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Evaluation of Advanced Oxidation Protein Products as a Novel Marker of Oxidative Stress in Postmenopausal Osteoporosis in a Tertiary Care Teaching Hospital

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ABSTRACT

Background: Postmenopausal osteoporosis (PO) is one of the most common bone diseases, characterized by low bone mineral density (BMD) and pathological fracture, which leads to significant morbidity. **Methods:** A total of 52 subjects were enrolled in the study out of which 26 postmenopausal women meeting osteoporosis diagnostic criteria of the World Health Organization (WHO) and 26 postmenopausal women without osteoporosis (in both have same aged; 45–64) with cessation of menses for at least one year were recruited in this study. **Results:** Mean FBS, MDA, AOPPs, BLAP, TRACP5b level were found increased in postmenpausal women with OP as compared to postmenopausal without OP women while BMD was found to decreased as shown in [Table 1] the plasma AOPPs levels were negatively cor¬related with BMD (r=–0.35, P<0.079) and Plasma MDA level was positively correlated with AOPPs(r=0.39, P<0.048), bone turnover markers BALP (r=0.42, P<0.032) and TRACP5b (r=0.41, P<0.037). However, plasma MDA levels were negatively correlated with BMD(r=-0.11, P=0.592) & BALP(r=-0.13, P=0.526) while positively correlated with TRACP5b(r=0.15, P=0.464) plasma in the postmenopausal osteopo¬rotic women. **Conclusion:** postmenopausal osteoporotic women elevated AOPPs is associated with reduced BMD and increased bone turnover markers. Because AOPPs is stable and easy to detect it may be used as a simple plasma marker to predict the severity of postmenopausal OP.

Keywords: Advanced Oxidation Protein Products, Oxidative Stress, Bone Density, Malondialdehyde, Osteoporosis & Postmenopausal.

INTRODUCTION

Postmenopausal osteoporosis (PO) is one of the most common bone diseases, characterized by low bone mineral density (BMD) and pathological fracture, which leads to significant morbidity.[1] Surgeon General's report (2004) on bone health and osteoporosis revealed that osteoporosis affected more than 8 million women and 2 million men in the USA, in addition to 34 million people with low bone mass.[2] These numbers are expected to increase steadily over time, with osteoporosis affecting an estimated 14 million people and low bone mass affecting about 48 million people by the year 2020;[3] thus, early diagnosis, prevention, and treatment of osteoporosis are extremely important.[4] An overhauled point of view of the pathogenesis in this illness from estrogen driven to oxidative stress (OS) has featured the need to distinguish solid markers for reflecting oxidative stress status in this malady.[5] Loss of estrogens diminishes guard against oxidative worry in bone, and this records for the expanded bone resorption and diminished bone development related with the intense loss of these hormones, which is the primary neurotic attribute of postmenopausal osteoporosis.[6] The contribution of oxidative worry in the improvement of postmenopausal osteoporosis has as of late been all around archived.[7] Oxidative stress happens because of increment in ROS as well as impairment in cell reinforcement limit.[8] Exact estimation of ROS to mirror the degree of oxidative worry in vivo is troublesome because of the dumbfounding assortment, low amount, high reactivity, and the very short half-existence of ROS created during every phone cycle.[9] Consequently, estimation of some peroxidation finished results is utilized to

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assess the oxidative stress status in vivo. Malondialdehyde (MDA), a finished result of lipid peroxidation, is broadly utilized as an oxidative stress parameter.[10] Be that as it may, the part of MDA in postmenopausal osteoporosis is still exceptionally far from being obviously true.[11] Advanced oxidation protein products (AOPPs) were first detected in the plasma of chronic uremic patients, and are considered to be a novel marker of oxidative stress because it is stable and easy to detect. AOPPs result mainly from the action of ROS (chlorinated compounds) in proteins, leading to the formation of dityrosine residues and protein crosslinking.[12] Currently, there is no consensus on the most appropriate biomarkers of OS for PO and the validity of many of the biomarkers in use needs to be confirmed. Aim of this present study was to evaluate of advanced oxidation protein products as a novel marker of oxidative stress in postmenopausal osteoporosis.

