DOI: 10.5350/BTDMJB.20170517070728

Quantitative Analysis of Lead and Nickel in Benign Meningioma and Glioblastoma Multiforme

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ÖZET

İyi huylu meningiom ve glioblastoma multiformede kurşun ve nikel düzeylerinin kantitatif analizi

Amaç: Bu çalışmanın amacı, iyi huylu meningiomlar ve glioblastoma multiforme doku örnekleri içerisindeki kurşun ve nikel seviyelerini karşılaştırmaktır.

Gereç ve Yöntemler: Bu çalışma, patolojik olarak iyi huylu olarak teşhis edilmiş ve cerrahi operasyonla elde edilmiş meningiom ve glioblastoma multiforme örnekleri üzerinde gerçekleştirilmiştir (her gruptan 20 örnek). Eser elementlerin ölçümü Shimadzu AA 680 atomik absorpsiyon spektrometresi ile gerçekleştirilmiştir. Değerlendirme, her gruptaki kurşun ve nikel seviyseindeki değişimle, $p<0.05$ istatistiksel anlamlılık içerisinde yapılmıştır.

Bulgular: İyi huylu meningiom örneklerindeki kurşun seviyesi glioblastoma multiforme örnekleriyle benzerdir ($p=0.817$). Nikel seviyesi ise iyi huylu meningiomlarda, glioblastoma multiforme örneklerine göre istatistiksel olarak yüksektir ($p=0.003$).

Sonuç: Glioblastoma multiformelerler ile karşılaştırıldığında iyi huylu meningiomlardaki yüksek nikel içeriği ve nikelin meningiom oluşumundaki muhtemel korelasyonu araştırılmalıdır. Bulgularımızın yeni çalışmalar için değerli bir veri olduğunu ve meningiom ve glioblastoma multiforme patojenezi hakkında önemli bilgi katkısında bulunacağı kanaatindeyiz.

Anahtar kelimeler: Glioblastoma multiforme, kurşun, meningiom, nikel

ABSTRACT

Quantitative analysis of lead and nickel in benign meningioma and glioblastoma multiforme

Objective: The aim of this study was to compare lead (Pb) and nickel (Ni) levels in tissue samples of benign meningiomas and glioblastoma multiformes.

Material and Methods: This study was performed in pathologically diagnosed benign meningioma and glioblastoma multiforme specimens (20 specimens in each group and a total of 40 specimens) obtained from operations. Measurements of trace elements were performed with Shimadzu AA 680 atomic absorption spectrophotometer. $p<0.05$ was considered as statistically significant.

Results: The level of lead in benign meningioma specimens was similar to that in glioblastoma multiforme specimens ($p=0.817$). The level of nickel in benign meningioma specimens were statistically higher than that in glioblastoma multiforme specimens ($p=0.003$).

Conclusion: The high Nickel content of benign meningiomas compared to that of glioblastoma multiformes and the possible correlation of nickel with meningioma formation should be further evaluated. We consider that our findings carry valuable data for new researches and can contribute to worthwhile information on pathogenesis of meningioma and glioblastoma multiforme.

Key words: Glioblastoma multiforme, lead, meningioma, nickel

Bakırköy Tıp Dergisi 2017;13:190-194

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Geliş tarihi / *Date of receipt:* 18 Nisan 2017 / April 18, 2017

Kabul tarihi / *Date of acceptance:* 17 Mayıs 2017 / May 17, 2017

INTRODUCTION

Primary brain tumors are the second most frequent malignancy in childhood and the sixth in adults (1,2). Trace elements are involved in the functions of biological systems by affecting activator or inhibitor systems, competing for binding regions with protein and other elements, and affecting the membrane permeability or other mechanisms (3). Trace elements can be found in benign and malignant tumors in different amounts. This difference is due to several factors. Benign tumors may have more time to collect some trace elements, some trace elements function in development of benign tumors and others function in development of malignant tumors. The difference in the amount of some trace elements in the environment can be important in determining the development of the benign or malignant tumors. Environmental exposure of the patients to some trace elements play some role in the development of benign and malignant tumors. Lead (Pb) and Nickel (Ni) are important elements in biological processes and have some kind of effect in the pathogenesis of brain tumors. The aim of this study is to compare Pb and Ni levels in tissue samples of central nervous system benign and malignant tumors; benign meningiomas and glioblastoma multiformes.

MATERIALS AND METHODS

Sample Collection and Preparation

This study was performed in benign meningioma and glioblastoma multiforme specimens obtained from 40 patients who were operated at Neurosurgery Clinic, Bakırköy Research and Training Hospital for Neurology, Neurosurgery and Psychiatry, Istanbul, Turkey. Twenty patients had benign meningioma as pathologic diagnosis and the other 20 patients had glioblastoma multiforme as pathologic diagnosis. Biopsy samples were taken from the tumor tissues in the operating rooms and then conserved in sterile plastic containers. Until they were used in experiments, these tissues were kept at -20°C in refrigerator. The pathological confirmations were obtained later and if the diagnosis was not benign meningioma or glioblastoma multiforme, the specimen was excluded from the study.

