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Original Research Article

Effect of 16 Weeks Soy Supplementation on Bone Metabolism and Body Composition in At Risk Osteoporotic Rajasthani Postmenopausal Women: A Randomized Controlled Study

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ABSTRACT

Background:- Menopause is a natural event associated with gradual reduction of estrogen production. Decrease level of estrogen cause physical and psychological changes that effect women's health. Soybean contains phytoestrogen, which are similar to the hormone estrogen. There is substantial evidence that soybean have the potential to address changes associated with menopausal transition.
Aim:- To investigate the effect of soy isoflavone consumption on bone metabolism and body composition in postmenopausal women of Udaipur city, Rajasthan.
Materials and method:- Sixty postmenopausal women at medium risk of osteoporosis were randomly divided into two groups (30 in each) treatment and control. Treatment group was supplemented with 40 g soyflour containing 52.62 mg isoflavones for 16 weeks. Another group of 30 subjects served as control. Biochemical profile (alkaline phosphatase, estrone, estradiol) and body composition (BMI, WHR, body fat per cent, body fat mass and fat free mass) were estimated at initial level (0 day) and after 16 weeks.
Results:- Results shows a significant increase in alkaline phosphatase, estrone, estradiol and fat free mass ($p<0.05$) and a significant ($p<0.05$) decrease in WHR in treatment group. Although there was a significant increase in weight and BMI also but it was still in the normal category. No significant changes in biochemical profile and body composition were found in the control group.
Conclusion:- The study reveals that consumption of soyflour enhances bone formation and can have positive effect on improving muscle mass in osteoporotic postmenopausal women.

Key Words:- Soyflour, Bone mass, Alkaline phosphatase, Body composition, Fat free mass

INTRODUCTION

Menopause is the permanent cessation of menstruation due to loss of ovarian follicular function, which results in decreased production of estradiol and other hormones. Women transitioning to menopause are at risk for central fat mass gain and associated health problems caused by hormone-related changes in appetite, energy expenditure, and body fat distribution. [1,2] Health problems associated with central fat mass, especially abdominal fat, in postmenopausal women include chronic diseases such as heart disease, hypertension, and osteoporosis. [3,4]

Estrogen deficiency is regarded as a leading cause of bone loss and osteoporosis in postmenopausal women. Estrogen has a critical role in bone health, positively regulating bone mass in both direct and indirect manners. Estrogen withdrawal during menopause includes metabolic changes that increase bone resorption and decrease bone formation. [5] In response to declining estrogen levels, women can lose substantial amounts of bone mass in the decade following menopause, which markedly increases their fracture risk. [6]

Isoflavones, chiefly derived from soybean are a group of biologically active substances shares the structural and functional homogeneity with estrogen and its important constituents are genistein, daidzein and glycitein. [7] Isoflavone exert its effect through selective estrogen receptor and promote its natural effect. Increasing the isoflavones naturally through diet may be an effective method in achieving health and preventing bone loss. Although phytoestrogens are not as potential as the endogenous estrogens, they are widely self-prescribed against the treatment of menopause and postmenopausal osteoporosis and are considered safe and beneficial in every part of the world. [8,9] A research group from China analyzed multiple published international clinical studies on the application of soy isoflavones to prevent osteoporosis, the central cause of hip fractures and other bone fractures, and concluded that soy isoflavones intake increase bone mineral density (BMD) and decrease bone resorption marker. [10] Besides preventing bone loss, soy products are a good substitute for creating beneficial effect also on regional body fat and lean tissue distribution in menopausal women. [11]

Clinical trials conducted so far have been either on effect of phytoestrogen isolate in its purified form or there are limited trials on dietary supplement among human subjects. Therefore, in the light of above facts there is a need to undertake more clinical trials to support medicinal benefits of soybean supplementation especially among Indian population group. Thus this research is aimed to examine the effect of soyflour containing isoflavones on bone metabolism and body composition of Rajasthani postmenopausal women.

