Measurement of Oxidized Low-Density Lipoprotein and Superoxide Dismutase Activity in Patients with Hypertension

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Background: Arterial hypertension is an important risk factor for coronary artery disease and cardiovascular-induced morbidity and mortality. It can cause end-organ damages such as cerebrovascular diseases, renal failure, and congestive heart failure. On the other hand, because of elevated blood pressure and rapid blood flow, there is an increase in oxidation and peroxidation reactions. The aim of this study was to evaluate the level of oxidized low-density lipoprotein and superoxide dismutase activity in sera of hypertensive patients.

Methods: In this case-control study, 70 hypertensive patients without any other important diseases such as congestive heart failure, cardiomyopathy, liver disease, diabetes mellitus, renal disease, or thyroid disease were compared with 70 age-and gender-matched controls. The participants' age range was from 30 to 75 years. Measurement of oxidized low-density lipoprotein in serum was performed by enzyme-linked immunosorbent assay. The activity of superoxide dismutase in serum was measured by enzymatic colorimetry method.

Results: The patients' mean age±SD was 52.2±14 years. The controls' mean age±SD was 45±13 years. The level of superoxide dismutase activity in the patients' group was 100±27 U/mL, and in the controls' group was 105±11 U/mL. The level of oxidized low-density lipoprotein in the patients' group was 14±4 μ/L, and in controls it was 7.7±3 μ/L.

Conclusion: Data of this study demonstrated an elevation of oxidized low-density lipoprotein in hypertensive group that may be the result of oxidation processes. Superoxide dismutase activity was decreased in hypertensive patients, which can be the result of elevated oxidation reactions.

Keywords: Hypertension • oxidized LDL • superoxide dismutase

Introduction

Hypertension is a common disease. It is an important cause of morbidity and mortality worldwide. Elevated systolic blood pressure is a major risk factor for cardiovascular diseases. Hypertension has been associated with an increased risk of certain cancers. It is also a major cause of cerebrovascular and coronary artery diseases, congestive heart failure, renal failure, peripheral vascular disease, and premature death.1,2

A better understanding of the pathophysiology of hypertension is indispensable to give optimal care to the 1.5 billion hypertensive patients who are estimated to exist by the year 2025.1

Hypertension is also a prevalent disease in Iran with overall prevalence of 23% and 50%, in 30–55- and >55-year-old population, respectively.2 Esteghamati et al. in a large national survey in Iran showed that approximately 25% or 6.6 million Iranians aged 25–64 years had hypertension and 46% or 12 million Iranians aged 25–64 years had prehypertension.3

Hypertension is classified based on its severity in The Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC) 7 classification.3 Regarding its etiology,
hypertension is classified as primary or secondary hypertension. Primary hypertension, also known as essential or idiopathic hypertension, accounts for as many as 95% of all cases of hypertension.6

Hypertension, known as “silent killer”, is a disorder that can damage many organs especially heart and brain.

Hypertension has unfavorable consequences on tissues, cells, and molecules, which in turn cause specific injuries; the most important of them is atherosclerosis.

Occurrence of oxidation and peroxidation is one of the unfavorable consequences of hypertension on molecular systems. In these oxidation processes, peroxides and free radicals are produced, which cause injuries and erosions in the wall of vessels. One of the most important oxidative processes is oxidation of lipids and lipoproteins such as oxidized low-density lipoprotein (Ox-LDL). Ox-LDL is a major cause of vessel wall injury and atherosclerosis. Antioxidants act against oxidants. There are two kinds of antioxidants; enzymatic, and non-enzymatic (glutathione, vitamin E, vitamin C, vitamin A, etc). The most important enzyme is superoxide dismutase (SOD).7–17

There is no study on Ox-LDL and SOD among Iranian patients; therefore, the aim of this study was to measure Ox-LDL and SOD levels in hypertensive patients and controls in Taleghani Hospital, affiliated to Shaheed Beheshti University of Medical Sciences. By finding any significant difference between the patient and control groups, it can be possible to prevent the undesirable consequences of hypertension.

Materials and Methods

In a case-control study, 70 patients with hypertension and 70 controls with the age range of 30 – 75 years were recruited. The patients who were the known cases of hypertension or had blood pressure measurements ≥140/90 mmHg in three occasions in rest were selected. The control group consisted of individuals without history of hypertension and with normal blood pressure in three times measurements. The excluded patients were those taking antilipid medications such as statins. Informed consents were taken before any measurement. Five mL of blood was taken from the patients and controls.

The level of Ox-LDL in serum and activity of SOD were measured. The measurement of the level of serum Ox-LDL was done by enzyme-linked immunosorbent assay (ELISA) method (Ox-LDL, ELISA Kit, Mercodia AB, Uppsala, Sweden). All of the tests were performed at the same time.