Analytical Procedure

These tumor tissues were put in the +4°C refrigerator to be thawed before the experiment. After the tumor tissues were thawed at +4°C they were weighed on precision balance; for each specimen 1 gram of tumor tissue was put into the teflon tube. Four ml of concentrated HNO3 (%65) was added over these samples and tube lids were closed. Teflon tubes were kept at acid bomb at +150°C for two hours. The materials that were converted into liquid forms were completed to 10 ml by adding de-ionized water and were placed in the fridge. All these operations were performed by using transparent plastic gloves. All plastic and glass materials used in the experiment were kept at 6 M (molar) HNO3 (%65) solution for a period of two days before they were used. The materials removed from the solution were washed six times with de-ionized water and dried in oven. These materials were kept in locked plastic bags until they were used in experiments. The measurements for Pb and Ni were performed by Shimadzu AA 680 atomic absorption spectrophotometer. Three measurements for Pb and Ni levels in the tissues were performed and the average of these measurements was calculated, and then these values were expressed as mg/kg as tissue concentrations.

Ethics Statement

Ethical considerations comply with the Helsinki Declaration. In all cases, patients were informed about the aim of the study and gave written consent for participation in the study and for data publication. The use of tissue in the investigations was permitted by the Bioethical Committee of the Istanbul Bakırköy Research and Training Hospital Neurology, Neurosurgery and Psychiatry.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows 12.0. For numeric and other variables, Paired Samples T Test and Independent Samples Students T Test were used, respectively and $p<0.05$ was considered as statistically significant.

Table 1: Demographic features and intracranial pathology of the patients

	Glioblastoma Multiforme	Meningioma	Total
Gender (Number of patients)			
male	17 (85%)	9 (45%)	25 (65%)
Female	3 (15%)	11 (55%)	15 (35%)
Age of the patients	48.45 (±14.45) years, (ranged from 20-77)	51.95 (±9.87) years, (ranged from 36-76)	50.2 (±12.35) years, (ranged from 20-77)

RESULTS

In this study there were 40 tumor specimens obtained from 40 different patients, 26 (65%) of these patients were male, 14 (35%) were female. In glioblastoma multiforme group, there were 17 males and 3 females; and in meningioma group, there were 9 males and 11 females. Gender and age characteristics for each intracranial pathology are summarized in (Table 1). The patients were evaluated according to the localization of the lesions; 3 lesions were found to be temporal, 6 parietal, 7 frontal, 5 parietooccipital, 7 temporoparietal, 3 parietotemporal, 7 frontoparietal, 1 frontotemporal and 1 lesion was at occipital (Table 2). The mean Pb and Ni levels in the whole sample were 1.69775 (±1.913908) and 0.14375 (±0.187680) mg/kg, respectively. The mean Pb, and Ni levels in patients with glioblastoma were 1.62650 (±1.918103) and 0.032 (±0.019620), mg/kg, respectively. The mean Pb and Ni levels in patients with meningioma were measured as 1.769 (±1.956802) and 0.2555 (±0.213603), mg/kg, respectively. The level of lead in benign meningioma specimens was similar to that in glioblastoma multiforme specimens (p=0.817). The level of nickel in benign meningioma specimens were statistically higher than that in glioblastoma multiforme specimens (p=0.003) (Table 3).

Table 2: Localization of meningioma and glioblastoma multiformes

Localization	n	%
Temporal	3	7.5
Parietal	6	15
Frontal	7	17.5
Parietooccipitial	5	12.5
Temporoparietal	7	17.5
Parietotemporal	3	7.5
Frontoparietal	7	17.5
Frontotemporal	1	2.5
Occipital	1	2.5

DISCUSSION

Trace elements are involved in the functions of biological systems by affecting activator or inhibitor systems. Trace elements compete for binding regions with protein and other elements, and affect the membrane permeability or other mechanisms (3). Trace elements are also involved in the functions of proteins which have enzyme activity.