MATERIALS AND METHODS

Study design and participants:- Three hundred twenty two postmenopausal women aged between 45-55 years were preliminary surveyed from Udaipur city, Rajasthan, India for the screening of subjects for intervention trial. Osteoporosis Self Assessment Tool for Asians (OSTA) was used for the identification of women with low, medium and high risk of osteoporosis. OSTA is a simple, effective, clinical risk assessment tool to identify elderly persons at risk of osteoporosis and to assess the likelihood of low bone mass in men and women. [12,13] To be qualified for this study, the subjects had to have on medium risk category of osteoporosis. The exclusion criteria were current or previous use of estrogen therapy, the consumption of soy products or supplements, treatment with insulin or oral hypoglycaemic, antihypertensive agents, aspirin, history of hyper and hypothyroidism, kidney, liver, infectious diseases, cancer, or allergic reaction to soy consumption. Finally, 60 women who met the inclusion criteria were chosen for this study. All participants were provided with the informed written consent form to sign. The present study was approved by the Research Committee of the University.

Study procedures:- This study was a 16-week randomized controlled trial. A questionnaire on demographic characteristics was completed at baseline. The participants were randomized into two groups (treatment and control) by the proportional randomization method using a table of random numbers generated by Microsoft Excel. Treatment group (n=30) received 40 g soyflour. Control group (n=30) received nothing instead, since the participants in the treatment groups were consuming natural soy products not pills, so it was impossible to apply any placebo for the control group. The control group was encouraged not to change their usual dietary habits and lifestyles and was instructed to avoid taking soybean and soybean products. The treatment group was provided with 7 packages of 40 g of soyflour for 1 week supply. Refills were provided the following week. They were trained on how they could prepare their chapatti (Indian bread) with soyflour. The nutrient composition of soyflour is shown in Table 1. Provided soyflour contained 52.62 mg isoflavones. Thus, the women in the treatment group received 52.62 mg of isoflavones per day. The participants were visited every week.

Measurements:- Participants' height was measured using a platform spring balance without shoes to the nearest 0.5 cm. Weight, Body mass index (BMI), body fat (%), body fat mass (kg) and fat free mass (kg) were measured with body composition analyzer (Tanita body composition analyzer). Waist circumference (WC) was measured just above the iliac crest. Hip circumference (HC) was assessed at the level of the greater trochanter. From these the waist-to-hip ratio (WHR) was calculated.

Fasting blood samples were collected from each participants for alkaline phosphates, estrone and estradiol estimation. Five millilitres of venous blood was collected by the trained technician in clean, dry and sterilized vials and allowed to stand at room temperature for 15 minutes. The supernatant (serum) was then separated, stored at 2-8°C temperature range and used for biochemical estimation. Measurements were assayed on fully autoanalyzer (COBAS INTEGRA). All measurements were recorded before and after the 16-week intervention.

Statistical analysis:- A paired t-test was run to determine changes for the 16-week intervention in each group. An independent t-test was applied to compare the means of variables before and after intervention. The percentage change for each variable was calculated by the formula $[(E - B)/B] \times 100$, while E is the value after intervention and B is the baseline value. P-value of less than 0.05 was considered significant. The statistical analyses were all performed by using SPSS (Statistical Package for Social Studies) version 20.

Table 1: Nutrient content of soyflour on dry weight basis (per 100 g)

Nutrients	Mean
Protein (g)	44.07
Fat (g)	19.14
Ash (g)	4.70
Crude fiber (g)	5.25
Carbohydrate (g)	26.82
Energy (kcal)	455.89
Calcium (mg)	198
Isoflavone* (mg)	131.55

* Fresh weight basis

RESULTS

Socio-demographic profile:-

All participants completed the entire study. Soyflour was well tolerated. There was no serious complain on the consumption of soy except for cause of flatulence for sometimes in small number of individuals. Demographic data showed that the average age, age at menopause and height of treatment group and control group was 54.53±0.85 years and 54.27±1.06 years, 47.11±2.97 years and 47.12±2.90 years, 151.97±4.87 cm and 150.90±6.66 cm respectively. In both groups all were married and a fairly large number were housewives, others employed in government and private jobs. Maximum subjects from both groups were vegetarian (Table 2).

