The Effect of Evening Primrose Oil and Soybean Oil on Menopausal Symptoms and Biochemical Parameters in Iraqi Postmenopausal Women: A Comparative Study.

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Abstract:

Background: Medicinal herbs as alternative therapies, commonly used to treat menopausal symptoms, and some studies have shown that they can be useful in treating menopausal syndrome, which have been linked to worse self-rated health, and decreased work productivity.

Aim of the study: This study compared the effectiveness of Evening Primrose Oil (EPO) and Soybean Oil herbal supplement in a sample of Iraqi postmenopausal women on treatment satisfaction and their quality of life.

Patients and methods: This prospective, randomized controlled, open-label clinical study was conducted on (40) post-menopausal women. The participants were divided into two groups randomly. The first group (G1, N=20) received 500 mg EPO/day while the second group (G2, N=20) received 233 mg soybean oil extract/day. The duration of treatment was 8 weeks for both groups. The subjective and clinical assessments of Menopause Symptom Treatment Satisfaction, and Menopause-Specific Quality of Life, which evaluated at baseline and after 2 months of treatment. Data was collected by the researcher via face-to-face interviews with women at baseline and after 2 months of treatment.

Results: In this study, Menopause Symptoms Treatment Satisfaction score was not significant within each group post treatment ($P>0.05$). While after 2 months of treatment, EPO significantly improved the quality of life by decreasing all MEN-QoL domains more than soybean oil, except for the sexual domain ($P<0.01$).

Conclusions: This study revealed that EPO and soya bean oil supplements had the beneficial effect of improving the postmenopausal quality of life with less treatment satisfaction.

Key words: Postmenopausal related symptoms, Evening primrose oil, Soybean Oil, MS-TSQ, MEN-QoL

تأثير زيت زهرة الربيع وزيت الصويا على أعراض سن اليأس والمتغيرات البيوكيميائية عند النساء العراقيات: دراسة مقارنة

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الخلاصة:

الخلفية: الأعشاب الطبية كعلاجات بديلة، التي يشيع استخدامها لعلاج أعراض انقطاع الطمث، وقد أظهرت بعض الدراسات أنها يمكن أن تكون مفيدة في علاج متلازمة انقطاع الطمث، والتي ارتبطت بتدهور انخفاض تقدير الذات، وانخفاض إنتاجية العمل.

الهدف من الدراسة: قارنت هذه الدراسة فعالية المكملات العشبية EPO وزيت فول الصويا في عينة من النساء العراقيات بعد سن اليأس على الرضا عن العلاج ونوعية الحياة.

طرق العمل: أجريت هذه الدراسة السريرية المرتقبة العشوائية المفتوحة التسمية على (40) امرأة بعد انقطاع الطمث. تم تقسيم المشاركين إلى مجموعتين بشكل عشوائي. تلقت المجموعة الأولى (G) (20=G1, N) 500 ملغم EPO / يوم بينما تلقت المجموعة الثانية (20=G2, N) 233 ملغم مستخلص زيت فول الصويا / يوم. كانت مدة العلاج 8 أسابيع لكلا المجموعتين. تم تقييم الرضا عن علاج أعراض انقطاع الطمث، ونوعية الحياة الخاصة بانقطاع الطمث في البدء وبعد شهرين من العلاج. تم جمع البيانات من قبل الباحث عن طريق المقابلات وجها لوجه مع النساء في البدء وبعد شهرين من العلاج.

النتائج: في هذه الدراسة، لم تكن درجة الرضا عن علاج أعراض انقطاع الطمث مهمة في كل مجموعة بعد العلاج (P<0.05). بينما بعد شهرين من العلاج، قامEPO بتحسين نوعية الحياة بشكل كبير من خلال تقليل جميع مجالاتMEN QoL أكثر من زيت فول الصويا، باستثناء المجال الجنسي (P<0.01).

الاستنتاجات: بحسب النتائج، أنه بعد شهرين من الاستخدام، كان هناك تغيير ذو قيمة إحصائية للدرجة الإجمالية لـ -MEN QoL بينما لم يكن هنالك تغيير ذات قيمة إحصائية فيما يخص الدرجة الإجمالية لـ MS-TSQ بين المجموعتين.

الكلمات المفتاحية: أعراض سن اليأس، زيت زهرة الربيع، زيت الصويا، إستبيان نمط الحياة الخاص بسن اليأس وإستبيان القناعة والرضا.

Introduction

Menopause, as defined is one of the most critical stages in a woman's Lifespan and is part of normal female physiology that represents a woman's shift from a reproductive to a non-reproductive status (1), distinguished by important endocrine, physiological, and clinical changes in women (2). At least one year of amenorrhea due to a deficiency of ovarian function marks the beginning of menopause, and it commonly happens between the ages of 45 and 55 (3). However, most women do not seek medical intervention until serious symptoms develop (4).

