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The Comparison of Trace Element Levels in Serum, Bone and Intervertebral Disc Tissues of Patients with Lumbar Spinal Stenosis and Lumbar Disc Herniation

Research Article

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Abstract

Aim: The aim of this study was to measure the levels of trace elements (TEs) in serum, bone and disc tissue of patients with lumbar spinal stenosis (LSS) and lumbar disc herniation(LDH) and so to evaluate the role TEs in the physiopathogenesis of in these pathologies.

Material and method: In this study, serum, bone, and disc tissue levels of 10 TEs including phosphorus (P), calcium (Ca), magnesium (Mg), manganese (Mn), vanadium (V), zinc (Zn), chromium (Cr), copper (Cu), selenium (Se), cobalt (Co) levels were measured in 20 patients with LDH and 30 patients with LSS by the way of Inductively Coupled Plasma - Mass Spectrometer (ICP-MS).

Results: While there was no significant difference in the serum levels of the two groups, statistically significant differences were observed in the amount of Ca, Co, P, and V elements in bone and disc tissues. In the LSS group, the Ca element was found to be higher in the bone tissues, whereas in the LDH group, the Co element was found to be higher in the bone tissue. In disc tissue, Ca, P and Co elements were found to be higher in LSS group.

Conclusion: The differences in trace element levels seen in these pathologies are discussed in terms of possible causes in the light of current literature. Although it is known that high doses of trace elements have toxic effects, it supports the hypothesis that these trace elements may have beneficial biological effects at pharmacological levels in accordance with the results obtained in our study.

Keywords: Intervertebral disc; Lumbar disc herniation; Lumbar stenosis; Trace element.

Introduction

About 96% of the human body is known to be composed of carbon, oxygen, hydrogen and nitrogen elements called major elements [1]. In addition, there are elements called semi-major elements such as potassium, sodium, calcium, phosphorus, magnesium which constitute 3-4% of the total body weight and whose biological functions are better understood. Apart from these, the presence of trace elements which are found naturally and which can be taken with various foods, daily intake not exceeding 100 mg per day, is known [2]. The metabolism and biological functions of these elements have not been clearly demonstrated. While trace elements may show toxicity depending on the dose, it is thought that a number of diseases may occur in their deficiencies [3].

In the presenting study, the trace element measurements of serum, bone, and disc materials obtained from LSS and LDH patients who were thought to have occurred with different etiological factors on the same anatomical structure were compared and the results of both groups were compared statistically. In this way, the role of trace elements in the physiopatho genesis of these different pathologies has been investigated. Moreover, the measurement of TEs levels at the same time in three different tissues (blood, bone, and disc) was done in our study for the first time.

Material and Method

After the approval of Clinical Research Ethics Committee of Yoz-

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gat Bozok University (12.10.2016 dated 12.10.2016/68), blood, bone (lamina), and degenerated disc tissue from the patients operated for lumbar spine pathology in Yozgat Bozok University Faculty of Medicine Department of Neurosurgery between 2016-2017 were taken. The trace element levels in the samples were measured by the ICP-MS (Inductively Coupled Plasma - Mass Spectrometer). Patients divided into two groups according to their preoperative magnetic resonance imaging (MRI) as lumbar spinal stenosis (LSS) and lumbar disc herniation (LDH) groups.

In addition, preoperative MRI (Magnetic Resonance Imaging) images were evaluated and divided into two groups as lumbar narrow canal (LSS) and lumbar disc herniation (LDH). Patients with rheumatic disease such as rheumatoid arthritis and ankylosing spondylitis, who were under 18 years of age, who had incomplete file information or had incomplete radiological examination, and who were operated for trauma were excluded from the study.

The diagnosis of LSS or LDH was established according to the clinical and radiological findings. 20 of 50 patients were diagnosed as LDH and remaining 30 were LSS. LSS group included the patient in whom discectomy was been performed included in the study. Patients only underwent laminectomy for LSS excluded from the study.

Obtaining of tissue specimens:

Tissue specimens from the patients were obtained from individuals who applied for surgery to the Department of Brain and Neurosurgery of Yozgat Bozok University. While the disc operation is being performed, lamina is taken (bone tissue) and disk tissue (cartilage tissue) is taken from the patients. For this purpose, an ethical file (12.10.2016 date, 12.10.2016/68 number) has been prepared and required permission has been obtained. Patients were asked to complete a questionnaire on smoking cessation, medical history and workplace conditions, and the necessary biochemical values were taken from hospital records.

