

Annual Research & Review in Biology
4(7): 1141-1149, 2014

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Comparison of the Effect of Vit E, VitB6, Calcium and Omega-3 on the Treatment of Premenstrual Syndrome: A Clinical Randomized Trial

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Authors' contributions

This work was carried out in collaboration between all authors. Author AA contributes to collect the data and follow up the treatment.

Original Research Article

Received 21st October 2013
Accepted 13th December 2013
Published 24th December 2013

ABSTRACT

Aims: The purpose of this study is to compare the effect of Vit E, B6, omega-3 and calcium on the treatment of this syndrome.

Study Design: A double blind clinical randomized trial study.

Place and Duration of Study: Department of midwifery, of Islamic Azad University, sari, branch Iran. Between March 2012 and October 2012.

Methodology: Two hundred girls with moderate and severe form of premenstrual syndrome were selected randomly and were divided into five groups. Group 1 received 1g of calcium during 7 final days of the cycle for three cycles. Group 2 received 100 mg of Vit E daily for three cycles. Group 3 received 1g of capsule of fish oil for three months. Group 4 received 40 mg of Vit B6 daily for three months. And group 5 received daily one tablet of placebo for three months and also filled Rosignol Bonlender check list during the use of the drugs. Data were analyzed by SPSS software, and severities of symptoms were compared before and after the intervention in each group and after the treatment in all five groups.

Result: Severity of physical, mental and physical and mental symptoms in patients who received Vit E, VitB6, calcium, omega-3 and placebo reduced ($p < 0.05$)

Conclusion: It E, Vit B6, calcium, and omega-3 are effective on PMS.

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Keywords: PMS; Vit E; Vit B6; calcium; omega-3.

1. INTRODUCTION

Premenstrual syndrome (PMS) is a regularly appearing cluster of somatic and psychological symptoms during luteal phase of menstrual cycle and is resolved by the end of menstruation [1-5]. The most common symptoms include breast tenderness, headache, backache, fatigue, clumsiness, tension, anxiety, irritability, depression, food craving, bloating and changes in sexual drive [3,6-10]. Approximately, 80% of women in reproductive age experience these symptoms and 40% of them, to some degree [11-16], experience the effect of these symptoms in their daily lives. Also, 3-9% of women suffer from severe forms of PMS [17-18]. A wide variety of strategies for the treatment of PMS have been proposed. Among them, the usual treatments for mild form of PMS include education, supportive counseling [19] and general self-care measures such as increasing and adopting a helpful diet. For women with severe form of PMS Fluoxetine, anxiolytic drug alprazolam, oral contraceptive, non-steroidal anti-inflammatory drugs, spironolactone and gonadotropin – releasing hormone agonists can be used. these treatments have many side effect, for example; fluoxetine as first line therapy could reduce libido, sleep disorder, alprazolam: drug addiction, oral contraceptive: headache, depression, thrombosis, non-steroidal anti-inflammatory drugs: GI (the digestive system) bleeding and renal complications, spironolactone: spitting, fatigue, abnormal uterine bleeding, gonadotropin – releasing hormone agonists: menopause symptoms [20].

Vit B6 is a factor in final stages of serotonin and dopamine synthesis [21]. Many studies suggested beneficial effects of Vit B6 on PMS treatment [22-23]. Disturbances of calcium regulation may play insignificant role in the path physiological aspect of PMS [21]. Also, reduction in concentration of extracellular calcium can stimulate neuromuscular junctions, irritability and mania. Recent studies demonstrate that calcium can reduce such symptoms as fatigability, changes in appetite and depression [24]. Omega-3 has anti-inflammatory effect and can reduce the pain of PMS by helping reduce inflammation in the body. Moreover, it can reduce physical and social symptoms [25]. Previous researchers demonstrated that VitE caused significant improvements in physical symptoms. Women with PMS do not have biochemical deficiency in Vit E, and their plasma surfaces of vitamin levels are not lower than those of women without PMS [11]. Previous studies investigated the role of each of these drugs in treatment of PMS; but none of them compared these drugs to select the best one.

This study was conducted to compare the effect of calcium, vit B6, vitE, fatty acid omega-3 and placebo on treatment of PMS in Islamic Azad University, sari, branch in 2012.