An etiologic relationship seems to exist between vasomotor symptoms/genital atrophic disorders and estrogen deficiencies during the post-menopausal transition (5). Most women, but not all, experience embarrassing symptoms during pre- and/or post-menopause. The symptoms are either physical or psychological in nature (6). Up to 80% of women experience somatic, vasomotor, sexual, and psychological post-menopause symptoms, which are related to poorer self-rated health, decreased workplace productivity, and higher usage of public health insurance resources, substantially diminishing their overall life satisfaction (7). Approximately 10-20% of all postmenopausal women experiencing intolerable symptoms that it disrupts their daily activities, but for others they are mild, and the transition is acceptable (8). Some symptoms of menopause might linger for years (9).

Hormone replacement treatment (HRT), also known as menopausal hormone treatment (MHT), is the most effective therapy to reach therapeutic support of numerous symptoms (10), like vasomotor symptoms especially hot flashes (11), prevention of the genitourinary syndrome, bone loss, as well as premature hypoestrogenism at any age (12), but many researchers advise keeping HRT sessions to a minimum by using the smallest

effective dosage for the shortest period possible (13).

Studies demonstrates that synthetic hormone formulations differ clinically in safety and efficacy (14). HRT can cause side effects like nausea, breast pain, bloating, vaginal bleeding, fluid retention, headaches, and leg cramps, but these side effects can be lessened by giving everyone the right dose (15). HRT has been linked to a rise in ER-rich tissue tumors that are dependent on hormones (e.g., endometrium and breast) (16).

Moreover, Pharmacological options are few and not as effective as HRT (17). As a result, a safe and effective alternative to HRT is needed for the treatment of hot flashes and other postmenopausal symptoms (18). Evidently, there is a gap between the need for effective treatment and the treatment options available.

Numerous non-hormonal treatments for post-menopause symptoms have been described as effective over-the-counter agents for symptomatic relief in clinical studies and the media generally (19). The WHO reports that 80% of global people use herbal remedies (20). Herbal supplements, such as those high in estrogen and traditionally used to cure postmenopausal manifestations, may be beneficial in alleviating the acute symptoms of the condition (21).

The genus *Oenothera*, which includes the evening primrose along with many other species, is part of the family *Onagraceae*. Premenstrual symptoms, breast pain, postmenopausal symptoms, and labor induction are just some of the women's health conditions for which EPO has been studied (22). As well as inhibiting platelet aggregation, EPO can alleviate psoriasis and menstrual problems symptoms and improve vasomotor symptoms experienced after menopause (23). EPO may cause mild gastrointestinal side effects, which may include loose stool and minor gastrointestinal upset (belching, abdominal bloating) (24), or decrease seizure tolerances in women taking antiepileptic drugs (25). EPO is available in a liquid or capsules form, the dose varies depending on manufacturer; but recommended dose of EPO is 8 to 12 capsules a day, at a dose of 500mg per capsule (26).

On other hand, Soy (*Glycine max*) and soy isoflavones are the most popular and extensively researched phytoestrogens for treating menopausal symptoms because they act similarly to estrogen and they are also antioxidants, so it had increasable interest in pharmaceutical industry (27,28). Some isoflavones have estrogenic properties, which lends credence to the idea that soy could serve as HRT for the treatment of postmenopausal symptoms. Postmenopausal women typically take 35–150 mg/day of isoflavone supplements (29). Soy is available as capsule in addition to topical products such as gels and moisturizers. Some people may experience thyroid function suppression, flatulence, diarrhea, and allergic reactions because of soy products (30).

There were few literature reviews, as our knowledge, to compare the efficacy of EPO and soybean oil in Iraqi postmenopausal women with menopause-related symptoms, as well as improvement in the quality of life, besides the lack of awareness by most postmenopausal women about these alternative treatments and these side effects. So, the present study aimed to compare the efficacy of EPO and soybean oil in postmenopausal women with post-menopause-related symptoms like vasomotor symptoms (hot flushes) and related metabolic and hormonal parameters.

Patients and Methods

Patients

This is a prospective comparative study conducted on 40 women, who visit the private clinic and obstetrics-gynecology department in Fallujah Teaching Hospital during the period from 10th November 2021 to 15th March 2022, in Fallujah city, Al-Anbar Province, all were diagnosed with post-menopause-related symptoms

under the supervision of an obstetrician-gynecologist; ages ranging from 45 to 59 years; were enrolled under the supervision of an obstetrician-gynecologist; all women completed the study and were treated according to the practice guidelines.

