Original Article

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The Effect of Vitagnus on Cyclic Breast Pain in Women of Reproductive Age

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ABSTRACT

BACKGROUND AND OBJECTIVE: One of the most common complaints in women is breast pain associated with reduced women quality of life and a lot of problems and costs. This study aimed to investigate the effect of vitagnus on severity of cyclic mastalgia in women of reproductive age.

METHODS: This study is a triple blind controlled clinical trial performed on 67 women with cyclic mastalgia. Women randomly entered to an intervention group (34 patients) or a placebo (n=33) groups and training and proper nutrition were done. Vitagnus daily was given for three months in the intervention group (8 ml) and eatable paraffin (1 ml) mixed with water and honey (a total of 10 ml) was given to the placebo group. The pain from two months before to three months after treatment with VAS and McGill measuring instruments were compared.

FINDINGS: The mean score of McGill in Vitagnus group decreased from 16.94±3.94 before the intervention to 9.50±5.32 in fifth month and in the placebo group decreased from 15.08±3.62 before the intervention to 13.08±4.29 in fifth month ($p<0.0001$). Mean VAS score in Vitagnus Group decreased from 6.59±3.35 before the intervention to 3.27±2.20 in fifth month and in the placebo group from 5.94±1.32 before the intervention to 4.94±1.81 in the fifth month ($p<0.0001$).

CONCLUSION: The results showed that Vitagnus can be used as an effective and low-cost treatment in the treatment of mastalgia.

KEY WORDS: *Cyclic Mastalgia, Vitagnus, Short Form Mcgill Questionnaire*.

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Introduction

The most common causes of anxiety and refer to health care centers among women is cyclic mastalgia (1). Cyclic mastalgia is defined as premenstrual breast pain and tenderness that usually happens on a regular basis in the luteal phase of the menstrual and disappears with starting of menstruation (2). 70 to 80 percent of women have experienced breast pain in their lifetime, mastalgia is responsible for 47-30% of clinical assessment.

In 15% of cases may be so severe that the patient needs repeated surveys and treatments. Impairment in sexual activity (48%), physical activity (37%), social activities (21%) and work or school activities (8%) also reported that these factors have played a significant role in lowering quality of life (3-5). Breast pain is rarely (5.4%) a symptom of breast cancer, but patients with but patients with unnecessary and multiple medical advice and various diagnostic procedures impose huge financial burden on health care systems (6, 7).

In many cases the cause of mastalgia is unknown, pro-inflammatory cytokines have been proposed as a cause of pain. Hormones, including estrogen and progesterone imbalance and slight increase of prolactin levels might be a possible cause for the symptoms that stimulates breast tissue and breast pain (7). Psychological factors, nutrition, increased levels of monounsaturated fatty acids to saturated polyester, increased sensitivity of receptors, water retention in the body are other cyclical factors of breast pain (3, 9, 8). According to unknown pathophysiology of Mastalgia and interfere with hormonal, nutritional, metabolic, and mental factors the treatment of mastalgia is complicated. History of mastalgia medical treatment included some confusing methods surrounding that the value of these techniques is also doubtful (10).

The most simple non-drug treatment is oral explanation and reassurance to women. known medical treatments for breast pain include analgesics, diuretics, hormone-altering medications, vitamins (including B6, E, etc.), food supplements, mechanical protection, reduction of fat intake and caffeine-derived methylxanthines (2,3). If conservative measures are not effective, other medication options include danazol, tamoxifen, bromocriptine, progesterone and its derivatives are used. Current drugs are associated with many side effects that limit their use (11-3). Several studies on the use of vitamins and herbal medicines in the treatment of mastalgia has been done. The most common and effective treatment are vitamin E and evening primrose (2, 14-12). Too much doses of vitamin E and for long periods are associated with skeletal muscle weakness, headache, pain, fatigue, nausea, diarrhea, abdominal cramps, abnormal gonadal activity, increased serum creatine kinase, total cholesterol, triglycerides, reduced serum thyroxine and triiodothyronine, increased urinary estrogen and androgen, creatinuria, sterile abscess, thrombophlebitis and contact dermatitis (15).

Administration of evening primrose have been reported with allergic and gastrointestinal complications such as difficulty breathing, hives and other skin reactions, however this plant does not grow in Iran (16). Vitagnus is the extract of Vitex agnus which contain flavonoids (casticin, Pandoltin, kriofanol D), alkaloids (viticin, Iridoidsaucubin, Agnuside) and water soluble flavonoids vitexin and Isovitexin.(10).

