Evanova in Menopause – An alternative to Hormone Replacement Therapy (HRT)

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Introduction

With the market increase in average life expectancy, women may now be spending up to one – third of their active social and professional lives in the postmenopausal (oestrogen-deficient) state. Managing the menopausal and postmenopausal woman involves ' helping her to replace what is lost and to remain feminine, thereby improving her quality of life'.

HRT has been effectively used to relieve the well-known symptoms of menopausal syndrome (e.g. hot flushes, insomnia, etc.) and to combat the adverse long-term sequelae (e.g. cardiovascular disease, osteoporosis). However, the benefits of HRT need to be weighed against possible risks associated with its long-term use, such as uterine or breast cancer and thromboembolic disease.

The judicious use of indigenous drugs an age-old science in India – adds a new dimension to management of the menopause. In this regard, Evanova, a compound preparation of 33 non-hormonal active ingredients, has been shown to be effective and safe in relieving the acute symptoms of menopause, without the risk of side effects.

Editor's Comment

'Back to nature' seems to be the answer to many health needs today, especially so with menopausal syndrome. HRT relieves the distressing symptoms and long term devastating disabilities of menopause, but has serious side effects. The Ayurvedic preparation Evanova, on the other hand, may be 'nature's gift' to menopausal women: effective in relieving symptoms, but without the demonstrable disadvantages of HRT.

Key Points

- Evanova, an Ayurvedic preparation, effectively relieves menopausal symptoms with no side effects.
- In the original study reported here, Evanova's efficacy was comparable to that of HRT, but without the demonstrable disadvantages.
- Evanova provides an alternative for women unwell and/or unable to take HRT for the menopausal syndrome.
- Further studies are needed to determine the long-term effects of Evanova on the cardiovascular and skeletal systems in postmenopausal women.

The present investigation was undertaken in order to

1. Assess the comparative efficacy of Evanova, conjugated (conj.) oestrogens and oestriol in menopausal syndrome.
2. Evaluate the safety of these drugs in Indian menopausal women.

Materials and Methods

This non-randomized, prospective study was undertaken in patients attending the Gynaecology Outpatient Department at St. John's Medical College Hospital, Bangalore, India. The study was approved by the ethics committee of the hospital and informed consent was obtained from each patient after explaining the treatment pattern and follow - up schedule. Sixty-six menopausal women aged between 40 and 52 years were included. Asymtomatic women, as well as those on hormonal treatment or on any drugs that could influence the variables being studied, were excluded.

Patients

The number of patients in each treatment group, together with the drug dose administered, are shown in table 1. Statistical analysis (see below) did not find any significant differences between the three groups in terms of type of menopause or duration of menopausal symptoms.

Parameters

At the start of the study, all patients were interviewed. A detailed history was obtained and a clinical assessment carried out. Subjects were then assessed for symptom relief every month for 6 months, noting subjective changes in intensity of symptoms and

side effects (if any). The following symptoms were clinically rated on a scale of 0 to 4 (0 = absence of symptoms; 4 – maximum severity)

- Vasomotor – hot flushes; headache; palpitations; vertigo.
- Psychomotor – insomnia; nervousness depression; fatigue; irritability
- Others – urethral syndrome; pruritus vulvae; arthralgia; breast tenderness; paresthesia.

Table 1. Distribution of Patients and drug doses

	Group		
	Evanova	Conj. Oestrogen	Oestriol
No. of Patients	34	15	17
-surgical menopause	24	13	11
- natural menopause	10	2	6
Dosage	2 Tablets TID	0.625 mg OD	1 mg OD
Abbreviations: TID = Three times daily; OD= once-daily			

In addition, the following investigations were done at 0.3, and 6 months, and the results were compared within each group and between groups:

- Hormonal – serum oestradiol: follicle stimulating hormone (FSH); leutinising hormone(LH).
- Biochemical – lipid profile; serum calcium and phosphorus: blood sugar and total proteins; creatinine.
- Others – haemoglobin; urine analysis; vaginal cytology.

At the end of the 6 – month study period, symptom relief and laboratory investigation findings were compared across the three treatment regimens.

Statistical Analysis

For the analysis of the results, repeated measures of analysis of the results, repeated measures of analysis of variance (RMANOVA) with 'Pillai' criterion was used to compare the frequency of distribution of symptoms across the three groups. A value of $p<0.05$ was considered statistically significant.

