

Isoflavone in Postmenopausal Women - Are They Really Effective? A Prospective Case Control Study.

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ABSTRACT

A prospective case control study was conducted at Medical College, Kolkata with the aim of evaluating the role of isoflavone (a class of phytoestrogen –plant compounds having the beneficial effects of estrogen but lesser risks and side effects) in postmenopausal women. 100 postmenopausal women (those who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy for different benign indications, aged between 40-50 years and who were menstruating before operation) were alternately distributed into two groups-Group A (n=50, received 60mg of isoflavone and 500mg of calcium per day for 6 months) and Group B (n=50, received 500mg of calcium per day only for 6 months). To evaluate the menopausal symptoms, the menopausal Kupperman index questionnaire was applied. Other outcomes measured were body mass index, blood pressure and lipid profile. Menopausal symptoms in Group A (those using isoflavones) were lower compared to Group B. The present study showed that Kupperman index decreased significantly in Group A (from 28.48 ± 2.03 to 16.32 ± 1.06 i.e. 45% decline) compared to Group B (from 24.56 ± 1.52 to 18.44 ± 1.11 i.e. 25% decline). No differences in blood pressure or body mass index were found during treatment between the two groups. In our study total cholesterol, triglycerides and low-density lipoproteins (LDL) decreased significantly in Group A compared to Group B. Therefore our clinical study indicates that isoflavone can be an invaluable resource for postmenopausal women for combating menopausal symptoms.

Keywords: Isoflavone, kupperman index, postmenopausal

INTRODUCTION

Estrogen replacement has long been therapy of choice for the treatment of climacteric symptoms in postmenopausal women as well as for the prevention of osteoporosis and cardiovascular diseases.¹⁻³ However, prolonged exposure to unopposed estrogen increases the risk of endometrial hyperplasia and neoplasia.³ Progestagen added with estrogen to decrease these risks can cause severe side effects in some patients.^{4,5} The identification of an alternative agent, which has the beneficial effects of estrogen but lesser side effects would be of considerable value. Isoflavones (a class of phytoestrogen) are plant compounds that are structurally or functionally similar to steroidal estrogens. The 3 major isoflavones found in soy (rich source of isoflavones) are genistin, daidzin, and glycitin. These compounds have both estrogenic and antiestrogenic activity.^{6,7} They function as pro-estrogens when estrogen deficiency is present and as antiestrogens when excess estrogen is present. If during menopause

the body's natural level of estrogen drops, isoflavones can compensate this by binding to the estrogen receptor, thereby easing menopause symptoms as a result.

METHODS

The study was conducted at Gynaecology & Obstetrics department of Medical College & Hospital, Kolkata from 1st January 2010 to 31st December 2010. It was a prospective case control study where 100 postmenopausal women (those who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy for different benign indications, aged 40-50 years and who were menstruating before operation) were alternately distributed into two groups-Group A (n=50, received 60mg of isoflavone and 500mg of calcium per day for 6 months) and Group B (n=50, received 500mg of calcium per day only for 6 months). In all cases written informed consent was taken and women with history of uncontrolled hypertension, stroke or transient ischemic attack, cancer diagnosed less than 5 years ago or previous myocardial infarction were

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excluded from the study. All subjects were not on any type of hormonal treatment during the previous 12 months and were also not using any lipid-lowering drugs, antidiabetic medications, soybean-derived products or herbal supplements. All women were queried about menopausal symptoms covered by Kupperman et al (1954) at the beginning of the study and at intervals of 3 and 6 months. The Kupperman index is a numerical conversion index and covers 11 menopausal symptoms: hot flashes (vasomotor), paraesthesia, insomnia, nervousness, melancholia, vertigo, weakness, arthralgia or myalgia, headache, palpitations and formication. Each symptom on the Kupperman index was rated on a scale from 0 to 3 for no, slight, moderate, and severe complaints. To calculate the Kupperman index, the symptoms were weighted as follows: hot flashes ($\times 4$), paraesthesias ($\times 2$), insomnia ($\times 2$), nervousness ($\times 2$), and all other symptoms ($\times 1$). Body mass index, blood pressure and lipid profile were recorded in all participants at baseline and at 3 and 6 months. Data collected were analyzed using standard statistical protocol.

OBSERVATIONS

A total of 100 postmenopausal women were alternately distributed into two groups-Group A(n=50, received 60mg of isoflavone and 500mg of calcium per day for) and Group B(n=50, received 500mg of calcium per day only). Both the groups had similar age, parity and duration since menopause distribution (vide table 1).