Table 2: Demographic characteristics of the participants

Variables	Treatment group (n=30)	Control group (n=30)
Age (y) (mean±SD)	54.53±0.85	54.27±1.06
Age at menopause (mean±SD)	47.11±2.97	47.12±2.90
Height (cm) (mean±SD)	151.97±4.87	150.90±6.66
Marital status		
Married	100 (30)	100 (30)
Unmarried	0 (0)	0 (0)
Occupation		
Service	33.33 (10)	40 (12)
Business	10 (3)	10 (3)
Housewife	56.66 (17)	50 (15)
Food habits		
Vegetarian	70 (21)	83.33 (25)
Non vegetarian	30 (9)	16.66 (5)
Ovo vegetarian	0 (0)	0 (0)

Values in parentheses indicate number of subjects

Effect of soyflour supplementation on biochemical profile:-

The serum level of alkaline phosphatase, estrone and estradiol are shown in Table 3. No significant difference in the baseline values of these variables was observed. In the treatment group there was a significant increase ($p<0.05$) in the mean values of serum alkaline phosphatase prior to and after the intervention period. The mean value increased from 101.29±15.85 U/l to 127.19±17.24 U/l with 25.5 per cent change indicating a good increase whereas control group showed not significant increase from the baseline to completion of the study. The intake of soyflour helped to increase the mean serum estrone from 22.10±4.74 pg/ml to 27.44±4.13 pg/ml after 16 weeks among treatment group. There was a significant increase of 24.1 per cent and it was found to be statistically significant ($p<0.05$). In control group serum estrone slightly decreased with 1.9 per cent change which was non-significant. Results of the estradiol level of the treatment group before and after the soyflour intervention showed significant increase from 18.36±10.62 pg/ml to 21.57±7.46 pg/ml with a per cent change of 17.4. In case of control group, there was decrease of 2.1 per cent in estradiol level prior and after the study.

Table 3: Biochemical characteristics of participants at baseline and after 16 weeks of intervention

Parameters	Treatment group (n=30)	Control group (n=30)	p^{ξ}-value
Alkaline phosphatase (U/l)			
Baseline	101.29±15.85	99.67±17.42	0.707^{NS}
Week 16	127.19±17.24	101.54±24.26	0.000*
p^{δ}-value	0.000*	0.575^{NS}	
Percent change	25.57 ↑	1.87 ↑	
Estrone (pg/ml)			
Baseline	22.10±4.74	23.25±5.28	0.381^{NS}
Week 16	27.44±4.13	22.79±4.90	0.000*
p^{δ}-value	0.000*	0.120^{NS}	
Percent change	24.16 ↑	1.97 ↓	
Estradiol (pg/ml)			
Baseline	18.36±10.62	17.94±8.63	0.869^{NS}
Week 16	21.57±7.46	17.55±8.03	0.049*
p^{δ}-value	0.001*	0.339^{NS}	
Percent change	17.48 ↑	2.17 ↓	

δ: p-value as calculated by t test, ξ: p-value as calculated by independent sample t test, *Significant at 5% level, NS – Non significant, ↑ indicates increase, ↓ indicates decrease

Effect of soyflour supplementation on body composition:-

Table 4 shows the mean values of body composition indicators in all groups at baseline and after 16 weeks of intervention. There were no significant differences seen among the groups with regard to any baseline variable. At baseline the participants of treatment and control group were classified as normal body weight. The mean BMI of treatment group showed an increase from 21.58±1.65 kg/m^2 to 22.27±1.65 kg/m^2. Thus, the per cent increase was 3.1 which was found to be significant ($p<0.05$). The increase in BMI was due to increase in weight of the subjects but the mean value after intervention was in the range of normal category (18.5-24.9 kg/m^2) as suggested by WHO/IASO/IOTF. [14] No significant increase in BMI was observed in control group. In case of waist and hip circumference, there was an increase of 0.2 per cent and 0.7 per cent respectively in treatment group. The per cent increase in the waist circumference was not significant but increase in hip circumference was found to be significant ($p<0.05$). Results of WHR showed a reduction of 1.1 per cent in treatment group and increase of 1.1 per cent in control group and both were found to be non significant.

