Effect of Environmental Tobacco Smoke on Plasma Iron, Zinc and Copper Concentrations in Infants

Ali Aycicek[1,*], Abdurrahim Kocyigit[2], Ozcan Erel[3], Sahbettin Selek[2] and Mehmet Resit Demirkol[4]

[1]*Kanuni Sultan Suleyman Research and Education Hospital, Pediatric Hematology/Oncology Clinic, 34303 Istanbul Turkey*

[2]*Bezm-i Alem Vakıf University, Medical Faculty, Research Hospital, Department of Clinical Biochemistry, Istanbul-Turkey*

[3]*Yıldırım Beyazıt University, Medical Faculty, Research Hospital, Department of Clinical Biochemistry, Ankara-Turkey*

[4]*Pediatrician, Children's Hospital at Sanlıurfa, Department of Pediatrics, Sanliurfa, Turkey*

Abstracts: The deleterious effects of cigarette smoking on trace elements concentrations are well known. Recent studies show that exposure of nonsmokers to environmental tobacco smoke (ETS) results in many biochemical processes and diseases. The aim of this study was to investigate the plasma concentrations of iron (Fe), zinc (Zn) and cooper (Cu) in 29 infants (14 boys and 15 girls, age range: 2-6 months, mean age: 3.6 months) who had been exposed to ETS (range 8-30 cigarettes/day mean 12.4 ± 4.7) for at least two months at home, while the control group included 30 infants (13 male, 17 female, age range: 2-6 months, mean age: 3.3 months) who had never been exposed to ETS. All infants had been breast fed. The plasma iron concentrations were determined by commercial kit, cotinine levels were determined by luminometric method. Cu and Zn concentrations were analyzed by atomic absorption spectrometry. The plasma Fe and Zn concentrations in the study group were significantly lower than in the controls ($P < 0.05$). However, plasma Cu levels were not different between the two groups ($P > 0.05$). In conclusion, the plasma Fe and Zn concentration decline in the ETS exposed infants.

Keywords: Environmental exposure, Tobacco, Copper, Zinc, İnfant.

INTRODUCTION

Infants are constantly exposed to the presence and are affected by the habits of household members. If parents smoke, the infant will be exposed to environmental tobacco smoke (ETS) for long periods. Exposure to ETS has been associated with numerous adverse health effects in young children, increased susceptibility to respiratory tract infections, increased infant mortality to higher rates of asthma, and sudden infant death syndrome [1-4]. Although smoking is recognized to be a significant health problem in older subjects [5], there is a surprising shortage of information on the health consequences of ETS in infants. Tobacco smoke can alter trace element concentrations.

Iron (Fe), zinc (Zn) and cooper (Cu) are essential for normal infant development [6]. Fe is in the structure of hemoglobin and myoglobin essential for O_2 and CO_2 transport, oxidative enzymes, cytochrome C and catalase. Fe deficiency redounds in the development of hypochromic microcytic anemia and growth failure [7]. Zn is an essential component of various enzymes other proteins and biomembranes. It is required to maintain the normal structure and/or function of multiple enzymes, including those that are involved in transcription and translation of genetic material and cell division. In animal models, Zn deficiency has been shown to affect skin, gastrointestinal, immune, respiratory, skeletal and reproductive systems [8-10]. Cu is essential for the production of red cells, catalyst in hemoglobin formation, absorption of and associated with activities of tyrosinase, catalase, uricase, cytochrome C oxidase, alfa-aminolevulinic acid dehydratase and xlylol oxidase. It was shown that active or passive smoking alters some blood trace element concentrations in teenage girls and adults [11, 12]. With respect to serum mineral concentrations, several investigators have reported that Zn concentrations are typically reduced in adult smokers, whereas Cu concentrations are typically increased [12-14]. It has been demonstrated that these trace element concentrations are subjected to change in smokers as well [15]. Nevertheless, it is not known whether there is an alteration in the plasma Zn and Cu concentrations in ETS exposed infants. In this study, we investigated whether plasma Zn, Cu and Fe concentrations of

*Address correspondence to this author at the Kanuni Sultan Suleyman Research and Education Hospital, Pediatric Hematology/Oncology Clinic, 34303 Istanbul TURKEY; Tel: +90 212 571 47 90; Fax: +90 212 404 15 00; E-mail: ayciceka@hotmail.com

E-ISSN: 2408-9877/15 © 2015 Cosmos Scholars Publishing House

infants exposed to ETS were altered, as compared to those of infants not exposed.