50 patients were included in the study. Bone and tissue specimens were taken from patients with disc degeneration during surgery, and 1 ml of blood was taken from the blood samples taken for surgical preparation of the patient prior to surgery. These samples were placed in 2 ml centrifuge tubes until the time of analysis and stored at -20 ° C until analysis.

Wet tissues were weighed on a precision scale and then transferred onto a glass table. The textures on the glass tray, together with the tray, were pre-conditioned at 75 ° C for 24 hours to dry. Tissue samples removed from the ovule were weighed to determine dry weights again with a precision scale and taken to the high temperature resistant teflon tubes of the microwave oven. 10 ml of 65% suprapure HNO3 was added to the tissues and acid etching was performed in the microwave (Milestone StartD) (Aliyev V. ve diğ., 2012). Analysis of these samples was determined by ICP-MS (Inductively Coupled Plasma Mass Spectrometry-Thermo Scientific ICAPQc) instrument at the Yozgat Bozok University Science and Technology Application and Research Center, Yozgat, Turkey. For this purpose, levels of phosphorus (P), magnesium (Mg), calcium (Ca), manganese (Mn), cobalt (Co), copper (Cu), zinc (Zn), vanadium (V), cobalt (Co) and selenium (Se) were measured in both tissues and blood.

Statistical Analysis:

These measured levels were grouped according to radiological findings. Three replicates were obtained for each sample analyzed and their mean value was taken into account for the concluded assessment. If the required statistics are given, it is evaluated by SPSS 20.0 statistical program. A normality test was used to determine whether sample data of groups a normally distributed. The correlations between toxicological variables among groups were assessed with Pearson correlation test. The parametric and nonparametric tests were carried out to determine the association of main parameters concerning among groups. All tests were considered significant at $p < 0.05$ and $p < 0.01$.

Results

Between January 2016 and December 2017, 20 of the 50 patients had LDH and 30 had LSS. The mean age was 45±9 years in LSS group and 59.6±11.1 years in LDH group. There was a statistically significant difference between the groups in terms of age ($p = 0.001$).

Ca element (p 0.025) (Graph1) and V element values ($p = 0.001$) (Graph2) were found to be higher in bone tissue of LSS cases, whereas Co values were higher in bone tissue of LDH group ($p = 0.004$) (Graph 3).There was no significant difference in serum concentration in both groups. In disc tissues, P ($p = 0.050$) (Graph 4), Ca ($p = 0.046$) (Graph 5) and Co ($p = 0.036$) (Graph 6) were higher in LSS cases.

Additionally, correlation analysis revealed that bone and serum P, Mg and Cu concentrations had a direct correlation in patients with LSS ($p = 0.001$, $p = 0.004$, $p = 0.001$, respectively). However, an inverse correlation was found between the Cr concentration of bone and serum in these patients ($p = 0.017$).

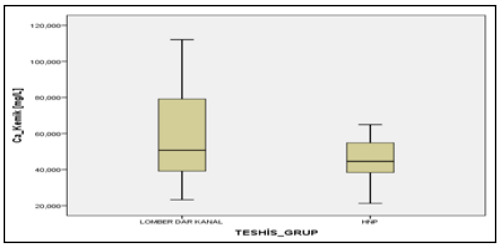
In the LDH group, correlation analysis revealed that bone Co, Zn, and Cu concentrations were found to be directly proportional to the serum concentrations ($p = 0.034$, $p = 0.025$ and $p = 0.001$, respectively), while V concentration in bone and disc were directly proportional ($p = 0.026$). However, in this group, it is found that Mg concentration in bone and disc and the Cr concentration of bone, serum, and, disc concentrations had inverse proportions ($p = 0.015$, $p = 0.026$, and $p = 0.012$, respectively).

Discussion

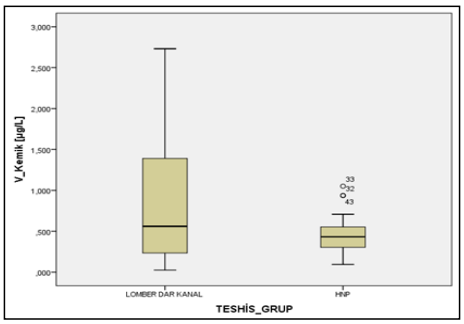
In this study, trace elements levels of bone, intervertebral disc tissues, and serum samples which were obtained from patients with LDH (n=20) and LSS (n=30) were examined. The levels of 10 trace elements which were phosphorus (P), calcium (Ca), Magnesium (Mg), Manganese (Mn), Vanadium (V), Zinc (Zn), Chromium (Cr), Copper (Cu), Selenium (Se), and Cobalt (Co) were determined and compared in each of the three tissues in patients with LDH and LSS. As a result of these tests, significant differences were found between Ca, V, Co and P elements in bone and disc materials in both groups.

