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Oxidative Stress Status in Patients with Lumbar Disc Herniation

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ABSTRACT

Lumbar disc herniation (LDH) is a degeneration process that causes nerve damage with mechanical and inflammatory effects. Data on oxidative stress's role in disease pathogenesis and prognosis are minimal. In this study, we analyzed oxidative stress parameters in LDH patients.

The study included 63 patients who were diagnosed with LDH by magnetic resonance imaging and decided to operate and the same number of healthy controls. Oxidative stress parameters were measured from the patients preoperatively and in the sixth postoperative month. The obtained values were compared among themselves and with the control group.

Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSHPx) levels were found to be significantly lower in the preoperative period compared to the control group, and postoperative period, meanwhile malondialdehyde (MDA) was higher (p=0.001). When postoperative patients were compared with the control group, it was revealed that SOD, CAT, and GSHPx were lower, and MDA was higher than the control group (p=0.001).

In this study, it was shown that surgery significantly improved the oxidative stress state in patients with LDH but could not eliminate it. In other words, oxidative stress and cellular damage continue at the molecular level.

Keywords: Lumbar disc herniation, disc herniation surgery, oxidative stress

Introduction

Lumbar disc herniation (LDH) is a degeneration process characterized by the protrusion of vertebral discs into the spinal canal due to excessive load (1). It is more common in 30-50 year aged men (2). Herniated disc causes neural tissue ischemia with direct mechanical effect or inflammatory response (3). Clinical findings vary according to the degree of compression and the affected nerve root. Patients usually complain of low back pain and sciatica. In the advanced period, sensory or motor losses in the lower extremities and urinary or stool incontinence may develop.

Free radicals are chemical molecules containing an unpaired electron generally very reactive. They are continuously formed as by-products of metabolism. The reactive free radicals may lead to cell death and tissue damage by oxidizing biomolecules (4). The term 'antioxidant' describes the molecules that stabilize or inactivate free radicals before injuring the cells (5). Free radicals oxidize unsaturated fatty acids in membranes through lipid peroxidation. Malondialdehyde (MDA) is a marker of oxidative stress and one of the end-products of lipid peroxidation. MDA level reflects the degree of lipid peroxidation. An increase in free radicals leads to the overproduction of MDA (6). Superoxide dismutase (SOD) is found in all aerobic cells and is involved in the defense against superoxide radicals formed in aerobic reactions. SOD, catalase, and glutathione reductase work together with enzymes that remove H2O2 (7). Reduced glutathione (GSH) plays a vital role in eliminating reactive oxygen radicals and maintaining enzymatic activities by catalyzing the reduction of oxidized glutathione to glutathione (8). Catalase (CAT) is found in peroxisomes and enables the conversion of hydrogen peroxide to water and oxygen (9). It was also shown that people with low CAT levels are prone to type 2 diabetes mellitus and hypertension (10).

In this prospective study, we compared oxidative stress parameters in LDH patients with healthy controls and evaluated how these parameters changed after surgical treatment. In addition, we aimed to reveal the effect of surgical treatment on the Visual Analogue Scale (VAS).

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Table 1. Oxidative Stress Parameters İn The Operative Patient Group and Healthy Controls (Total Number Of 63 İn Each Group)

Parameters	Mean ± SD	P value
Preoperative MDA	2,08 ± 0,03	0,001
Control MDA	0,96 ± 0,04	
Preoperative SOD	3,34 ± 0,02	0,001
Control SOD	6,52 ± 0,27	
Preoperative GSHPx	13,29 ± 0,89	0,001
Control GSHPx	28,44 ± 1,33	
Preoperative CAT	5,96 ± 0,35	0,001
Control CAT	12,32 ± 0,28	

MDA, Malondialdehyde; SOD, Superoxide dismutase; GSHPx, Glutathione peroxidase; CAT, Catalase

Materials and Methods

The study included 63 patients between the ages of 18-65 who were diagnosed with LDH by magnetic resonance imaging (MRI) and the same number of healthy controls. Patients with a surgical decision for LDH were included, while those with comorbid diseases were excluded from the study. LDH types were classified as bulging, protruded, extruded, and sequestered. The clinical and biochemical data of the patients were recorded before the operation and in the sixth month after the operation. For preoperative samples, 4 mL of venous blood was drawn from the brachial vein, and serum was obtained by centrifuging the samples at 5000 rpm for 5 minutes. The sera were stored at -20 °C until the time of analysis. With the same method, blood was taken from the patients in the 6th month after the operation, and serums were separated. SOD, CAT, GSH, and MDA levels were measured spectrophotometrically in the sera of both groups after thawing in preoperative samples. Preoperative and postoperative oxidative stress pathway enzyme levels were compared among themselves and with the control group.

Biochemical Measurements: SOD, CAT, GSH, and MDA activities were determined using the method described by Popov, Aebi, Beutler, and Gutteridge, respectively (11-14).

Statistics Analysis: Descriptive statistics were expressed as mean and standard deviation (SD). The Kolmogorov-Smirnov test was used to test the normality of the distribution of data. Student t-test was used in cases with normal distribution. Mann Whitney U test was used in cases where normal distribution was not evident. The statistical significance level was set at $p<0.05$, and the SPSS statistical software (ver.19.0 Armonk, NY: IBM Corp.) was used for analyses.

Results

Of the 63 patients included in the study, 34 (54%) were male, and 29 (46%) were female. The mean age of the patients was 46.32 ± 12.8 years. Fifty-seven (90.5%) and 6 (9.5%) patients had ASA (American Society of Anesthesiologists) scores of 2 and 3, respectively. Sixteen (25.4%) patients had protruded, 43 (68.3%) patients had extruded, and 4 (6.3%) patients had sequestered LDH.