MATERIALS AND METHODS

Study location: Department of Orthopedics, Narayan Medical College and Hospital, Jamuhar, Sasaram, Bihar in collaboration with Department of Biochemistry during the period from January,2018 to February,2019.

Study design: Cross-Sectional study.

Ethics approval: Study was approved by the Institution-al ethics committee and informed consent was taken from the participants or from the blood relatives.

Methodology: A total of 52 subjects were enrolled in the study out of which 26 postmenopausal women meeting osteoporosis diagnostic criteria of the World Health Organization (WHO) and 26 postmenopausal women without osteoporosis (in both have same aged; 45–64) with cessation of menses for at least one year were recruited in this study. We excluded patients with secondary osteoporosis, diseases known to be associated with increased oxidative stress (dementia, cardio- and cerebrovascular disease, diabetes, renal or hepatic insufficiency, and inflammatory diseases), use of antioxidant vitamins in the 6 months before enrollment, or malnutrition. We also excluded subjects who had received medications potentially involving bone mineral metabolism within the last 6 months (including corticosteroids, heparin, and anticonvulsants) or who had previous or current use of active bone agents such as selective estrogen receptor modulators or estrogen replacement therapy, strontium ranelate, teriparatide or PTH, calcitonin, and denosumab. Demographic data of all subjects were recorded.

Biochemical Laboratory Diagnosis:

Seven ml of blood sample was drawn under aseptic conditions. Sample was allowed to stand at room temperature for 3-5 minutes for clotting. Then serum was separated by centrifugation at 3000 rpm for 8 minutes. Following parameters were studied; Fasting Blood Glucose by GOD POD method; MDA by Kei Satoh; AOPP by spectrophotometric method; Specific markers of bone turnover, BALP and TRACP 5b by ELISA kits and BMD measurement: Measurement of BMD by dual-energy X-ray absorptiometry at the spine, hip, and/or forearm is the gold standard for establishing the diagnosis of osteoporosis. In this study, BMD was measured at the lumbar spine region (L2-L4) by dual-energy X-ray absorptiometry. The diagnosis of osteoporosis is defined as a T score of −2.5 or less, indicating a BMD that is at least 2.5 SD less than the mean of young adults.

Statistical Analysis:

The results were expressed as mean ± standard deviation (SD) values. Data analysis was performed with Microsoft Excel. The statistical differences between cases and controls were determined by student independent sample t test. Pearson's correlation coefficient was calculated to determine the correlation between parameters. The p-value<0.05 was considered significant. All the analysis was carried out on IBM SPSS -18.0 version.

RESULTS

This cross-sectional study was carried out in the department of Orthopedics, Narayan Medical College and Hospital, Jamuhar. The present study describes a novel oxidative stress marker, referred to as advanced oxidation protein products (AOPP) and its possible clinical relevance in postmenopausal osteoporosis. Basically, there was no statistically significant difference in age or years since menopause between the two groups. Mean ages of postmenopausal with OP and postmenopausal without OP women were 52.24 ± 14.6 and 53.6 ± 14.7 (P; 0.37), respectively. Mean height and BMI were increased in postmenpausal women with OP as compared to postmenopausal without OP women while weight was slight increase in postmenpausal women with OP as compared to postmenopausal without OP women.

Mean FBS, MDA, AOPPs, BLAP, TRACP5b level were found increased in postmenpausal women with OP as compared to postmenopausal without OP women while BMD was found to decreased as shown in [Table 1]. The plasma AOPPs levels were negatively correlated with BMD (r=–0.35, P<0.079) and Plasma MDA level was positively correlated with AOPPs(r=0.39, P<0.048), bone turnover markers BALP (r=0.42, P<0.032) and TRACP5b (r=0.41, P<0.037). However, plasma MDA levels were negatively correlated with BMD(r=-0.11, P=0.592) & BALP(r=-0.13, P=0.526) while positively correlated with TRACP5b(r=0.15, P=0.464) plasma in the postmenopausal osteoporotic women.