Lead is used in building construction, lead-acid batteries, bullets and shot, weights, as part of solders, pewters, fusible alloys, and as a radiation shield. Exposure to lead and lead chemicals can occur through inhalation, ingestion and dermal contact. Lead exposure mostly occurs through ingestion. Lead paint is the major source of lead exposure for children. Lead can be

Table 3: Comparison of lead and nickel levels in classic meningioma and glioblastoma multiforme specimens

	Pathology	Number	Average (mgr/kg)	Standard deviation	P
Pb	Glioblastoma	20	1.6265 (ranged from 0.1 - 8.1)	1.9181	p=0.817
	Meningioma	20	1.769 (ranged from 0.06 - 5.88)	1.9568	
Ni	Glioblastoma	20	0.032 (ranged from 0.01 - 0.084)	0.01962	p=0.003
	Meningioma	20	0.2555 (ranged from 0.02 – 0.65)	0.2136	

The level of nickel in bening meningioma specimens were statistically higher than glioblastoma multiforme specimens at p<0.05.

ingested through fruits and vegetables contaminated by high levels of lead in the soils they were grown in. Soil is contaminated through particulate accumulation from lead in pipes, lead paint and residual emissions from leaded gasoline. Lead Inhalation is the second major pathway of exposure, especially for workers in lead-related occupations. Almost all inhaled lead is absorbed into the body, the rate is 20–70% for ingested lead; children absorb more than adults. Dermal exposure may be significant for a narrow category of people working with organic lead compounds, but is of little concern for general population. Lead is a highly poisonous metal affecting almost every organ and system in the body. Long-term exposure to lead or its salts can cause nephropathy, and colic-like abdominal pains. Chronic, high-level exposure has been shown to reduce fertility in males. Exposure to high lead levels can severely damage the brain and kidneys in adults or children; and ultimately cause death. In pregnant women, high levels of exposure to lead may cause miscarriage. The main target for lead toxicity is the nervous system, both in adults and children. In children high blood levels of lead were found to be significantly negatively correlated with the developmental quotients of adaptive behavior, gross motor performance, fine motor performance, language development, and individual social behavior (4). Long-term exposure of adults is associated with persistent brain lesions, and may cause progressive decline in cognitive functions (5). Bhatti et al., stated that lead may cause glioblastoma multiforme and meningioma through mechanisms related to oxidative damage (6). In our study we found that the level of lead in benign meningioma specimens was statistically similar to that in glioblastoma multiforme specimens ($p=0.817$). Regarding this finding, there is no difference in lead content of benign meningioma and glioblastoma multiforme; and no specific conclusion can be done for the relation of the amount of Pb in tissue and formation of benign meningioma and glioblastoma multiforme.

Nickel is one of the four elements that are ferromagnetic around room temperature. The metal is chiefly valuable in the modern world for the alloys it forms; about 60% of world production is used in nickel-steels. Other common alloys, as well as some new superalloys, make up most of the remainder of world nickel use, with chemical uses for nickel compounds consuming less than 3% of production. As a compound, nickel has a number of niche chemical manufacturing uses, such as a catalyst for hydrogenation. Although not recognized until the 1970s, nickel plays important roles in the biology of microorganisms and plants. The plant enzyme urease (an enzyme that assists in the hydrolysis of urea) contains nickel. A nickel-tetrapyrrole coenzyme, Cofactor F430, is present in the methyl coenzyme M reductase, which powers methanogenic archaea. One of the carbon monoxide dehydrogenase enzymes consists of an Fe-Ni-S cluster. Other nickel-containing enzymes include a rare bacterial class of superoxide dismutase and glyoxalase I enzymes in bacteria and several parasitic eukaryotic trypanosomal parasites (this enzyme in higher organisms, including yeast and mammals, uses divalent zinc, Zn^{2+}). Nickel can have an impact on human health through infectious diseases arising from nickel-dependent bacteria. Nickel released from Siberian Traps volcanic eruptions is suspected of having a significant impact on the role played by Methanosarcina, a genus of euryarchaeote archaea that produced methane during the biggest extinction event on record. Large amounts of nickel leach into food cooked in stainless steel. Nickel sulfide fume and dust are believed to be carcinogenic, and various other nickel compounds may be as well. Occupational exposure to Ni compounds through inhalation is a big health concern for workers involved in the different stages of Ni processing (7,8). Sensitized individuals may show an allergy to nickel, affecting their skin, known as dermatitis (9-11). Nickel is an important cause of contact allergy, partly due to its use in jewellery intended for pierced ears. Nickel allergies affecting pierced ears are often marked by itchy, red skin. Many earrings are now made nickel-free due to this problem. Nickel was voted Allergen of the Year in 2008 by the American Contact Dermatitis Society. The most important adverse health effects due to occupational exposure to nickel and its compounds are skin allergies, lung fibrosis, and lung cancer (12). Epidemiological studies have reported an increased incidence of lung and nasal cancer among workers in nickel refinery (13-15). In our study, we found that the level of nickel in benign meningioma specimens were statistically higher than that in glioblastoma multiforme specimens ($p<0.05$). There is no study that investigated the relation of nickel with meningiomas. The high

nickel content of meningiomas should be investigated. Meningiomas develop in a long time, however most glioblastomas develop in a shorter time, so we may think that meningiomas have long time to collect trace elements, but Pb is also a trace element and there is no statistically important difference in the Pb content of glioblastomas and meningiomas. There is an enormous difference in the nickel content of glioblastomas and meningiomas ($p=0.003$). The high Ni content of meningiomas, and the relation between meningioma formation and Ni should be further investigated. More studies should be done to understand the relation between meningioma formation and nickel.