Results

Symptoms

Data analysis of only those patients who experienced symptoms indicated that overall, treatment with Evanova, conjugated oestrogens, or oestriol was equally effective in relieving a range of vasomotor and psychomotor symptoms (table 2). Evanova and oestrogens were equally efficacious in relieving specific symptoms such as vertigo, formication, vaginal dryness, pruritus vulvae, and urethral symptoms ($p>0.05$, Chi Square test), although the incidence of these was very low in the patient population studied.

Laboratory Investigations

Biochemical data of the patients who completed the trial were analyzed (table 3). Baseline oestradiol levels in all three groups were below the normal range. Over the 6-month study period, oestradiol levels increased significantly in patients on conjugated oestrogens as compared to those on Evanova and oestriol ($p<0.05$, RMANOVA; figure 2). Although oestradiol levels increased significantly in the Evanova group after 3 months they fell again after 6 months ($p<0.05$, RMANOVA; figure 1).

FSH levels in all three groups were within the normal range. During the study, FSH levels remained unchanged in the Evanova group, whereas they fell significantly in the conjugated oestrogen and oestriol groups ($p<0.05$, RMANOVA; figure 2).

Table 2. Effect of Evanova, conjugated oestrogen, and oestriol on menopausal symptoms

Symptom	Drug	Follow – up (months)		
		0	3	6
Hot Flushes	Evanova	3.33 ± 0.89	1.03 ± 0.62	0.22 ± 0.39
	Conj. Oestrogen	3.33 ± 1.18	0.82 ± 0.54	0.07 ± 0.27
	Oestriol	3.35 ± 0.79	0.90 ± 0.57	0.10 ± 0.28
Paresthesia	Evanova	0.10 ± 0.19	0.25 ± 0.50	0.03 ± 0.13
	Conj. Oestrogen	0.40 ± 0.80	0.07 ± 0.27	0.0 ± 0.00
	Oestriol	0.71 ± 0.84	0.17 ± 0.36	0.00 ± 0.00
Anxiety	Evanova	1.26 ± 0.37	0.20 ± 0.36	0.00 ± 0.00
	Conj. Oestrogen	0.20 ± 0.16	0.21 ± 0.58	0.0 ± 0.00
	Oestriol	0.82 ± 1.28	0.20 ± 0.56	0.00 ± 0.00
Fatigue	Evanova	2.38 ± 1.26	0.82 ± 0.75	0.07 ± 0.26
	Conj. Oestrogen	2.20 ± 1.21	0.29 ± 0.47	0.70 ± 0.27
	Oestriol	2.18 ± 1.47	0.60 ± 0.71	0.00 ± 0.00
Depression	Evanova	1.12 ± 1.27	0.28 ± 0.78	0.05 ± 0.20

	Conj. Oestrogen Oestriol	1.53± 1.45 1.05 ± 1.24	0.29 ± 0.61 0.10 ± 0.28	0.00 ± 0.00 0.00 ± 0.00
Somatisation	Evanova Conj. Oestrogen Oestriol	2.26 ± 1.34 0.87± 1.25 2.12 ± 1.58	0.87 ± 0.76 0.21 ± 0.43 0.90 ± 9.95	0.17± 0.47 0.0 ± 0.00 0.07 ± 0.26
Headache	Evanova Conj. Oestrogen Oestriol	1.41 ± 1.33 0.87 ± 1.36 0.71 ± 1.16	0.32 ± 0.53 0.0 ± 0.00 0.27 ± 0.46	0.07 ± 0.26 0.00 ± 0.00 0.00 ± 0.00
Palpitation	Evanova Conj. Oestrogen Oestriol	0.08± 0.01 70.20± 0.56 0.42 ± 0.79	0.07 ± 0.25 0.0 ± 0.00 0.00 ± 0.00	0.00 ± 0.00 0.00 ± 0.00 0.00 ± 0.00
Insomnia	Evanova Conj. Oestrogen Oestriol	1.74 ± 1.40 1.73 ± 1.49 1.94 ± 1.30	0.65 ± 0.77 0.50 ± 0.70 0.21 ± 0.43	0.10 ± 0.28 0.0 ± 0.00 0.00 ± 0.00
Irritability	Evanova Conj. Oestrogen Oestriol	1.71 ± 1.33 2.07 ± 1.87 1.82 ± 1.55	0.37 ± 0.54 0.39 ± 0.74 0.53 ± 0.74	0.03 ± 0.19 0.0 ± 0.00 0.00 ± 0.00

