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HEALTH SCIENCES

The Association of Passive Smoking and Serum Urotensin-II Levels in Children

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Abstract: Urotensin-II (UT-II) is the most powerful vasoconstrictor agent and is known to play a role in heart failure, diabetes, pulmonary hypertension and asthma. The effect of passive smoking on UT-II levels is unknown. The present study aims to evaluate serum UT-II levels in children exposed to passive smoke. The study included a total of 120 children; 47 children not exposed to passive smoke were included in Group 1 (control group), and 73 children exposed to passive smoke were included in Group 2. Serum samples of the participants were stored at -80 °C after centrifugation and were assessed at least two times with high-precision human ELISA kits. Serum UT-II levels were significantly higher in the children exposed to passive smoke than in the children not exposed. Furthermore, Group 2 was grouped according to the number of cigarettes smoked at home per day, type of passive smoking (second-hand smoke or third-hand smoke), and how many people in their family and/or living together smoked. There was a positive correlation between the number of cigarettes they were exposed to per day and serum UT-II levels. Passive smoking in childhood may be associated with high serum UT-II levels.

Key words: passive smoking, disease, child, UT-II, risk factors.

INTRODUCTION

It is known that under many chronic diseases in adulthood, proinflammatory processes occur in childhood and inflammatory mediators start to be released at the cellular level when clinical findings have not yet occurred (Libby 2007). The endothelial dysfunction process that begins with the release of these inflammatory mediators is the basic pathophysiological process for many diseases (Drexler & Hornig 1999). Smoking is often blamed for the onset of these pathological processes. And in the light of today's scientific data, we know that, smoking is a risk factor for many diseases due to the toxins and other chemical agents in cigarettes (Cao et al. 2015). Active or passive exposure to smoking has been shown to induce many inflammatory mediators, disrupt endothelial integrity and predispose to oxidative stress and inflammation (Golbidi et al. 2020). In a large study of patients aged 55-74 with different types of cancer, smoking has been shown to be effective on at least 10 different immunomodulatories (Shiels et al. 2014). Passive smoking is known to exert harm through the inhalation of the toxins in smoke. We know that passive smoking causes intrauterine growth retardation and low birth weight during the fetal period, sudden infant death syndrome and growth retardation during infancy, and decreased lung function and increased risk for cardiac diseases in advanced age (Hwang et al. 2012, Banderali et al. 2015). The effect of smoking through which mediators in this process is continuously investigated. In a

recent study of 378 children with asthma, it was observed that passive smoking increased IL17A and IL-23, and FoxP3 (Forkhead / winged helix transcription factor) and tumor growth factor-decreased (Jing et al. 2019).

UT-II is a vasoactive polypeptide that was first found approximately 40 years ago in the pituitary glands of fish and subsequently identified in many species (Vaudry et al. 2010). UT-II is the most powerful vasoconstrictor and is thought to play a key role in the onset of many diseases (Ross et al. 2010). UT-II is synthesized in many organs in the human body such as the heart, lung, kidney, and pituitary. UT-II has proliferative, proinflammatory, carcinogenic, and profibrotic properties at the cellular level (Ross et al. 2010). There are studies showing that UT-II increases in many diseases with endothelial dysfunction such as HT, pulmonary hypertension and diabetes mellitus, and increases in body fluids in these patients (Guler et al. 2020, Bozkurt et al. 2021).

We also studied the UT-II serum levels of growth-restricted children and observed dramatically increasing UT-II levels in growth-restricted children that were negatively correlated with serum IGF-1 and IGFBP3 levels (Yayla et al. 2019). Based on clinical studies in children, it is thought that UT-II may play a role in the pathophysiology of many diseases (Rong et al. 2012). Regarding our topic, Gold et al. (2007) in their study showed that active smoking increased serum UT-II levels in adult male patients (Gold et al. 2007). However, there is no information about how passive smoking affects serum UT-II levels, especially in children who are exposed to cigarette smoke by their parents or caregivers. Therefore, the present study aims to evaluate serum UT-II levels in children exposed to passive smoke.