2. MATERIALS AND METHODS

This study was a double blind clinical trial study for the evaluation of the effect of calcium, Vit E, Vit B6 and omega-3 on premenstrual syndrome treatment. In this study, all female students of Islamic Azad University, sari, branch entered in our study according to the inclusion and exclusion criteria. In this study, they filled Rosignol Bonlender questionnaire for 3 months. This questionnaire was a standard check list to assess the severity of premenstrual syndrome. The validity of this check list demonstrated previously [26]. First section of check list was about physical symptoms and second section was about mental symptoms. The severity of each symptom was characterized with 4 scores (0, 1, 2 and 3). Score 0 means: don't have any symptom, score 1 means: the person have symptoms but

don't any effect on their activity , score 2 means : the symptoms effect on their activity, score 3 means: the symptoms induced disability in their life. We considered sum of severity of physical & mental symptoms, if the mean of this score during 3 months was equal or higher than 17, the intensity of this syndrome was moderate and severe form. In our study, the inclusion criteria were: single girls, age between 18-30 years old, regular menstruation, duration of cycle between 21-35 days and moderate and severe form of premenstrual syndrome according to the standard measurement (Rosignol Bonlender check list) [26]. The exclusion criteria were: breast feeding, use of hormonal contraceptive, having a history of psychological disease such as depression, acute traumatic problem during the last 2 months, using drug such as anti-depression and herbal medicine since six months ago. Two hundred girls who had moderate and severe forms of premenstrual syndrome were selected randomly and were divided into five groups. According to $\alpha=0.2$ (error type 1), $\beta = 0.8$ (error type 2), $p=0.433$, $b=0.2$ and $p<0.05$ (significant level) and power 80% having 31 girls in each group were enough, but for preventing release of samples we decided to include forty girls in each group. The flowchart of this study appears in Fig. 1.

The first group received 1 g of calcium (that was produced by the Osveh Pharmacy-Iran), during 7 final days of the cycle for three cycles. The second group received 100 mg of Vit E (that was produced by the Osveh Pharmacy-Iran) daily for three cycles. The third group received 1g of fish oil capsule (that was produced by the American 21stCentury Company) for three months. The fourth group received 40 mg of Vit B6 (that was produced by the Iranian hormone –Tehran Company) daily for three months and the fifth group received daily one tablet of placebo (starch tablet that was produced by Razi Hospital Pharmacy-Iran) for three months. Also, this group filled Rosignol Bonlender check list during the use of drug. Duration of filling the questionnaire and collecting the data was between March 2012 and October 2012. The samples were visited once a month for being given drug and checking the questionnaires and to make sure if they had filled it correctly or not. Finally, severity of physical symptoms, mental symptoms, and physical and mental symptoms after receiving drug was compared with that of pre-treatment. This clinical trial was accepted by the ethical committee of the University and the consent form was signed by the patients. SPSS 11 software was used for data analysis. For matching groups for quantitative and qualitative variables, ANOVA, chi square, and Kruskal Wallis were carried out respectively. Wilcoxon test was applied for comparing severity of symptoms before and after the treatment in each group. Kruskal Wallis test was used for comparing severity of symptom after the treatment in five groups. (The registration number of this study was: IRCT2012123010705N1).

3. RESULTS AND DISCUSSION

One hundred and fifty five girls who had moderate and severe form of premenstrual syndrome were divided into 5 groups (each group: 31 girls). Mean age of girls who used Vit E was 22.6 ± 2.25 , Vit B6 23.19 ± 2.1 , omega-3 22.7 ± 1.8 , calcium 22.7 ± 2.1 and placebo 22.4 ± 1.9 . These 5 groups did not show any statistically significant differences regarding age ($p= .74$), BMI ($p=.89$), field of education ($p=.64$), level of education ($p=.83$), severity of physical symptoms before treatment ($p=.23$), severity of mental symptom before treatment ($p=.25$) and severity of physical and mental symptom before the intervention ($p =.36$).

Effect these treatments on physical, social, physical and social symptoms are shown in Table 1.

Table 1. Effect these treatments on physical, social, physical and social symptoms

Symptom Group	Social symptom		Physical symptom		Social & physical symptom	
	before	after	before	after	before	after
Vit E	11.26±1.9	10.06±2.09	7.74±1.8	6.23±2.2	19.03±2.41	16.29±3.43
Calcium	11.9±1.77	10.61±1.25	7.52±2.6	6.45±1.6	19.42±3.45	17.32±2.37
Omega-3	11.81±1.93	11.1±2.15	7.35±1.11	6.39±2.15	19.19±2.3	17.10±3.40
Placebo	12.1±2.46	11.48±2.44	7.71±1.21	7.35±1.6	19.81±2.53	18.58±2.46
Vit B6	11.97±2.33	10.74±1.67	7.35±1.17	6.16±1.71	19.48±2.6	16.74±2.16

In the group receiving Vit E, there were statistically meaningful differences after the treatment regarding their physical symptoms ($p=.000$), mental symptoms ($P=.001$) and their physical and mental symptoms ($P=.000$).