Another study stated that the level of Zinc in benign meningioma specimens were statistically higher than that in glioblastoma multiforme specimens (16). In this study we found that the level of nickel in benign meningioma specimens were statistically higher than that in glioblastoma multiforme specimens ($p=0.003$). These two studies showed that some trace elements are more concentrated in meningioma specimens. There might be a relation between trace elements and formation of benign meningiomas.

CONCLUSION

The level of Nickel in benign meningioma specimens were statistically higher than that in glioblastoma multiforme specimens ($p<0.05$). The measurement of trace element levels in glioblastomas and classic meningiomas in our study is not sufficient in terms of reaching meaningful results because there is no complementary study on this subject in the literature. For the interpretation of these results, there is a need for further well-randomized researches. Future researches should compare the cerebrospinal and normal tissue levels of trace elements with the levels in tumor tissues. We consider that our findings cary valuable data for new researches and can contribute to worthwhile information on this issue.

Acknowledgements: This research did not receive any specific grant from funding agencies in the public commercial, or not-for-profit sectors.

Conflict of interest: The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

REFERENCES

1. Garcia DM, Fulling KH. Juvenile pilocytic astrocytoma of the cerebrum in adults. A distinctive neoplasm with favorable prognosis. J Neurosurg 1985; 63: 382-386.
2. Katsetos CD, Krishna L. Lobar pilocytic astrocytomas of the cerebral hemispheres: I. Diagnosis and Neurology Clin Neuropath 1994; 13: 295-305.
3. Cavallo F, Gerber M, Marubini E, Richardson S, Barbieri A, Costa A. Zinc and copper in breast cancer. A joint study in northern Italy and southern France. Cancer 1991; 67: 738-745.
4. Hou S, Yuan L, Jin P, Ding B, Qin N, Li L. A clinical study of the effects of lead poisoning on the intelligence and neurobehavioral abilities of children. Theor Biol Med Model 2013; 10: 13.
5. Stewart WF, Schwartz BS, Davatzikos C, Shen D, Liu D, Wu X, et al. Past adult lead exposure is linked to neurodegeneration measured by brain MRI. Neurology 2006; 66: 1476-1484.
6. Bhatti P, Stewart PA, Hutchinson A, Rothman N, Linet MS, Inskip PD, et al. Lead exposure, polymorphisms in genes related to oxidative stress, and risk of adult brain tumors. Cancer Epidemiol Biomarkers Prev 2009; 18: 1841-1848.
7. Polednak AP. Mortality among welders, including a group exposed to nickel oxides. Arch Environ Health 1981; 36: 235-242.
8. Grimsrud TK, Berge SR, Resmann F, Norseth T, Andersen A. Assessment of historical exposures in a nickel refinery in Norway. Scand J Work Environ Health 2000; 26: 338-345.
9. Boonchai W, Chaiwanon O, Kasemsarn P. Risk assessment for nickel contact allergy. J Dermatol 2014; 41: 1065-1068.
10. Fabbro SK, Zirwas MJ. Systemic contact dermatitis to foods: nickel, BOP, and more. Curr Allergy Asthma Rep 2014; 14: 463.
11. Ricciardi L, Arena A, Arena E, Zambito M, Ingrassia A, Valenti G, et al. Systemic nickel allergy syndrome: epidemiological data from four Italian allergy units. Int. J Immunopathol Pharmacol 2014; 27: 131-136.
12. Zhao J, Shi X, Castranova V, Ding M. Occupational toxicology of nickel and nickel compounds. J Environ Pathol Toxicol Oncol 2009; 28:177-208.
13. Doll R, Morgan LG, Speizer FE. Cancers of the lung and nasal sinuses in nickel workers. Br J Cancer. 1970; 24: 623-632.
14. Roberts RS, Julian JA, Muir DC, Shannon HS. Cancer mortality associated with the high-temperature oxidation of nickel subsulfide. IARC Sci Publ 1984; 53: 23-35.
15. Roberts RS, Julian JA, Muir DC, Shannon HS. A study of mortality in workers engaged in the mining, smelting, and refining of nickel. II. Mortality from cancer of the respiratory tract and kidney. Toxicol Ind Health 1989; 5: 975-993.
16. Adilay U, Demirgil BT, Günaldı Ö, Tuğcu B, Belivermiş M, Güçlü B. Comparison of levels of zinc, iron and cadmium in classic meningioma and glioblastoma multiforme. Journal of Neurological Sciences 2016; 33: 325-330. [Turkish]