Body fat, the fraction of the total body mass that is adipose tissue is often used as an index to monitor progress during intervention. The mean body fat per cent of the treatment group before intervention was 30.56±2.13 per cent and after intervention it was 30.15±3.07 per cent exhibiting 1.3 per cent decrease which was non significant. In control group, there was 1.6 per cent increase in the body fat before and after the study and this increase was also found to be non significant. Results regarding fat mass showed an increase of 1.6 per cent and 2.3 per cent in treatment group and control group respectively and both were found to be non significant. Fat free mass of treatment group increased from 33.93±0.81 kg to 35.21±1.77 kg at the end of the study, with a significant ($p<0.05$) increase of 3.7 per cent. Control group did not show any change in the fat free mass.

Table 4: Body composition indicators of participants at baseline and after 16 weeks of intervention

Indicators	Treatment group (n=30)	Control group (n=30)	p^{ξ}-value
Body weight (kg)			
Baseline	48.82±1.48	49.16±0.97	0.303^{NS}
Week 16	50.36±1.67	49.56±1.60	0.065^{NS}
p^{δ}-value	0.000*	0.084^{NS}	
Percent change	4.32 ↑	0.81 ↑	
BMI (kg/m^2)			
Baseline	21.58±1.65	21.39±1.35	0.620^{NS}
Week 16	22.27±1.65	21.53±1.15	0.049*
p^{δ}-value	0.000*	0.141^{NS}	
Percent change	3.19 ↑	0.65 ↑	
Waist circumference (cm)			
Baseline	84.29±7.34	85.16±5.87	0.616^{NS}
Week 16	84.49±7.03	85.51±5.91	0.547^{NS}
p^{δ}-value	0.210^{NS}	0.120^{NS}	
Percent change	0.23 ↑	0.41 ↑	
Hip circumference (cm)			
Baseline	94.14±5.95	93.38±6.00	0.621^{NS}
Week 16	94.87±5.84	93.63±6.19	0.429^{NS}
p^{δ}-value	0.038*	0.140^{NS}	
Percent change	0.77 ↑	0.26 ↑	
WHR			
Baseline	0.89±0.04	0.90±0.03	0.115^{NS}
Week 16	0.88±0.04	0.91±0.03	0.018*
p^{δ}-value	0.107^{NS}	0.222^{NS}	
Percent change	1.12 ↓	1.11 ↑	
Body fat (%)			
Baseline	30.56±2.13	30.10±2.42	0.526^{NS}
Week 16	30.15±3.07	30.61±3.68	0.602^{NS}
p^{δ}-value	0.277^{NS}	0.422^{NS}	
Percent change	1.34 ↓	1.69 ↑	
Body fat mass (kg)			
Baseline	14.90±1.38	14.81±1.34	0.814^{NS}
Week 16	15.15±1.73	15.16±2.16	0.985^{NS}
p^{δ}-value	0.218^{NS}	0.271^{NS}	
Percent change	1.67 ↑	2.36 ↑	
Fat free mass (kg)			
Baseline	33.93±0.81	34.35±1.08	0.099^{NS}
Week 16	35.21±1.77	34.39±1.41	0.055^{NS}
p^{δ}-value	0.000*	0.807^{NS}	
Percent change	3.77 ↑	0.11 ↑	

δ: p-value as calculated by t test, ξ: p-value as calculated by independent sample t test, *Significant at 5% level, NS – Non significant, ↑ indicates increase, ↓ indicates decrease

