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The Relationship Between Atherosclerosis and Patients Who Have Chronic Lower Back Pain and Lumbar Disc Hernia

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Abstract: Background: In the presence of comorbid disease potential benefits and harms of Surgical operation for lumbar disc hernia must be known . It was thought that local inflammatory response; which detected at lumbar disc hernia and factors ;which considered as involved with atherosclerotic vascular diseases; which developed after an inflammatory process, were same or caused by atherosclerosis. This study has been started to search; the influence of known relationship between atherosclerotic risk factors; insulin resistance(IR), hypercholesterolemia (HC), hyperlipidemia (HL), sero-reactive protein (CRP) and inflammation to development of lumbar disc hernia. Methods: In our study, 52 patients whose chronic low-back pain related to lumbar disc hernia named as study group and 52 patients whose chronic low-back pain could not be related with non-mechanic pain named as control group. Magnetic Resonance Imaging (MRI), Electro-Myo-Graphy. (EMG), sero-reactive-protein (CRP), fasting blood glucose, insulin, cholesterol, triglycerides (TG) levels of all patients were measured. Insulin resistance was measured with the homeostatic method for insulin resistance (HOMA-IR). All of the patients were selected from the non-obese patients whose body mass indexes are lower than 30kg/m2. Results: In this study, 52 patients whose chronic low-back pain is related to lumbar disc hernia were 30 female (%57.6) and 22 male (42.6). 52 Patients who were selected to control group whose chronic low-back pain is not related to any mechanic reasons were 36 female (%69.2) and 16 male (%30.8). There were no significant statistical differences between these two groups in sex and ages (p=0,36). Significant Pearson correlation statistical analyze differences were found in Herniated disc chronic low-back pain group in LDL (r=0.33, p=0.001), T cholestrol (r=0.28, p=0.006), HDL (r=0.32, p=0.001), TG (r=0.31, p=0.001), fasting insulin (r=0.44, p=*0.0001), fasting glucose(r=0.45, p=*0.0001) ve insulin resistance HOMA-IR(r=0.49, p=*0.0001) . Conclusions: Significant differences were found in the presence of comorbid disease, increasing atherosclerosis risk at the patients who have lumbar disc hernia; Between the blood tests and statistical analyses of groups whose low-back pain is related to disc hernia and whose low-back pain is not related to any mechanic reason : LDL (r=0.33, p=0.001), T cholesterol (r=0.28, p=0.006), HDL (r=0.32, p=0.001), TG (r=0.31, p=0.001),fasting Insulin (r=0.44, p=*0,0001), fasting glucose (r=0.45, p=*0,0001) and HOMA-IR(r=0.49, p=*0,0001).

Key words: Comorbid disease · Lumbar disc herniation · Atherosclerotic risk factors

INTRODUCTION

Comorbidity refers to the simultaneous presence of additional diseases besides the one that is being treated. The rate of comorbidity in patients rises with the patients' age [1]. Comorbidity can lead to problems in the medicinal or surgical treatment of the primary disease if the secondary diseases have not been identified.

It has been found in previous investigations that no all positively identified disc herniations cause pain. The discs that cause pain have been shown to have different histological properties. It has been determined that the nucleus pulpozus and annulus fibrozusun have more granulation tissue vascularity than normal discs in extruded regions and that neopeptides like substance P are released at increased levels [2]. Studies on the relationship between the risk factors for atherosclerosis and the immuno-reactive activity of neuropeptides like substance P are currently being conducted on animal subjects. The results of these studies are expected to lead to developments in the treatment of chronic lumbar pain.

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Lumbar disc hernia (LDH) is the protrusion of the annulus fibrozusun's posterior longitudional ligament of the disc located between the lumbar vertebrae toward the spinal canal or foramen, or the extruding of that ligament into the canal that passes between the fibers of the ligament. This condition can also involve local inflammation, which reduces the volume of the canal and puts pressure on the neural and vascular structures that pass through it and can thus cause pain. Mechanical pressure is not the only factor that can cause pain. The secretion of inflammatory neuroactive substances like invertrebal disc fosfolipaz A2, prostoglandins, nitric oxide, interlucin -6 and various cytokines can contribute to the process of inflammation. Studies have shown that secreted mediators can play a role in this process [3,4]. In the presence of LDH, it is thought that these substances, which are related to disc material, are active [5]. Even where LDH is not present, it has been shown that these substances have a high concentration [6]. When these substances cause inflammation in the area of the nerve root, they can potentially raise the activity level of the dorsal root ganglion. Even in the absence of LDH, this can cause pain [7-9]. The result that emerges from these facts is that mechanical pressure is not the sole cause of pain-pain can be present even in the absence of mechanical pressure. One study indicates that LDH is the cause of 39% of lower lumbar region pain. In another study that that is intended to look at the correlation between cardiovascular risk factors and incidence rates of lumbar disc hernia, it has been found that cardiovascular risk factors are independently and significantly correlated with symptomatic lumbar disc herniation.