Inclusions Criteria

- Women who have entered menopause, those age between 45 to 59.
- Women with post-menopausal symptoms, such as vasomotor symptoms (hot flushes (HFs), night sweats (NSs), psychological symptoms (migraine, insomnia, irritability), or genitourinary symptoms (dyspareunia, vaginal dryness) (31).
- Women who is ready to sign a permission form indicating they understand the risks and benefits of taking part in the clinical trial.

Exclusion Criteria

- Post-menopausal women on warfarin or other antithrombotic (the γ-linolenic acid present in EPO may also slow blood clotting and even exacerbate the effects of blood thinners, like warfarin, causing bleeding and bruising (24)).
- Post-menopausal women with history of neurological disorders (EPO aggravation of temporal lobe epilepsy (32)).
- Post-menopausal women with comorbid diseases, diabetic neuropathy or malignant tumor, and serious illnesses such as cardiovascular, cerebrovascular (CVD), Renal, Liver, and hematopoietic system (16).
- Post-menopausal women with mental illness take sedatives or anti-anxiety drugs regularly.
- Postmenopausal women have been utilized HRT within the past three months.
- Post-menopausal women who cannot cooperate with the treatment.

Ethical Consideration

- The scientific and Ethics Committee in the Mustansiriyah University / College of Pharmacy reviewed and approved the protocol. Field authorities accepted the project.
- The patient agreed to take part in the study both verbally and in writing after the objective of this study was fully explained and the accuracy of the data was guaranteed.

Study Design

This prospective, simple randomized controlled, open-label clinical study compares the effectiveness of two herbal complements: evening primrose oil (EPO) and Soybean Oil on menopause-related symptoms in postmenopausal women. The selected patients were randomly assigned into two main groups, to receive either of the following two treatments as a sole treatment:

Group 1: include 20 postmenopausal women who received 1000mg Evening Primrose oil (EPO) per day, as 2 capsules twice a day for 8 weeks.

Group 2: include 20 postmenopausal women who received 466mg of soybean oil extract per day, as 2 capsules twice a day for 8 weeks.

The patients were informed to take the complement with or after meals, then followed up for any adverse effects until the end of the study.

Methods

Data Collection

Data were collected by the researcher; a special data collection sheet was designed by the research team to match the study goals and the information was collected from the patient's case sheets regarding their demographic data, which include age, residency, Body Mass Index (BMI), and medical history, were collected from women via face-to-face interviews with the researcher. The subjective and clinical assessments of the current study included Menopause Symptoms Treatment

Satisfaction (MS-TSQ) (33), and Menopause Specific Quality of Life (MENQOL) (34) using the Arabic translation(in Appendix) . The questionnaires were professionally translated from English into Arabic, and then they were reviewed by a bilingual speaker before being translated back into English. A panel of specialists from the same profession examined the content for applicability, language simplicity, and clarity in reading. Their suggestions were considered, and the questionnaire was adjusted as needed.

Assessment of Menopause Symptoms Treatment Satisfaction (MS-TSQ)

Treatment satisfaction was measured using the Menopause Symptoms Treatment Satisfaction Questionnaire (MS-TSQ) (33). The MS-TSQ, includes eight questions that assess satisfaction with the treatment's control of hot flushes (day and night); the treatment's effects on sleep, mood, libido, and ability to concentrate; treatment tolerability; and overall satisfaction with the treatment.

Participants rated their satisfaction with each item on a five-point scale, ranging from ''extremely satisfied'' to ''extremely dissatisfied'' (33) as the following (35):

I. Extremely Dissatisfied: [1-1.80)
II. Dissatisfied: [1.80-2.60)
III. Neutral: [2.60-3.40)
IV. Satisfied: [3.40-4.20)
V. Extremely Satisfied: [4.20-5].

Assessment of Menopause-specific Quality of Life (MEN-QOL)

The development and initial overview of the psychometric properties of the Menopause-Specific Quality of Life questionnaire (MEN-QoL) were published in 1996 (36). The final 29-item questionnaire included the highest three items ranked by importance score from each combined dimension, now renamed a domain, followed by the remaining items, ranked together by importance score, and assigned according to their dimension of origin to the four domains of the questionnaire (34).

The final version of MEN-QOL consists of a total of 29 items in four domains:

I. Vasomotor domain (1-3): consists of hot flushes or flashes, night sweats, and sweating.
II. Psychosocial domain (4-10): consists of being dissatisfied with my personal life, feeling anxious or nervous, experiencing poor memory, accomplishing less than I used to, feeling depressed, down, or blue, being impatient with other people, and feeling wanting to be alone.
III. Physical domain (11-26): consists of flatulence (wind) or gas pains, aching in muscles and joints, feeling tired or worn out, difficulty sleeping, aches in the back of the neck or head, decrease in physical strength, decrease in stamina, feeling a lack of energy, drying skin, weight gain, increased facial hair, changes in appearance, texture, or tone of your skin, feeling bloated, low backache, frequent urination, and in voluntary urination when laughing or coughing.
IV. Sexual domain (27-29): consists of change in your sexual desire, vaginal dryness during intercourse, and avoiding intimacy.

