

Original Research Article

Does copper deficiency predispose children to otitis media with effusion?

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ABSTRACT

Background: Both otitis media with effusion (OME) and copper or selenium have been associated to the immune system, hence it could be proposed that copper and/or selenium deficiency predisposes children to OME through immune cells dysfunction. The aim of this study was to determine the serum levels of Copper and Selenium in an immunodeficient-linked disease - OME – in childhood.

Methods: This cross-sectional study was conducted between July 2015 and December 2016 including 80 patients age 1 to 8 years old who were divided into two groups: otitis media with effusion (OME) consisted of 40 patients and the control (n=40). Patients who did not recover after three months conservative treatments were included. Serum levels of Copper and Selenium were measured using graphite furnace atomic absorption spectrometry.

Results: Statistical analysis showed no significant differences regarding age and sex were noted between groups. Patients with OME had significantly lower serum copper levels than the control group (p=0.007). However, there was no statistically significant difference in serum selenium levels between groups. The analysis also showed a significant positive correlation between serum copper level and age (correlation coefficient=0.348, p=0.028), whereas, there was no correlation between the measured selenium level and age.

Conclusions: The results of the present study showed that serum level of copper might play a role on development of otitis media with effusion in childhood.

Keywords: Copper, Otitis media with effusion, Selenium

INTRODUCTION

Otitis media with effusion (OME) is an inflammatory condition of the middle ear cleft with a collection of fluid in the middle ear with an intact tympanic membrane.¹ The etiology of OME is multi-factorial, but an immature function of the immune system and dysfunction of the Eustachian tube are the most important etiologic factors.² Otitis media is one of the most common infections in the presentation of immune deficiency. Studies of otitis media-prone children yield humoral immune abnormalities as compared with other children.³

Selenium, an essential trace element, is a structural component of several enzymes with physiological antioxidant properties.⁴ Dietary selenium is an essential micronutrient that plays a role in the maintenance of optimal immune responses.⁵ Copper has also been shown to play a role in the development and maintenance of the immune system. Experimental studies have demonstrated that copper status alters several aspects of neutrophil, monocyte, and T-cell function in the immune system.⁶

The literature review revealed both OME and trace elements, copper and selenium, are linked to the immune

system. Therefore, we hypothesized that there might be an association between serum level of these elements and OME. This study was designed to determine whether the serum copper and selenium play a role in the development of OME in childhood.

METHODS

Forty patients, 1 to 8 years old, with the clinical diagnosis of OME, were included in this cross-sectional study from July 2015 to December 2016. All patients underwent an audiogram to confirm the diagnosis. Patients were placed on non-surgical treatments according to American Academy of pediatrics guidelines; those who did not recover during three months were included. Exclusion criteria were children with immune defects, craniofacial abnormalities, cleft palate, Down syndrome, passive smokers and failure to thrive. The following deviations from the norm were considered as failure to thrive: weight-to-length ratio less than 70% or body mass index less than 3rd percentile for age, weight lower than 3rd percentile and lack of increase in length and/or weight with percentile deviations more than two main percentiles.⁷

Controls were matched age-group children (N=40) from the same community who were attending the ENT department clinics for tonsillectomy. All controls had normal otoscopic examination and audiogram as well. Parents of all patients were provided with a written informed consent was obtained before participation. A questionnaire was used to collect information on demographic, health-related and some socioeconomic characteristics. This study received ethical approval code

from Clinical Research Ethics Committee. A venipuncture sample was collected and serum stored at -20 celsius degrees. Serum copper and selenium were measured by Graphite-furnace atomic absorption spectrometry (Varian 222, Australia Inc.) as microgram per liter. Data analysis was performed using SPSS software (version 21, Chicago, IL, USA). The characteristics of the study groups are summarized using means or frequency counts as appropriate, with 95% confidence intervals. Definitive and analytical tests; the chi-square, t-test and ANOVA were used for data analysis.