In fact, the determination of trace elements in bone and intervertebral disc tissues is not a new study area. Takata et al. investigated trace element differences in normal cortical and trabecular bones

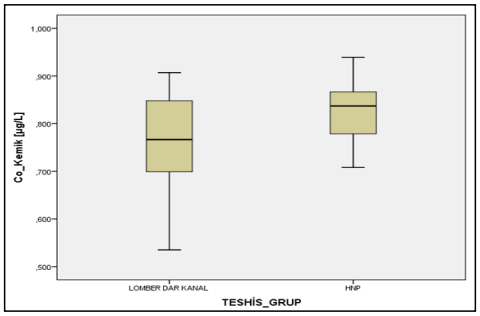
Graphic 1: Comparison of Ca amounts in bone tissue in LSS and LDH groups.



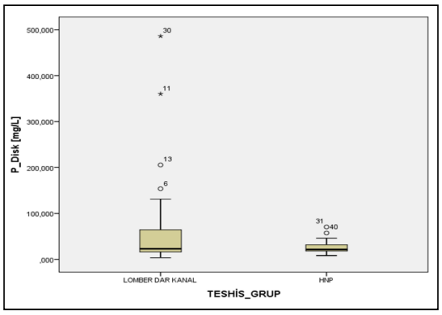
Graphic 2: Comparison of V amounts in bone tissue in LSS and LDH groups.



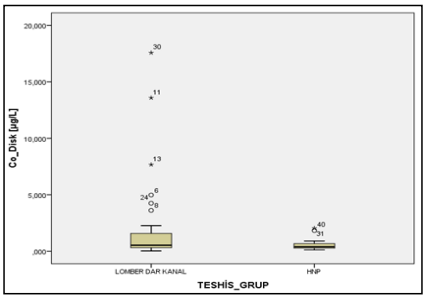
Graphic 3: Comparison of Co amounts in bone tissue in LSS and LDH groups.



Graphic 4: Comparison of P amounts in DİSC tissue in LSS and LDH groups.



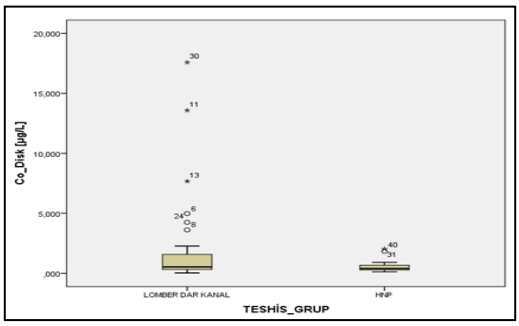
Graphic 5: Comparison of Ca amounts in disc tissue in LDK and LDH groups.



[4]. Now akovski et al. studied the effect of trace elements in degenerative disc diseases [5, 6]. Kubaszewski et al. suggested that the trace element concentrations in intervertebral disc and bone tissue were different [7]. Zaichick et al. were performed the determination of trace element in osteomyelitis and Ewing sarcoma [8].

In our study, we found that the levels of Ca in bone and disc tissue obtained from LSS cases were higher than LDH cases. In fact, patients with LSS are older and they thought to have osteoporosis or osteopenia. However, it seems that this finding which was higher Ca levels in bone tissue in patients with LSS is inconsistent with our general knowledge. Basle et al. showed that cortical and trabecular bone mineral contents, especially Ca and P concentra-

Graphic 6: Comparison of Co amounts in disc tissue in LDK and LDH groups.



tions, did not change in elderly and osteoporotic spine, however, they suggest that decreased bone densitometry was due to the decreased bone mass [9]. Dequeker mentioned about the effect of aging on bone and stated that there was no change in bone composition with increasing age. Dequeker additionally stated the presence of some references which stated the increased Ca content in bone with increasing age [10]. In a similar study Totter et al reported that decrease in bone mineral density was not prominent with the increasing age [11]. Vogt Herman and Tonsager stated the increased Ca concentration with the increased age [12]. However, in a study performed by Havaldari et al, the presence of a correlation between the aging and bone mineral density was reported [13]. Sapcanin and Sofic reported that Ca has no effect on the regulation of bone resorption, however, they concluded that Ca is an effective factor on bone formation [14].

Although the increase of Ca mineral in aged bone may be considered as a result of increased bone and Ca metabolism, it can be said that this issue may be a new clinical research subject for further studies. In our study, the high level of Ca levels in LSS patients with a high mean age supports the high level of Ca al in bone tissue in elderly patients. Similarly, we found high Ca levels in disc tissues in these patients. This result has been shown both radiologically and biochemically in cases with degenerative cases of adolescent scoliosis in which early degeneration has been started [15, 16].

