STUDY ON THE EFFECTS OF PHYTOESTROGENS ON BONE RESORPTION IN MENOPAUSE

Ţiţ Delia-Mirela[*], Lazăr Liviu[**], Bungău Simona*, Iovan Ciprian*

[*]Oradea University, Faculty of Medicine and Pharmacy, 23 N. Jiga St., Oradea, Romania, e-mail: mirela_tit@yahoo.com
[**]Oradea University, Faculty of Medicine and Pharmacy, 10 Decembrie 1 St St., Oradea, Romania, e-mail: lvlazar@yahoo.com

Abstract

Postmenopausal osteoporosis is the most common form of osteoporosis and is determined by the decrease of the endogenous estrogen which is a characteristic of the menopause. This study aims to assess the effects of phytoestrogens on the bone metabolism ,by monitoring bone resorption using a specific biochemical maker, namely deoxypyridinoline . The study was conducted on a total of 62 menopausal women, aged between 47 and 57, who were divided into two groups/ lots: one group that was given phytoestrogens available as OTC preparations and a control group which was not given any kind of treatment . The duration of the study was 6 months, patients were evaluated twice, initially and after 6 months. After the statistical evaluation it was found that in the case of the patients who were administered phytoestrogens, there was better preservation of the bone, and a decrease in bone resorption in 18.8 % of cases after 6 months of treatment.

Key words: phytoestrogens, urinary deoxypyridinoline, bone resorbtion, menopause

INTRODUCTION

Postmenopausal osteoporosis is caused by an imbalance between the mechanisms that control bone remodeling by increasing bone resorption especially in the trabecular bone (Marcu et al, 2011; Raisz, 2005). The decrease of estrogen secretion during menopause causes changes in bone, thus producing bone loss of 2-5% per year in the early years postmenopausal (Arnaud, 1990) and up to 10-15% in the first 10 -15 years of menopause (SL et al, 1998).

Numerous studies show that the administration of a hormone replacement therapy during menopause significantly reduces the risk of osteoporosis and the fracture incidence, but it is accompanied by a number of contraindications and an increased risk of estrogen-dependent cancers and cardiovascular diseases (Winkler, 1992). Phytoestrogens, phytochemicals with similar structure to that of the estradiol represent a natural alternative to hormone replacement therapy, the only one of the alternatives that seems to be effective in preserving the bone and preventing osteoporosis (Setchell et al, 2003).

Phytoestrogens are compounds of vegetable origin which present estrogenic action, having the property of binding to the estrogen receptors and act either as agonists or as antagonists of estrogen

(http://www.elsevierhealth.com.) Their action at the cellular and molecular level is influenced by a number of factors such as: the concentration, the presence or absence of endogenous hormones, the receptor status, the type of the tissue. There are three main groups of phytoestrogens: isoflavones or flavonoids; coumestans with chemical structures close to isoflavones, lignans. (http://www.elsevierhealth.com.).

Although the clinical diagnosis of osteoporosis and the assessment of the fracture risk is based on bone density measurement, mainly by dual X-ray absorptiometry (DEXA) (Kanis, 2002), in recent decades, the interest in biochemical markers of bone transformations able to assess faster changes in bone activity has increased greatly. (SL et al, 1998). A specific marker of bone resorption is deoxypyridinoline. It is released into circulation during the bone resorption and is excreted unchanged in the urine (Delmas et al, 1993), thus being useful in monitoring bone resorption induced in menopause, and the effectiveness of antiresorptive therapy (Rubinacci et al, 1999).

The main objective of this study is to assess the effects of some standardized extracts of phytoestrogens on bone resorption in naturally menopausal women.

MATERIAL AND METHOD

The study was conducted over a period of 6 months on a number of 62 women with physiological menopause, aged between 47 and 57 years.

Inclusion criteria: women at the natural menopause without hormone therapy without antiresorptive therapy without chronic diseases affecting bone metabolism.

Exclusion criteria: induced menopause, hormonal therapy, chronic illness affecting bone metabolism, corticosteroid treatment, anticonvulsants, heparin, presence of bilirubin or red blood cells in urine.

Women were divided into two homogenous groups: group I, 31 women with the average age of 53.5 years, who were given supplements with phytoestrogens in the form of standardized extracts of soy, alfalfa, red clover and mixtures of phytoestrogens derived from various plants, and group II, 31 women with the average age of 54.2 years, who had no treatment administered .