MATERIALS AND METHODS

Ethical approval

Permission was obtained from the Local Ethics Committee (80576354-050-99/15, 26.12.2018).

Informed consent

Informed consent was obtained from all individual participants included in the study.

Study population

This cross-sectional study was conducted between 1 December 2018 and 31 January 2019. The formula of $n= Nt^2pq / (d^2(N-1) + t^2pq)$ was used to calculate the sample size (Sumbuloglu & Sumbuloglu 2016). In order to determine the size of the universe, the number of applications for routine health control, excluding duplicates in the same months of previous year, were considered. When the prevalence of passive smoking was taken as 50%, the confidence interval as 95% and the sampling error as 5%, the sample size to be reached representing the universe was calculated as 120 patients. In this process, we included the first 120 children who applied to our hospital for routine health control and agreed to participate in the study.

Design

The inclusion criteria for the study were presenting at our healthy child polyclinic for follow-up regarding child growth and development or being brought in for routine health controls, being in the 2- to 16-year age range, having no chronic diseases, having neither malnutrition nor obesity, being born full-term, having no acute infection, having no anaemia or polycythaemia. The children's body weight and height were measured and recorded. The age, sex, and place of residence of the children and the educational status of their parents were recorded. Smoking data

were collected from the children's family members in a face-to-face interview by a trained paediatrician using a structured questionnaire. Children were consecutively enrolled. Children from families in which no one smoked formed Group 1, while those whose family included at least one member at least 6 months who smoked formed Group 2. At the administration smoking parents with 0-6 months, accepted, new smokers and excluded from this study. The children, especially adolescents and teenagers were asked if they smoke and active smokers were excluded from the study. Furthermore, Group 2 was grouped according to the total number of cigarettes smoked at home per day (<10 cigarettes/day, 10-20 cigarettes/day, >20 cigarettes/day) regardless the number of smoking person number (for example 2 person smoking, 5 cigarettes/day each other, so total 10 cigarettes/day; 1 person smoking, 20 cigarettes/day, so recorded 20 cigarettes/day); whether their mothers smoked, type of passive smoking (second-hand or third-hand) and how many people in their family (1 person or more than 1 person) smoked. When a child is physically in the same environment as someone smoking nearby and is directly exposed to this smoke, it is considered Second-hand tobacco smoking (SHS). If cigarettes are smoked while the child is not in the living environment, or if cigarettes are smoked outside of the living environment, it is considered third-hand tobacco smoking (THS) because of the cigarette smoke that sticks to clothes and other items.

Before data and samples were collected, an informed consent form was obtained from all parents, and local ethics committee approval was received (2018/80576354-050-99/15).

Data collection and biochemical analysis

Blood samples were collected at the first administration simultaneously with questionnaire application. Blood collected from the children was centrifuged in a tube containing a special gel that separates blood cells from serum at 4000 rpm and 4 °C for 10 min, and the sample was stored at -80 °C until analysis. UT-II levels of each sample were measured with a high-precision human enzyme linked immune assay (ELISA) kit (Cloud-Clone, Product No: CEA362Hu, China) with 2 replicates. This ELISA kit is for research use only and is not meant for therapeutic or diagnostic applications. The intensity of color is measured spectrophotometrically at 450 nm in a microplate reader. A standard curve is plotted that relates the intensity of the color (O.D.) to standards. The UT-II concentration of each sample is interpolated from this standard curve. Intra-assay precision (precision within an assay) was CV% < 10%. Inter-assay precision (precision between assays) was CV% < 12%. The detection range was 12.35 pg/ml-1000 pg/ml.

Statistical analysis

Statistical methods: SPSS 20.0 software was used for statistical analysis of the data. Frequencies and percentages were used in the descriptive table, the Chi-squared test was used for binary comparisons. The conformity of the measurement data for normal distribution was evaluated with the Kolmogrov Smirnov test. Student T test was used in the data that provided parametric assumptions. Mann Whitney U test and Kruskal Wallis Variance analysis were used for data where parametric assumptions could not be provided. Results were evaluated within the 95% confidence interval. $p<0.05$ was accepted as statistically significant.