In the group receiving Vit B6, there were statistically meaningful differences after the treatment regarding their physical symptoms ($p=.000$), mental symptoms ($P=.000$) and their physical and mental symptoms ($P=.000$).

In the group receiving calcium, there were statistically meaningful differences after the treatment regarding their physical symptoms ($P=.01$), mental symptoms ($P=.001$) and their physical and mental symptoms ($P=.000$).

In the group receiving omega-3, there were statistically meaningful differences after the treatment regarding their physical symptoms ($p=.007$), mental symptoms ($P=.002$) and their physical and mental symptoms ($P=.000$).

In the group receiving placebo, there were statistically meaningful differences after the treatment regarding their physical symptoms ($p=.03$), mental symptoms ($P=.01$) and their physical and mental symptoms ($P=.001$).

According to the results of comparison of symptoms after intervention in five groups, only physical symptom ($p=.03$) and physical and mental symptoms ($p=.02$) were different.

The comparison between two groups regarding physical, physical and mental symptoms are shown in Table 2.

Table 2. Comparison between groups, regarding physical symptoms and physical and mental symptoms of premenstrual syndrome after the intervention

Groups	Physical symptoms P value	Physical and mental symptoms- P value
Vit E- B6	0.007	0.5
Vit E-calcium	0.5	0.2
Vit E-omega-3	0.3	0.4
Vit E-placebo	0.006	0.006
Vit B6-calcium	0.5	0.6
Vit B6-omega-3	0.4	0.9
Vit B6-placebo	0.007	0.008
Omega-e –calcium	0.8	0.6
Calcium –placebo	0.01	0.02
Omega-3-placebo	0.04	0.01

PMS is cyclic recurrence of a group of symptoms that occur in luteal phase. These symptoms are repeated, and if severe degrees of symptoms appear, PMS can interfere with some aspects of lifestyle. About 25 to 50% of women in reproductive age suffer from this disorder monthly [27]. According to similar studies, many confounding variables, such as age, BMI, marriage status, field of education, level of education and place of residency, can affect this syndrome; therefore, we matched these groups along these variables.

In the group receiving Vit E, a significant relationship was found regarding their physical symptom, mental symptom, and physical and mental symptoms after the treatment. A single – blind trial reported that PMS treatment with 400 IU/day can improve physical symptoms [11]. Although Poormohsen reported that more than 50% of women with PMS who took Vit E with calcium experienced less symptom severity, we evaluated the effect of calcium on symptoms and observed the reduction of severity of PMS symptoms. In Poormohsen's study they used calcium and Vit E together, and they did not exactly determine which one was effective. It appears that they should have designed a cross over study. There have been long histories of scientific examinations about the correlation between calcium and menstrual cycle. Women with this syndrome have lower plasma calcium level and if they receive diet containing calcium e.g. 1336 mg/day or take 1200 mg/day calcium carbonate, they will feel improvement in their symptoms [11]. Furthermore, Akhlaghi demonstrated that along with taking calcium 1000 mg/day, 61% of physical and 62% of mental symptom improved [28]. Another study, likewise, confirmed the same effect [24,29].

In the group receiving Vit B6, significant effects were seen regarding their physical, mental and physical and mental symptoms after the treatment. In 1970, a study reported the beneficial effects of Vit B6 on depression. Vit B6 is a cofactor in the synthesis of neurotransmitters and has a significant role in mental symptoms alleviation of PMS [11]. A study done in Iran showed efficacy of Vit B6 on premenstrual symptoms [22]. Another study showed pyridoxine effect of Vit B6 on just emotional symptom of PMS [30]. Differences in doses of VitB6 between this research and our study may have led to different effects of Vit B6 on physical symptoms. In omega-3 group, significant differences were seen after the treatment regarding physical, mental, physical and mental symptoms. Studies performed in Iran showed efficacy of omega-3 in PMS alleviation [25]. In our study the group treated with placebo had significant improvement in severity of symptoms. The placebo effect in reducing the severity of symptoms expressed in other studies(as a placebo effect), even in control group that didn't receive any placebo, just filled the daily checklist reducing the severity of symptoms were seen [31].

