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Nadia Khalaf Atia [(1)]

Israa H Abid Al-Karim[(2)]

(1) Ministry of Health, Salahuddin Health Department, Iraq

(2) Department of Obstetrics and Gynecology, College of Medicine, University of Tikrit. Iraq

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Flaxseed effect on Menopausal Symptoms and Quality of Life

ABSTRACT

Flaxseed has the highest concentration of lignan, which is one of the major phytoestrogen groups. Lignan has non-hormonal effects in addition to its estrogenic and anti-estrogenic properties. The improvement of the symptoms of premenstrual syndrome are one of the indications of this plant, therefore this study aimed to determine the effects of using flaxseed throughout the menopausal period on women's menopausal symptoms and quality of life.

Patients and Methods:

double blind clinical trial done in Salahadeen general hospital/ gynecology outpatient clinic 1st January to 15th July 2021, including convenient sample of 60 menopause women divided into 3 groups: Intervention group receive 5 g of flaxseed daily (20 patient) group A. HRT group receive 2 mg of estradiol hemihydrate + 1 mg of norethindrone acetate (20 patient) group B. And Control group who did not receive any medical or complementary treatment (20 patients) group C. All 3 groups followed for 3 months.

Results:

Flaxseed had significant effect in decreasing the total MRS with mean (-4.5) score after treatment in comparison to (-6) of hormonal therapy and (4.5) in control group, its effect is lower than the hormonal therapy but had good effect. In the post treatment there were significant higher mean total physical SF-36 score among group A (44.98 ± 7.58), and B (40.7 ± 6.46) than group C (30.8 ± 3.92).

Conclusions:

flaxseed had significant positive effect in reducing the postmenopausal symptoms and had good effect in improving the quality of life among menopause women.

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*Corresponding author E mail : nadiaalakedy00@gmail.com

Introduction:

The symptoms of menopause are reflected not only in the female genital tract but also in the skeletal, cardiovascular and psychological system. With increasing life expectancy, women are likely to face long periods of menopause accounting to approximately one-third of their age. This has resulted in higher burden of morbidities.[1] Menopause, with its signs and symptoms, occurs at a time in a woman's life when she is often actively engaged in family upbringing and/or handling a full-time job, during which time she might also have the responsibility of caring for ageing parents. Women are often puzzled by the remarkable changes in mood, sleep patterns, memory and body shape that occur, as well as the onset of vasomotor and urogenital symptoms. [2] As menopausal symptoms can be very distressing and considerably affect a woman's personal and social life, health-care providers caring for women at all levels of the health care system must be well prepared to guide patients through this transition and provide advice to improve quality of life [3]. Flaxseed has the highest concentration of lignan, which is one of the major phytoestrogen groups. Lignan has non-hormonal effects in addition to its estrogenic and anti-estrogenic properties. [4, 5] The improvement of the symptoms of premenstrual syndrome is one of the indications of this plant. The aim of this study is to determine the effects of using flaxseed throughout the menopausal period on women's menopausal symptoms and quality of life.

Patients and Methods: Prospective Cohort study design was adopted, double blind clinical trail done in Salahadeen general hospital/ gynecology outpatient clinic 1st January to 15th July 2021, using convenient sample of 60 menopause women divided into 3 groups: Intervention group receive 5 g of flaxseed daily (20 patient) group A. HRT group receive 2 mg of estradiol hemihydrate + 1 mg of norethindrone acetate (20 patient) group B. And

Control group who did not receive any medical or complementary treatment (20 patients) group C. All 3 groups followed for 3 months. Data collected using: (1) questionnaire for demographic and general characteristics if the patient, (2) Menopause Rating Scale for symptoms assessment , and (3) SF-36 Quality-of-Life Scale.

Results

The distribution of the study groups show non- significant difference between groups regarding age, age at menopause, marital status and body mass index, as shown in table 3.1. This similarity between study groups rollouts the selection bias. Regarding the general characteristics among the whole sample, most of the menopause women were aged 56-60 years 28(46.7%), followed by 51-55 years 18(30%). The mean age at menopause as reported by the menopause women was 46.8 ± 4.6 years. The marital status show that the commonest marital status was married 36 (60%), followed by widow 17 (28.3%). The commonest BMI was (30-39.9 Kg/m ^{2}) which defined as obese 25 (41.7%), as shown in table 1.