The monitoring of bone resorption was achieved with the IMMULITE / IMMULITE 1000 Pyrilinks-D kit , which measures the amount deoxypyridinoline in urine, as an aid in monitoring type 1 collagen resorption changes.

IMMULITE / IMMULITE 1000 Pyrilinks-D is a solid phase, enzime labeled chemiluminescent competitive immunoassay. The solid phase is coated with monoclonal murine antideoxypyridinoline antibody. The liquid

phase consists of alkaline phosphatase conjugated to deoxypyridinoline (IMMULITE / IMMULITE 1000 Pyrilinks-D (PIELKPD-2 {14}, 2010-09-09))

Urine samples were collected from the first urine in sterile plastic containers at all women included in the study, and were stored at-20^{O} until their processing.

Patients included in the study were assessed in two stages: initially and at six months.

RESULTS AND DISSCUSIONS

The distribution of the cases according to the the amount of D-Pyr, after the initial assessment and and at 6 months is presented in Table 1.

Table 1

Distribution of cases according to the D-pyr value

D-Pyr (nM/mM creatine)	Untreated				Treated			
	Baseline		At 6 months		Baseline		At 6 months	
	No.	%	No.	%	No.	%	No.	%
3-3.9	1	3.3	0	0.0	1	3.1	4	12.5
4-4.9	3	10.0	3	10.0	4	12.5	4	12.5
5-5.9	6	20.0	3	10.0	4	12.5	2	6.3
6-6.9	12	40.0	11	36.7	12	37.5	11	34.4
7-7.9	6	20.0	9	30.0	8	25.0	8	25.0
>=8	2	6.7	4	13.3	3	9.4	3	9.4
M±SD	6.37±2.37		6.93±2.65		6.52±2.41		6.26±2.47	

In the group of women untreated with phytoestrogens, initially 66.7% had values of D-Pyr over 6 nM / mM creatine, and after 6 months this percentage increased by 13.3% to 80.0% ($p = 0.035$), the average increased from 6.37 to 6.93 nM / mM creatine.

In the group of women treated with phytoestrogens, initially 71.9% had values of D-Pyr over 6 nM / mM creatine, and after 6 months this percentage decreased by 3.1% to 68.8% ($p = 0.093$), the average decreased from 6.52 to 6.26 nM / mM creatine (figure 1).

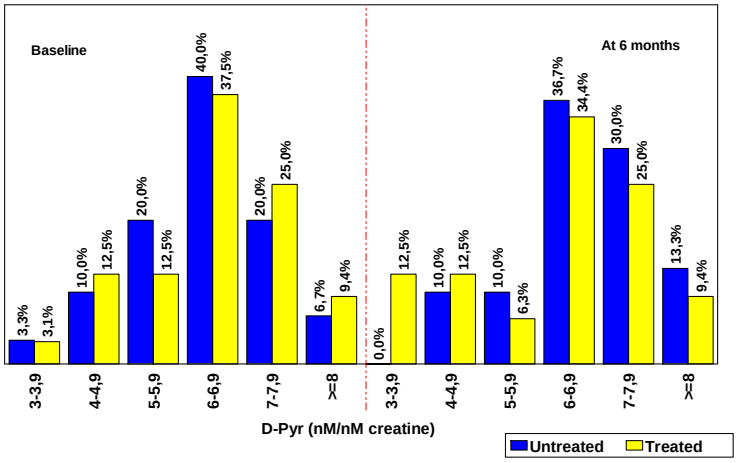

Fig.1. Distribution by D-Pyr values

Changes that have taken place at the level of D-Pyr quantity from urine, both in control group and in group therapy, at the six months evaluation are presented in Table 2.

Table 2

Evolution of D-Pyr values

D-Pyr (nM/mM creatine)	**Baseline**	**At 6 months**					
		3-3.9	**4-4.9**	**5-5.9**	**6-6.9**	**7-7.9**	**>=8**
		Untreated					
3-3.9	1	0	1				
4-4.9	3		2	1			
5-5.9	6			2	3	1	
6-6.9	12				8	3	1
7-7.9	6					5	1
>=8	2						2
		0	**3**	**3**	**11**	**9**	**4**
		Treated					
3-3.9	1	1					
4-4.9	4	2	2				
5-5.9	4	1	1	2			
6-6.9	12		1	0	10	1	
7-7.9	8				1	7	
>=8	3						3
		4	**4**	**2**	**11**	**8**	**3**

From the analysis of D-Pyr on value ranges results that in the group without treatment in 11 cases bone resorption has increased (36.7%) significantly more than in the group treated with phytoestrogens (3.1%), group where we have a reduction of bone resorption in 6 cases (18.8%) (figure 2).