For each item, participants were asked to indicate if they had experienced each symptom or problem within the past month and, If 'no', she goes to the next item; however, if 'yes', she rates how bothered she was by the item on a 7-point Likert scale ranging (37) as the following (35):

I. Extremely Unbothered: [0-0.86)
II. Unbothered: [0.86-1.71)
III. Somewhat Unbothered: [1.71-2.57)
IV. Neutral: [2.57-3.43)
V. Somewhat bothered: [3.43-4.29)
VI. Bothered: [4.29-5.14)
VII. Extremely bothered: [5.14-6].

Each domain score was the average of the item scores in that domain (higher scores indicated a poorer quality of life) (38).

Calculation of Body Mass Index

The body mass index measured for all women at baseline according to the following equation:

$$BMI\left(\frac{Kg}{m^2}\right) = \frac{Weight\ (Kg)}{\left(Height\ (m)\right)^2}$$

BMI classified as the following (39):

- BMI < 18.5: Underweight
- BMI = 18.5-24.9: Normal Weight
- BMI = 25.0-29.9: Overweight
- BMI = 30.0-34.9: Obesity (1st Class)
- BMI = 35.0-39.9: Severely Obesity (2nd Class)
- BMI ≥ 40: Extreme Obesity (3rd Class)

Statically Analysis

The data were analyzed using the Microsoft Excel 2023 and SPSS IBM-version 26.0 software. The results reported in this study were expressed as mean ± SD (Standard Deviation) and frequencies were expressed as percentages. For comparison of distributed groups, Paired Samples Test, Analysis of Variance (ANOVA), & Analysis of Covariance (ANCOVA) were performed. The chi-squared test was used to compare reported proportions of subject satisfaction scores. Probability values (p-value) less than 0.05 were considered biologically significant difference while probability values less than 0.01 were regarded as highly significant.

Result

Demographics and Disease Characteristics of Participants

In the current study, forty post-menopause aged women were enrolled, most of women in group 1 were aged between 50- to 54 years and aged between 55- to 59 years as 7 (35%) for each category, while most of women in group 2 were aged between 50- to 54 years old as 10 (50%). There were no statically significant differences between both groups with respect to age categories, and BMI Classification, with (P>0.05).

Most women in this study were without any chronic disease in group 1 and group 2, (70%, and 65%, respectively), and all the women in group 2 were without any medication history, but in group 1 (80%) of women. There was no statically significant difference between both groups with respect to chronic diseases, with (P>0.05); but there was a statically significant difference between groups with respect to medication history, with (P<0.05).

The mean duration of Menopausal Symptoms of women in group 1 was (14.55±7.4) months, who presented with less than 7 times hot flushes per day (60%). While the mean duration of Menopausal Symptoms of women in group 2 was (11.95±4.5) months, who presented with less than 7 times hot flushes per day (55%). There were no statically significant differences between both groups with respect to the duration of menopausal symptoms, and the number of hot flushes, with (P>0.05).

Table 1 Scio-Demographic characteristics of the study groups

SDV.s		Study Groups		Total (N=40)	Sig.
		G1 (N=20)	G2 (N=20)		
Age Categories	45-49yrs	6 (30%)	7 (35%)	13(32.5%)	0.1 N.S.
	50-54yrs	7 (35%)	10 (50%)	17(42.5%)	
	55-59yrs	7 (35%)	3 (15%)	10 (25%)	
BMI Classification	Normal Weight	0 (0%)	1 (5%)	1 (2.5%)	0.3 N.S.
	Overweight	9 (45%)	6 (30%)	15 (37.5%)	
	1st Obese	3 (15%)	7 (35%)	10 (25%)	
	2nd Obese	6 (30%)	5 (25%)	11 (27.5%)	
	3rd Obese	2 (10%)	1 (5%)	3 (7.5%)	
Residence	Urban	14 (70%)	18 (90%)	32 (80%)	**0.05***
	Rural	6 (30%)	2 (10%)	8 (20%)	
Chronic Diseases	With	6 (30%)	7 (35%)	13 (32.5%)	0.6 N.S.
	Without	14 (70%)	13 (65%)	27 (67.5%)	
Medication History	No	16 (80%)	20 (100%)	36 (90%)	**0.03***
	Yes	4 (20%)	0 (0%)	4 (10%)	
Number of Hot Flushes per day	<7 times/day	12 (60%)	11(55%)	32 (57.5%)	0.7 N.S.
	>7 times/day	8 (40%)	9 (45%)	17 (42.5%)	

G1: group 1 who received EPO, G2: group 2 who received Soybean oil. Data presented as Mean ± SD, (N) is number of patients and (%) is percentage. Chi-square were used for categorical variables. *(P-value<0.05) is considered Significant differences. (P-value>0.05) is considered not significant (N.S.).

