



**COMPARISON OF THE EFFECT OF RED CLOVER AND PASSION FLOWER
CAPSULES ON SLEEP DISORDERS AMONG POSTMENOPAUSAL WOMEN**

**SIMIN TAAVONI¹, MINA SAFARIAN^{2*}, NEDA NAZEM EKBATANI³, ASHRAFODIN
GOUSHEHGIR⁴, HAMID HAGHANI⁵**

1. M.Sc. in Midwifery and M.Sc. in Medical Education, PhD Student in Medical Education, Faculty of Medicine, Tehran University of Medical Sciences, Researcher and Faculty Member in Iran University of Medical Sciences.

2. Graduate Student of Midwifery, School of Nursing and Midwifery, Tehran University of Medical Sciences.

3. PhD Student in Reproductive Health, Faculty of Medicine, Tehran University of Medical Sciences.

4. Internalist, Research Institute for Islamic & Complementary Medicine, Iran, Islamic Republic of Iran, (RICM, IUMS)

5. PhD student in statistics, Faculty Member of Statistics department, School of Medical Management and Information, Iran University of Medical Sciences

*** Corresponding Author: E Mail: neda40012@gmail.com**

ABSTRACT

Sleep disorders are common problem for postmenopausal women that can affect their quality of life. To overcome this problem, there are some remedy that are used for postmenopausal women. Among non-hormonal and complementary therapy, herbal remedies and between plants, phytoestrogenal plants have a special place. Therefore, this study was performed to evaluate the efficacy of oral capsules of red clover on sleep disorders in postmenopausal women. This study was a randomized, triple blind and clinical trial performed on 80 postmenopausal women referred to Tehran general hospital in 2014. Participants were assigned in one of two groups of red clover and placebo by simple randomly sampling. Each participant used 2 capsules per day

for 1 month. All women were evaluated after 1 month. The data collection tool was a questionnaire. The results showed that mean score of sleep disorders before the intervention in red clover group was 11.62 ± 1.98 and in placebo group 11.47 ± 2.17 . The T- test showed that there was no significant differences between the groups in terms of sleep disturbance score before the intervention. The T- test showed significant differences between the groups in terms of sleep disturbance score one month after the intervention ($P= 0.027$). The use of oral capsules of red clover and placebo could improve sleep disturbance score in two groups. Red clover impact on improving sleep disturbance is greater than placebo. So, we can use red clover to improve sleep disorders in postmenopausal women.

Keywords: Postmenopausal, Sleep disturbances, Red clover

INTRODUCTION

Menopause is a natural stage of a woman's life, but is associated with symptoms such as neurological disorders, vasomotor, urogenital disorders and sleep disorders that the onset of these symptoms can affect the quality of women's life. Menopausal age is between 50 to 51 years in most countries (1). Due to increased life expectancy, also high population of women at this period, knowing the symptoms of menopause and its prevention and treatment is of special importance (2).

On the other hand, one of the disorders which occurs with increased age is sleep disturbance. Sleep is one of the necessities of life, as human allocate about a third of their life to sleeping (3). Increased age is the most important reason of the increased prevalence of sleep disorders. Sleep disorders have been greatly affected by gender that these problems are most

observed during pregnancy and menopause (4). Lack of sleeping has a major negative impact on quality of life (5). Lack of sleeping significantly decreases the daily performance in terms of emotional, social, and physical aspects. Chronic lack of sleeping may prone the postmenopausal women to moodiness, increased depression and anxiety disorders. It may also cause daytime sleepiness, impaired attention and memory consumption of hypnotic drugs (6). This is most common during postmenopausal period, so that Novi et al. in their study showed that 68% of postmenopausal women are suffering from sleep disorders. Taavoni et al. concluded that 75% of women are complicated by lack of sleeping (7). In other study, Taavoni and colleagues concluded that 70% of postmenopausal women in West of Tehran suffered from sleep disorders (8). Due to the

mentioned frequency for sleep disorder and a high population of these women in the country, because according to the statistics of Iran in 2006, the population of women aged 40 to 65 years old has been 5,854,763 (9), there is need to do more researches in this field.

Different treatments are used to solve the problem of sleep disorders for postpostmenopausal women. Prior to 2002, hormone therapy was considered as the first choice to relieve the symptoms of menopause. But with publication of the results of women's health pioneers center about the possibility of increased risk of the diseases such as endometrial cancer, ovarian cancer, breast cancer and thromboembolic disease, although today the above results are completely unacceptable, but has led to the decreased recommendation by some doctors (10). On the other hand, 10% of postmenopausal women due to medical conditions such as hypertension and diabetes are contraindicated to use these drugs (11). According to the above issues in recent decades, the use of alternative and complementary treatments has been somewhat extended (12).