The exact mechanism of its effectiveness is unproven but seems that by impact on hypothalamic-pituitary axis leads to reducing the release of FSH, prolactin and increases the release of LH from pituitary (17). Another theory is that Vitagnus with inhibition of type 2 dopamine receptors in the pituitary prevents from the release of prolactin and can therefore be effective in the treatment of mastalgia (18). Vitagnus effect on premenstrual syndrome and dysmenorrhea have been more reported compared to mastalgia and its complications (10, 18-25).

But not commonly prescribed in the treatment of breast pain. Because the prescription of Vitagnus is not common in Iran, despite its availability in pharmacies and due to the fact that in previous studies on Vitagnus, pain before the study is not definitive and longitudinally review, as well as in some cases the treatment was only for two months and proper education regarding to use of bra and proper nutrition had not given and also only Visual Analogue Scale tool VAS (Visual) has been used, and most of them were double-blind, in the present study, we tried to confirm absolutely pain for two months and to give the necessary training for use of bras and proper nutrition during this period and then to intervene for three months as triple-blind, as well as with VAS and McGill short form questionnaire to compare the Vitagnus effect with placebo on the levels of cyclic mastalgia at the same in order to if it is effective, Vitagnus could be recommend as a treatment method with more reliability in this field .

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Methods

This three blind randomized control clinical with Clinical Trial Code; IRCT: 201104304785N3 was done on 72 women with cyclic mastalgia referred to the breast cancer Institute of Tehran University after obtaining permission from the ethics committee of Tehran University of Medical Sciences. The number of samples in each group was 30 and due to the long duration of the study, 36 patients were determined by calculating 20% loss. Subjects were randomly assigned to the intervention group (Vitagnus syrup=36) and control (placebo syrup=36 cases).

Written informed consent was obtained from patients. Educated women, ages 49-15 years, with no history of suspicious lesions, malignancies, physical illness, mental and breast surgery, pregnancy and lactation failure, lack of addiction to drugs, alcohol and cigarettes, the VAS 4 and more than 4, not using drugs such as pain killers and anti-inflammatory drugs, etc., for the treatment of mastalgia (two months before the intervention) were enrolled and in case of sensitivity, lack of desire to continue cooperation and regular drug use (more than 2 days and 4 days alternately) as well as in case of severe pain requiring regular consumption of analgesic drug were excluded from study.

The severity of breast pain before intervention in two months and after the intervention to three months by using the VAS tool and Short Form Questionnaire McGill (reliability and validity have proven in studies) (27, 26) were evaluated, the participants at first were trained regarding the appropriate use of Bras, low-fat and low xanthine diet. Then, McGill short questionnaire and VAS tool were trained and provided to assess the type and severity of breast pain. After determining the type and severity of breast pain, they described and recorded their pain scores daily for 2 months and they reported for researchers weekly by phone call. The mean pain intensity and pain was measured in two months. People with minimum score of their pain intensity using visual analogue scale during these two months was 4 and more than 4 were entered interventional stage. Participants randomly selected one of the A and B codes that were given to them in separate boxes. Patients, researchers and statistical analysts were not aware of drugs code (three blind). The pharmacist had determined drugs code, after data collection and end of the study the codes were decoded. The intervention group was prescribed 10 milliliters (two tablespoons) of Vitagnus syrup equal to 60 drops of vitagnus (8 ml) mixed with water and honey (to taste better) (available in pharmacies and used in other studies) (8, 24) and the placebo group 10 ml (two tablespoons) of syrup containing 1 ml of Paraffin oil (available in pharmacies and used in other studies) (28) mixed with water and honey for 3 months (shape and color of glasses were the same).

Drugs were made by the Institute of Medicinal Plants of University of Karaj. During three-month intervention, severity of breast pain was recorded by patients and reported for researchers weekly by phone call. The monthly mean pain was measured and compared with degree of pain before intervention. After collecting the data, comparison of pain intensity were performed at different times. During the study, acute complication was not observed in none of the groups, only in the Vitagnus group 2 patients (one person had flushing and one person had increased bleeding of period) and in the placebo group 3 patients (one patient had intolerance of tasting, one patient had readmission, and one patient had irregular consumption) began to fall out. Finally, we compared the results between 34 people in the intervention group and 33 people in the placebo group, in five times (two months before and three months after intervention). The data were statistically analyzed using SPSS version 18 and chi-square tests, Reapted Meature ANOVA, Green house, Giesier Indepented T-Test and $p<0.05$ was considered significant.