Table 1. Comparison of age ,parity and duration since menopause

	Group A (Isoflavone and calcium)	Group B (Only calcium)
Age (years)	45.00 \pm 3.33	45.58 \pm 2.6
Parity	2.96 \pm 0.19	3.38 \pm 0.21
Duration since menopause(years)	2.2 \pm 0.3	1.94 \pm 0.2

Menopausal symptoms in Group A (those using isoflavones) were lower compared to Group B (vide table 2). Mean KI (Kupperman index) in Group A reduced from 28.48 \pm 2.03 to 16.32 \pm 1.06(p- value<.01) whereas in Group B it reduced from 24.56 \pm 1.52 to 18.44 \pm 1.11(p-value<.05) at the end of 6 months (vide table 2). There was no significant difference between blood pressure and body mass index between the two groups (vide table3). Total cholesterol, triglycerides and low-density lipoproteins (LDL) decreased significantly in Group A compared to Group B. Total cholesterol in Group A decreased from 191.37 \pm 2.79 to 169.71 \pm 2.74mg/dl, triglycerides from 153.28 \pm 3.59 to 130.68 \pm 4.40mg/dl whereas low-density lipoproteins (LDL) from 119.48 \pm 2.83 to 96.59 \pm 3.28mg/dl. In Group B total cholesterol decreased from 181.31 \pm 5.50 to 180.35 \pm 5.13mg/dl whereas low-density lipoproteins (LDL) decreased from 109.27 \pm 5.88 to 106.05 \pm 5.65mg/dl. The high-density lipoproteins (HDL) increased in both groups after treatment(vide table3).

Table 2: Comparative study of menopausal symptoms by Kupperman index

		0 month	3 months	6 months
Vasomotor symptoms	Group A	7.36 \pm 0.75	5.92 \pm 0.70	4.48 \pm 0.78**
	Group B	7.68 \pm 0.76	7.04 \pm 0.70	6.40 \pm 0.73*
Paresthesias	Group A	4.24 \pm 0.31	3.52 \pm 0.30	2.48 \pm 0.24**
	Group B	3.52 \pm 0.17	3.44 \pm 0.18	3.04 \pm 0.26*
Insomnia	Group A	3.12 \pm 0.55	1.12 \pm 0.39	0.96 \pm 0.23**
	Group B	3.22 \pm 0.55	2.56 \pm 0.41	2.19 \pm 0.17*
Nervousness	Group A	2.16 \pm 0.54	2.16 \pm 0.54	0.48 \pm 0.15**
	Group B	1.92 \pm 0.39	1.60 \pm 0.35	1.28 \pm 0.28*
Depressed Mood	Group A	1.36 \pm 0.25	1.16 \pm 0.21	1.00 \pm 0.1*
	Group B	0.88 \pm 0.16	0.88 \pm 0.16	1.00 \pm 0.2*
Vertigo	Group A	0.84 \pm 0.26	0.84 \pm 0.26	0.84 \pm 0.26
	Group B	0.92 \pm 0.24	0.92 \pm 0.24	0.92 \pm 0.24
Weakness/ Fatigue	Group A	2.80 \pm 0.10	2.72 \pm 0.11	2.48 \pm 0.12**
	Group B	2.60 \pm 0.12	2.32 \pm 0.13	2.08 \pm 0.1**
Arthralgia + Myalgia	Group A	2.20 \pm 0.08	2.16 \pm 0.09	1.96 \pm 0.12
	Group B	2.68 \pm 0.10	2.52 \pm 0.10	1.96 \pm 0.16*
Headache	Group A	1.36 \pm 0.27	1.28 \pm 0.26	0.32 \pm 0.56**
	Group B	1.32 \pm 0.29	1.20 \pm 0.24	1.12 \pm 0.56
Palpitation	Group A	0.48 \pm 0.21	0.44 \pm 0.19	0.32 \pm 0.14
	Group B	0.32 \pm 0.14	0.32 \pm 0.14	0.32 \pm 0.14
Formication	Group A	0.24 \pm 0.12	0.24 \pm 0.14	0.20 \pm 0.13
	Group B	0.08 \pm 0.06	0.08 \pm 0.06	0.08 \pm 0.06
Mean KI	Group A	28.48 \pm 2.03	24.64 \pm 1.49	16.32 \pm 1.06**
	Group B	24.56 \pm 1.52	22.52 \pm 1.27	18.44 \pm 1.11*

