MEDIA MEDIKA INDONESIANA

Phytoestrogen Genistein and Black Cohosh and Marker of BMD in Menopausal Women

Rizani Amran *, Adenan Abadi *, Theodorus **, Elvi Widiastuti *

ABSTRACT

Background: In Indonesia, phytoestrogens can be found in the market as supplement to resolve climacteric complaint and osteoporosis. This phytoestrogens has not been proven scientifically to have benefit in overcoming the climacteric complaints and osteoporosis in menopausal women. Therefore, it is important to have clinical test searching data for knowing the increase of bone mineral density (BMD).

Methods: The design was comparison clinical test in the form of "add on" with double blind in Hospital of Mohammad Hoesin Palembang started in August 2010 until February 2011 putting subjects into fitoestrogen and placebo groups randomly. T-score of spine and femur were measured using done densitometry before and after 6 months supplementation.

Results: In the beginning of study, it was found that the average of spine T-score in the group of phytoestrogens was -1.455±0.264 after 6 months it increased to -1.295±0.223 with change 0.160±0.153 (p=0.001). Whereas in placebo group the average of spine T-score at the beginning of the study was -1.295±0.223 becoming -1.560±0.414 with decrease of -0.100±0.273 (p=0.118). Femur T-score level, of phytoestrogens group at the beginning of the study was -1.415±0.215, after 6 months it became -1.270±0.141 with change of 0.145±0.170 (p=0.001). In placebo group, the average of femur T-score was -1.475±0.202 becoming -1.595±0.421 with of decrease -0.120±0.33 (p=0.124). The status of spine and femur T-score BMD both in, phytoestrogens and placebo group was osteopenia at the beginning of the study. After 6 months, spine T-score in phytoestrogens group did not change, and in placebo group, 2 subject showed osteoporosis with spine T-score and femur T-score -2.7 and -2.75(±0.212).

Conclusions: The administration of phytoestrogens is able to maintain bone mineral density and prevent the occurrence of osteoporosis.

Keywords: Phytoestrogens, BMD, T-score, menopause

ABSTRAK

Fitoestrogen genistein dan black cohosh dan penanda BMD pada perempuan menopause

Latar belakang: Di Indonesia, fitoestrogen beredar di pasaran sebagai suplemen untuk mengatasi keluhan klimakterik dan osteoporosis. Fitoestrogen ini belum terbukti secara ilmiah bermanfaat untuk mengatasi keluhan klimakterik maupun osteoporosis pada perempuan menopause. Oleh karena itu uji klinik ini dilakukan untuk mencari data guna mengetahui meningkatnya gambaran BMD.

Metode: Desain adalah uji klinik berpembanding dalam bentuk add on, secara tersamar ganda di RS Dr. Mohammad Hoesin Palembang bulan Agustus 2010 sampai dengan Februari 2011 pada subyek yang dibagi dalam kelompok fitoestrogen dan placebo secara acak. Variabel yang diukur adalah skor T tulang vertebra dan femur menggunakan bone densitometer sebelum dan setelah 6 bulan mendapat suplemen.

Hasil: Pada awal penelitian rerata T-skor tulang belakang kelompok fitoestrogen -1,455±0,264 setelah 6 bulan menjadi -1,295±0,223 dengan perubahan 0,160 ± 0,153 (p=0,001). Sedangkan kelompok plasebo rerata T-skor tulang belakang pada awal penelitian -1,295±0,223 menjadi -1,560±0,414 dengan penurunan -0,100±0,273 (p=0,118). Pada kadar T-skor femur, di awal penelitian kelompok fitoestrogen -1,415±0,215 setelah 6 bulan menjadi -1,270±0,141 dengan besaran perubahan 0,145±0,170 (p=0,001). Pada kelompok plasebo rerata T-skor femur pada awal penelitian -1,475±0,202 menjadi -1,595±0,421 dengan perubahan -0,120±0,33 (p=0,124). Status BMD T-skor tulang belakang dan femur di awal penelitian, kelompok fitoestrogen dan kelompok

* Department of Obstetrics and Gynecology, Faculty of Medicine University of Sriwijaya/Dr. Mohammad Hoesin General Hospital, Jl. Jend. Sudirman Km 3.5 Palembang 30126, Email: rizani_amran@yahoo.com

5. Tice JA, Ettinger B, Ensrud K. Phytoestrogen supplements for the treatment of hot flashes: the isoflavone clover extract (ICE) study: a randomized controlled trial. JAMA. 2003; 290(2):207-14.

6. Williams RE, Kalilani L, DiBenedetti DB, Zhou X, Granger AL, Fehnel SE, et al. Frequency and severity of vasomotor symptoms among peri and postmenopausal women in the United States. Climacteric, 2008;11:32-43.