Results

Two groups were matched for age, height, weight, BMI, and were matched for breast pain period. Average score of McGill in Vitagnus group decreased from 16.94±3.94 before the intervention to 9.5±5.32 in the fifth month and in the placebo group decreased from 15.08±3.62 before the intervention to 13.08±4.29 in the fifth month ($p<0.0001$) (table 1). The trend of McGill score in two groups was a downward trend, but the decline or the reduction of pain, was not similar in both groups and the difference between groups was statistically significant, so that in the Vitagnus group, the trend of pain reduction was sharper. From the third month or the first month of intervention until the fifth month of study, prominent decline was seen in the Vitagnus group (Fig 1). Also evaluation of mean VAS score in Vitagnus group showed a decrease from 6.59±1.35 before the intervention to 3.27±2.2 in the fifth month and in the placebo group from 5.94±1.32 before the intervention to 4.94±1.81 which was

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statistically significant (p<0.0001). So that the mean pain severity in the three months after the intervention and in particular the fourth and fifth months in the placebo group was higher than Vitagnus (table 2 and Fig 2) indicating that the palliative effect of Vitagnus was much greater than placebo.

Table 1. Comparison of mean scores of McGill in considered times in Vitagnus (B) and placebo groups.

Time of study(month) group	Before Intervention Mean±SD		After Intervention Mean±SD			P-Repeated meature ANOVA
	First	Second	Third	Forth	Fifth	
Vitagnus	16.94±3.94	16.67±4.20	15.32±3.76	11.92±4.34	9.5±5.32	0.0001
Placebo	15.08±3.62	15.03±3.71	14.52±3.65	13.77±3.95	13.08±4.29	0.0006

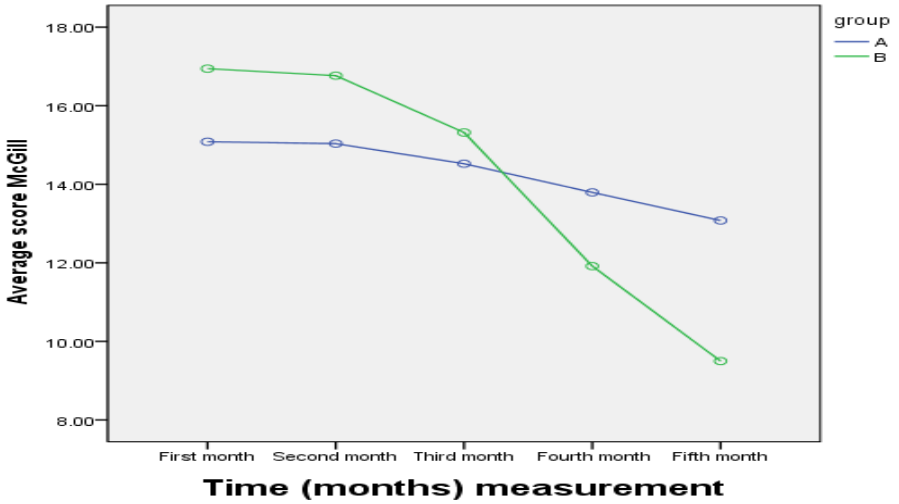


Figure 1. The trend of mean score changes of McGill in studied times in Vitagnus and placebo groups (placebo=A and Vitagnus=B)

Table 2. Comparison of the mean VAS score during the time of study in placebo and Vitagnus groups

Time of study group	first month Mean±SD	Second month Mean±SD	Third month Mean±SD	Forth month Mean±SD	Fifth month Mean±SD
Placebo	5.9±1.32	5.29±1.37	5.64±1.38	5.34±1.57	4.94±1.81
Vitagnus	6.59±1.35	6.35±1.42	5.8±1.35	4.31±1.78	3.27±2.2
Indepented T-Test	0.031	0.045	0.001	0.0001	0.0001