Table 3.1. The general characteristics of menopausal women according to study groups.

General characteristics	Group A No.(%)	Group B No.(%)	Group C No.(%)	Total No.(%)	P value
Age (years)					0.6 >0.05
46 - 50	4(20%)	6(30%)	4(20%)	14(23.3%)	
51 - 55	7(35%)	5(25%)	6(30%)	18(30%)	
56 - 60	9(45%)	9(45%)	10(50%)	28(46.7%)	
age at menopause (years) mean ±SD	47.6± 3.9	46.9±4.2	47.3±4.4	46.8 ± 4.6	0.8>0.05
marital status					0.8 >0.05
Unmarried	1(5%)	1(5%)	0(0%)	2(3.3%)	

Married	12(60%)	11(55%)	13(65%)	36(60%)	
Widow	6(30%)	5(25%)	6(30%)	17(28.3%)	
Divorced	1(5%)	3(15%)	1(5%)	5(8.3%)	
BMI					
18.5-24.9 Kg/m ^{2} (Normal)	6(30%)	4(20%)	6(30%)	16(26.7%)	0.9 >0.05
25-29.9 Kg/m ^{2} (Overweight)	5(25%)	5(25%)	4(20%)	14(23.3%)	
30-39.9 Kg/m ^{2} (Obese)	8(40%)	8(40%)	9(45%)	25(41.7%)	
≥ 40 Kg/m ^{2} (Extreme obesity)	1(5%)	3(15%)	1(5%)	5(8.3%)	
Total	20(100%)	20(100%)	20(100%)	60 (100%)	

There was no significant difference between mean total MRS among study groups A, B, C in pretreatment visit (21.20 ± 10.46), (22.7± 9.64), (18.65± 7.04), respectively while in the post treatment there were significant lower mean total MRS score among group A (16.6 ±10.22), and B (16.7 ± 9.87) than group C (23.15 ± 6.51), as shown in table 3.2. To measure the difference in score among each group paired t test used; there were significant difference in mean in post treatment visit than the pretreatment visit in group A (21.20 ± 10.46), (16.6 ±10.22), respectively the mean score change was (- 4.6). There were significant difference in mean total MRS in post treatment visit than the pretreatment visit in group B (22.7± 9.64), (16.7 ± 9.87) respectively the mean score change was (- 6). While in group C there was significant increase in mean total MRS score in the post treatment visit (23.15 ± 6.51), than pretreatment visit (18.65± 7.04), with mean increase of (4.5) scores, as shown in table 3.2.

Table.2. Mean total Score of the Menopause Rating Scale in pre & post treatment

MRS according to visit	group A		group B		group C		ANOVA P value
	Mean	SD	Mean	SD	Mean	SD	
pre treatment	21.20	10.46	22.70	9.64	18.65	7.04	> 0.05
post treatment	16.60	10.22	16.70	9.87	23.15	6.51	< 0.05
Mean difference (post treatment mean– pretreatment mean)	-4.6		-6		4.5		
Paired t- test p value	< 0.05		< 0.05		< 0.05		

SD; standard deviation , ANOVA; analysis of variance

There was no significant difference between mean total physical SF-36 among study groups A, B, C in pretreatment visit (39.5± 6.5), (36.8± 5.87), (36.28± 5.91), respectively while in the post treatment there were significant higher mean total physical SF-36 score among group A (44.98 ± 7.58), and B (40.7 ± 6.46) than group C (30.8 ± 3.92), as shown in table 3.3. There was significant increase in mean in post treatment visit than the pretreatment visit in group A (44.98 ± 7.58), (39.5± 6.5), respectively the mean score change was (5.48). There was significant difference in mean in post treatment visit than the pretreatment visit in group B (40.7 ± 6.46), (36.8± 5.87), respectively the mean score change was (3.9).