Preoperative SOD, CAT, and glutathione peroxidase (GSHPx) were significantly lower than the control group, while MDA was higher (table 1). There was a significant increase in the postoperative mean values for SOD, CAT, and GSHPx compared to the preoperative values ($p=0.001$). On the other hand, there was a significant decrease after surgery for MDA (table 2). Finally, when the postoperative enzyme levels were compared with the control group, SOD, CAT, and GSHPx were significantly lower than the control group. In contrast,e MDA was higher (table 3).

Preoperative VAS waist and leg mean scores were significantly higher than postoperative scores (table 4).

Discussion

A wealth of evidence indicates that oxidative stress may be responsible to varying degrees in the onset and/or progression of various diseases such as cancer, diabetes, metabolic disorders, atherosclerosis, or cardiovascular diseases (15). Today, LDH constitutes a significant health burden regarding workforce loss and treatment costs. There is no standardization regarding treatment indications, response, and patient follow-up. In our study, we aimed to evaluate

Table 2. Oxidative Stress Parameters In Preoperative and Postoperative Patients (Total Number of 63 Patients)

Parameters	Mean ± SD	P value
Preoperative MDA	2,08 ± 0,03	0,001
Postoperative MDA	1,05 ± 0,02	
Preoperative SOD	3,34 ± 0,02	0,001
Postoperative SOD	5,87 ± 0,36	
Preoperative GSHPx	13,29 ± 0,89	0,001
Postoperative GSHPx	21,43 ± 0,92	
Preoperative CAT	5,96 ± 0,35	0,001
Postoperative CAT	10,75 ± 0,35	

MDA, Malondialdehyde; SOD, Superoxide dismutase; GSHPx, Glutathione peroxidase; CAT, Catalase

Table 3. Oxidative Stress Parameters In The Postoperative Patient Group and Healthy Controls (Total 63 İn Each Group)

Parameters	Mean ± SD	P value
Postoperative MDA	1,05 ± 0,02	0,001
Control MDA	0,96 ± 0,04	
Postoperative SOD	5,87 ± 0,36	0,001
Control SOD	6,52 ± 0,27	
Postoperative GSHPx	21,43 ± 0,92	0,001
Control GSHPx	28,44 ± 1,33	
Postoperative CAT	10,75 ± 0,35	0,001
Control CAT	12,32 ± 0,28	

MDA, Malondialdehyde; SOD, Superoxide dismutase; GSHPx, Glutathione peroxidase; CAT, Catalase

Table 4. Preoperative and Postoperative VAS Waist and Leg Scores of Patients (Total Number of Patients 63)

Parameters	Mean ± SD	P value
Preoperative VAS waist	1,75 ± 0,69	0,001
Postoperative VAS waist	1,21 ± 0,44	
Preoperative VAS leg	1,92 ± 0,74	0,001
Ppostoperative VAS leg	1,06 ± 0,24	

VAS, Visual Analogue Scale

these patients' preoperative and postoperative oxidative stress parameters in terms of treatment response.

Yucetas et al. found that low catalase activity, an indicator of increased oxidative stress, was associated with hypertrophy of the ligamentum flavum, which causes lumbar canal stenosis (16). Our study also shows that a low CAT level is associated with LDH. In addition, in our study, SOD and GSHPx, other oxidative stress parameters, were significantly lower in preoperative patients compared to the healthy control group. In groups, MDA was found to be higher.

It is not known how the level of oxidative stress changes with surgical treatment in patients with LDH. In our study, oxidative stress parameters at preoperative and postoperative six month. We found a significant increase in SOD, GSHPx, and CAT levels and a substantial decrease in MDA levels. This shows that oxidative stress is significantly reduced with surgery. In addition, we analyzed the oxidative stress status in the postoperative patient group compared to the healthy population. While the postoperative mean values of SOD, CAT, and GSHPx were significantly lower thanin the control group, MDA was higher. In other words, although postoperative oxidative stress decreases in patients compared to preoperatively, there is still a significantly higher oxidative stress state compared to the healthy group. Aydin M.et al.l revealed no significant decrease in stress levels in patients who had liver transplantatio. They argued that new transplantation with liver transplantation would be destroyed by oxidative stress (17). In our study, we reached results that support this theory. In other words, we cannot eliminate oxidative stress

with surger; we can only improve the patientsurgeryrent condition and symptoms. As the invisible part of the iceberg, oxidative stress continues to cause tissue damage.

Considering the VAS score, which is the postoperative clinical symptom score of the patients, it is clear that the patients benefited clinically from the operation. In our study, the difference between the preoperative VAS waist, VAS leg group mean and post-operative VAS waist, VAS leg group represent was statistically significant.

In conclusion, our study found clinically significant improvement in LDH patients with a surgical operation. The operation also significantly improved the oxidative stress state but could not eliminate it. In other words, oxidative stress and cellular damage continue at the molecular level. There need to be more studies on when this one oxidative stress will manifest clinically. It is not yet clear whether molecular damage causes new symptoms or mechanical effects increase oxidative stress in patients with recurrent symptoms. Further studies are needed on this subject.

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List of abbreviations: CAT, Catalase; GSH, glutathione; GSHPx, Glutathione peroxidase; LDH, Lumbar disc herniation; MDA, Malondialdehyde; MRI, Magnetic resonance imaging; SOD, Superoxide dismutase; VAS, Visual Analogue Scale.

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