ORIGINAL ARTICLE

ROLE OF PHYTOESTROGEN IN SUPPRESSING BONE TURNOVER IN A GROUP OF POSTMENOPAUSAL WOMEN

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Background: Osteoporosis has emerged a major health hazard in postmenopausal women. The process of osteoporosis accelerates two year prior to menopause, reaching the peak level during first 3 years of menopause when women loss 3–5% of their bone mass per year. This study tried to find out the role of phytoestrogne in improving the bone mineral density and bone related biochemical parameters in group of postmenopausal women. **Methods:** Fifty postmenopausal women with age range 50–60 years were included in the study. Phytoestrogen with mineral supplement were given twice daily for 3 months. Biochemical parameters like serum calcium, magnesium, alkaline phosphatase, uric acid, total protein and oestrogen were determined before and after phytoestrogen therapy by autoanalyser and ELIZA (oestrogen assay). T-score before and after phytoestrogen were find out by densitometer DEXA. **Results:** The level of serum calcium, magnesium, uric acid and oestrogen was increased in women after taking phytoestrogen but significant difference ($p<0.01$) was only observed in case of serum calcium. Level of serum alkaline phosphatase and total serum protein were slightly increased with no significant different before and after phytoestrogen therapy. Value of T-score was although markedly decreased after phytoestrogen therapy but it showed no significant difference. **Conclusion:** It is concluded that as the early years of menopause are a period of rapid bone loss, and the risk for osteoporosis increases substantially, the habitual intake of soy protein and isoflavones may play a role in the retardation of bone loss.

Keywords: Osteoporosis, Phytoestrogen, Postmenopausal status

INTRODUCTION

Osteoporosis has emerged a major health hazard in postmenopausal women. It is defined as a skeletal disorder characterised by impaired bone strength which predisposes to an increased risk of fracture. There is decrease mass per unit volume (density) of bone matrix (osteoid) maintaining the bone brittle and labile to break especially hip, vertebrate and wrist.[1] The process accelerates two year prior to menopause, reaching the peak level during first 3 years of menopause when women loss 3–5% of their bone mass per year.[2]

The prevalence of osteoporosis in female population is variable in different age groups, i.e., in the age range of 50–59 years, the incidence of osteoporosis is 13.5%, in age range of 60–69 years, it is 78% and above 70 yrs of age the frequency of osteroporosis rises up to 100%. After the age of 40, slow resorption of bones occurs in both sexes but after menopause women loss of additional bone mass for a decade leading to decreased bone mineral density (BMD). The process of BMD actually starts prior to menopause due to oestrogen deficiency[3] and become more marked often menopause due to rapid decline in oestrogen level.[4] Pakistani women with age over 45 years one more susceptible to osteoporosis (32.4%) and osteoporosis (6.7%).[5]

Oestrogen replacement therapy has been remained a popular therapy to alleviate menopausal symptoms, to minimised the rise of osteoporosis and provide effective protection against the activation of bone turnover.[6] Oestrogen is helpful in maintaining bone health by increasing osteoclast apoptosis and decreasing cytokines which promote osteoclast activity.[7] However the use of HRT may increase the risk of breast and endometrial cancer.[8]

Phytoestrogens are plant derived compounds with estrogenic activity found in natural diet including soybean, soy product and alfafa fodders used widely for prevention and treatment of osteoporosis.[9] Phytoestrogens mainly consist of isoflavone, lignans and coumestans. Soy Isoflavone are heterocyclic phenols have similar structure to 17 beta estradiol and selective oestrogen receptor modulator and its important constituents are genistein, daidzein and glycitein.[11] Isoflavone exert its effect through oestrogen receptor inducing receptor dimerization and promote its natural effect.[12] Their action is depend on the target tissue, receptor status of the tissues and level of endogenous oestrogen.[13] These are the best known phytoestrogen used for the prevention of postmenopausal osteoporosis by stimulating osteoblasttic activity and inhibit osteoclast formation.[14,15] They influence human health by means of genomic and non genomic mechanism. It is proposed that due to low molecular weight, they pass through the cell membrane and interact with oestrogen receptor (genomic) to shows estrogenic effects while this effect is inhibited via tyrosine kianse (non genomic).[16,17]