Among alternative and non-hormonal treatments, plant therapy and among plants, phytoestrogens plants (containing estrogen-like compounds) have a special status and

have been recommended for the treatment of postmenopausal symptoms (1). phytoestrogens are estrogen-like compounds found in plant products (13). A variety of phytoestrogens include aloe vera, valerian, lavender, mimosa, chamomile, licorice, five fingers, soya, lemon balm, Jinseng, hops, passion flower, and red clover (14).

In terms of Iran traditional medicine, red clover has anti-cancer, anti-seizure effects, cleaning blood and removing the problems such as cough, asthma, muscular pains, swelling of the skin, itching, arthritis, rheumatism and swollen testicles and is used in different methods (15). In a study conducted by Luis and colleagues that was performed to evaluate the effects of red clover on postmenopausal symptoms with daily administration of 80 mg of red clover on two times concluded that red clover has significant effect in reducing postmenopausal symptoms including sleep disorder (16). While in the study performed by Stacie and Geller, sleep disorder in postpostmenopausal women was evaluated using the Pittsburgh Sleep Disorder Tool and with administration of red clover concluded that the plant has no significant impact on the treatment of sleep disorders in postpostmenopausal women (17). Taavoni and colleagues also performed a study with aim to evaluate the effect of red clover on

postmenopausal symptoms and they came to the conclusion that although the use of red clover had resulted in a significant reduction in postmenopausal symptoms, but had no effect on sleep disorders, as well as didn't cause any complication in the consumers (8).

Considering the above, and since there are conflicting results of various studies about the effectiveness of red clover plants that are

Materials and Methods

This triple blind clinical trial was performed on 80 postmenopausal women aged 50-60 years suffered from sleep disorders referred Jame hospital, Tehran University of Medical Sciences during 2014-2015. This study was conducted with the approval of the ethics committee of Tehran University of Medical Sciences. A written informed consent was obtained from the participants of the study. With evaluation of Petersburg sleep disorder questionnaire, the women who obtained the score ≥ 5 were identified until the samples were reached to 80 cases. At the next stage that was the intervention stage, the samples were randomly divided into two groups of 40 cases, including one test group and one control group, so that at the beginning of entrance, code of 1, 2 was given to each one.

native to Iran, and sleep disorders are common at this time that have negative impact on quality of life in postmenopausal women; also, since so far no study is recorded about the effectiveness of this plant in this field in Iran, it seems necessary to perform a study using this plant to evaluate their effectiveness on sleep disorders in postmenopausal women.

The capsules which the pharmacist was only aware from their contents up to the end of analysis were distributed as the same forms, so that the test group received oral tablet containing 40 mg of red clover leaf and the placebo group, 40 mg oral capsules containing starch. So that, the consumption of capsules was two capsules daily (morning and night) for one month. To monitor the consumption, checklist of drug consumption was given to complete during usage.

The researcher controlled the correct use of capsules by phone call each week. Although oral administration of this plant has no side effects, but the women were asked to follow up any problems and the researchers have to be informed. In the third stage which took place one month after the intervention, the subjects were again asked to refer to the center and to complete the Petersburg sleep disturbance questionnaire. For those who

participated in this study, at the end of the study, breast exam was performed for free as a reward. It should be mentioned that the research group, samples and the person who analyzed the data were not aware of the contents of the capsule until the end of analysis, so the study was triple blind research.

Inclusion criteria were volunteers female without known disease who had passed the postmenopausal age and have not gone through menopause due to surgery, no use of tobacco, narcotics and alcohol, no use of any hormonal drugs, and body mass index < 28. Exclusion criteria included the occurrence of any physical or mental illness during the study which cause sleep disorder, significant change of condition affecting sleep as unpredictable situations such as travel, change in life' location, the occurrence of any crisis during the research process, including the death of relatives, divorce, etc. as well as any adverse event during the study which cause sleep disorder or exacerbates it.

Instruments used in this study included: Demographic questionnaire including 16 questions and Pittsburg Sleep Quality Index (PSQI). This questionnaire evaluated the sleep disorder during the past one month and consisted of 9 items, so that the questions of 1-4 were open, short, single answer and

question No. 5 (with 10 sub-questions) and the questions of 6-8 were as four answers and were scored in one of the options of never (score 0), less than once a week (score 1), one or two times a week (score 2), three or more a week (score 3). Question No. 9 was set as response to the options of very good (score 0), relatively good (score 1), relatively bad (score 2) and very bad (score 3).

Totally, the questionnaire was consisted of seven areas of the person general description of the sleep quality, the delay in going to work, actual sleep duration, sleep efficiency including the actual sleep duration of total time spent in bed, sleep disorders (sleep fragmentation), the hypnotic drugs consumption and daily performance as degradation problems caused by lack of sleep. After final scoring, obtaining the score of ≥ 5 indicated sleep disorder.