Trial group: Age (years): 49.2±9.4, blood insulin (μIU/mL): 20.2±8.7, blood glucose (mg/dL): 119.9±14.5, triglyceride (mg/dL): 201.8±80.8, total cholesterol (mg/dL): 206.8±44.3, HDL (mg/dL): 43.7±12.5, LDL (mg/dL): 112.7±35.5, CRP (mg/L): 0.5±0.4, insulin resistance (HOMA-IR): 6.1±3.0

Control group: Age (years): 47.5±9.3, blood insulin (μIU/mL): 12.1±8.1, blood glucose (mg/dL): 105.7±13.6, triglyceride (mg/dL): 149.7±78.2, total cholesterol (mg/dL): 182.4±43.6, HDL (mg/dL): 52.6±13.3, LDL (mg/dL): 88.5±34.9, CRP (mg/L): 0.4±0.5, insulin resistance (HOMA-IR): 3.1±2.2

Our results give further confirmation to the results of other studies that have shown that the atherosclerosis spinal disc can degenerate [10]. atherosclerosis of the abdominal aorta can hinder blood flow at branching points and this reduced blood flow can cause a variety of back problems [11]. Most patients with chronic lower back pain have congested lumbar and center sacral arteries due to atherosclerosis and it has been found that blockage of these arteries might be correlated with disc degeneration [12].

Clinical panels have come to the conclusion that aterosclersis (AS) leads to a loss of elasticity and a thickening of the walls of the aorta, iliac artery, coronary, popliteal artery vessel walls. This development is in addition to the effects of primary and secondary risk factors.

Hypercholesterolemi (HC) constitutes a risk for AS and studies have shown that when levels of blood cholesterol are lowered, the development of AS can be stopped or even reversed [13]. Hyperlipidemi has been shown to result from hemodynamic pressure on the endothelium of the veins that is caused by hypertension and the buildup of lipids in these areas as a result of the damage caused by that pressure [14]. Diabetes Mellitus (DM) and insulin resistance have been clearly shown to increase the risk of atherosclerotic heart and veins and cerebrovascular disease [15]. Additionally, they are known to lead to diabetic neuropathies in the spinal nerves [16, 17]. In a recent study, after correcting for comorbidity related to inflammation and pain, it was shown that the risk for chronic pain nearly doubled in the presence of metabolic syndrome and insulin resistance causing general obesity. The prevalence of chronic pain was determined in that study to be 52%. It was shown that metabolic syndrome was the most strongly correlated factor for pain. The correlation of general obesity, insulin resistance and inflammation with pain has been found to increase in the presence of osteoarthritis or neuropathy [18].

With this study, an attempt is made to determine whether the presence of disc hernia in patients who are admitted with complaints of chronic lower back pain is correlated with atherosclerosis. For the present study, the atherosclerosis risk factors that will be considered are ID, HC, HL, LDL, HDL and CRP.

MATERIALS AND METHODS

The test subjects for this study were selected from the patients who came to our clinic between January and July of 2011 with complaints of chronic lower back pain. The 52 patients chosen for the trial group had been given both magnetic resonance imaging MRI and electromyography (EMG) scans and those with LDH

(lower back pain with mechanical causes) were selected. 30 of the patients were women (57.6%) and 22 were men (42.4%). The 52 patients in the control group included 36 women (69.2%) and 16 men (30.8%) and had chronic lower back pain unrelated to mechanical causes. There was not a statistically significant difference between the age and gender distributions of the two groups (p=0.36).

Patients undergoing operations, as well as ones with polyneuropathy, rheumatismal sickness, malignitis, vascular pathology, congenital anomalies, hypertension and heart disease were not admitted to the study.