Regular physical exercise, adequate intake of calcium, magnesium, vitamin D, avoidance of steroids potentiates the estrogenic effects.[18]

BMD is a key determinant for osteoporotic changes in postmenopausal women is a reflection of peak bone mass attained in young adulthood and the mass lost during perimenopausal age.[19] A T-score between -1.7 to 0 and above is normal while women with a T-score between -1.7 to -2.3 are prone to develop osteroporosis. A T-score <-2.3 indicate osteopenia.[20] Effect of phytoestrogen on BMD is evaluated by T-score of bone carried out by bone densitomenter before and after 6 months of their administration. The results are compared and in most cases revealed an increase in BMD and reduced bone bio markers thereby reduce the risk of fracture.[21]

Present study tried to find out the role of phytoestrogne in improving the bone mineral density and bone related biochemical parameters in group of postmenopausal women.

MATERIAL AND METHODS

Fifty post menopausal women attending the Gynaecology and Orthopaedics OPD of Sir Ganga Ram Hospital, Lahore with age range 50–60 years were included in the study. Commercially available Phytoestrogen capsule, and Calcium tablets were given for 3 months. Biochemical parameters like serum calcium, magnesium, alkaline phosphatase, uric acid, total protein and oestrogen were determined before and after phytoestrogen therapy by autoanalyser and ELIZA (oestrogen assay). T-score before and after phytoestrogen were find out by densitometer DEXA. Subjects included in the study were the teaching staff of Fatima Jinnah Medical College, Lahore, Orthopaedic ward of Sir Ganga Ram Hospital Lahore and local clinic of Lahore city. Detail history of women was recorded in Performa. Letter of consent was also taken from each subject. Our study was done in accordance with ethical standards for human experimentation and was approved by the Ethics Committee of medicine.

RESULTS

Bone related biochemical parameters before and after phytoestrogen therapy in osteoporotic postmenopausal women are tabulated (Table-1). It was observed that the level of serum calcium, magnesium, uric acid and oestrogen was increased in women after taking phytoestrogen as compared to before taking phytoestrogen but significant difference (p<0.01) was only observed in case of serum calcium. Level of serum alkaline phosphatase and total serum protein were slightly increased with no significant different before and after phytoestrogen therapy. Value of T-score was although markedly decreased after phytoestrogen therapy but it showed no significant difference (Figure-1 and Table-1).

Table-1: Bone related biochemical parameters before and after phytoestrogen therapy in osteoporotic post menopausal women

Biochemical parameters	Before phytoestrogen	After phytoestrogen
Serum calcium (mg/dl)	7.98±0.79	8.62±0.76*
Serum magnesium (mg/dl)	1.92±0.58	2.27±0.64
Serum alkaline phosphatase (U/L)	219.32±27.51	222.07±25.97
Serum uric acid (mg/dl)	4.44±1.22	4.09±1.17
Serum total protein (gm/dl)	7.16±0.52	7.37±0.43
Serum oestrogen (ρg/ml)	93.4±51.14	123.6±62.53
T-score	-1.67±1.2	-0.99±1.28

*p<0.01=Significant

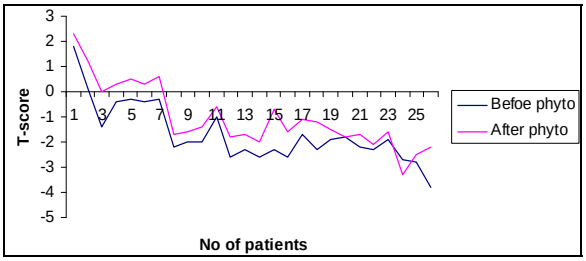

Figure-1: Values of T-score before and after phytoestrogen therapy

DISCUSSION

In recent years, isoflavones have increased in popularity as an alternative to conventional hormone replacement therapy for the relief of hot flashes and other symptoms associated with menopause. Currently, isoflavones are available as tablets, capsules, powders (particularly soy protein powders), drinks and bars as well as a component of traditional soy foods. Typically, supplements provide 25–100 mg total isoflavones if consumed according to package directions.[22]