Table 1: Comparison of demographic & biochemical parameters in both group.

Variables	Postmenopausal women		P Value
	With Osteoporosis (n=26) (Mean±S.D.)	Without Osteoporosis (n=26) (Mean±S.D.)	
Age in years	52.24 ± 14.6	53.6 ± 14.7	0.37
BMI kg/m2	26.4 ± 8.02	25.04 ± 7.26	0.46
FBS (mg/dl)	99.84±32.06	84.7±27.5	0.04
MDAnmol/L	7.23 ±1.34	6.54 ±1.02	0.62
AOPPs µmol/L	126.2 ±42.06	64.8 ±17.2	0.01
BLAP	44.3±13.02	32.7±11.6	0.01
TRACP5b	5.4±1.06	3.2±1.0	0.01
BMD gm/cm^2	0.58±0.10	0.87±0.5	0.01

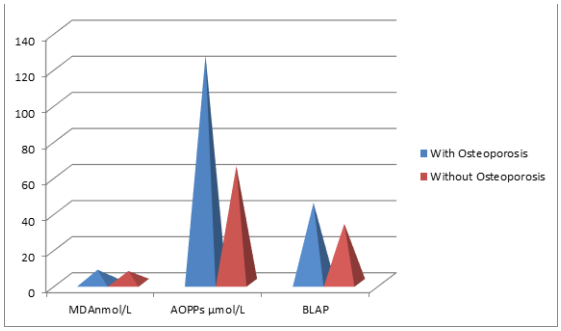

Figure 1: Shows the mean level of MDA, AOPPs & BLAP in both group.

DISCUSSION

In the present study, we measured plasma AOPPs and MDA levels to evaluate the level of oxidative stress, and found that AOPPs levels was increased in postmenopausal osteoporotic women compared with controls. AOPPs levels were negatively correlated with lumbar BMD and positively correlated with bone turnover markers, while MDA levels were not correlated with lumbar BMD or bone turnover markers. Morphologic examinations and estimations of certain biochemical markers have shown that bone redesigning is quickened at the menopause, as the two markers of resorption and forma-tion are expanded.[13] BALP, which advances bone mineralization, is viewed as fundamentally an indication of expanded activity of osteoblasts and optionally as a remedial response because of expanded bone resorption.[14] Levels of this serum bone turnover marker are significant in surveying foundational bone turnover in postmenopausal osterporetic.[15] Osteoclasts contain the TRACP5b as bone-explicit compound, the serum convergence of which for the most part mirrors the degree of bone resorption.[16] In this investigation, we found that the plasma BALP and TRACP5b concentrations were higher in postmenopausal osteoporotic women contrasted and controls. Many laboratory methods are available in the literature that are of help in establishing the presence of oxidative stress in vivo, but none of them proved to be unequivocally superior to the others.[17] One of the most damaging effects of oxidative stress is lipid peroxidation, the end product of which is MDA, which is one of the most frequently used indicators of lipid peroxidation.[18] MDA is known as a potential biomarker of oxidative stress and possesses the ability to promote osteoclast genesis. There have been some debates about using MDA as a marker for OP in postmenopausal women in the last decade. It has been reported that total femoral BMD measurements significantly correlated with MDA levels in a limited sample of postmenopausal osteoporotic women. However, the results of the present study suggest that MDA levels were not correlated with lumbar BMD or bone turnover markers. Therefore, the use of MDA levels may not assist estimation of the severity of postmenopausal OP, which is highly consistent with results of published studies with larger sample sizes. Prior to lipid and other cellular components, proteins are the primary target of ROS.[19] Oxidative damage to proteins is reflected by increased levels of AOPPs, which therefore serve as a novel biomarker of oxidative stress.[20] In addition to chronic uremia levels of AOPPs are also elevated in patients with different oxidative stress-related diseases, such as diabetes,[21] coronary artery disease and chronic inflammatory bowel diseases.[22] In the present study, we also found that AOPPs seemed to be a more relevant marker to reflect the severity of postmenopausal OP than MDA after we investigated the relationship between AOPPs and BMD or bone turnover markers. Apart from being regarded as an oxidative stress maker, AOPPs have also been shown to be a novel molecular basis of oxidative stress, participating in many biological events by inducing the production of intracellular ROS.[23] Postmenopausal OP is thought to be a type of high-turnover osteoporosis and is characterized by excessive bone resorption and inadequate bone formation, which is regulated by the coupling of osteoblasts and osteoclasts.[24] ROS can affect the genesis and lifespan of osteoblasts and osteoclasts. In precursors of osteoclasts, RANKL-induced activation of RANK stimulates ROS production, which is essential for osteoclastogenesis. In osteoblastic cells, ROS is an essential me-diator of apoptosis. More recently, an in vitro study has revealed that OS results in increased content of AOPPs in cultured mouse MC3T3-E1 osteoblast-like cells. In addition, AOPPs can inhibit proliferation and differentiation of os-teoblast cells through the ROS-dependent NF-kB pathway. Taken