All of the patients admitted had a body mass index of less than 30kg/m2, meaning that they were not obese. The 104 patients admitted to the study were given tests for blood sugar, blood insulin, triglyceride, total cholesterol, LDL, HDL and CRP. The following tests were preformed in our hospital's biochemical and microbiological laboratories:

- Blood glucose (spectro photometric method)
- Blood insulin (spectro photometric method)
- Lipids (spectro photometric method)
- CRP (nephelometric method)
- Insulin Resistance (homeostatic method, HOMA-IR)
- HOMA-IR = blood glucose (mg/dL) x blood insulin () /405

Statistical Analysis: for statistical calculations, The statistics program SPSS 11.5 for Windows was used.

The results are presented as an average ± the standard deviation. The ages, CRP, lipid, blood insulin, blood glucose and insulin resistance values of the trial and control group were were calculated using the student t-test and the Mann-Whitney U test. For the group with chronic lower back pain and disc hernia, the correlation between age and other markers of atherosclerosis was measured using a Pearson correlation analysis. The results were considered significant if the p value was below 0.05.

A statistically significant relation was found between the trial group and the control group via a Pearson correlation analysis of the LDL (r=0.33, p=0.001), T cholesterol (r=0.28, p=0.006), HDL (r=0.32, p=0.001), TG (r=0.31, p=0.001), blood insulin (r=0.44, p=*0.0001), blood glucose (r=0.45, p=*0.0001) and HOMA-IR (r=0.49, p=*0.0001) (Table 1).

Findings: The 52 patients in this study, all of whom had chronic lower back pain connected to lumbar disc problems, consisted of 30 women (57.6%) and 22 men (42.4%). The patients selected for the control group, who had chronic lower back pain unconnected to mechanical causes, consisted fo 52 people, with 36 women (69.2%) and 16 men (30.8%) (Table 2). There was not a statistically significant difference between the groups in terms of gender and age (p=0.36).

Table 1: Patients with chronic lower back pain and with and without disc hernia, age, CRP, lipid, blood insulin, blood glucose values and insuline resistance.

	Trial Group (n=52) (Average ± SS)	Control Group (n=52) (Average ± SS)	P
Age (years)	49.2±9.4	47.5±9.3	0.36
Blood Insulin (µIU/mL)	20.2±8.7	12.1±8.1	*0.0001
Blood Glucose (mg/dL)	119.9±14.5	105.7±13.6	*0.0001
TG (mg/dL)	201.8±80.8	149.7±78.2	0.001
T Cholestrol (mg/dL)	206.8±44.3	182.4±43.6	0.006
HDL (mg/dL)	43.7±12.5	52.6±13.3	0.001
LDL (mg/dL)	112.7±35.5	88.5±34.9	0.001
CRP (mg/L)	0.5±0.4	0.4±0.5	0.70
HOMA-IR	6.1±3.0	3.1±2.2	*0.0001

LDL: low density lipoprotein, T Cholesterol: total cholesterol, HDL: hi density lipoprotein

TG: triglyceride, CRP: C-reactive protein, HOMA-IR: homeostatic model for insulin resistance

Table 2: Distribution of Gender

	Trial Group n=52	Control Group n=52	Combined Group n=104
Women	30 % 58	36 % 69	66 % 63,5
Men	22 % 42	16 % 31	38 % 36,5

Blood Insulin: (µIU/mL)(20.2±8,7)(p=*0.0001), blood glucose: (mg/dL)(119.9±14.5)(p=*0.0001), triglycerides: (mg/dL)(201.8±80.8) (p=0.001), total cholesterol: (mg/dL)(206.8±44.3)(p=0.006), HDL: (mg/dL)(43.7±12.5)(p=0.001), LDL: (mg/dL)(112.7±35.5) (p=0.001), HOMA-IR:(6.1±3.0)(p=*0.0001). The average blood test values for the trial group were significantly higher than that of the control group and the insulin resistance was also determined to be significantly stronger. No statistically significant difference (p=0.70) was found between the trial and control group's average CRP test results (Table 1). Considering these atherosclerosis risk factors, the trial group was more at risk than the control group. Only the CRP test did not reveal a statistically significant result, because the nephelometric method for CPR testing was not sensitive enough.