RESULTS

A total 40 OME patients (21 male and 19 female) age from 1 to 8 years old (mean=3.85±1.86) and 40 controls (22 male and 18 female) aged from 2 to 8 years old (mean 4.93±1.50) were enrolled (Table 1). No significant differences regarding age or gender were noted between groups. There were also no significant differences regarding the mother's education, the household income and FTT (p=0.44, p=0.26 and p=0.41 respectively). Comparison of the patient groups showed that OME had significantly lower serum copper levels than the control group (p=0.007). However, there was no statistically significant difference in serum selenium levels (Table 2). The serum level of copper based on gender, mothers' education and FTT was not different significantly. The analysis also showed a significant positive correlation between serum Copper level and age (correlation coefficient=0.348, p=0.028), whereas, there was no correlation between the serum selenium level and age.

Table 1: Demographic characteristics of the two groups in this study.

Parameter	OME (n=40)	Control (n=40)	P value
Age (mean±SD)	3.85±1.86	4.93±1.50	0.62
Sex (Female/Male)	19/21	18/22	0.53

OMD: Otitis media with effusion; SD: Standard deviation.

Table 2: Serum trace elements concentration in case and control (Microgram/Liter).

Mineral	Case		Control		P value
	Mean*±SD	Range	Mean*±SD	Range	
Copper	17.10±4.75	11.35-38.09	20.73±6.81	14.49-56.31	0.007
Selenium	1.53±0.66	0.34-2.99	1.45±0.57	0.41-2.66	0.578

* 95% confidence interval; SD=Standard deviation

DISCUSSION

The close interactions among nutrition, infection and health have been recognized for many decades.⁵ Adequate intake of micronutrients is required for the immune system function. A large number of the studies have shown that copper affects the functions immune system.⁶ Although the mechanisms by which copper homeostasis is altered within specific organs in response to infection are unknown, these changes may form adaptive responses of the innate immune system to mobilize copper toward

sites of infection to aid in bacterial killing by macrophages. Consistent with this concept, various studies have shown that copper deficiency increases the susceptibility to various pathogens.⁸⁻¹³ Conversely, other studies have shown that copper supplementation is protective against *E. coli* induced mastitis in dairy cattle.¹⁴ Although the underlying mechanisms by which the copper status of the host impacts susceptibility to infection are unknown, it is likely that the bactericidal activity of phagocytic cells of the innate immune system is partially responsible because the respiratory burst

capacity of and the bacterial killing by these cells are reduced by copper deficiency.¹⁵⁻¹⁷

A review of the literature, a few human studies specifically examining the association between copper and selenium status and middle ear diseases was identified. In our study, we found a significant difference among groups concerning serum copper levels. The results of present study showed that the serum level of copper in otitis media patients with effusion was significantly lower than control group. Aydogan and colleagues' results showed the serum copper levels among otitis media patients and the control group was not different significantly.⁵ Elemraid et al also reported significantly higher serum copper and lower selenium levels in patients with chronic suppurative otitis media.¹⁸ These findings are not in accordance with our results. They studied chronic suppurative otitis patients with perforated tympanic membrane, whereas we selected those with effusion and an intact tympanic membrane. Another reason for the inconsistency of the different results may be due to different geographical sampling, as serum selenium depends on diet and soil selenium concentration.¹⁹ This is the reason that we selected all patients from the same community and the same geographical region.

Although this is one of the few controlled studied in the literature evaluating serum trace elements in patients with OME, it has limitations. Due to the cross-sectional design of this study, we cannot address causal relationships. Although the population size was not too small, if the sample size were greater, it would be more accurate. We assessed serum levels of metals, and these values may not always correlate with definite functions at the ear tissue level.

In conclusion, we found that the serum levels of copper were lower in otitis media with effusion patients than the control group. As both OME and copper are linked to the immune system, it could be proposed that Copper deficiency may predispose children to otitis media by immune cell abnormalities. The results also showed that the serum level of selenium might not play a role in the development of OME. Further controlled clinical studies are recommended to elucidate the predisposing or preventive effects of micronutrient in the pathogenesis of OME.

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Conflict of interest: None declared

Ethical approval: The study was approved by National Clinical Research Ethics Committee (ir.kmu.rec 1394/324)

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