The relationship of ceruloplasmin and neural tube defects

Seruloplasmin ve nöral tüp defektleri arasındaki ilişki

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Abstract

Objective: To compare the levels of ceruloplasmin (cp) in the amniotic fluids and maternal bloods of second trimester fetuses with and without neural tube defects (NTD).

Materials and Methods: 66 pregnant women were included in the study. Amniocentesis was performed in 32 women in a patient group diagnosed as NTD or anencephaly and 34 pregnants in a control group with positive Down Syndrome screening test. Maternal bloods were also taken. Cp was measured with Erel's ceruloplasmin measurement method.

Results: The cp levels of the amniotic fluid of patients and controls were not statistically different ($p>0.05$). The cp levels of the maternal bloods were not different in two groups ($p>0.05$).

Conclusion: As an antioxidant, no relation was found between cp and NTD.

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Key words: Ceruloplasmin, Antioxidant, Neural tube defect

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Özet

Amaç: Bebeklerinde intrauterin nöral tüp defekti (NTD) olan ve olmayan ikinci trimesterdeki gebe kadınlarda amnion sıvısı ve anne kanındaki seruloplasmin değerlerinin karşılaştırılması.

Gereç ve Yöntem: Çalışmaya 66 kadın dahil edildi. NTD veya anensefali tanısı konulan hasta grubundaki 32 gebe ile Down sendrom taraması pozitif olan 34 gebe kadına amniosentez yapıldı ve anne kanları alındı. Amnion sıvıları ile anne kanlarında Erel'in metodu ile seruloplasmin bakıldı.

Bulgular: Hasta ve kontrol grubunun amnion sıvısı ile anne kanlarındaki seruloplasmin seviyeleri arasında anlamlı fark saptanmadı ($p>0.05$).

Sonuç: Antioksidan olarak seruloplasmin ve NTD arasında herhangi bir ilişki saptanamamıştır.

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Anahtar kelimeler: Seruloplasmin, Antioksidan, Nöral tüp defekti

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Introduction

Ceruloplasmin (Cp) is an acute phase response protein with two important potential functions: first; transportation of copper to the tissue sites; and second; functions such as oxidase activity of aromatic amines and serum antioxidation. In this setting, Cp acts as an extracellular scavenger of free radicals and superoxide ions, and then endogenously modulates inflammatory responses and so synthesis and secretion of Cp can be markedly increased during inflammation, infection, and in diseases such as diabetes, cancer, and cardiovascular disease, as well as during pregnancy (1, 2).

Neural tube defects (NTD) are a group of heterogenous and complex congenital anomalies of the central nervous system (CNS). Commonly included in this group are anencephaly, spina bifida and encephaloceles (3). The exact etiology of NTD is rather complex and poorly understood. Recently, oxidative metabolism was considered to be related with congenital anomalies including CNS (4, 5).

This study aims to compare the levels of cp in the amniotic fluids and maternal bloods of second trimester fetuses with and without NTD.

Materials and Methods

66 pregnant women admitted to Obstetrics and Gynecology Clinic of Gaziantep University Faculty of Medicine were included in the study. In addition to the local ethics board approval, the informed consent form was obtained from all the parcipitants of the study.

Design of Study: The Patient Group consisted of 32 women, diagnosed with NTD or anencephaly by ultrasonography, in the 16-20th gestational week and termination of pregnancy was decided on. Amniocentesis was performed using a 22 gauge spinal needle by ultrasound guidance before the termination of the pregnancy. 5 cc amniotic fluid was taken during the procedure. Simultaneously, 5 cc maternal blood sample was taken from the antecubital vein.

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The Control Group consisted of 34 pregnants with positive screening of first and second trimester biochemical test results (>1/250 for trisomy 18 and/or trisomy 21) but having normal ultrasonografic findings. In this group, during the amniocentesis procedure which was performed for chromosomal analysis, similar to the patient group's procedure, an extra 5 cc amniotic fluid was taken. Simultaneously, a 5 cc blood sample was also taken from the antecubital vein.

Maternal serum samples and amniotic fluid samples were stored at-80^0 C.

Ceruloplasmin measurement: Erel's ceruloplasmin measurement method was used. This method is automated, colorimetric, and based on the enzymatic oxidation of ferrous ion to ferric ion. The results were expressed in milligrams per deciliter, and the precision of this assay is within 3% (6, 7).