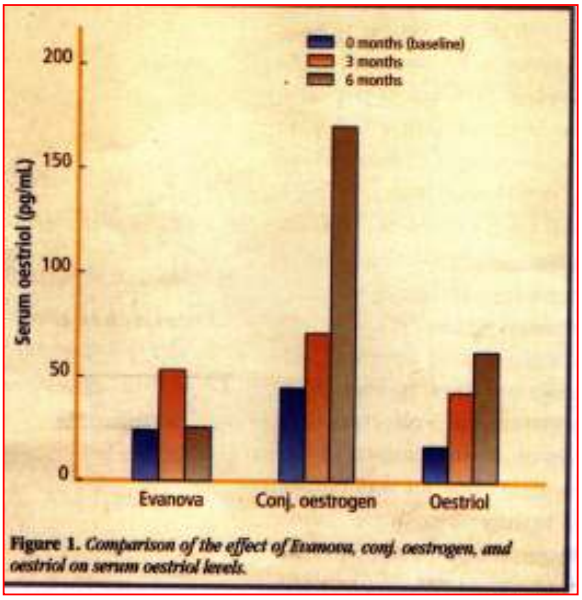

Figure 1. *Comparison of the effect of Evanova, conj. oestrogen, and oestriol on serum oestriol levels.*

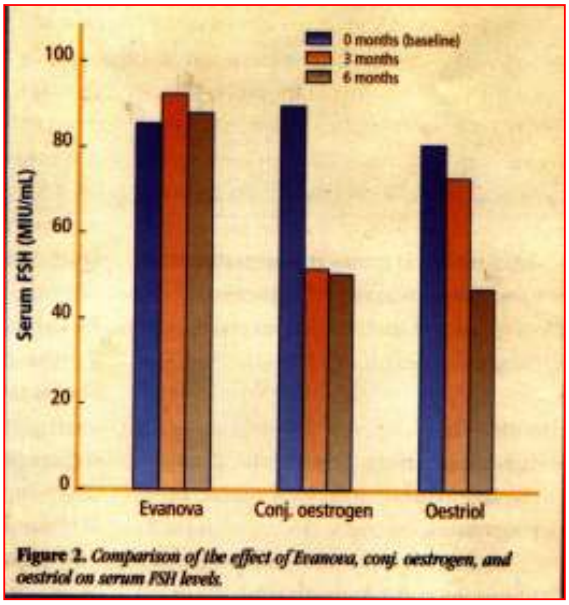

Figure 2. *Comparison of the effect of Evanova, conj. oestrogen, and oestriol on serum FSH levels.*

Table3. Effect of Evanova, conjugated oestrogen, and oestriol on laboratory investigations:

Investigation (normal range)	Drug	Follow-up (months)		
		0	3	6
Oestradiol (pg/ml) [30-70]	Evanova Conj. Oestrogen Oestriol	25.76 ± 31.04 44.71 ± 36.92 16.80 ± 12.40	53.16 ± 23.92 70.70± 79.33 43.88 ± 65.48	27.36±10.35 171.43±22.98 63.79 ± 33.77
FSH (MIU/ml) [50-150]	Evanova Conj. Oestrogen Oestriol	85.78 ± 29.33 89.91 ± 42.35 80.95 ± 27.22	92.76 ± 36.22 51.96 ± 30.41 73.08 ± 39.89	88.08± 32.35 50.59±28.80 57.32± 17.33
LH (MIU/mL) [50-100]	Evanova Conj. Oestrogen Oestriol	73.22 ± 59.61 60.89 ± 32.52 64.02 ± 21.09	65.24 ± 21.83 55.98 ± 35.02 55.76 ± 29.89	40.44± 14.41 48.41± 32.72 52.16± 32.10
Calcium (mg%) [9-11]	Evanova Conj. Oestrogen Oestriol	9.29 ± 0.64 9.57 ± 0.59 9.39 ± 0.70	9.22 ± 0.69 9.10 ± 0.64 9.32 ± 0.53	9.11 ± 0.26 9.30 ± 1.25 9.03 ± 0.59
Phosphorous (mg %) [2.5-3.4]	Evanova Conj. Oestrogen Oestriol	3.93 ± 1.02 3.75 ± 0.66 3.93 ± 0.48	3.63 ±0.59 3.35 ± 0.82 3.82 ± 0.52	3.50 ± 0.69 3.43 ± 0.52 3.64 ± 0.39
Somatisation	Evanova Conj. Oestrogen Oestriol	2.26 ± 1.34 0.87 ± 1.25 2.12 ± 1.58	0.87 ± 0.76 0.21 ± 0.43 0.90 ± 9.95	0.17± 0.47 0.0 ± 0.00 0.07 ± 0.26
Cholestrol (mg%) [150-250]	Evanova Conj. Oestrogen Oestriol	225.09 ± 44.50 198.00 ± 32.83 232.65 ± 52.44	215.41± 47.70 201.43± 23.92 239.13±62.82	214.97± 55.60 208.57± 28.09 226.40± 49.60
Triglycerides(mg%) [80-110]	Evanova Conj. Oestrogen Oestriol	171.82± 79.11 131.20± 64.72 192.82± 89.17	154.59± 55.78 137.64± 84.47 187.40± 83.53	150.93± 66.96 140.64± 73.07 179.33± 79.28
HDL (mg%) [35-80]	Evanova Conj. Oestrogen Oestriol	52.73 ± 10.93 50.93 ± 8.52 54.29 ± 1.30	54.00 ± 9.88 55.43 ± 9.11 50.87 ± 9.67	50.62 ± 9.14 56.43 ± 15.06 52.20 ± 7.48
LDL (mg%) [60-170]	Evanova Conj. Oestrogen Oestriol	139.36 ± 41.48 121.13 ± 28.65 140.41 ± 52.72	126.28± 41.49 122.36± 20.83 152.93± 55.95	133.41± 47.49 123.50± 33.74 138.53± 48.72
Fasting Blood Sugar (mg%) [70-110]	Evanova Conj. Oestrogen Oestriol	86.53± 7.95 97.18 ± 27.41 92.12 ± 15.07	126.28± 41.49 87.48 ± 20.32 87.27 ± 9.54	133.41± 47.49 91.76 ± 26.71 86.33 ± 11.32
Hb (gm%) [12-14.5]	Evanova Conj. Oestrogen Oestriol	12.78 ± 1.03 12.06 ± 1.38 12.63 ± 1.15	13.00 ± 1.36 12.86 ± 1.61 12.51 ± 0.93	13.07±1.01 13.07 ±1.02 12.52 ±1.16
Protein (gm%) [6.3 –7.9]	Evanova Conj. Oestrogen Oestriol	7.60 ± 0.42 7.73 ± 0.37 7.73 ± 0.37	7.63 ± 0.40 7.70 ± 0.55 7.73 ± 0.57	7.66 ± 0.04 7.61 ± 0.57 7.69 ± 0.59
Creatinine (mg%) [0.6-1.8]	Evanova Conj. Oestrogen Oestriol	0.79 ± 0.10 0.75 ± 0.07 0.80 ± 0.1	0.79 ± 0.31 0.80 ± 0.16 0.82 ± 0.14	0.80 ± 0.11 0.79 ± 0.19 0.83 ± 0.17

Analysis of the remaining investigations revealed no significant differences as a result of treatment with Evanova, conjugated oestrogens or oestriol (table 3)

Discussion

Data available from large – scale, double blind, randomized, cross – sectional studies have reported beneficial effects with HRT. The results of the present study indicate both exogenous oestrogen and Evanova were equally efficient in relieving various symptoms of menopausal syndrome over the total duration of treatment. The three types of medication had no significant effect on laboratory parameters, except on oestrogen and FSH during the 6 months of therapy.

Compared with patients on Evanova (or oestriol), a significant increase in oestrogen levels was noted in those on conjugated oestrogen therapy at the end of 6 months. There was in fact, a similar increase in oestrogen levels after 3 months in all three groups, after which levels continued to rise in the conjugated oestrogen group only; they fell back in the other two groups. The reason for this could be that conjugated oestrogen contains potent oestrogen whose administration could have elevated oestrogen to high levels. Evanova also temporarily increased oestrogen levels, an effect which may be due to its oestrogen like effect by indirectly stimulating oestrogen secretion. In any event , patients were relieved of their presenting symptoms at the lower oestrogen levels achieved with Evanova.

Vaginal Cytology

Vaginal Cytology was employed in the assessment of hormonal status. Conjugated oestrogen had a prominent oestrogenic effect (figure 3), whereas Evanova and oestriol showed little or no effect (figures 4 and 5, respectively).