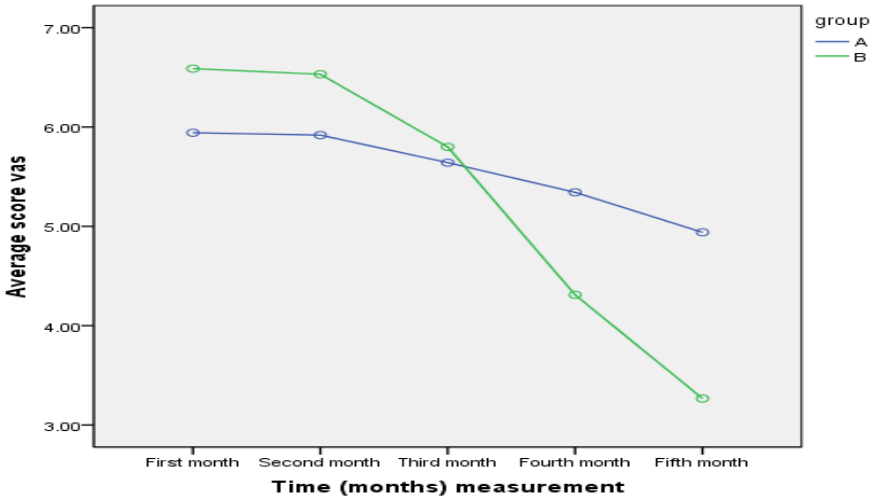


Figure 2. Comparison of average VAS score in the studied times in groups (placebo = A and Vitagnus = B)

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Discussion

The findings of the study showed that Vitagnus in women who use bras and have a good nutrition with moderate to severe breast pain, certainly relieves pain. These findings were obtained using two tools McGill and VAS and after three months of intervention. In the present study, in both groups, a significant decrease in the severity of mastalgia was observed after the intervention than before, but mastalgia reduction in the intervention group compared to the placebo group was higher than the others. Although the reduction of pain in the placebo group was not just similar to intervention group, it could be due to the effectiveness of psychotherapy. Halaska and colleagues in their study on 97 patients concluded that in the group receiving Vitagnus the lower mastalgia was more significant compared to placebo (8).

It is worth noting that although in their study they conducted prescribed Vitagnus for three months, but in the third month than the second month was not observed more reduction in pain.

This may be because they did not train patients for nutrition and also had no control on this. As well as other difference with this study was that they just measured the pain at first until fourth days of each cycle by VAS tool. While in this study the pain in all days was measured and the average was calculated. In study of Sekhavat and colleagues on 117 women with breast pain using the VAS tool indicated that 88/4% of patients responded to Vitagnus and pain was relief compared to 17/7% in placebo group (24). Although the results of this study are similar to the results of their study, the present study has shown the effectiveness of Vitagnus with the primarily two-month control of samples before intervention and also using two tools.

Another point is that in both recent study, loss of samples in the Vitagnus group was mainly due to drug intolerance, while in this study in order to create better tasting, Vitagnus as syrup (mix with honey) was prepared, so attrition in this study was not due to drug intolerance. Two sample loss were due to the flushing and increased bleeding of menstruation which were not side effects of Vitagnus, because patient believe this and unwillingness to continue taking drugs, subjects were excluded. In another study, Seraji and colleagues with comparing VAS pain score before and after the intervention in groups showed that pain intensity compared to before intervention in patients receiving Vitagnus than the other two groups (evening primrose and placebo) significantly reduced (10).

Although the results of our study have shown the effectiveness of Vitagnus compared to placebo, it should be noted that in their study Vitagnus tablet contains 40 mg of active ingredient was administered while patients in the present study received up to 3.5 mg (60 drops) Vitagnus each day.

This suggests that Vitagnus in much smaller amounts and less side effects has its palliative effects in the treatment of mastalgia. Since the results of the above studies indicate palliative effect of Vitagnus in mastalgia and according to the results of this study regarding to effectiveness of Vitagnus using two tools and the final two months of follow-up of patients with moderate to severe mastalgia and the use of bras and proper nutrition during their study and measurement of pain in all days of the monthly cycle, it seems that Vitagnus is effective in the treatment of cyclic mastalgia. Given that Vitagnus Syrups generally has a palliative effect, could be used in combination with other drugs in the treatment of cyclic mastalgia. Use of Vitagnus for the treatment of mastalgia can be an effective, safe and low cost method and in administrated dose of this study could be well tolerated by patients.

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