together, these results show that AOPPs may be a reliable indicator in estimation of the severity of postmenopausal OP as well as an important factor in the patho-genesis of this disease. A few impediments of our examination ought to be recognized. To begin with, we were unable to gauge BMD at the femoral area. Besides, we didn't evaluate plasma levels of some other cell reinforcements. Further examinations exploring connection between AOPPs, cell reinforcements levels, and femoral BMD ought to be performed. Taking into account the fact that the oxidative modification of LDL is an important factor in the development of atherosclerosis,[25] it is highly probable that AOPP and oxidized lipoproteins act in concert in this process.

CONCLUSION

In conclusion, the postmenopausal osteoporotic women elevated AOPPs is associated with reduced BMD and increased bone turnover markers. Because AOPPs is stable and easy to detect it may be used as a simple plasma marker to predict the severity of postmenopausal OP. Subsequently, plasma levels of AOPPs may be utilized as a novel marker of oxidative worry to anticipate the seriousness of postmenopausal osteoporosis.

REFERENCES

1. M.N. Weitzmann, R. Pacifici, "Estrogen deficiency and bone loss: an inflammatory tale," Journal of Clinical Investigation, vol. 116, no. 5, pp. 1186–1194, 2006.
2. J. Iwamoto, Y. Sato, T. Takeda, and H.Matsumoto, "Whole body vibration exercise improves body balance and walking velocity in postmenopausal osteoporotic women treated with alendronate: Galileo and Alendronate Intervention Trail (GAIT)," Journal of Musculoskeletal Neuronal Interactions, vol. 12, no. 3, pp. 136–143, 2012.
3. D. L. Diab and N. B. Watts, "Postmenopausal osteoporosis," Current Opinion in Endocrinology, Diabetes and Obesity, vol. 20, no. 6, pp. 501–509, 2013.
4. S. Das and J. C. Crockett, "Osteoporosis—a current view of pharmacological prevention and treatment," Drug Design, Development and Therapy, vol. 7, pp. 435–448, 2013.
5. Manolagas SC: From estrogen-centric to aging and oxidative stress: A revised perspective of the pathogenesis of osteoporosis. Endocr Rev, 2010; 31: 266–300
6. Di Gregorio GB, Yamamoto M, Ali AA et al: Attenuation of the self-renewal of transit-amplifying osteoblast progenitors in the murine bone marrow by 17 beta-estradiol. J Clin Invest, 2001; 107: 803–12
7. Ozgocmen S, Kaya H, Fadillioglu E et al: Role of antioxidant systems, lipid peroxidation, and nitric oxide in postmenopausal osteoporosis. Mol Cell Biochem, 2007; 295: 45–52.
8. Halliwell B: Free radicals, antioxidants, and human disease: Curiosity, cause, or consequence? Lancet, 1994; 344: 721–24
9. Fan LM, Li JM: Evaluation of methods of detecting cell reactive oxygen spe-cies production for drug screening and cell cycle studies. J Pharmacol Toxicol Methods, 2014; 70: 40–47