RESULTS

Sociodemographic features of the children and their families

A total of 120 healthy children were included in the study. Group 1 consisted of 47 children, and Group 2 consisted of 73 children. The mean age of the children was 5.9±3.2 years; 55.8% were male, and 44.2% were female. There was no significant difference in terms of age or sex between Group 1 and Group 2. The smoking rate was higher among those whose mothers had low educational levels, but the difference was not statistically significant (p=0.088). The smoking rate was significantly higher among those whose fathers had lower educational levels (p=0.028). The rate of passive smoking was 56.1% in children who were living in urban zones compared with 71.1% in those who were living in rural zones, but no statistically significant difference was found (p=0.118) (Table I).

Urotensin-II Levels in children with passive smoking and for independent variables

There was no significance between serum UT-II levels and the children's age. Additionally, UT-II levels did not differ according to the children's sex (p>0.05). The mean weight and height of the children were 21.90±10.08 kg and 112±18 cm, respectively. We calculated the BMI values and percentiles of the children according to their age, weight and height. We analyzed the relation between BMI of children and their serum UT-II levels. However, there was no significance between serum UT-II levels and BMI values of the children.

UT-II levels were significantly higher in Group 2, i.e., in children who were exposed to passive smoking (p=0.001). Group 2 was sub-grouped according to the number of total cigarettes smoked at home per day (<10 cigarettes/day, 10-20 cigarettes/day, >20 cigarettes/day) regardless the number of smoking person number. There

Table I. Sociodemographic features of group 1 (children not exposure to smoke) and group 2 (passive smoking children).

	Group 1 n=47	Group 2 n=73	Total n=120	*p value*
Age (years, mean±std.)	5.3±2.53	6.2±3.57	5.9±3.2	0.134[t]
Gender Male(n,%) Female(n,%)	27 (40.3) 20 (37.7)	40 (59.7) 33 (62.3)	67 (55.8) 53 (44.2)	0.775[x]
Living region City (n,%) Rural (n,%)	36 (43.9) 11 (28.9)	46 (56.1) 27 (71.1)	82 (68.3) 38 (31.7)	0.118[x]
Mother's education level Secondary school and lower (n,%) High school and above (n,%)	17 (30.9) 30 (46.2)	38 (69.1) 35 (53.8)	55 (45.8) 65 (54.2)	0.088[x]
Father's education level Secondary school and lower (n,%) High school and above (n,%)	7 (22.6) 40(44.9)	24(77.4) 49 (55.1)	31(25.8) 89 (74.2)	***0.028*[x]**

[x]**Chi-square,** [t]**Student T Test, std=standart deviation, p<0.05 is significant.**

was a positive correlation between the number of cigarettes smoked per day and UT-II levels (p=0.003) (Figure 1). The prevalence of children who were SHS group was 60.8%, the prevalence of those whose family included more than 1 smoker was 38.3%. No statistically significant difference was identified between the groups regarding the type of passive smoking and the number of smokers (p=0.604; 0.905, respectively). There was also positive correlation between BMI and UT-II levels. According to this when we compare the groups there was a significance between Group 1 (non smoker) and Group 2 (passive smoker) but there was no significance between SHS and THS group (Figure 2). The prevalence of those whose mothers smoked was 22.5% and when we classify mothers of children according to whether they smoke or not, we see that serum UT-II level is higher in the mother-smoker child (p=0.046). Mothers smoked during pregnancy was 10.9%, but there was no significance between groups (Table II).

DISCUSSION

In our study, UT-II levels were significantly higher in Group 2, seemed to be related to the total number of cigarettes smoked per day; the total number of cigarettes smoked directly increased exposure to both SHS and THS. Both of our groups consisted of healthy individuals. Therefore, we investigated UT-II levels in healthy children with smoking exposure. Because there was no clinical evidence in the early period, we looked for an answer to the question of whether UT-II levels provide some insight into the pathophysiological effects of passive smoking.

