43).

Notably, some studies have found no significant association between PMS experience and academic performance, suggesting that other factors, such as the length of menses, may play a more direct role (44). Various studies have shown that focusing solely on the treatment or management of maternal premenstrual syndrome (PMS) is usually not sufficient to improve children's educational outcomes, and that it is also necessary to consider broader factors such as the family environment and psychosocial support. (45-47).

In summary, future research should adopt a holistic approach, considering not only maternal health but also the broader family environment, psychosocial support, and nutritional status, to more effectively

promote children's academic achievement and overall well-being (44).

5- CONCLUSION

Based on the findings of this study, which included 251 women diagnosed with premenstrual syndrome (PMS) and 150 of their daughters, all three treatment groups—Hypericum perforatum (St. John's Wort), vitamin B6, and placebo—demonstrated a reduction in PMS symptom severity. Although the greatest improvement was observed in the Hypericum perforatum group, the differences between the groups were not statistically significant. Baseline characteristics such as age, weight, and height were well-matched across the groups, confirming the comparability of the study populations.

With respect to the impact of maternal treatment on daughters' academic performance, while a trend toward improvement in school activities was noted, these changes did not reach statistical significance, and none of the interventions showed a clear advantage over the others. This indicates that improvement in maternal PMS symptoms alone does not significantly influence the academic performance of their daughters.

These results suggest that both Hypericum perforatum and vitamin B6 are safe and potentially beneficial options for managing PMS symptoms, particularly in reducing physical and behavioral manifestations. However, since neither treatment demonstrated a statistically significant advantage over placebo in this study, their selection may be guided by patient preference or clinical judgment, with consideration given to individual tolerance and response. Importantly, the lack of a significant impact on daughters' academic outcomes highlights the complex interplay of factors affecting child well-being, which extends beyond maternal symptom management.

6- CONFLICT OF INTEREST: None.

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