While in group C there was significant decrease in mean total physical SF-36 score in the post treatment visit (30.8 ± 3.92), than pretreatment visit (36.28±

5.91),with mean increase of (-5.84) scores, as shown in table 3.3

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Table 3 Mean physical health SF-36 Score in pre and post treatment among study groups

physical SF-36 score according to visit	group A		group B		group C		ANOVA P value
	Mean	SD	Mean	SD	Mean	SD	
pre treatment	39.5	6.5	36.8	5.87	36.28	5.91	> 0.05
post treatment	44.98	7.58	40.7	6.46	30.8	3.92	< 0.05
Mean difference (post treatment - pretreatment	5.48		3.9		-5.84		
Paired t test p value	< 0.05		< 0.05		< 0.05		

SD; standard deviation, ANOVA; analysis of variance

There was no significant difference between mean total mental health SF-36 among study groups A, B, C in pretreatment visit (40.2± 7.4), (40.1± 4.01), (38.35± 5.38), respectively while in the post treatment there were significant higher mean total mental health SF-36 score among group A (42.6 ± 4.3), and B (41.2 ± 3.93) than group C (36.25 ± 3.75), as shown in table 4. There was significant increase in mean score in post treatment visit than the pretreatment visit in group A (42.6 ± 4.3), (40.2± 7.4), respectively the mean score change was (2.4). There was significant difference in mean in post treatment visit than the pretreatment visit in group B (41.2 ± 3.93), (40.1± 4.01), respectively the mean score change was (1.1). While in group C there was significant decrease in mean total mental health SF-36 score in the post treatment visit (36.25 ± 3.75), than pretreatment visit (38.35±

5.38), with mean decrease of (-2.1) scores, as shown in table 4.

Table 4. The mean mental health Score in pre and post treatment among study groups

Mental health SF-36 score according to visit	group A flaxseed		group B hormonal		group C control no treatment		ANOVA P value
	Mean	SD	Mean	SD	Mean	SD	
pre treatment	40.2	4.7	40.1	4.01	38.35	5.38	> 0.05
post treatment	42.6	4.3	41.2	3.93	36.25	3.75	< 0.05
Mean difference (post treatment - pretreatment	2.4		1.1		-2.1		
Paired t test p value	< 0.05		< 0.05		< 0.05		

SD; slandered deviation, ANOVA; analysis of variance

Abdominal pain was reported among 1(5%), 1(5%), 2(10%) of the group A,B, and C, this relation was statistically not significant as shown in table 3.5. moderate abdominal distension reported among 1(5%),0(0%), and 0(0%) of the group A,B, and C, this relation was statistically not significant as shown in table 3.5. diarrhea was reported among 3(15%), 2(10%), 2(10%) of the group A,B,and C, this relation was statistically not significant as shown in table 3.4. Flatulence was reported among 7(35%), 4(20%), 5(25%) of the group A, B, and C, this relation was statistically not significant as shown in table 5. Nausea and pain was reported among 1(5%), and 3(15%), of the group A, B, and C, this relation was statistically not significant as shown in table 5.

Table 5. The side effect among the study groups

	group A flaxseed		group B hormonal		group C control		P value
	No.	%	No.	%	No.	%	
Abdominal pain							> 0.05
NO	19	95.00%	19	95.00%	18	90.00%	
Yes	1	5.00%	1	5.00%	2	10.00%	
Abdominal distension							> 0.05
No	18	90.00%	19	95.00%	18	90.00%	
Mild	1	5.00%	1	5.00%	2	10.00%	
Moderate	1	5.00%	0	0.00%	0	0.00%	
diarrhea							> 0.05
No	17	85.00%	18	90.00%	18	90.00%	
Yes	3	15.00%	2	10.00%	2	10.00%	
Flatulence							> 0.05
No	13	65.0%	16	80.0%	15	75.0%	
Yes	7	35.0%	4	20.0%	5	25.0%	
Nausea							> 0.05
No	19	95.00%	17	85.00%	19	95.00%	
Yes	1	5.00%	3	15.00%	1	5.00%	

Discussion:

After treatment for 3 months there were significant lower mean total MRS score among group flaxseed group (16.6 ±10.22), and hormonal therapy group (16.7 ± 9.87) than group control (23.15 ± 6.51), also significant deference within the group in comparison to the baseline score. This goes with Cetisli NE et al 2015 in Turkey [6] who found