7. Suzanne C, Yu-ming C Jean LF. Educational level and osteoporosis risk in postmenopausal chinese women. American Journal of Epidemiology, 2004;161:680-90

8. Elizabeth A, Kathleen AR, Daniel JM, Toni I. The relationship between parity and bone mineral density in women characterized by a homogeneous lifestyle and high parity. The Journal of Clinical Endocrinology & Metabolism, 2005;90(8):4536-41.

9. Rosen HN. Biochemical markers of bone turnover: clinical utility. Curr Opin Endocrinol Diabetes. 2003; 10:387-93.

10. Ravn P, Hosking D, Thompson D. Monitoring of alendronate treatment and prediction of effect on bone mass by biochemical markers in early postmenopausal intervention cohort study. J Clin Endocrinol Metab. 1999;84:2363-68.

11. Cosman F, Nieves J, Wilkinson C. Bone density change and biochemical indices of skeletal turnover. Calcif Tissue Int. 1996;58:236-43.

12. Tsourounis C. Clinical effects of phytoestrogens. Clinical obstetrics and gynecology. 2001;44:836-42.

13. Wagner JD. Soy phytoestrogens: research on benefits and risks. Clinical Obstetry and Gynecology. Lippincott Williams and Wilkins, Inc; 4;2001:843-52.

14. Speroff L, Glass RH, Kasse NG. Regulation of menstrual cycle. In: Speroff L. Clinical Gynecologic Endocrinology and Infertility. 7th ed Baltimore Maryland: Williams & Wilkins, 2005:183-230.

15. Kyung K. Han, Jose M. Soares, Mauro A. Haidar. Benefits of soy isoflavone therapeutic regimen on menopausal symptoms Obstet Gynecol. 2002;99:389-94

16. Wise LA, Krieger N, Zierler S. Lifetime socioeconomic position in relation to onset of perimenopause. J Epid Comm Health. 2002;56:851-60.

Table 4. T-score result in femur examination of research subjects

Examination	Phytoestrogens (average±SD)	p^*	Placebo (average±SD)	p^*	p^*
Research onset	-1.415 ± 0.215		-1.475 ± 0.202		0.370[c]
After 6 months	-1.270 ± 0.141	0.001[a]	-1.595 ± 0.421	0.124[b]	0.002[d]
The change	0.145 ± 0.170		-0.120 ± 0.333		0.004[e]

* t-test   SD = standard deviation
[a]. Natrium phytoestrogens group: Onset: After
[b]. Placebo group: Onset: After
[c]. Onset: Phytoestrogens group: placebo group
[d]. After: Phytoestrogens group: placebo group
[e]. Change: Phytoestrogens group: placebo group

Table 5. Bone mineral density status in spine and femur

BMD status	Phytoestrogens (average±SD)	Placebo (average±SD)
Research onset		
Spine :		
Osteopenia	20(-1.455 ± 0.264)	20(-1.460 ± 0.223)
After 6 months		
Osteopenia	20(-1.295 ± 0.223)	18(-1.433 ± 0.149)
Osteoporosis	0(0)	2(-2.700 ± 0.000)
Femur :		
Osteopenia	20(-1.415 ± 0.215)	20(-1.475 ± 0.202)
After 6 months		
Osteopenia	20(-1.270 ± 0.141)	18(-1.467 ± 0.145)
Osteoporosis	0(0)	2(-2.750 ± 0.212)

The examination result of subject's femur was not far different with examination on spine, in the beginning of research, the average of femur T-score in phytoestrogens group was -1.415±0.215 and it had increase to -1.270±0.141 with change amount of 0.145±0.170 with p=0.001. In placebo group it had decrease where the average of femur T-score in research onset was -1.475±0.202 becoming -1.595±0.421 with decrease amount of -0.120±0.33 and there was not significant correlation (p=0.124). Based on statistical analysis of t-test, there was significant difference between average change of femur T-score in phytoestrogens group with placebo group (p=0.001). The average of femur T-score in the two groups can completely be seen in Table 4.

It can be seen in Table 5, BMD status of spine and femur T-score in research onset, phytoestrogens and placebo group was osteopenia. After 6 months, in phytoestrogens group there was not change of BMD status and in placebo group there were 2 persons whose bone mineral density had change becoming osteoporosis with the average of spine T-score was 2.70 and femur T-score was -2.750±0.212.

DISCUSSION

Characteristics of subject

The age interval of research subject in phytoestrogens and placebo group largely constituted in interval of 51-55 years old, namely 11 subjects (55.0%) in phyto-

(65.0%). The average of age in this research is almost same with the average of subject age in research done by Tice JA, et al. (52.3 year), William RE, et al. had interval of 50-54 years with amount of 41% and Suzanne C, et al. (48-63 years).

General characteristic in this research is not far different with research performed by Suzanne C, et al. which reported that body mass index was low and high energy diet, calcium, phosphor, vegetable protein, soybean protein, and fresh fruits. Elizabeth, et al. reported that there was significant correlation on high parity with increase of hip BMD at old woman and largely with higher body mass index.

