Atherosclerosis in Patients with Osteoporosis

Osteoporoz Hastalarında Ateroskleroz Riski

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Dear editor, bone is metabolically active throughout life, the primary actors of the continuous process of renewal and repair termed as "bone remodeling." This remodeling requires the coordinated actions of osteoclasts and osteoblasts to attach to a specific area of bone, remove old bone, and fill this pit with new bone (1, 2).

Oxidative stress has been recently suggested to play a part in the development of osteoporosis (3). Reactive oxygen species (ROS) are oxygen-containing molecules that are produced during normal metabolism. When the production of damaging ROS exceeds the capacity of the body's antioxidant defenses to detoxify them, a condition known as oxidative stress occurs (4). ROS can cause tissue damage, particularly in the endothelial tissue (5). Lipids and lipoproteins are also affected by ROS.

The oxidative modification hypothesis suggests that lipid and protein oxidation in the vascular wall may cause atherosclerosis. Further, oxidative stress characterized by oxidized low density lipoprotein (LDL) contributes to atherogenesis (6). Enzymatic protection against ROS and the breakdown products of peroxidized lipids and oxidized protein is provided by many enzyme systems, such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx). Apart from these important enzymatic antioxidants, paraoxonase-1 (PON1) appears to have antioxidative properties as well (7). PON1 is an enzyme with three subtypes -paraoxonase (PON), arylesterase (ARE) and dyazoxonase.

PON1 hydrolyzes organophosphates, such as paraoxon, aromatic esters, e.g., phenyl acetate, and also lipid peroxidation products, and reduces their accumulation. Thus, PON1 prevents the acceleration of atherosclerosis and assumes an antiatherogenic property (8).

Osteoporosis and cardiovascular disease are major public health problems leading to increased morbidity and mortality. Recently, it has been suggested that there is an association between increased atherosclerosis risk and osteoporosis (9). We have thus focused mainly on the oxidative stress parameters and PON/ARE activities in patients with osteoporosis.

A total of 39 postmenopausal women and 26 healthy controls were included in the study. A detailed history was taken from each woman including relevant lifestyle parameters and risk factors, and their weight and height measurements were recorded. Bone mineral density (BMD) in the lumbar and femoral neck regions was measured by dual-energy X-ray absorptiometry. According to the World Health Organization (WHO), osteoporosis was defined as a lumbar BMD value more than 2.5 standard deviations (SD) below the T-score, corresponding to 0.759 g/cm2 (10). Serum PON and ARE activities were measured spectrophotometrically (11, 12). Oxidative and antioxidative status were evaluated by measuring serum lipid hydroperoxide (LOOH) level, total antioxidant status (TAS) and total oxidative status (TOS) (13, 14). The demographic and clinical data of the subjects are summarized in Table 1. There were no significant differences in age and body mass index between patients with osteoporosis and healthy controls. Laboratory findings of the patients and controls are also presented in Table 1. PON and ARE activities were significantly lower and LOOH levels were significantly higher in patients with osteoporosis compared to controls ($p<0.001$, for all). Serum TOS was higher in patients than in healthy controls ($p<0.001$). Serum TAS was lower in patients than in healthy controls ($p<0.001$). Our data indicated that

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Table 1. Demographical properties and clinical findings in patients with postmenopausal osteoporosis and controls

	Osteoporosis (n=39)	Control (n=29)	p
Age (Years)	54.15±58	56.7±9.4	0.1
BMI (kg/m²)	26.5±4.2	27.4±5.2	0.4
Lumbar BMD (g/cm²)	0.74±0.8	0.96±1.6	<0.001
Femoral neck BMD (g/cm²)	0.70±0.1	0.91±0.8	<0.001
TOS (μmolH2O2/L)	9.1±3.4	7.3±1.3	<0.001
TAS (mmolTroloxEquiv/L)	1.4±0.1	1.7±0.1	<0.001
Paraoxonase (U/L)	204.0±17.2	321.7±19.2	0.01
Arylesterase (kU/L)	227.3±54.3	260.5±41.3	0.006
LOOH (μmolH2O2)	4.9±0.8	4.4±0.5	0.006

BMI: Body Mass Index; CTx: C- Telopeptide; PTH: Parathormon; ALP: alkaline phosphatase; BMD: Bone Mineral Density; TOS: Total Oxidant Status; TAS: Total Antioxidant Status; OSI: Oxidative Stress Index.
The values represent mean ± SD, *Significance was defined as p<0.05

increased LOOH levels and TOS and decreased PON/ARE activities and TAS may be implicated in the presence of oxidative stress in osteoporosis. Thus, it was thought that increased consumption of PON1 for the prevention of oxidation may have a role in the decrease of PON1 activity in osteoporosis. We suggest decreased serum PON and ARE activities may be potential risk factors for developing atherosclerosis in patients with osteoporosis.

However, the nature of this link, and whether it is direct or indirect, remains to be explored. Clearly, further studies are needed to substantiate this possible relationship.

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