Apparatus: A Cecil 3000 spectrophotometer with a temperature controlled cuvette holder (Cecil) and an Aeroset automated analyzer (Abbott) were used (6).

Statistical Analysis: Statistical analyses (t test) were performed by using commercial program SPSS (Statistical Package for Social Sciences) 11.0. Values of $p<0.05$ were considered to be significant.

Results

The mean ages of the patients and controls were 28.59 (±5.09), and 30.17 years (±5.65) respectively. The mean value of BMI were patients and controls were 25.16 (±1.20) and 24.72 (±0.37). Mean gestational ages of the patients and controls were 17.7 (±1.3), 17.8 weeks (±1.4) respectively. The two groups were similar according to age, BMI and gestational age ($p>0.05$).

The ceruloplasmin levels of the amniotic fluid of patients and controls were 304.96 (±20.1) mg/dl and 305.31 (±14.9)mg/dl. There were no statistical differences between the groups ($p>0.05$).

The ceruloplasmin levels of the maternal bloods were 888.20 (±99.3) and 853.14 (±119.21) mg/dl for the patients and controls respectively. The value of the ceruloplasmin in maternal bloods were not found to be statistically different in the two groups ($P>0.05$).The results were summarized in Table 1.

Discussion

Ceruloplasmin is one of the most important acute phase response proteins of the organism. The oxidation of aromatic amines is the important activity of cp in terms of antioxidation (1, 2).

Despite years of intensive epidemiological, clinical and experimental research, the exact etiology of NTD remains rather complex and poorly understood. Genetic and environmental factors contribute to NTD. However, it is generally agreed that most NTD cases are of multifactorial origin, having a significant genetic component in their etiology that interacts with a number of environmental risk factors (3, 8, 9).

Many physical agents (e.g. X-irradiation, hyperthermia, stress), drugs (e.g. thalidomide, folate antagonists, androgenic hormones, antiepileptics ,hypervitaminosis A), chemical agents (e.g. organic mercury, lead), airborned chemicals (polyvinyl chloride) and maternal infections (e.g. rubella, cytomegalovirus, *Toxoplasmo gondii*, syphilis), are capable of causing congenital malformations of the central nervous system structures (3).

These factors are probably affecting the closure mechanisms of NTD at gene level. Also, most of these chemical and physical agents are also effective in the production of oxidative stress, which can effect the CNS. At this point antioxidation mechanisms become an important activity of the organism in order to prevent biofunctional disorders.

In the light of previous datas about the etiology of CNS anomalies, they seem to be related to oxidant chemical and physical agents (3-5, 10). Ceruloplasmin was considered to be effective as an antioxidant in NTD.

However, in a study Jenkins et al. have found that pregnancies that went successfully to term were associated with increased levels of ceruloplasmin early in the first trimester. This change was thought to offer the cell protection from the damage caused by the increased oxidative stress associated with pregnancy (11).

In our study we investigated whether there is a relation between the NTD and Cp. We could not find a significant relationship between Cp and NTD. The limitation of our study is the gestational week of the parcipitants. Although it was documented that NTD was a very early onset anomaly (early first trimester), the patients in our study were in the second trimester. On the other hand, cp is only one of the many antioxidants in the body. Maybe the other antioxidants, but not cp,are effective in NTD development. This is an other aspect in order to investigate the probable etiology of NTD, and different studies about these antioxidants need to be planned.

Also, a study evaluating a larger patient group in early first trimester may document significant cp values related with NTDs.

Table 1. Results of the patient ant control groups

	Patient group	Control group	P*
MaternalAge	28.59 (±5.09)	30.17 (±5.65)	>0.05
Gestational age	17.7 (±1.3)	17.8 (±1.4)	>0.05
BMI	25.16 (±1.20)	24.72 (±0.37)	>0.05
Cp values of amniotic fluid (mg/dl)	304.96 (±20.1)	305.31 (±14.9)	>0.05
Cp values of maternal blood (mg/dl)	888.20 (±99.3)	853.14 (±119.21)	>0.05

*p>0.05 is not statistically significant

In summary; according to this study, cp is not a marker related with NTD yet. However, this result does not mean that cp and other antioxidants are definitely not effective on NTD. Larger and well structured studies are needed for more accurate results.

Conflict of interest

None declared

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