MATERIALS AND METHODS

The subjects, who were breast fed 2-6 months infants, were randomly selected. All of the subjects and their mothers were healthy and we were informed and assured that they had never used any drug and mineral compounds until recently and during the study. Parents were asked about the frequency of smoking and the number of cigarettes smoked per a day. The number of cigarettes smoked in the household per day was calculated. The plasma cotinine concentrations were also determined to confirm the environmental tobacco smoke status of the infants. Infants from mothers who had been active smokers, or infants below the 10^{th} percentile in weight were excluded. Parents were fully informed about the aim of the investigation and they consented to take part in the study. Besides, the local ethic committee approved the study.

Fifty-nine infants aged 2-6 months were divided into two groups: the study group included 29 infants (14 boys, 15 girls, mean age: 3.6 months) who had been exposed to ETS via at least 8 cigarettes (range=8-30 cigarettes/day; mean 12.4 ± 4.7 cigarette) per day for at least the last 2 months in their house, while the control group included infants (13 male, 17 female, mean age: 3.3 months) who had never been exposed to ETS.

METHODS

Venous blood was drawn into tubes containing the heparin and the disodium salt of ethylenediaminetetraacetic acid (EDTA). The blood with EDTA was used for analysis of hematological parameters. White blood cell and hemoglobin were measured by a Cell-Dyn 1700 (Abbott) system within 30 minutes from taking the blood sample. The heparinised tubes were separated from the cells by centrifugation at 1500 g for 10 min. The plasma samples were stored at –80 ^{o}C until analysis. The plasma samples were diluted with ultra deionized, distilled water for Cu and Zn measurements and determined by atomic absorption spectrometer (Varian Spectr AA 250 Plus, Australia) and values were expressed as µg/dL. The plasma Fe concentration was determined by colorimetric method with a commercial kit (Boehringer Mannheim, Germany) using an automatic analyzer (Hitachi 911, Boehringer Mannheim, Germany). ETS status of the subjects was determined by measuring the levels of the plasma cotinine by luminometric method using a commercial kit (DPC, USA) with an automated hormone analyzer (Immulite, USA). This kit's lowest detection limit is 10 (ng/mL).

STATISTICAL ANALYSIS

All results were expressed as mean ± standard deviation; differences were considered statistically significant at $P < 0.05$. The data were analyzed by using Student's *t* test and Mann-Whitney U test. The relationships between parameters were assessed with Spearman's correlation analyses. All statistical analyses were performed with the program Statistical Package for the Social Sciences (SPSS) for Windows, version 11.5 (SPSS Inc.)

RESULTS

The demographic data and number of cigarettes smoked per day in study and control group are given in Table **1**. The mean age of the study group was slightly higher than that of the control group.

Table 1: Comparison of Demographic Data in the Study Group and the Control Group. Data are Given as Mean ± SD

	Study Group (*n* = 29)	**Control Group (n = *30)***	***p***
Age (months)	3.6 ± 1.4	3.3 ± 1.5	0.354 [a]
Height (cm)	64.2 ± 4.3	64.6 ± 5.2	0.775 [a]
Body Weight (g)	6545 ± 1528	6658 ± 1372	0.462 [a]
Head circumference (cm)	41.6 ± 2.5	41.9 ± 1.9	0.624[a]
Sex (B/G)	14/15	13/17	0.615[b]
Cigarettes/day	12.4 ± 4.7	0	

[a]Student's *t* test
[b]Chi-square test

The mean of body weight, height and head circumference tended to be slightly low in the study group than in the control group. There was not statistically significant difference in the age, body weight, height and head circumference between cases the study group and the control group ($P > 0.05$). The plasma mean (SD) cotinine concentration was 36.4 ± 7 (ng/mL) in the study group but not detectable in the controls (Table **2**). The plasma mean Fe concentrations were significantly lower in study group (58.7 ± 14.2) than in the control group (78.6 ± 15.4) ($P = 0.002$). Also, the plasma mean Zn concentrations were significantly lower in the study group (53.7 ± 5.9) than in the control group (90.7 ± 10.1) ($P = 0.001$).

The plasma Cu levels were not different between the two groups. There are negative correlations between the plasma cotinine and trace element concentration but this correlation was not statistically significant ($P > 0.05$).