*P< 0.05; **P<0.01

Table 3: Comparative study of Lipid profile, body mass index and blood pressure

		0 month	3 months	6 months
Serum Cholesterol (mg/dl)	Group A	191.37 \pm 2.79	184.58 \pm 3.12	169.71 \pm 2.74**
	Group B	181.31 \pm 5.50	179.80 \pm 5.34	180.35 \pm 5.13
Serum Triglycerides (mg/dl)	Group A	153.28 \pm 3.59	143.92 \pm 4.15**	130.68 \pm 4.40**
	Group B	155.80 \pm 3.03	157.04 \pm 3.69	162.68 \pm 4.28
Serum HDL (mg/dl)	Group A	43.58 \pm 1.41	43.96 \pm 1.52	44.84 \pm 1.36
	Group B	40.84 \pm 1.22	39.52 \pm 1.57	42.42 \pm 1.42
Serum LDL(mg/dl)	Group A	119.48 \pm 2.83	109.99 \pm 3.04*	96.59 \pm 3.28**
	Group B	109.27 \pm 5.88	108.72 \pm 5.92	106.05 \pm 5.65
BMI(kg/m ²)	Group A	24.2 \pm 0.5	24.3 \pm 0.5	24.4 \pm 0.52
	Group B	25.4 \pm 0.6	25.4 \pm 0.6	25.6 \pm 0.6
Max B.P.(mm Hg)	Group A	133 \pm 3	133 \pm 2	133 \pm 2
	Group B	131 \pm 2	131 \pm 2	131 \pm 1
Min B.P.(mm Hg)	Group A	84 \pm 2	84 \pm 2	84 \pm 1
	Group B	84 \pm 2	84 \pm 2	85 \pm 1

**P<0.01; *P<0.05

DISCUSSION

Most women experience some effects of estrogen deficiency during menopause. Effects range from short-term discomfort to long-term changes that can have a profound effect on a woman's health. The present clinical study was done to evaluate the short-term effects of soy isoflavones (which is a class of phytoestrogen that are structurally or functionally similar to steroidal estrogens but with lesser side effects) in postmenopausal women. In our study, a total of 100 postmenopausal women were alternately divided into two groups-Group A(n=50, received 60mg of isoflavone and 500mg of calcium per day) and Group B(n=50, received 500mg of calcium per day only). In our study the average age of women was approximately 45 years with average time since menopause ranging from 2 to 2.2 years. The age at menopause in our study was similar to the earlier studies which have reported menopause at 43 to 49 years in developing countries.^{8,9} The present study showed that Kupperman index decreased significantly in Group A (from 28.48 ± 2.03 to 16.32 ± 1.06 i.e. 45% decline) compared to Group B (from 24.56 ± 1.52 to 18.44 ± 1.11 i.e. 25% decline) Our findings are in contrast to earlier report by Germain et al where no improvement in menopausal index was seen with either soy proteins or soy isoflavones after 24 weeks.¹⁰ However, Murkies et al have demonstrated significant decrease in menopausal symptoms in soy supplemented group within 6 weeks as compared to wheat flour group.¹¹ In our study total cholesterol, triglycerides and low-density lipoproteins (LDL) decreased significantly in Group A (Total cholesterol decreased from 191.37 ± 2.79 to 169.71 ± 2.74 mg/dl, triglycerides from 153.28 ± 3.59 to 130.68 ± 4.40 mg/dl and low-density lipoproteins (LDL) from 119.48 ± 2.83 to 96.59 ± 3.28 mg/dl) compared to Group B (total cholesterol decreased from 181.31 ± 5.50 to 180.35 ± 5.13 mg/dl, low-density lipoproteins (LDL) decreased from 109.27 ± 5.88 to 106.05 ± 5.65 mg/dl whereas triglycerides increased from 155.80 ± 3.03 to 162.68 ± 4.28 mg/dl. Numerous other clinical studies have shown that soy protein can cause significant reduction in serum total cholesterol, LDL-Cholesterol and triglycerides.^{12,13,14} Isoflavones as part of soy protein have been postulated to account for the hypocholesterolemic effect of soy protein.¹⁵⁻¹⁷ However, several other investigations also do not support the hypocholesterolemic role of soy isoflavones.^{12,18-20} Therefore our clinical study indicates that isoflavone can be an invaluable resource for postmenopausal women for combating menopausal symptoms.

CONCLUSION

Estrogen replacement has long been considered as therapy of choice for the treatment of climacteric symptoms in postmenopausal women but estrogen has numerous side effects and prolonged exposure to unopposed estrogen also increases the risk of endometrial hyperplasia and

neoplasia. Isoflavones (a class of phytoestrogen) act as selective estrogen enzyme modulators functioning as pro-estrogens when estrogen deficiency is present and as antiestrogens when excess estrogen is present and they delicately balance the estrogen metabolism in the body. Our clinical study indicates that isoflavones can be of great use for combating menopausal symptoms in postmenopausal women and can be effectively used as an alternative agent, which has the beneficial effects of estrogen but considerable lesser risks and side effects when compared to estrogen.

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