Bone related biochemical parameters before and after phytoestrogen therapy in osteoporotic post menopausal women were estimated. It was observed that the level of serum calcium was significantly increased (p<0.001) in women after taking phytoestrogen and supplement of calcium as compared to before taking phytoestrogen. Our study is in line with a study that reported that isoflavone (IP), prevents bone loss associated with ovarian hormone deficiency. This protective effect of IP may be partly due to its ability to enhance calcium absorption.[23]

Level of serum magnesium, uric acid and oestrogen was non-significantly increased in women after taking phytoestrogen with minerals as supplement as compared to before taking phytoestrogen. Our study is in accord with a study who reported that oral magnesium supplementation suppresses bone turnover in postmenopausal

osteoporotic women.[24] Our study is in contrast to the study who used isoflavone and observed that intestinal bacteria metabolize the soy isoflavone daidzein to O-desmethylangolensin or equol. The study found that the Equol product decreased the level of serum uric acid.[25]

An increased level of oestrogen after taking phytoestrogen was also noted. Our study is in line with a number of studies. It is reported that estrogens exert a protective action in maintaining bone health by increasing osteoclast apoptosis and decreasing cytokines which promote osteoclast activity.[26]

Other studies observed that phytoestrogen compound is able to elicit an estrogenic response, regardless of the mechanism involved (via the oestrogen receptor or not).[27,28] However phytoestrogens are able to act not only estrogenically as oestrogen agonists, but also antiestrogenically as antagonists by blocking or altering ERs, thus they are more closely resemble natural selective oestrogen receptor modulators.[29] It means that they perform a complex function as agonists or antagonists depending on the tissue, ER type and quantity and the endogenous hormonal milieu.[30]

Level of serum alkaline phosphatase and total serum protein were slightly increased with no significant different before and after phytoestrogen therapy. Our study is in contrast to some studies who observed a direct relationship of phytoestrogen with alkaline phosphatase. One of the study stated that phytoestrogens is able to bind to oestrogen receptors and to stimulate the AlkP activity 2- 4-fold. This may increase the rate of bone formation and bone density in some bones, suggesting the bone loss preventive role.[31,32] It is reported that phytoestrogens present in the extract bound to serum protein showed antioxidant properties.[33]

Mean value of T-score before phytoestrogen therapy showed that the women with postmenopausal status were prone to develop osteoporosis. Present study observed that the value of t-score was markedly decreased after phytoestrogen therapy. A study found that Isoflavones may alter bone turnover in postmenopausal women by decreasing bone resorption and increasing bone formation.[34] It is proposed that phytoestrogens perform their antiosteoporotic effect by stimulating osteoblastic activity through an oestrogen receptor mediated action[35] or by increasing the production of insulin-like growth factor-I[23], which may enhances osteoblastic activity.[36] Our study is in contrast to many studies. A group of workers found that 150 mg of isoflavone taken twice daily for 6 months by 37 postmenopausal women showed no significant efficacy of the phytoestrogen treatment.[37] A study failed to find any significant efficacy on BMD of 99 mg of isoflavones taken daily.[38]

CONCLUSION

Many human trials have evaluated the effects of phytoestrogens on menopausal women. The results are conflicting above all because of a great methodological variability: different subjects with regards to hormonal status, premenopausal or postmenopausal, as well as early or late postmenopause, a factor which is very important for the evaluations of osteoporotic problems because bone turnover is usually different in these periods. Moreover, the phytoestrogens used were different as regards type and dosage, and the number of patients and duration of the studies was usually too short. However, it is concluded that as the early years of menopause are a period of rapid bone loss, and the risk for osteoporosis increases substantially, the habitual intake of soy protein and isoflavones may play a role in the retardation of bone loss.

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