DISCUSSION

Tobacco smoke can alter trace element concentrations. However, to the best of our knowledge, all of the published studies related to the alteration of ETS are about teenagers or adults, whereas this is the first report showing an association between trace element concentrations in exposed to ETS infants. In this study, we found that the plasma Fe and Zn concentrations were lower in infants exposed to ETS than in infants of the control group ($P = 0.002$; $P = 0.001$, respectively).

It is important to recognize that cotinine is a quantitative biomarker for smoking, and it is unlikely that cotinine or its parent compound, nicotine, is responsible for all of the adverse outcomes associated with smoking [16]. Combinations of the measurement of body fluids cotinine with the interview-derived information are accepted to be the optimal method for assessing ETS exposure in children. Therefore, we used both methods in this study [17]. The plasma cotinine level in the study group was 36.4 ng/mL in this study while the controls had undetectable concentrations. The level of exposed infants was similar to ETS infants in the literature [18]. On the other hand, Strauss RS [19] determined that cotinine levels were 2 ng/mL and 15 ng/mL in ETS group. The difference of the plasma cotinine levels may relate to measuring methods or the degree of ETS, because, Straus RS [19] was determined serum cotinine levels by liquid chromatography, whereas we determined them by luminometric method.

Trace element abnormalities can generally be traced to nutritional or environmental factors. Both kinds of abnormalities can be diagnosed by analyses of trace elements in plasma or other tissues. The children coming from the tobacco-smokers' families often present with disorders of Fe metabolism, hemoglobin formation, or red blood cell metabolism, leading to the development of anemia during the first year of life [20]. Fe concentrations in ETS exposed infants are considered below necessary levels to meet the infant's requirements for growth and development [21]. In this study, we found that Fe concentrations were at normal limits in ETS exposed infants. However, Fe concentrations were lower in the study group than in the control group. Fe concentrations may be lower than normal limits in a long period in ETS exposed infants. We suggested that this Fe metabolism disorders begin at infancy period in ETS exposed infants.

Various studies have been reported that Zn concentrations are typically reduced in adult smokers

Table 2: Comparison of Iron, Zinc, Copper, WBC and Hemoglobin Levels Between the Study Group and the Control Group. Data are given as Mean ± SD

	Study Group ($n = 29$)	Control Group ($n = 30$)	P^a
Iron (µg/dL)	58.7 ± 14.2	78.6 ± 15.4	0.002
Zinc (µg/dL)	53.7 ± 5.9	90.7 ± 10.1	0.001
Copper (µg/dL)	77.9 ± 27.6	66.4 ± 26.8	0.746
WBC /mm^3	10.6 ± 3.8	10.2 ± 3.8	0.745
Hemoglobin mg/dL	10.3 ± 1.6	10.7 ± 1.7	0.347
Cotinine (ng/mL)	36.4 ± 7	< 10‡	NA

[a] Student's *t*-test
‡ Mesurable concentrations were present in a single case only (24 ng/mL).

[11-13]. In this study, we were demonstrated that in ETS exposed infants have lower the plasma zinc concentrations than in the control group. The hypozincemia that are often observed in adult smokers have been attributed to the acute-phase response that can be triggered by tissue damage [11]. Owing to the fundamental role that Zn plays in cellular metabolism, its effect is substantial in cells with a rapid turnover such as the immune system and is therefore said to modulate host resistance to various infections [9, 22].

Several investigators have reported Cu concentrations are typically increased in adult smokers [1, 13, 23]. On the contrary common findings our data displayed that in ETS exposed infants statistically significant hypercupremia was not observed. This is probably related to long exposure time to cigarette smoke in active smoker than ETS exposed infants [24]. We also found that a slightly negative relationship between the plasma Fe and Zn and the plasma cotinine concentrations.

The decreasing Fe and Zn, increasing Cu concentration in ETS exposed infants may be dependent on several factors. One factor, toxic heavy metals that are naturally found in tobacco, especially in the tar phase, acts antagonistically to Zn [25]. Another factor, the decreasing content of Zn, Fe, and increasing content of Cu, may be dependent on the inflammatory response due to tobacco smoking. It has been demonstrated that tobacco smoke increases the inflammatory processes and causes increased expression of inflammatory mediators such as interleukin 1 (IL-1) (IL-2) (IL-6) (IL-8), and serum eosinophil cationic protein [26, 27]. Other finding of inflammation in this study is increased WBC counts in ETS exposed infants. WBC may serve as an important biomarker for these processes. Similarly, Panagiotakos and colleagues [28] were compared with who were not exposed to ETS, those exposed more than 3 days per week had higher white blood cell counts.