DISCUSSION

The following were the results for the trial group: age (years): 49.2±9.4, blood insulin (μIU/mL): 20.2±8.7, blood glucose: (mg/dL): 119.9±14.5, triglycerides (mg/dL): 201.8±80.8, total cholesterol (mg/dL): 206.8±44.3, HDL (mg/dL): 43.7±12.5, LDL (mg/dL): 112.7±35.5, CRP (mg/L): 0.5±0.4, insulin resistance (HOMA-IR): 6.1±3.0. The results for the control group were: age (years): 47.5±9.3, blood insulin (μIU/mL): 12.1±8.1, blood glucose (mg/dL): 105.7±13.6, triglycerides (mg/dL): 149.7±78.2, total cholesterol (mg/dL): 182.4±43.6, HDL (mg/dL): 52.6±13.3, LDL (mg/dL): 88.5±34.9, CRP (mg/L): 0.4±0.5, insulin resistance (HOMA-IR): 3.1±2.2). In our trial group tests for the atherosclerosis risk factors of blood insulin, blood glucose and insulin resistance revealed significantly higher results than for the control group (Table 1).

These results, as well as other risk factors that lead to atherosclerosis, have been shown to raise the risk of developing lumbar disc hernia. Recently, the incidence rates of atherosclerotic heart vein disease as well as lumbar disc hernia have been steadily rising. HC constitutes a risk for AS and studies have shown that reducing blood cholesterol levels can halt or even reverse the development of AS [13]. It can be imagined that if one reduces the risk factors that lead to atherosclerosis, one will also reduce the risk of heart and vein diseases as well as lumbar disc hernia. It has been shown that HL is when lipids accumulate in areas where hemo-dynamic pressure on veins exposed to hypertension has caused damage [14]. It has also been shown that DM and insulin resistance clearly raise the risk of atherosclerotic heart and veins and cerebro-vascular diseases [15]. In a study utilizing computer tomographic discography, the amount of calcification and the level of disc degeneration were shown to be correlated [19]. In a study carried out by Boleaga Dura, it was found that 10% of atherosclerotic lower lumbar region pain starts at age 20-29 and 80% starts between the ages of 30 and 69 [20]. It can be understood from this that attempts to reduce atherosclerotic risk factors should start at an early age. These studies also show the need for the new treatment methods, as well as the increased use of additional diagnostic methods when choosing medical and surgical treatments for older patients, in case of atherosclerotic comorbid diseases and radiologically diagnosed lumbar disc hernias. Because the inflammation caused by disc hernia is minimal, very sensitive serum tests are required in order to detect it.

High sensitivity CRP (HsCRP) is an extremely sensitive test. The cytokines released by inflamed cells include macraphages and monosites and are produced in response to tissue damage. Pro-inflammation cytokines are responsible for CRP synthesis in the liver [21]. Previous research has found no correlation between serum concentration of CRP, MRG and clinical symptoms. Many studies have indicated that CRP concentration is high prior to operation and low after operation and this has been interpreted as a sign of improvement. The base level of concentration of CRP for women and men gives an indication of future myocardial infarction and ischemic stroke. The relation between CRP concentration and atherosclerosis is unclear [22]. It has been shown that in the post-op period, if CRP is high, the recovery phase is likely to be longer. CRP level is also a small but important cause of LDH and chronic inflammation of the nerve root area. The level of disc herniation was found to be higher than the control group [23].

Researchers have become interested in the relationships between LDH and growth hormone (GH). Animal tests performed to study this subject have shown that some growth factors play a role in intervertebral disc development and degeneration. Exogenic growth factors have been shown to increase the production of proteoglicans and collagens during disc cell reproduction. Using growth factors in disc treatment has been shown to be effective in the repair of degeneration and in new construction. Despite the fact that the role of growth factors in cartilage tissue care and maintainance has been widely studied, the response of invertebral discs to growth factors has not yet been researched. Cartilage tissue has been observed to respond differently to different growth factors of the nucleus pulposus and annulus fibrosus. In animal studies, it has been shown that epidermal, fibroblast, transformational and insulin growth factors are made in the liver along with the effect of GH. In the near future, GH might be used as medicine for the treatment of LDH [24, 25].