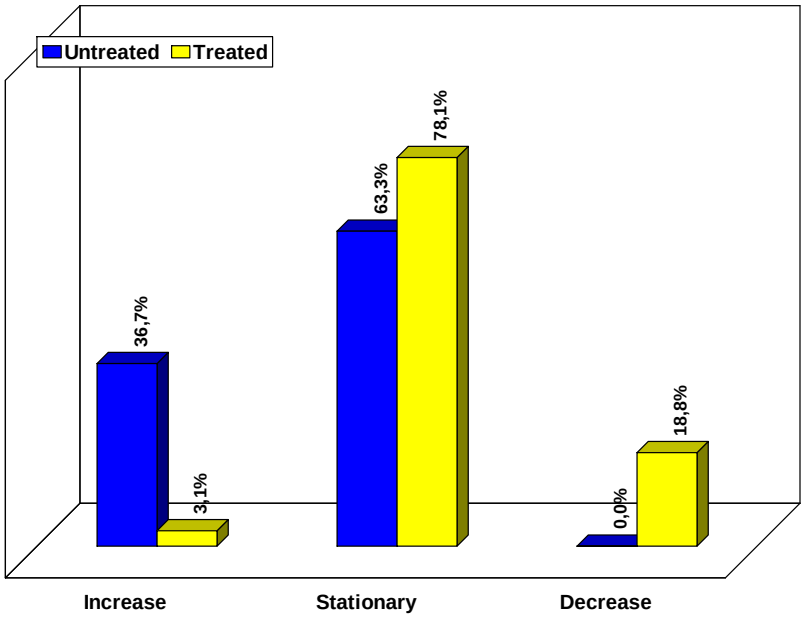

Fig.2. Evolution of bone resorption

We note that of the 6 cases whose D-Pyr values were reduced, 5 had baseline values under 6 nM/mM creatine.

CONCLUSIONS

From the statistical analysis it is found that between the two groups studied there are significant differences in the changes in urine deoxypyridinoline, respectively in bone resorption.

Treatment with phytoestrogens has been shown to be effective both in preserving bone mass (78.1% compared to 63.3% in the control group) as well as in the decline in bone loss (18.8% compared to 0.0% in control group).

REFERENCES

1. Arnaud C., D, Sanchez S., D, 1990, The role of calcium in osteoporosis. Annual Review of Nutrition 10:397-414.
2. Delmas P., D., Ginezts E., 1993, Immunoassay of pyridinoline crosslink excretion in normal adults and in Paget`s disease, J. Bone Mener Res, 8, 643-8. http://www.elsevierhealth.com.au/media/anz/samplechapters/9780443069925/Sample%20Chapter_9780443069925.pdf
3. IMMULITE / IMMULITE 1000 Pyrilinks-D (PIELKPD-2 {14}, 2010-09-09.
4. Kanis J., A , 2002, Diagnosis of osteoporosis and assessment of fracture risk. Lancet 359(9321)**:**1929-36.
5. Marcu F., Mihai L., L., 2011, Morfofiziologia, diagnosticul şi tratamentul osteoporozei, Editura Universității din Oradea, Oradea.
6. Raisz L., G, 2005, Pathogenesis of osteoporosis: concepts, conflicts, and prospects, Journal of Clinical Investigation 115(12):3318-25.
7. Rubinacci A., Melzi R., Zampino M., Soldarini A., Villa I.,1999, Total and free deoxypyridinoline after acute osteoclast activity inhibition, Clinical chemistry 45 (9): 1510-6.
8. SL Yu, LM Ho, BC Lim, ML Sim, Urinary Deoxypyridinoline is a Useful Biochemical Bone Marker for the Management of Postmenopausal Osteoporosis. Ann Acad Med Singapore 1998; 27:527-
9. Setchell K., D., R., Lydeking-Olsen E., 2003, Dietary phytoestrogens and their effect on bone: Evidence from in vitro and in vivo, human observational, and dietary intervention studies, American Journal of Clinical Nutrition, 78, 3:593S-609S.
10. Winkler U., H, 1992, Menopause, hormone replacement therapy and cardiovascular disease: a review of haemostareological findings. Fibrinolysis: 6 (suppl 3), pp. 5-10.