In active smoker mother's infants height were significantly lower in infants and was higher in the third months, caused by slower height growth. Smoking affected infant's height during breastfeeding, attributed to an eventual impaired bioavailability of essential nutrients [29]. In the present study, heights, body weights and head circumferences were slightly lower in the study group than in the control group. ETS exposure may be extensive effect in infant growth in a long time. The lack of development may be caused by bioavailability of essential nutrients, adverse effect of nicotine and other contains of tar phase cigarette [30].

The limitations of the study were that limited trace elements were measured. Also, there was not to investigate relationship between trace elements and oxidative stress changes in this group.

When considering changing mineral concentrations in ETS infants, any deviations from the central measurement trend can have important consequences on the understanding of infant nutrition requirements. Children's ETS exposure to increased rates of respiratory tract infections, otitis media, and childhood asthma, with the severity of these problems increasing with increased exposure [31]. The decreasing Fe and Zn, increasing Cu concentration in ETS exposed children may be contribute in these health events.

In conclusion, the plasma Fe and Zn concentration decrease in the ETS exposed infants.

ACKNOWLEDGEMENTS

We are most grateful to the technical staff of the Laboratory Unit, Children's Hospital and Harran University Medical School for their assistance in conducting this study.

REFERENCES

[1] Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Increase incidence of asthma in children of smoking mothers. Pediatrics 1992; 89: 21-26.

[2] Haglund B, Cnattingius S. Cigarette smoking as a risk factor for sudden infant death syndrome: a population-based study. Am J Public Health. 1990; 80: 29-32. http://dx.doi.org/10.2105/AJPH.80.1.29

[3] Weiss ST, Tager IB, Schenker M, Speizer FE. The health effects of involuntary smoking. Am Rev Respir Dis 1983; 128: 933-942.

[4] Jacobs-van der Bruggen MA, Wijga AH, Brunekreef B, *et al*. Do parents who smoke underutilize health care services for their children? A cross sectional study within the longitudinal PIAMA study. BMC Health Serv Res. 2007: 12; 7: 83.

[5] Aycicek A, Erel O, Kocyigit A. Decreased total antioxidant capacity and increased oxidative stress in passive smoker infants and their mothers. Pediatr Int. 2005; 47: 635-9. http://dx.doi.org/10.1111/j.1442-200x.2005.02137.x

[6] Hurley LS. The roles of trace elements in fetal and neonatal development. Philos Trans R Soc Lond B Biol Sci 1981; 294: 145-152. http://dx.doi.org/10.1098/rstb.1981.0095

[7] Schumann K, Elsenhans B, Maurer A. Iron supplementation. J Trace Elem Med Biol 1998; 12: 129-140. http://dx.doi.org/10.1016/S0946-672X(98)80001-1

[8] Bhatnagar S, Natchu UC. Zinc in child health and disease. Indian J Pediatr 2004; 71: 791-795. http://dx.doi.org/10.1007/BF02828114

[9] Shankar AH, Prasad AS. Zinc and immune function: the

biological basis of altered resistance to infection. Am J Clin Nutr 1998; 68: 447S-463S. http://dx.doi.org/10.3200/AEOH.58.2.68-73

[10] Kilburn KH. Stop inhaling smoke: prevent coronary heart disease. Arch Environ Health 2003; 58: 68-73.

[11] Kim SH, Kim JS, Shin HS, Keen CL. Influence of smoking on markers of oxidative stress and serum mineral concentrations in teenage girls in Korea. Nutrition 2003; 19: 240-243. http://dx.doi.org/10.1016/S0899-9007(02)01002-X

[12] Kocyigit A, Erel O, Gur S. Effects of tobacco smoking on plasma selenium, zinc, copper and iron concentrations and related antioxidative enzyme activities. Clin Biochem 2001; 34: 629-633. http://dx.doi.org/10.1016/S0009-9120(01)00271-5

[13] Dubick MA, Keen CL. Influence of nicotine on tissue trace element concentrations and tissue antioxidant defense. Biol Trace Elem Res 1991; 31: 97. http://dx.doi.org/10.1007/BF02990418

[14] Keen CL, Clegg MS, Ferrell F. Hypertension induced alterations in copper and zinc metabolism: a link to vascular disease? In: Sorenson JRJ, Clifton NJ, editors. Biology of copper complexesed. Humana Press, 1987. p. 141. http://dx.doi.org/10.1007/978-1-4612-4584-1_11