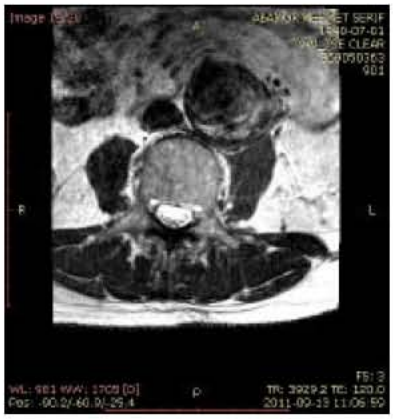
The 52 patients we selected for the trial group were ones with chronic lower back pain who were diagnosed with disc hernia at a routine checkup and were radiologically confirmed to have LDH. EMG's showed one-sided and bilateral pressure on roots at various levels. The patients were not overweight (BMI=less than 30kg/m2) and were not known to have any chronic diseases. The age and gender of the selection was selected randomly. The 52 patients in the control group also had chronic lower back pain. There was no neurological deficit found in checkups. There was no

radiological evidence of extruded discs and the EMG showed no evidence of pressure. No chronic diseases were diagnosed. They had not been operated on for LDH. Their age and gender range was randomly selected. The only thing that differentiated the two groups was that the control group did not have any evidence of mechanical pressure. The two groups underwent the same blood tests and the blood insulin, blood glucose and insulin resistance values of the trial group were significantly much higher than those of the control group. TG, TC, HDL and LDL were found to be significantly higher. As in a study by Longo UG and his colleagues, the blood lipid level of the patients in the trial group was high, which they indicated to be a possible risk factor for LDH [26]. Despite the fact that CRP was found to be higher with the nephelometric method, the difference was not statistically significant (Table 1). When these results are analyzed, the risk factors for atherosclerosis can be seen to be in effect in the development of LDH. In this respect our study supports the results of previous studies. Successfully combating risk factors of atherosclerosis should be of use for patients with risk of LDH.

Studies of LDH have shown that there is a close relationship between symptoms of risk of atherosclerosis and cerebro-vascular disease.

For one 71-year-old male patient in our study, who had been treated for high cholesterol, total lipid value and cerebro-vascular diseases, we performed an MRG to examine chronic lower back pain and found L4-L5 and L5-S1 extruded LDH,and in L3 the abdominal aorta fed a thrombosis aneurism (Figure 1,2,3). The patient reported that after the operation to address the aneurism, the lower back pain subsided.

Small branches of the mid sacral artery (MSA) provide vascularization for the L5 vertebra's 2 lower and 2 upper discs. The MSA comes out from the rear face of the abdominal aorta's bifurcation. Along with the increased incidence of atherosclerosis with rising age, the atherom plates that form in these regions hinder the blood flow in the MSA and cause ischemic variations. The subsequent inflammatory reaction and neovascularization can lead to cartilage tissue resorption and degeneration. This degeneration can at first encourage the development of lumbar disc hernia and after a while spontaneous regeneration of the (sekestre?) disc and thus lead to an eventual reduction of existing pain [27]. For this reason, as patients get older, if there is no neurological deficit, delaying potential operations to address disc hernia should be taking into consideration.



Resim: 1: L3 location, thrombose aneurism of the abdominal aorta

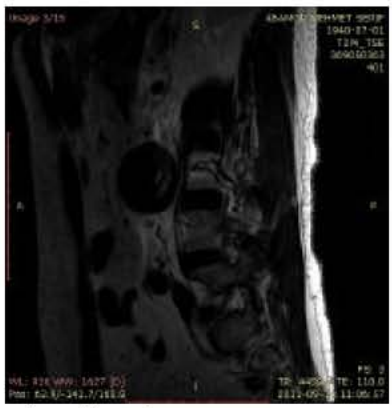


Fig. 2: Thrombose Aneurism

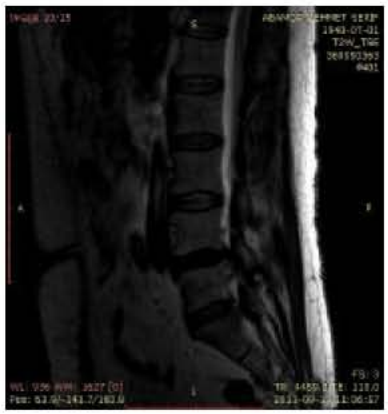


Fig. 3: L4-L5 ve L5-S1 location extruded LDH.

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