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RELATION BETWEEN LUMBAR DEGENERATIVE DISC DISEASE AND HUMAN 8-HYDROXYDEOXYGUANOSINE (8-OHDG) SERUM LEVEL

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ABSTRACT

Aim: Lumbar degenerative disc disease (LDDD) identified as multifactorial, irreversible and degenerative discopathy. The 8-hydroxy-2 deoxyguanosine (8-OHdG) is a nucleoside oxidation of DNA marker of oxidative stress. Present study aim to investigate 8-OHdG levels in patient with LDDD as a marker of oxidative stress.

Material and Methods: The study group included 45 patients with LDDD and 49 healthy individuals for control group. Patients with LDDD were examined with lumbar Magnetic Resonance Imaging (MRI), Oswestry Disability Index (ODI) scores, Visual Analoge Scale (VAS) scores and neurogical examination. Serum 8-OHdG levels determined with The Enzyme-Linked Immunosorbent Assay (ELISA) method.

Results: Patients with LDDD had significantly increased levels of 8-OHdG than healthy control group ($p<0.0001$). Also there was positive correlation between Oswestry and VAS parameters and 8-OHdG serum levels ($p<0.0001$).

Conclusion: In this study evaluated the 8-OHdG serum levels in the risk of LDDD. Increased 8-OHdG serum levels were having negative impact on severity of LDDD.

Keywords: 8-OHdG, Lumbar degenerative disc disease, oxidative damage

Level of Evidence: Prospective case-control study, Level II

INTRODUCTION

Lumbar degenerative disc disease (LDDD) being significantly associated with non-specific low back pain (LBP) and generally lead to reduced physical activity and decreased quality of life. LDDD is a mechanical and irreversible dysfunction and also identified as degenerative process with multifactorial factors [(2)].

The numerous evidences have been displayed that oxidative stress induced damage play important role in pathogenesis of degenerative disorders [(4)]. Reactive oxygen species (ROS) cause severe damage to cellular macromolecules such as DNA. DNA damage is detected by sensor proteins and in irreparable circumstances it give rise to cell cycle arrest or the activation of apoptotic pathways. The 8-hydroxy-2 deoxyguanosine (8-OHdG) and 8-hydroxyguanosine (8-OHG) are the most important products of nucleotide oxidation [(5)].

Therefore, in this study, we aimed to investigate the association between 8-OHdG serum levels and development or prognosis of LDDD.

MATERIAL AND METHODS

Study population

Our study was a prospective case-control study included 45 patients with lumbar degenerative disc disease and 49 healthy individuals for control group. The clinical data of the patients were recorded and followed-up prospectively. All partipiciants were recruited from Neurosurgery Department. Clinical investigations of LDDD patients were determined according to neurological examination, lumbar magnetic resonance imaging (MRI) studies, visual analog scale (VAS) scores to define pain level and Oswestry disability index (ODI) scores. Demographic characteristics of patients and controls were collected from hospital records. Inclusion criteria were leg pain

and low back pain as a result of lumbar radiculopathy and lumbar intervertebral disc protrusion diagnosed on MRI. Exclusion criteria were traumatic patients, oncological pathologies, osteoporosis, spinal stenosis, spondylolisthesis, vertebral fractures and deformities of spine.

All patients were questioned for the level of pain and scored with VAS and questioned with ODI for quality of life analyze. Subject cob stent was obtained in agreement with the Declaration of Helsinki and the local ethic committee and informed consent forms from all patients was provided.

Biochemical assays

Serum samples were extracted and frozen at -20 °C. In the serum samples 8-OHdG levels were determined by enzyme-linked immunosorbent (ELISA) assay.

Statistical analysis

Statistical analysis were performed using SPSS Ver. 23 software (SPSS Inc, Chicago, IL, USA). The significant difference between groups were examined by Student's t-test and demographic information were compared by Chi square and Fisher's exact tests, $p<0.05$ denoted as statistically significant.

RESULTS

The analysis included 45 LDDD patients and 49 controls. Demographic characteristics of the two groups and mean values of VAS and ODI scores are displayed in Table-1 and Figure-1.

The mean age of the patients with LDDD and healthy control group were 37.29 ± 8.30 and 34.98 ± 4.47 years, respectively. There were no significant differences between LDDD and control groups in terms of median age ($p=0.074$). The frequency of gender was 46.7 % male and 53.3 % female for patients; 38.8 % male and 61.2 % female for controls. There were no significant difference with genders ($p=0.044$).

The serum levels of 8-OHdG determined in this study, 8-OHdG levels of patient group was 10.30±4.37 ng/ml and control group was 5.24±4.52 ng/dl. The patient group had significantly higher 8-OHdG levels compared to the control group ($p<0.0001$).

Another important outcome of present study was we determined that there was positive correlation between Oswestry and 8-OHdG serum levels ($p<0.001$) (Figure 2).

Increase in 8-OHdG serum levels were significantly parallel with Oswestry. Moreover there were positive correlation between VAS and 8-OHdG serum levels ($p<0.001$) (Figure-3).