DISCUSSION

Bone alkaline phosphatase catalyses the hydrolysis of phosphate esters at the osteoblast cell surface to provide a high phosphate concentration for the bone mineralization process as part of the osteoblast cell role in bone remodelling. Therefore, during periods of active bone formation and bone growth alkaline phosphatase levels are raised in the circulation. [15] Animal or in vitro studies had proposed that isoflavones might improve bone health through estrogenic activity in the inhibition of bone resorption or stimulation of bone formation, or via estrogen receptor α-dependent mechanisms. [16,17] It seems isoflavones of soyflour can be effective on alkaline phosphatase activity through curbing bone resorption in soy group as was demonstrated in subjects of the present study. This is somewhat in agreement with study on postmenopausal women supplemented with red clover derived isoflavone suggesting that isoflavones stimulate bone formation. [18] In an another study, Hanachi et al. [19] found that the total alkaline phosphatase activity in soymilk consumption and exercise plus soymilk was significantly ($p<0.05$) increased, compared with the baseline time, 190.82±42.3, 211.91±43.1, 170.58±39.6, 183.67±58.9 (IU/L) respectively. Alekel et al. [20] showed a modest effect of soy isoflavone on bone particularly at femoral neck. Other studies have also shown beneficial effect of soy isoflavone on bone health and maintain a healthy bone structure during menopause. [21,9,22] This indicates that consumption of soy isoflavones offers protection against osteoporosis.

In postmenopausal women, a reduction occurs in the number and activity of estrogen receptors in tissues, and therefore more potent endogenous or exogenous estrogens are not necessary in this period. Estrogen therapy significantly increases the serum levels of estrone far above the levels observed in postmenopausal women. [23] Estrone is also the main precursor of the small amount of estradiol still present in postmenopausal women. Estrone can then be the most suitable endogenous estrogen during the postmenopausal period for maintenance of basic physiological needs at this time. In a study, it was found that reduced serum estradiol concentrations with age leads to increased bone turnover, which is a risk factor for fractures. [24] In the present investigation estradiol hormone level was elevated when postmenopausal women were supplemented with soyflour. This result is in agreement with Brook et al. [25] who reported that supplementation with flaxseed improve the decline level of estrogen in postmenopausal women to great extent. Meta-analysis by Hooper et al. [26] also showed an increase in estradiol level in postmenopausal women consuming isoflavone rich soy products but Sapbamrer et al. [27] found no significant effects. The conflicting results were might be due to the differences in terms of the form of soy supplementation, intake amount, duration of supplementation and individual absorption ability.

Furthermore, it is important to note that in soy group, body weight and fat free mass increased significantly. In this sense, it has been demonstrated that soyflour normally engenders an increase in fat free mass that includes muscles, bone and body water. Similar results regarding significant increase in fat free mass was reported by Myle`ne et al. [28] Maesta et al. [29] observed a significant increase of 1.3 kg in muscle mass after 16 weeks of intervention in both soy protein plus resistance exercise and placebo plus resistance exercise groups which is comparable to the findings of the present study. Similarly, Liu et al. [11] conducted a randomized placebo-controlled trial among 180 postmenopausal Chinese women and observed a mild but significant favourable effect on body composition with supplementation of soy protein with isoflavones. They found a mean difference of percentage change in body fat percentage between the soy and the iso groups was -3.7 per cent, and between the soy and the placebo groups was -2.5 per cent. Another study stated that after 12 week intervention of soy there is a mild favourable effect on body composition in postmenopausal women. [30] These finding suggest that an isoflavone rich diet is associated with increased fat free mass and may play a role in the prevention of chronic diseases.

CONCLUSION

The results of the present study demonstrated that intake of 40g of soyflour daily for 16 weeks significantly increases levels of alkaline phosphatase, estrone and estradiol. Soyflour also helps to increase fat free mass of postmenopausal women. No adverse effect of soyflour was observed on the health status of treated subjects. These data may suggest that consumption of 40 g soyflour containing 52.62 mg isoflavones for 16 weeks enhances bone formation. Soyflour can have positive effects on improving body fat distribution, though this effect was little. However, being consistent in reducing total body fat and abdominal fat and in increasing fat free mass, the results are all pointing out that there is a potential capacity of soy in these improvements.

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