Menarche and menopause duration

From this study result it was got the average of menars age in phytoestrogens group was 13.25±1.25 years whereas in placebo group was 13.05±1.35 years. For duration variable of menopause experienced by research subject, it was gained that the average in phytoestrogen group was 36.60±14.29 month and placebo group was 40.20±16.64 months. In the study of Suzanne C, et al. it was reported that the average of menopause duration was 4.6±2.8 years with interval of menarche age from 12.5 years.

Spine and femur T-score

Rosen HN (2003) in Australia reported that the change of bone marker may benefit on osteoporosis in

plasebo adalah osteopeni. Setelah 6 bulan kemudian, pada kelompok fitoestrogen tidak terdapat perubahan status BMD sedangkan pada kelompok plasebo terdapat 2 orang yang densitas mineral tulangnya mengalami perubahan menjadi osteoporosis dengan rerata T-skor tulang belakang -2,70

dan T-skor femur -2,750 ± 0,212.

Simpulan: Pemberian fitoestrogen dapat mempertahankan densitas mineral tulang dan mencegah terjadinya osteoporosis.

BACKGROUND

The best choice and standard medication for climacteric complaint and osteoporosis is hormonal therapy (estrogen + progesterone/estrogen) based on the cause, that is the lack of estrogen hormone. In 2004, WHI *(women's health initiative)* stated, based on its research, that hormonal therapy on menopause women increased the risk of breast cancer. This statement decreased the hormonal therapy users, and women altered to supplement use including fitoestrogen for therapy of climacteric complaint and osteoporosis. However, has not had enough study proofs about the benefit of fitoestrogen.[1]

In Indonesia, phytoestrogens strongly circulates in market with category of supplement and has been used by people to overcome climacteric complaint and osteoporosis. This phytoestrogens has not been proven scientifically to have benefit in overcoming the climacteric complaints and osteoporosis in menopausal women.

This study chose the age of 45-55 years old age estrogen hormone production decrease, is an ideal age to prevent the occurrence of osteoporosis. Therefore, it is important to know and analyze effect of fitoestrogen supplementation on BMD.

METHOD

This study was comparing clinical test in the form of add on with double blind. The proposal was approved by Bioethics and Humanities Unit of Medical Faculty of Sriwijaya University. Number of samples was calculated using the following equation :

$$n = \frac{Pt(1-Pt) + Pc(1-Pc)}{(Pt-Pc)^2} \times f_{(\alpha,\beta)}$$

The subjects in this study were women with menopausal age. The examination of BMD marker was done twice, before and after 6 months of administration of fitoestrogen genistein and black cohosh. Placebo was given in the same form. The examination of BMD marker was executed in YK. Madira Palembang. The success parameter in this research was to maintain bone mineral density of spine and femur.

Study variables include: demographic characteristics (age, age of menars, education, parity and old menars),

femur), and the dependent variable (fitoestrogen). Fitoestrogen given were 15 mg soya genistein + 3 mg black cohosh twice daily.

Data collection was done by way of each participant who filled the inclusion and exclusion criteria would accept identification number and card as research subject. All research results of anamnesis, physical examination, laboratory, the result of spine T-score and femur T-score was noted in research sheets. The examination of bone mineral density was done twice before and after 6 months of giving phytoestrogens in YK. Madira Palembang. Data were analyzed using chi-square and T-test.

RESULTS

Forty subjects were recervited starting August 2010 until February 2011. Subjects into 2 groups, namely phytoestrogens group and placebo group which were randomly assigned.

General characteristic distribution of subject is completely figured out in Table 1.

Table 1 shows no significant difference on age between both group. Similarly, for education of graduate (S1) in phytoestrogens group was 8 subjects (40.0%) and in placebo group was 10 subjects (50.0%) with $p=0.810$. Only 11 subjects (55.0%) and 15 subjects (65.0%) in both group that can be evaluated at the end of the study.

It was found that the average of menars age in phytoestrogens group was 13.25±1.25 years while the placebo group was 13.05±1.35 years. Statistically there was no significant difference in menars age in the both groups ($p=0.631$). Menopause duration experienced by study subjects, it in phytoestrogens group was 36.60±14.29 month while in placebo was 40.20±16.64 month. Statistically there was not significant difference in menopause duration in the both groups ($p=0.468$). Characteristic of menars age and menopause duration of research group can completely be seen in Table 2.

In the beginning of study, it was found that the average of spine T-score in the group of phytoestrogens was -1.455±0.264 and it increased to -1.295±0.223 with change amount of 0.160±0.153 and had significant correlation ($p=0.001$). Whereas in placebo group it had decrease where the average of spine T-score in research onset was -1.295±0.223 becoming -1.560±0.414 with