10. Kilic N, Yavuz TM, Guney Y et al: An investigation into the serum thiore-doxin, superoxide dismutase, malondialdehyde, and advanced oxidation protein products in patients with breast cancer. Ann Surg Oncol, Ann Surg Oncol, 2014; 21(13): 4139–43
11. Maggio D, Barabani M, Pierandrei M et al: Marked decrease in plasma an-tioxidants in aged osteoporotic women: Results of a cross-sectional study. J Clin Endocrinol Metab, 2003; 88: 1523–27
12. Witko-Sarsat V, Friedlander M, Capeillere-Blandin C et al: Advanced oxi-dation protein products as a novel marker of oxidative stress in uremia. Kidney Int, 1996; 49: 1304–13.
13. Ishii S, Miyao M, Mizuno Y et al: Association between serum uric acid and lumbar spine bone mineral density in peri- and postmenopausal Japanese women. Osteoporos Int, 2014; 25: 1099–105.
14. Parfitt AM, Villanueva AR, Foldes J, Rao DS: Relations between histologic indices of bone formation: Implications for the pathogenesis of spinal os-teoporosis. J Bone Miner Res, 1995; 10: 466–73.
15. Ebeling PR, Atley LM, Guthrie JR et al: Bone turnover markers and bone density across the menopausal transition. J Clin Endocrinol Metab, 1996; 81: 3366–71.
16. Seibel MJ: Clinical use of markers of bone turnover in metastatic bone dis-ease. Nat Clin Pract Oncol, 2005; 2: 504–17, quiz 533.
17. Miller PD: Bone disease in CKD: A focus on osteoporosis diagnosis and management. Am J Kidney Dis, 2014; 64: 290–304.
18. Jung K, Lein M: Bone turnover markers in serum and urine as diagnostic, prognostic and monitoring biomarkers of bone metastasis. Biochim Biophys Acta, 2014; 1846: 425–38.
19. Selmeci L: Advanced oxidation protein products (AOPP): Novel uremic tox-ins, or components of the non-enzymatic antioxidant system of the plas¬ma proteome? Free Radic Res, 2011; 45: 1115–23.
20. Nielsen F, Mikkelsen BB, Nielsen JB et al: Plasma malondialdehyde as bio-marker for oxidative stress: Reference interval and effects of life-style fac¬tors. Clin Chem, 1997; 43: 1209–14.
21. DeAtley SM, Aksenov MY, Aksenova MV et al: Adriamycin induces protein oxidation in erythrocyte membranes. Pharmacol Toxicol, 1998; 83: 62–68.
22. Witko-Sarsat V, Friedlander M, Nguyen KT et al: Advanced oxidation pro-tein products as novel mediators of inflammation and monocyte activa¬tion in chronic renal failure. J Immunol, 1998; 161: 2524–32.
23. Kalousova M, Skrha J, Zima T: Advanced glycation end-products and ad-vanced oxidation protein products in patients with diabetes mellitus. Physiol Res, 2002; 51: 597–604.
24. Xie F, Sun S, Xu A et al: Advanced oxidation protein products induce intes-tine epithelial cell death through a redox-dependent, c-jun N-terminal ki¬nase and poly (ADP-ribose) polymerase-1-mediated pathway. Cell Death Dis, 2014; 5: e1006.
25. Maggi E, Bellazzi R, Falaschi F, Frarfoni A, Perani G, Finardi 0, Gazo A, Nat M, Romanini D, Bellomog: Enhanced LDL oxidation in uremic patients: An additional mechanism for accelerated atherosclerosis? Kidney mt 45:876—883, 1994.

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