Effect of Evening Primrose Oil and Soybean Oil on MS-TSQ

As presented in Table 2, there were significant differences in the MS-TSQ score between both groups at pre- and post-treatment (P<0.01) in some variables. After 2 months of treatment, there was significant difference in in some variables at EMM with (P<0.05). After 2 months of treatment, post menopause women in group 1 who received EPO showed an increase in total MS-TSQ score of (6.76%) and a decrease in group 2 who received soybean oil of (-8.76%), but it was not significant with (P>0.05).

Table 2 Effect of the study interventions on Menopause Symptoms Treatment Satisfaction Questionnaire (MS-TSQ) after 2 months

Variables		G1	G2	P-value
During the past 4 weeks, how satisfied have you been with the ability of the study medication to control your hot flashes during the day?	Pre-treatment	3.65±0.59	4.1±0.64	**0.026***
	Post-treatment	3.6±0.6	3.45±0.51	0.399$^{N.S.}$
	P-value	0.716$^{N.S.}$	**0.001****	
	% Difference	-1.37%	-15.85%	
	EMM	3.67±0.12	3.38±0.12	**0.03***
During the past 4 weeks, how satisfied have you been with the ability of the study medication to control your hot flashes during the night?	Pre-treatment	3.25±0.64	4.05±0.69	**0.000****
	Post-treatment	3.95±0.76	3.45±0.61	**0.027***
	P-value	**0.003****	**0.01****	
	% Difference	21.54%	-14.81%	
	EMM	3.97±0.17	3.43±0.17	0.7$^{N.S.}$
During the past 4 weeks, how satisfied have you been with the effect of the study medication on the quality of your sleep?	Pre-treatment	3.6±0.6	3.9±0.72	0.159$^{N.S.}$
	Post-treatment	3.7±0.66	3.55±0.51	0.425$^{N.S.}$
	P-value	0.629$^{N.S.}$	**0.031****	
	% Difference	2.78%	-8.97%	
	EMM	3.72±0.13	3.53±0.13	0.2$^{N.S.}$
During the past 4 weeks, how satisfied have you been with the effect of the study medication on your mood or emotions?	Pre-treatment	3.4±0.5	3.55±0.83	0.492$^{N.S.}$
	Post-treatment	3.9±0.55	3.6±0.6	0.108$^{N.S.}$
	P-value	**0.014***	0.716$^{N.S.}$	
	% Difference	14.71%	1.41%	
	EMM	3.92±0.12	3.58±0.12	**0.03***
During the past 4 weeks, how satisfied have you been with the effect of the study medication on your interest in sex?	Pre-treatment	3.45±0.61	3.8±0.62	0.078$^{N.S.}$
	Post-treatment	3.8±0.7	3.55±0.51	0.203$^{N.S.}$
	P-value	0.13$^{N.S.}$	0.262$^{N.S.}$	
	% Difference	10.14%	-6.58%	
	EMM	3.75±0.14	3.60±0.14	0.08$^{N.S.}$
During the past 4 weeks, how satisfied have you been with the effect of the study medication on your ability to concentrate?	Pre-treatment	3.35±0.67	3.8±0.77	**0.056***
	Post-treatment	3.55±0.61	3.55±0.61	1.000$^{N.S.}$
	P-value	0.297$^{N.S.}$	0.135$^{N.S.}$	
	% Difference	5.97%	-6.58%	
	EMM	3.60±0.13	3.50±0.13	0.08$^{N.S.}$
While taking some medications, some people may experience side effects. How satisfied have you been with the tolerability (lack of bothersome side effects) of the study medication, during the past 4 weeks?	Pre-treatment	3.55±0.51	3.7±0.57	0.387$^{N.S.}$
	Post-treatment	3.85±0.59	3.6±0.5	0.156$^{N.S.}$
	P-value	0.083$^{N.S.}$	0.577$^{N.S.}$	
	% Difference	8.45%	-2.70%	
	EMM	3.85±0.12	3.60±0.12	0.8$^{N.S.}$
During the past 4 weeks, overall, how satisfied have you been with the study medication?	Pre-treatment	4.1±0.64	4.1±0.72	1.000$^{N.S.}$
	Post-treatment	3.95±51	3.9±0.45	0.744$^{N.S.}$
	P-value	0.481$^{N.S.}$	0.258$^{N.S.}$	
	% Difference	-3.66%	-4.88%	
	EMM	3.95±0.11	3.90±0.11	0.7$^{N.S.}$
Total Score of MS-TSQ	Pre-treatment	3.55±0.18	3.88±0.39	**0.001****
	Post-treatment	3.79±0.19	3.54±0.15	**0.000****
	P-value	**0.000****	**0.001****	
	% Difference	6.76%	-8.76%	
	EMM	3.80±0.04	3.53±0.04	0.7$^{N.S.}$