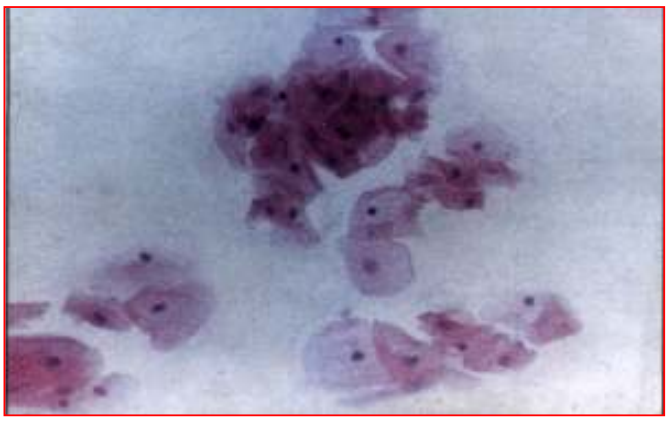

Figure 3. Effect of conjugated oestrogen on vaginal cytology

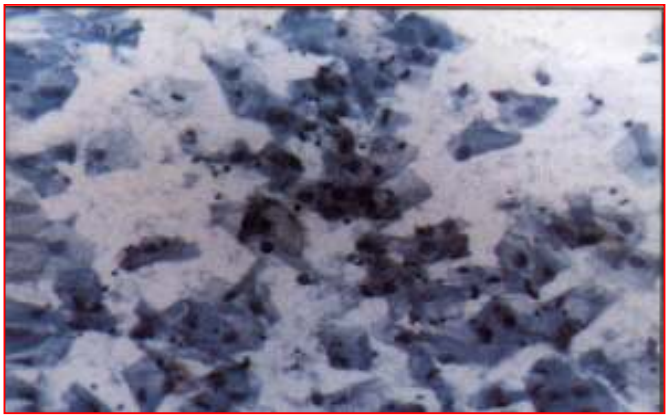

Figure 4. Effect of Evanova on vaginal cytology

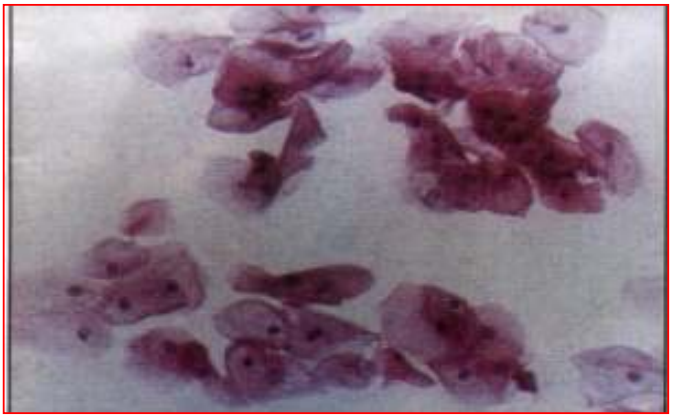

Figure 5. Effect of oestriol on vaginal cytology

Evanova had no adverse effects on various laboratory parameters (e.g. haemoglobin, cholesterol, triglycerides, etc.) indicating its safety for clinical use.

The efficacy of oestrogen in relieving symptoms of vasomotor irritability and genital tract atrophy is well established. It has been recognized for many years that these benefits, together with relief of psychological problems, can improve a woman's quality of life. Despite this may women are apprehensive about HRT, due to fears of potential adverse events, particularly cancer. Evanova is one such herbal, non-hormonal preparation which can serve in the management of menopausal syndrome. Prominent among the 33 ingredients in this Ayurvedic medicine, are the following medicaments:

- Ashoka – which controls all abnormal and excessive secretions.
- Jeera – which has a demonstrable oestrogenic activity.

- Chandan – which acts as an anxiolytic agent.
- It has been suggested that Evanova stimulates optimum functioning of the hypothalamo-pituitary-ovarian axis,thus restoring hormonal balance. Certainly our study has shown that this non hormonal pro- oestrogenic preparation is highly efficacious and safe and provides benefits comparable to exogenous oestrogen, but without the demonstrable disadvantages of HRT. However, long term controlled studies are needed to determine its effects in terms of cardiovascular disease and osteoporosis prevention. Meanwhile Evanova provides a much needed non hormonal alternative (to HRT) which is effective and safe in managing menopausal syndrome.

Conclusion

Evanova is effective in relieving menopausal syndrome, with no adverse effects; its efficacy is comparable to that of oestrogen therapy. Thus it is suggested that Evanova can be given as an alternative to HRT for the management of menopausal syndrome, especially in patients for whom replacement therapy is contraindicated or where women are reluctant to take HRT.

Relevant Reading

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