The inter-tests changes in the three ranges (low, moderate, and high) were less than 87%.

The activity of SOD was measured by enzymatic-colorimetric method (SOD activity Kit, Jal CA, Shizuo KA, Japan). All of the tests were done at the same time. The inter-tests changes in the three ranges (low, moderate, and high) were less than 74%.

Results

The data were collected from both genders. The mean age±SD in the patients group was 52.2±14 years, and in the controls, it was 45±13 years. It was shown that the level of SOD activity in patients group was 100±27 U/mL, and in control group it was 105±11 U/mL. The level of Ox-LDL in patients group was 14±4 μU/mL, and in the control group it was 7.7±3 μU/mL (Figures 1 – 4).

![Figure 1. Serum levels of superoxide dismutase activity in the patients.](image-url)
The level of SOD activity in patients group was 5.2 units less than the control group. This difference was not significant. The level of Ox-LDL in patients group was 6 units higher than the control group, which was significant ($P<0.001$, Table 1).

**Discussion**

Arterial hypertension is one of the most common diseases, and an important risk factor for coronary artery disease and cardiovascular-induced morbidity and mortality. Hypertension may induce multiple changes in lipoproteins and oxidation-peroxidation processes. Ox-LDL is an important risk factor in this respect. SOD activity is the first antioxidant enzymatic defense that correlates with these processes.

The results of this study indicated that the serum level of SOD activity in the control group was higher than the patient group. This difference was not significant. In previous studies, Fukai et al. showed that angiotensin II and hypertension increased the vascular oxidant stress. They examined how these might affect expression of the extracellular superoxide dismutase (ecSOD), a major form of SOD.\(^{18}\) In mice angiotensin II infusion (1.1 mg/kg for seven days) increased systolic blood pressure from 107±3 mmHg to 152±9 mmHg and caused a three-fold increase in ecSOD, but there was no change in the systolic Cu\(^{++}/Zn\(^{++}\) SOD protein. Induction of ecSOD by angiotensin II was not due to hypertension alone, because hypertension caused by norepinephrine (5.6 mg . Kg\(^{-1}\) . d\(^{-1}\)) had no effect on ecSOD. Similarly, exposure of mice aortas to angiotensin II (100 nmol/L) in organoid culture increased ecSOD by approximately two folds. This effect of angiotensin II on ecSOD expression may modulate the oxidative state of vessel wall in pathologic processes in which the renin-angiotensin system is activated.\(^{18}\)
Congura et al. concluded that angiotensin II-induced hypertension increased the vascular ecSOD. They proposed that this was a compensatory mechanism that blunted the hypertensive response. To test this hypothesis, they studied ecSOD-deficient mice and found that hypertension caused by angiotensin II was greater in ecSOD (-/-) compared with wild type mice (168 versus 147 mmHg, respectively, \( P < 0.01 \)).

Ferroni et al. found that superoxide anion was a major determinant of nitric oxide (NO) biosynthesis and also acted as a vasoconstrictor. Increased level of biomarkers of lipid peroxidation and oxidative stress had been found in patients with hypertension.

Other researchers such as Raij et al., el Hafidi and Baños, Pierdomenico et al., Vaziri et al., Lerman et al., and Donmez et al. also investigated oxidation and peroxidation. They indicated that hypertension caused increased oxidation processes, which emphasized on importance and usefulness of antioxidants. Because SOD is the first enzymatic antioxidant defense, its low level in hypertensive patients may be due to excess of oxidative stress. The results of this study on Ox-LDL showed that its level in the patient group was six units higher than the control group. This increase was significant (\( P < 0.001 \)). The results of this study are similar to the results obtained by Raij et al., Pierdomenico et al., Tokkia et al., Quinines-Galvan et al., and Brookes, and indicate that oxidative processes increase in hypertension and cause increasing level of serum Ox-LDL.

### Table 1. Serum level of Ox-LDL and SOD activity in the patient and control groups.

<table>
<thead>
<tr>
<th></th>
<th>Patient group</th>
<th>Control group</th>
<th>( P ) value</th>
</tr>
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<tbody>
<tr>
<td>SOD U/mL</td>
<td>100±27</td>
<td>105±11</td>
<td>NS</td>
</tr>
<tr>
<td>Ox-LDL mu/L</td>
<td>14±4</td>
<td>7.7±3</td>
<td>(&lt;0.001)</td>
</tr>
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Ox-LDL=oxidized low-density lipoprotein, SOD=superoxide dismutase, NS=nonsignificant.

### References

8. el Hafidi M, Baños G. *In vivo* plasma lipid oxidation in...