Reliability of the questionnaire was tested in different studies. So that, in the study conducted at Tehran School of Nursing and Midwifery by Malekzadegan et al. (23), test-retest was used to determine its reliability and correlation coefficient of $r=0.84$ was obtained. In another study performed by Nassiri Ziba and colleagues (24), correlation coefficient of $r=0.87$ was mentioned.

One month after the intervention, Pittsburgh questionnaire was again completed by the

experimental and control groups. Data was analyzed using SPSS software (version 14) and descriptive and inferential statistics (paired t-test, independent t). $P < 0.05$ was considered significant.

Results

The mean age of women in red clover group was 55.05 ± 2.90 years and in control group, 54.30 ± 3.19 years. The mean age of menopause in red clover group was 49.27 ± 2.07 years, and in control group, 49.15 ± 1.14 years. Other features of the subjects were described in table 1.

One month after the intervention, it was showed that 55.7% of women consumers of red clover and only 55% of the placebo

group showed improvement in their sleep status. So that, their sleep disturbance score decreased at least 5 points that the difference was statistically significant ($P = 0.027$).

The mean score of sleep disorders in red clover group before and one month after the intervention was 11.62 ± 1.98 , 8.10 ± 2.55 respectively that the difference observed in this group was also statistically significant. (Table 2).

Table 1: Demographic characteristics of two groups of red clover and placebo

Demographic characteristics		Placebo N (%)	Red clover N (%)
Age (yrs)	50-54	(65)26	(52.5)21
	55-59	(32.5)13	(47.5)19
	≥ 60	(2.5)1	(0)0
Menopausal age (yrs)	47-45	(10)4	(17.5)7
	48-50	(80)32	(50)20
	51-55	(10)4	(32.5)13
Educational level	Illiterate	(22.5)9	(10)4
	Elementary	(32.5)13	(32.5)13
	Secondary	(42.5)17	(57.5)23
	High school and college	(2.5)1	(0)0
Job status	Household	(82.5)33	(77.5)31
	Employed	(17.5)7	(22.5)9
Marital status	Single	(10)4	(5)2
	Married	(60)24	(67.5)27

	Widow	(30)12	(22.5)11
Parity	0-3	(14.3)5	(10.8)4
	4-6	(62.9)22	(45.9)17
	7-9	(22.9)8	(43.2)16
Gravity	0-3	(16.7)6	(15.8)6
	4-6	(27.3)26	(63.2)24
	7-9	(11.1)4	(21.1)8
Number of married children	0-3	(38.9)14	(34/2)13
	4-6	(58.3)21	(63/3)24
	7-9	(2.8)1	(2/6)1
Number of family members	0-1	(0)0	(7.5)3
	2-3	(55.6)20	(47.5)19
	4-5	(38.9)14	(27.5)11
	6-7	(5.6)2	(17.5)7

Table 2: The distribution of mean score of sleep disorders before and after the intervention among the subjects in two group.

Groups Time	Placebo		Red clover	
	Mean	SD	Mean	SD
Before the intervention	11.47	2.17	11.62	1.98
One month after the intervention	9.12	2.25	8.1	2.55
T-test analyse	$T=1.12$		$F=3.73$	
	$pvalue:0.02$			

DISCUSSION

This study showed that red clover significantly reduced sleep disturbances in postmenopausal women.

The study of Luise and Hidalgo (16) was performed on 60 patients with a daily intake of 80 mg of red clover for 90 days, the results showed that red clover isoflavones significantly decrease postmenopausal symptoms including sleep disturbance ($P<0.05$). In contrast, the study of Stacie and Geller (17) performed on 80 cases, they

evaluated the results from taking medication at 3, 6, 9 and 12 after the intervention, the results showed that black cohosh and red clover had no significant impact in reducing the symptoms of menopause such as not sleeping compared with medroxyprogesterone acetate. The study of Taavoni et al.(2013) demonstrates that only massage and aromatherapy massage can improve sleep problem in postmenopausal women(18).

The study of Ngan and Condui (20) which was conducted on 82 people, they received daily decoction of 2 g red clover as tea for one week. The results showed that red clover leads to a significant increase in sleep quality and improved all the criteria that were evaluated in this study. The study off Fahami F. et al (25) was performed on 59 postmenopausal women. The samples were randomly divided into two group of Hypericum (30 cases) and red clover (29 cases). In this study, 160 mg tablets of Hypericum 3 times a day and red clover drops 3 times a day (10 drops) and 30 drops before bedtime were used. The results of this study showed that red clover and Hypericum had a significant effect in reducing postmenopausal symptoms including sleep.

CONCLUSION

The main findings of this study showed that oral capsules of red clover improve sleep disturbances in postmenopausal women.

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