G1: group 1 who received EPO, G2: group 2 who received Soybean oil. All domains were calculated as total measured. Data presented as Mean ±SD. Analysis of Variance (ANOVA) was used to compare between two means between both groups. Paired Samples Test had been used to compare between Pre- & Post-treatment for each group. Analysis of Covariance (ANCOVA)

had been used to compare the Estimated Marginal Means (EMM) (pre-treatment-adjusted mean) of post-treatment between study groups. *(P-value<0.05) is considered Significant differences. **(P-value<0.01) is considered Highly Significant differences. (P-value>0.05) is considered not significant (N.S.).

Effect of Evening Primrose Oil and Soybean Oil on MEN-QoL

As presented in Table 3, there were significant differences in the MEN-QoL score between both groups at pre- and post-treatment (P<0.01) in all variables. After 2 months of treatment, in this study, EPO had significantly improved the quality of the life through decrease all MEN-QoL domains more than soybean oil, except with sexual domain (P<0.01). After 2 months of treatment, post menopause women in group 1 who received EPO showed a decrease in total MEN-QoL score of (-74.69%) and a decrease in group 2 who received soybean oil of (-68.69%), and it was significant with (P<0.05).

Table 3 Effect of the study interventions on Menopause-specific Quality of Life (MEN-QoL) Questionnaire after 2 months

Variables		G1	G2	P-value
Vasomotor	Pre-treatment	3.13±0.89	3.02±0.81	0.609$^{N.S.}$
	Post-treatment	0.77±0.52	0.87±0.55	0.491$^{N.S.}$
	P-value	**0.000****	**0.000****	
	% Difference	-75.40%	-71.19%	
	EMM	0.78±0.12	0.87±0.09	**0.03***
Psychosocial	Pre-treatment	3.31±0.69	3.13±0.66	0.333$^{N.S.}$
	Post-treatment	0.81±0.47	1.08±0.5	**0.047***
	P-value	**0.000****	**0.000****	
	% Difference	-75.53%	-65.50%	
	EMM	0.80±0.11	1.08±0.08	**0.02***
Physical	Pre-treatment	3.27±0.55	3.18±0.53	0.551$^{N.S.}$
	Post-treatment	0.95±0.28	1.26±0.47	**0.008****
	P-value	**0.000****	**0.000****	
	% Difference	-70.95%	-60.38%	
	EMM	0.97±0.09	1.26±0.06	**0.000****
Sexual	Pre-treatment	3.25±0.63	3.18±0.64	0.697$^{N.S.}$
	Post-treatment	0.77±0.43	0.72±0.51	0.704$^{N.S.}$
	P-value	**0.000****	**0.000****	
	% Difference	-76.31%	-77.36%	
	EMM	0.76±0.11	0.71±0.08	0.3$^{N.S.}$

Total Score of MEN-QoL	Pre-treatment	3.24±0.51	3.13±0.47	$0.395^{N.S.}$
	Post-treatment	0.82±0.32	0.98±0.32	$0.076^{N.S.}$
	P-value	**0.000****	**0.000****	
	% Difference	-74.69%	-68.69%	
	EMM	0.82±0.07	0.98±0.05	**0.006***

G1: group 1 who received EPO, G2: group 2 who received Soybean oil. All domains were calculated as total measured. Data presented as Mean ±SD. Analysis of Variance (ANOVA) was used to compare between two means between both groups. Paired Samples Test had used to compare between Pre- & Post-treatment for each group. Analysis of Covariance (ANCOVA) had used to compare the Estimated Marginal Means (EMM) (pre-treatment-adjusted mean) post-treatment (pre-treatment-adjusted mean) between study groups. *(P-value<0.05) is considered Significant differences. **(P-value<0.01) is considered Highly Significant differences. (P-value>0.05) is considered not significant (N.S.).

Discussion

Recently, menopause has been the focus of medical researchers worldwide, especially in developing nations (40), because it causes physical, glandular, and psychological differences in women that can last for some years and affect their daily lives and activities (41).