significant decrease in MRS score after treatment with 5 g of flaxseed for 3 months. Udani, J.K etb al 2013[7] found that reduction in the mean number of weekly hot flashes, & severity of hot flushes. Pruthi S et al 2012 [8] found that mean score of hot flash was reduced 4.9 score in the flaxseed group compared to 3.5 in the placebo group. Colli MC et al 2012 [9] found that the Kupperman index decreased from (10.23 ± 4.38) at baseline to (7.18 ± 3.30) after 6 month of flaxseed meal and the hot flashes intensity decreased from (4.54 ± 3.14) at basline to (3.50 ± 2.06) after 6 months. Lewis JE et al 2006 [10] found a significant decrease in the severity of hot flashes for those on flaxseed. In contrast of our finding a study by Simbalista et al 2010 [11], found no differences between the control group and the experimental group (to whom 25 g of flaxseed per day was given for 12 weeks). [11] The effect of flaxseed may be explained by the fact that estrogenic action of certain metabolites of flaxseed suggested a potentially positive effect on these post-menopausal symptoms. In a study of 140 postmenopausal women, menopausal symptoms decreased and the quality of life increased in women who ingested a flaxseed supplemented diet [12]

In the post treatment there were significant higher mean total physical SF-36 score among group A (44.98 ± 7.58), and B (40.7 ± 6.46) than group C (30.8 ± 3.92). Also there is significant increase in mean score in post treatment visit than the pretreatment visit in group A (44.98 ± 7.58), (39.5± 6.5), respectively the mean score change was (5.48). This goes with Cetisli NE *et al* 2015 in Turkey [6] who found significant increase in physical quality score after treatment with 5 g of flaxseed for 3 months from (38.93 ± 8.53) to (49.00 ± 8.55), also in HRT group it decreased from (37.29 ± 5.98) to (34.65 ± 6.71) while in control it was decreased from (34.94 ± 6.15) to (33.82 ± 5.29). Dodin, S *et al* 2013 [13] found that flaxseed group had decreased in impairment of quality of life −0.23 ±

0.62 score while control group decreased by −0.14 ± 0.58. Sun N, *et al* 2018 [14] found that menopausal symptoms decreased the quality of life. This may be explained by findings of Zhang *et al*. (2012) [15] that androgen replacement not only improves androgen deficiency associated symptoms, but enhances comprehensive improvement in psychological issues and health related quality of life. Sourinejad H, et al 2019 [16] found that flaxseed has a positive effect on the improvement of symptoms of menopause and hot flashes. It reduces the risk of breast cancer and improves cyclic mastalgia and premenstrual syndrome.

There was significant increase in mental score in the post treatment among group A (42.6 ± 4.3), and B (41.2 ± 3.93) and is more than group C (36.25 ± 3.75). There was significant increase in mean in post treatment visit than the pretreatment visit in group A (42.6 ± 4.3), (40.2± 7.4), respectively the mean score change was (2.4). There was significant difference in mean in post treatment visit than the pretreatment visit in group B (41.2 ± 3.93), (40.1± 4.01), respectively the mean score change was (1.1).

While in group C there was significant decrease in mean total Mental health SF-36 score in the post treatment visit (36.25 ± 3.75), than pretreatment visit (38.35± 5.38), with mean decrease of (-2.1) scores. This goes with Cetisli NE et al 2015 in Turkey [6] who found significant increase in mental quality score after treatment with 5 g of flaxseed for 3 months from (40.63 ± 8.01) to (42.39 ± 5.00), also in HRT group it increased from (40.02 ± 6.62) to (41.13 ± 7.08) while in control it was decreased from (41.37 ± 6.99) to (39.29 ± 7.18).

El Tanbouly et al 2017 [17] confirmed the efficacy of flaxseed oil in alleviating biochemical changes associated with postpartum depression, which is considered a predisposing factor for menopause related depression , the study done on rat model . Linolenic acid is an essential omega-3 fatty acid; it is essential for

normal cell function. Dietary sources of alpha-LA are nuts, vegetable oils, flaxseed oil, and soybean oil. [18] Different mechanisms of action and theories had been proposed for the role of Linolenic acid to improve depression. One of them, Linolenic acid can cross the blood brain barrier and interrelate with mood related molecules inside the brain. Another theory, Linolenic acid has anti-inflammatory actions that may help in relieving depression. Meta-analyses studies suggested that the omega-3 fatty acids were effectives, but reabilities of these researches are controversial, because of variability between doses and ratios of eicosapentaenoic acid to docosahexaenoic acid [19] . Depressed women who are overweight and have elevated inflammatory markers are good candidates for omega-3 fatty acid supplement [20]

Conclusions: flaxseed had significant positive effect in reducing the postmenopausal symptoms and had good effect in improving the quality of life among menopause women.

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