In our study, P amount was significantly higher in disc materials of patients with LSS. Wu et al reported that P is required for the calcification and initiates apatite crystal formation [17]. In another in vitro study, Ca/P ratio was stated to affect the hydroxyapatite degradation [18]. With these results, it is possible to say that P has an effect on helping the precipitation of Ca ion and calcification.

In our study, Co element levels were found to be higher in the bone tissues of LDH patients, whereas it was found higher in the degenerative disc materials of the LSS patients. In fact, Co is one of the essential trace elements that must be taken with the diet and found in the vitamin B12 as cobalamin. Although this is the only known physiological function to date, in some studies, it has also been shown that this element physiologically presents in different enzyme groups(methionine aminopeptidase, prolidase, nitrile hydratase, glucose isomerase, methylmalonyl-CoA carboxytransferase, aldehyde decarbonylase, lysine-2,3-aminomutase, and bromoperoxidase) [19]. However, our knowledge level about the toxic effects of Co is still more than their physiological function [20]. Moshtaghie et al reported that toxic dosages of Co may lead to bone destruction like a osteoporotic agent by the way of impairing bone metabolism[21]. However, it is known that it activates bone regeneration at physiological levels and therefore Co is used in making bioactive glass particles [22]. The responding mechanism in this situation is the activation of the revascularization and regeneration of the ischemia-sensitive bone tissue by the way of ischemia formation in the tissue. Reduction of tissue oxygenation leads to release of hypoxia-inducible factor 1 (HIF1) [23]. This factor is important in the adaptation of tissue hypoxia and is a heterodimeric transcriptional factor with two subgroups, α and β [24]. HIF-α is rapidly degraded by an enzyme called prolyl hydroxylases in normal oxygen levels. Co inhibits this enzyme to help the HIF stay longer in the medium and ultimately help in revascularization of the tissue[25]. It is known that clinical picture is more acute and mechanical stresses are important in disc degeneration in patients with LDH. In addition, in most of these cases, paravertebral muscle spasm is observed to reduce nerve compression and as a result of paravertebral spasm leg and/or back pain are frequently accompany to the clinical picture. The paravertebral muscle spasm is said to decrease the tissue oxygenation and blood flow by the way of increasing the intra muscular pressure [26]. The intermediate branch of the lumbar artery has been shown to be divided into three in microangiographic studies and the posterior branch has been shown to supply lamina and facets [27]. These branches are closely related to the posterior paravertebral muscles and may be affected by spasm, and the body's adaptation mechanisms as a result of tissue hypoxia may be involved in increasing the HIF and thereby increasing the body Co resources, thereby ensuring the continuity of adaptation due to this physiological hypoxia. In patients with LSS, clinical picture is mostly due to the chronic neural compression and disc degeneration. Paravertebral spasm is less common in these patients. It is expected that these patients may have higher Co levels in disc tissue which is degenerated and prone to ossification. Certainly these hypotheses should be supported by laboratory and clinical studies.

In our study, another trace element found high in the bone tissue of LSS cases is Vanadium (V). V is an element that is considered to be the most interesting and has many treatment potentials in recent years [28]. It has insulin and growth factor-like effects in pharmacological doses and has been shown to have osteogenic activation [29]. Even more, it has been stated that some V compound have antitum oral properties. It has been suggested that V compounds induce DNA and collagen synthesis in fibroblast cell cultures and cause osteoblastic differentiation. Paglia et al reported that local V usage increases the bone healing in shorter period by increasing the chondrogenesis and angiogenesis in a rat model of femoral bone fracture [30]. It may be thought that the V element may have been increased in order to increase osteoblastic activity in bone tissue, possibly due to a number of intrinsic factors or metabolic controls that have not been disclosed in patients with LSS who had older age in our study. Again, it is obvious that

this suggestion should be clarified by planning new clinical and laboratory studies.

In conclusion, as trace element studies increased, our knowledge about trace elements which are determined under normal or pathological conditions increased in the light of new data. Although it is known that high doses of trace elements have toxic effects, it supports the hypothesis that these trace elements may have beneficial biological effects at pharmacological levels in accordance with the results obtained in our study. In addition, it is impossible to argue that the reason for the increase in bone or disc tissue of the trace elements in our study is due to a physiological defense mechanism or to initiate or maintain a pathological process. However, it is possible to design new clinical and laboratory studies and discover the metabolic pathways of the trace elements through the data and hypotheses obtained as a result of these studies.

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