The post menopause women enrolled in this study were in age range between 45- to 59 years similar menopausal age reported in previous studies (45 and 54 years) (42–44). The mean age of onset of the menopausal transition is 47.5 years and commonly lasts approximately 4 to 5 years (45). The enrolled women were mostly overweight (37.5%), and those within class 2 obesity and class 1 (27.5%, and 25%, respectively). Longitudinal studies show that higher BMI is a risk factor for vasomotor symptoms (46). Obesity and abdominal obesity were found to negatively correlate with physical (but not mental) quality of life in a linear model analysis (47). High BMI was also related to a lower score of symptoms of 1156 postmenopausal women aged between 45- to 64-years (48).

In the current study, out of 40 postmenopausal women, 13 (32.5%) presented with a history of chronic illness. This was in agreement with previous study reported out 666 post-menopausal women (58.9%) of them suffered with chronic diseases (49).

The mean duration of menopausal symptoms of enrolled women was (13.25±6.2) months mostly of <7 times/day of hot flushes, though 42.5% of them presented with more than 7 times of hot flushes episodes of duration is often 2 to 3 minutes with a range from a few seconds up to one hour and there is a wide variety in frequency (50). As mentioned early that approximately 70% of women experience symptoms associated with menopause presenting as hot flushes, sweating, palpitations, and insomnia (51). Different studies evaluated the effect of phytoestrogenic plants on hot flashes in postmenopausal women, that herbal compounds could be used as complementary therapies in treating menopausal symptoms instead of hormonal replacement therapies.

Many tools have been created to evaluate postmenopausal distress, but very few have proven to be standardized, valid, and reliable. The most used measures are built on women's own self-reports of the existence, intensity, and recurrence of clinical manifestations, such as hot flashes. Such tools include diaries in which women record the onset of postmenopausal symptoms like HF and NS and, frequently,

a rating of the severity of each episode (e.g., mild, moderate, or severe) (52).

In the present study, assessment of post menopause satisfaction (MS-TSQ) overall score revealed notable increased in women satisfaction after receiving EPO, and slight decrease among those received soybean oil, significantly regarding the ability of the study medication to control hot flashes during the day the effect of the study medication on mood or emotions. Most post menopause were neutrally satisfied with treatment before and after treatment as MS-TSQ indexed, however, patient convenience with herbal medications still underestimated.

The MEN-QoL represents 4 domains as sub-scales are vasomotor, psychosocial, physical, and sexual domains, which assess health-related quality of life in middle-aged women (aged 47-62 years) in the years closely afar the onset of menopause, 2-7 years beyond post-menopause (34). In the current study, post menopause women respond with [Somewhat bothered: 3.43-4.29) symptoms that affect their QoL, hence after 2 months of treatment the MEN-QOL scores were significantly improved after both supplements ($P < 0.01$), as they respond with [Unbothered: 0.86-1.71) symptoms, nevertheless, improvement in EPO group was significantly superior to that of soybean oil.

In this study, after 2 months of treatment, all MEN-QOL scores, except for the sexual domain, were significantly enhanced in two groups ($P < 0.01$), but the percentage of enhancement in EPO group was significantly improved to the soybean oil group. Basaria S. *et al.* reported significant improvements in all QOL subscales (vasomotor, psychosexual, physical, and sexual) among women treated with isoflavones (20g-160 mg of total isoflavones) for 12 weeks, but the placebo group (20 g whole-milk protein) did not see any changes. Basaria S. *et al.* found that high dosages of isoflavones are related to enhanced quality of life (QOL) among women in the early phases of menopause, suggesting that isoflavones as alternatives to HRT may be effective and safe in relieving symptoms of menopause (53).

Conclusion

The current study revealed that after two months of intervention, there was a significant change in the total score of MEN-QoL but a non-significant change in the total score of MS-TSQ between post-menopausal women maintained on EPO and those on soybean oil.

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استبيان نمط الحياة الخاص بسن اليأس (MENQAL)

تم اعادة الطباعة من قبل هيلديتش واخرون في عام 1996 بأذن من ايلسيفير

حدد، في كل من الفقرات التالية ما اذا كنت قد واجهت المشكلة المشار اليها في الشهر الماضي. اذا حدث معك ذلك، حدد مدى تأثرك بالمشكلة.