In the present study we assessed a collection of physical and social symptoms. It was, of course, better to investigate each symptom (such as: depression, anxiety, headache...) before and after treatment individually. We suggest conducting a study in the future to compare the effect of herbal medicine with the current treatment on PMS.

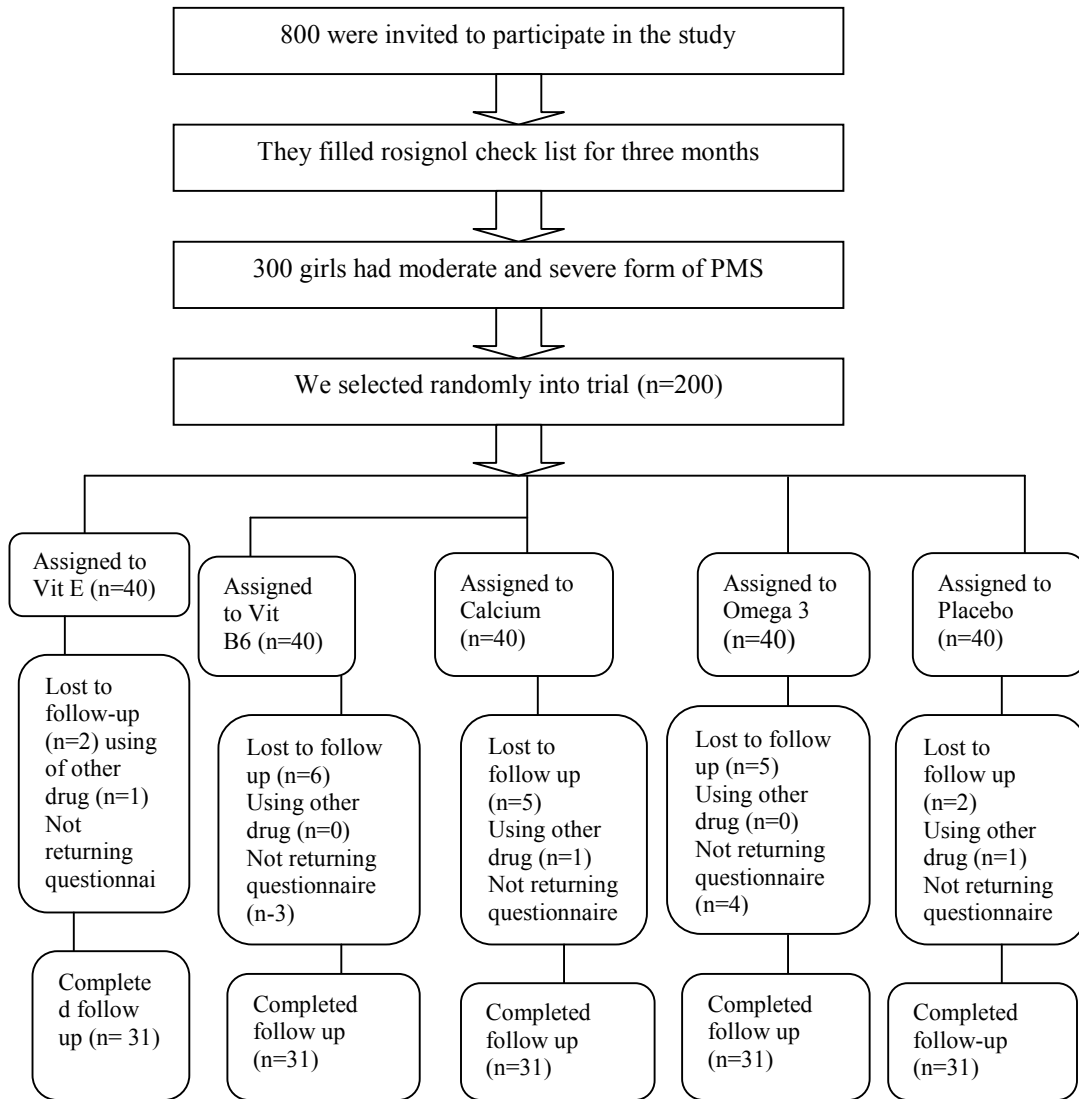


Fig. 1. Flowchart of this study

CONCLUSION

Vit E, Vit B6, calcium and omega-3 are effective treatment on PMS.

CONSENT

The consent form was signed by the patients.

ETHICAL APPROVAL

This clinical trial was accepted by the ethical committee of the Islamic azad University Sari branch. Iran and registered in IRCT.

ACKNOWLEDGEMENTS

We thank all the persons who helped us with this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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