Table-1. Demographic Characteristics of Patient and Control Groups

Parameter	Control (n=49)	LDDD (n=45)	p-Value
Age (Mean±SD)	34.98±4.47	37.29±8.30	0.074
Gender (Male/Female)	19/30	21/24	0.44
VAS (Mean±SD)	-	48.92±19.79	-
Owestry (Mean±SD)	-	64.90±23.01	-

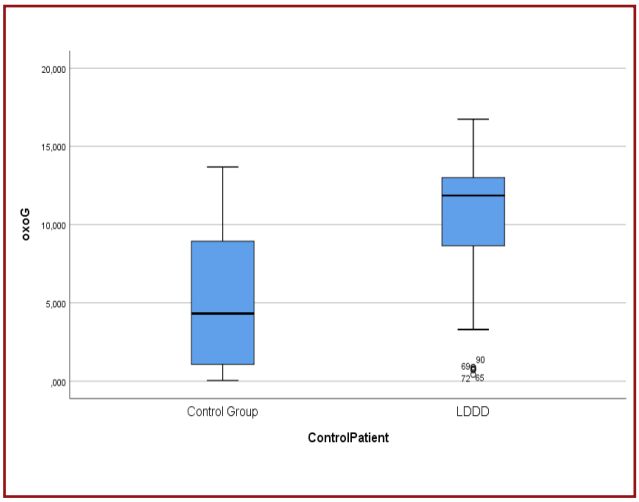

Figure-1. 8-OHdG Serum Levels

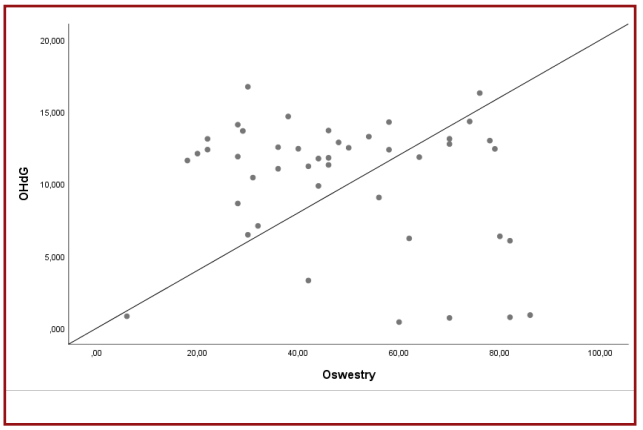

Figure-2. Correlation graphic of 8-OHdG serum levels and Oswestry

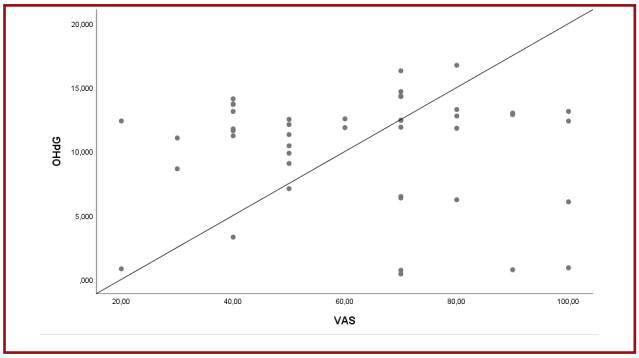

Figure-3. Correlation graphic of 8-OHdG serum levels and VAS

DISCUSSION

LDDD is the most common cause of low back pain (LBP) and sciatica costing millions to the economy each year [1]. The degenerative process is identified as multifactorial, irreversible and associated with a mechanical dysfunction. LDDD is a condition which has prevalence of which may be as much as 80% with rate of an annual prevalence of 25–60 % [6].

The oxidative stress, as the cellular redox status, is established by the balance between the rates of production and breakdown of reactive oxygen species (ROS) [7]. Recent studies have also reported that the oxidative stress was associated with disc degeneration. Over production of ROS could directly damage the intervertebral disc cells and irritate the disc matrix homeostasis, including reduced proteoglycan synthesis and increased matrix metalloproteinase levels [3]. Evidence of oxidative stress exists in disc degeneration, but it is unclear how it affects disc metabolism. Another study revealed that oxidative stress, resulting from overproduction of ROS, was implicated in Intervertebral disc degeneration (IDD) by inducing premature senescence, promoting catabolic metabolism, and causing the apoptosis of intervertebral disc cells [9].

The relationship between oxidative stress and disc degeneration is complicated. Han et al (2017) determined oxidative stress pathways in apoptosis. It has been demonstrated that oxidative stress has a crucial role in programmed cell death and oxidative stress could induce apoptosis in cartilaginous endplate cells. They found that oxidative stress induced by molecules increased the apoptosis and subsequently the calcification in the cartilage cells. While decreased oxidative stress species were advantageous for the survival of cells and also it could delay the physiopathology of disc degeneration [8].

The biomarkers of oxidative damage reflecting the disease risk or severity could be detectable in body fluids such as serum. In present study we evaluated 8-OHdG serum levels as a marker of oxidative stress in LDDD. Another study conducted by Gmitterova et al (2009). They analyzed 8-OHdG levels in neurodegenerative disorders as degeneration marker. They suggested that 8-OHdG levels in cerebrospinal fluid could be use for diagnostic biomarker [10].

CONCLUSION

To the best of our knowledge, this is the first study to evaluate the 8-OHdG serum levels in LDDD. We observed that patients with LDDD had significantly increased 8-OHdG serum levels than healthy controls. Furthermore positive correlations between 8-OHdG serum levels and clinical parameters showed that enhanced 8-OHdG serum levels were having negative impact on severity of LDDD.

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