لم انزعج على الاطلاق _____ منزعج جداً

6 5 4 3 2 1 0

1. هبات ساخنة	نعم	كلا	6 5 4 3 2 1 0
2. التعرق الليلي	نعم	كلا	6 5 4 3 2 1 0
3. التعرق	نعم	كلا	6 5 4 3 2 1 0
4. غير مقتنع بحياتي بالخاصة	نعم	كلا	6 5 4 3 2 1 0
5. اشعر بالقلق او التوتر	نعم	كلا	6 5 4 3 2 1 0
6. اعاني من فقدان الذاكرة	نعم	كلا	6 5 4 3 2 1 0
7. انجز اقل مما كنت افعل	نعم	كلا	6 5 4 3 2 1 0
8. اشعر بالاكتئاب او الاحباط او الحزن	نعم	كلا	6 5 4 3 2 1 0
9. اشعر بقلة الصبر مع الاشخاص الاخرين	نعم	كلا	6 5 4 3 2 1 0
10. اشعر بالرغبة بالبقاء وحيداً	نعم	كلا	6 5 4 3 2 1 0
11. انتفاخ البطن والام الغازات	نعم	كلا	6 5 4 3 2 1 0
12. الألم بالعضلات والاطراف	نعم	كلا	6 5 4 3 2 1 0
13. الشعور بالتعب والانهاك	نعم	كلا	6 5 4 3 2 1 0
14. الصعوبة في النوم	نعم	كلا	6 5 4 3 2 1 0
15. الام في مؤخرة الرقبة او الرأس	نعم	كلا	6 5 4 3 2 1 0
16. قلة القوة البدنية	نعم	كلا	6 5 4 3 2 1 0
17. قلة التحمل	نعم	كلا	6 5 4 3 2 1 0
18. اشعر بانعدام الطاقة	نعم	كلا	6 5 4 3 2 1 0
19. بشرة جافة	نعم	كلا	6 5 4 3 2 1 0
20. زيادة الوزن	نعم	كلا	6 5 4 3 2 1 0
21. زيادة شعر الوجه	نعم	كلا	6 5 4 3 2 1 0
22. تغييرات في مظهر او درجة لون البشرة	نعم	كلا	6 5 4 3 2 1 0
23. الشعور بالانتفاخ	نعم	كلا	6 5 4 3 2 1 0
24. الم الظهر السفلي	نعم	كلا	6 5 4 3 2 1 0
25. التبول المتكرر	نعم	كلا	6 5 4 3 2 1 0
26. التبول اللاإرادي عند الضحك او السعال	نعم	كلا	6 5 4 3 2 1 0
27. التغير في الرغبة الجنسية	نعم	كلا	6 5 4 3 2 1 0
28. المشاكل المهبلية عند المضاجعة	نعم	كلا	6 5 4 3 2 1 0
29. تجنب العلاقة الحميمية	نعم	كلا	6 5 4 3 2 1 0

استبيان مدى الرضى على علاج اعراض سن اليأس

نحن مهتمون برأيك عن الحبوب التي تستخدمها كجزء من هذه الدراسة خلال الاربع اسابيع الماضية. الرجاء الإجابة على كل سؤال باختيار إجابة واحدة في المربع.

1- ما هو مدى رضاك خلال الأربع أسابيع الماضية على إمكانية دراسة العلاج للسيطرة على الهبات الساخنة خلال النهار.

راض بشدة راض اعتيادي غير راض غير راض بشدة

2- ما هو مدى رضاك خلال الأربع أسابيع الماضية على إمكانية دراسة العلاج للسيطرة على الهبات الساخنة خلال المساء.

راض بشدة راض اعتيادي غير راض غير راض بشدة

3- ما هو مدى رضاك خلال الأربع أسابيع الماضية على إمكانية دراسة العلاج للسيطرة على الهبات الساخنة وتأثيرها على نومك.

راض بشدة راض اعتيادي غير راض غير راض بشدة

4- ما هو مدى رضاك خلال الأربع أسابيع الماضية على إمكانية دراسة العلاج للسيطرة على الهبات الساخنة وتأثيرها على المشاعر والمزاج.

راض بشدة راض اعتيادي غير راض غير راض بشدة

5- ما هو مدى رضاك خلال الأربع أسابيع الماضية على إمكانية دراسة العلاج للسيطرة على الهبات الساخنة وتأثيرها على الرغبة في الجنس.

راض بشدة راض اعتيادي غير راض غير راض بشدة

6- ما هو مدى رضاك خلال الأربع أسابيع الماضية على إمكانية دراسة العلاج للسيطرة على الهبات الساخنة وتأثيرها على التركيز.

راض بشدة راض اعتيادي غير راض غير راض بشدة

7- اثناء تناول بعض من هذه العقاقير يعانون بعض الناس من اعراض جانبية. ما هو رأيك في انعدام الاعراض الجانبية المزعجة في هذا العلاج خلال الأربع أسابيع الماضية.

راض بشدة راض اعتيادي غير راض غير راض بشدة

8- بشكل عام ما هو مدى رضاك على دراسة العلاج خلال الأربع أسابيع الماضية.

راض بشدة راض اعتيادي غير راض غير راض بشدة