[15] Lapena D, Mezetti A, De Gioida S, Pierdomenico SD, Daniele F, Cuccurullo F. Plasma copper and lipid peroxidation in cigarette smokers. Free Radic Biol Med 1995; 19: 849-852. http://dx.doi.org/10.1016/0891-5849(95)00056-4

[16] Mascola MA, Van Vunakis H, Tager IB, Speizer FE, Hanrahan JP. Exposure of young infants to environmental tobacco smoke: breast-feeding among smoking mothers. Am J Public Health 1998; 88: 893-896. http://dx.doi.org/10.2105/AJPH.88.6.893

[17] Tutka P, Wielosz M, Zatonski W. Exposure to environmental tobacco smoke and children health. Int J Occup Med Environ Health 2002; 15: 325-335.

[18] Luck W, Nau H. Nicotine and cotinine concentrations in serum and urine of infants exposed via passive smoking or milk from smoking mothers. J Pediatr 1985; 105: 816-820. http://dx.doi.org/10.1016/S0022-3476(85)80427-3

[19] Strauss RS. Environmental tobacco smoke and serum vitamin C levels in children. Pediatrics 2001; 107: 540-542. http://dx.doi.org/10.1542/peds.107.3.540

[20] Gavalov SM, Soboleva MK, Deriagina LP, Demchenko AE. Effect of active and passive smoking on the course of pregnancy in women and on the establishment of the erythrocytic system in their children. Ter Arkh 1991; 63: 126-30.

[21] Dorea JG (2000) Iron and Copper in Human Milk. Nutrition 16: 209-220 http://dx.doi.org/10.1016/S0899-9007(99)00287-7

[22] Milnerowicz H, Ściskalska M, Dul M. Pro-inflammatory effects of metals in persons and animals exposed to tobacco smoke. J Trace Elem Med Biol. 2015; 29: 1-10. http://dx.doi.org/10.1016/j.jtemb.2014.04.008

[23] Di Gioacchino M, Forcucci R, Tiboni GM, Kouri S, Di Gioacchino F, Boscolo P. The influence of menopause and habitual smoking upon serum zinc, serum copper and the cardiovascular and immune parameters of women. Int J Immunopathol Pharmacol 2000; 13: 91-97.

[24] Kocyigit A, Gur S, Erel O, Gurel MS. Associations among plasma selenium, zinc, copper, and iron concentrations and immunoregulatory cytokine levels in patients with cutaneous leishmaniasis. Biol Trace Elem Res 2002; 90: 47-55. http://dx.doi.org/10.1385/BTER:90:1-3:47

[25] Preston AM. Cigarette smoking-nutritional implications. Prog Food Nutr Sci 1991; 15: 183-217.

[26] Derentowicz P, Czerwinska-Kartowicz I, Markiewicz K, Wnuk A, Rytwinski K, Wawrzyniak M, Bulawa E. The effect of tobacco smoking on the human immune system Med Wieku Rozwoj 1999; 3: 495-501.

[27] Lodrup K, Carlsen C, Halvorsen R, Carlsen KH. Serum inflammatory markers and effects of age and tobacco smoke exposure in young non-asthmatic children. Acta Paediatr 1998; 87: 559-564. http://dx.doi.org/10.1111/j.1651-2227.1998.tb01504.x

[28] Panagiotakos DB, Pitsavos C, Chrysohoou C, Skoumas J, Masoura C, Toutouzas P, Stefanadis C; ATTICA study. Effect of exposure to secondhand smoke on markers of inflammation: the ATTICA study. Am J Med 2004; 116: 145-150. http://dx.doi.org/10.1016/j.amjmed.2003.07.019

[29] Berlanga Mdel R, Salazar G, Garcia C, Hernandez J. Maternal smoking effects on infant growth. Food Nutr Bull 2002; 23: 142-145.

[30] Emmons KM, Thompson B, Feng Z, Hebert JR, Heimendinger J, Linnan L. Dietary intake and exposure to environmental tobacco smoke in a worksite population. Eur J Clin Nutr 1995; 49: 336-345.

[31] DiFranza JR, Aligne CA, Weitzman M. Prenatal and postnatal environmental tobacco smoke exposure and children's health. Pediatrics 2004; 113: 1007-1015.

Received on 06-07-2015 Accepted on 09-07-2015 Published on 30-7-2015

http://dx.doi.org/10.15379/2408-9877.2015.02.02.02

© 2015 Aycicek *et al.*; Licensee Cosmos Scholars Publishing House.
This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.