Passive smoking is a critical health problem worldwide. According to recent data from the World Health Organization, it is the third most common preventable cause of death. There are 1.1 billion smokers worldwide. The number of passive smoker is much higher, and more than half of the children in the world are thought to be affected (Asma et al. 2014). Passive smoking is a predisposing factor for many diseases in children, such as lower respiratory tract

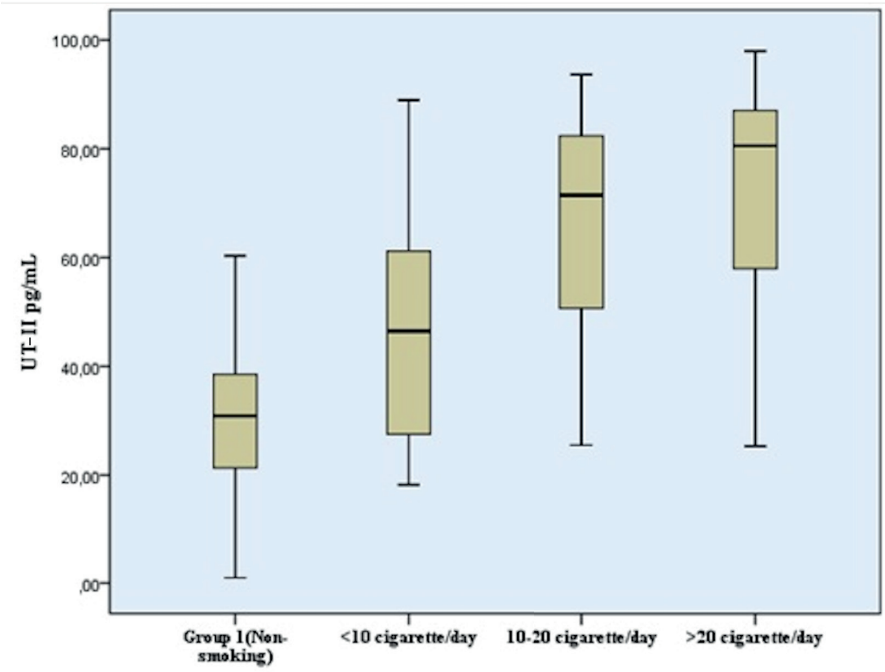

Figure 1. Evaluation of passive exposure to cigarette smoke and UT-II levels according to the numberof cigarettes smoked per day.

infections, otitis media, asthma, autism, and obesity (Li et al. 1999, Mangrio et al. 2010, Matt et al. 2011, Jones et al. 2012, Jung et al. 2017). These diseases are caused by the more than 4000 chemicals and more than 50 carcinogenic substances in cigarettes (Talhout et al. 2011). However, there is no certain information regarding the mechanisms of the effects of these substances. Therefore, elucidation of the physiopathology of clinical problems caused by passive smoking is of great importance for the development of new treatment strategies for diseases.

UT-II is a vasoactive proinflammatory polypeptide. UT-II is thought to play a key role in the development of pulmonary hypertension associated with congenital heart disease, autism, chronic kidney disease, and insulin resistance in children (Li et al. 2016, Uğur et al. 2018). Passive smoking is a risk factor for respiratory diseases in children. Studies have linked smoking or passive smoking in expectant women and the exposure of children to passive smoke during infancy with wheezing and allergic airway diseases (Vardavas et al. 2016). Smoking may trigger these pathological conditions both through the action of harmful substances and through UT-II. Gold et al. (2007) showed that active smoking increased serum UT-II levels in adult male patients (Gold et al. 2007). To the best of this author's knowledge, the present study is the first to evaluate the effects of passive smoking on UT-II levels. Our study found significantly higher serum UT-II levels in children exposed to passive smoke than in those not exposed to passive smoke. A positive correlation between the number of cigarettes smoked per day in the family and the serum UT-II levels of the children was detected. Children who do not smoke but are exposed to passive smoke may become predisposed to many future health problems through the UT-II pathway due to the

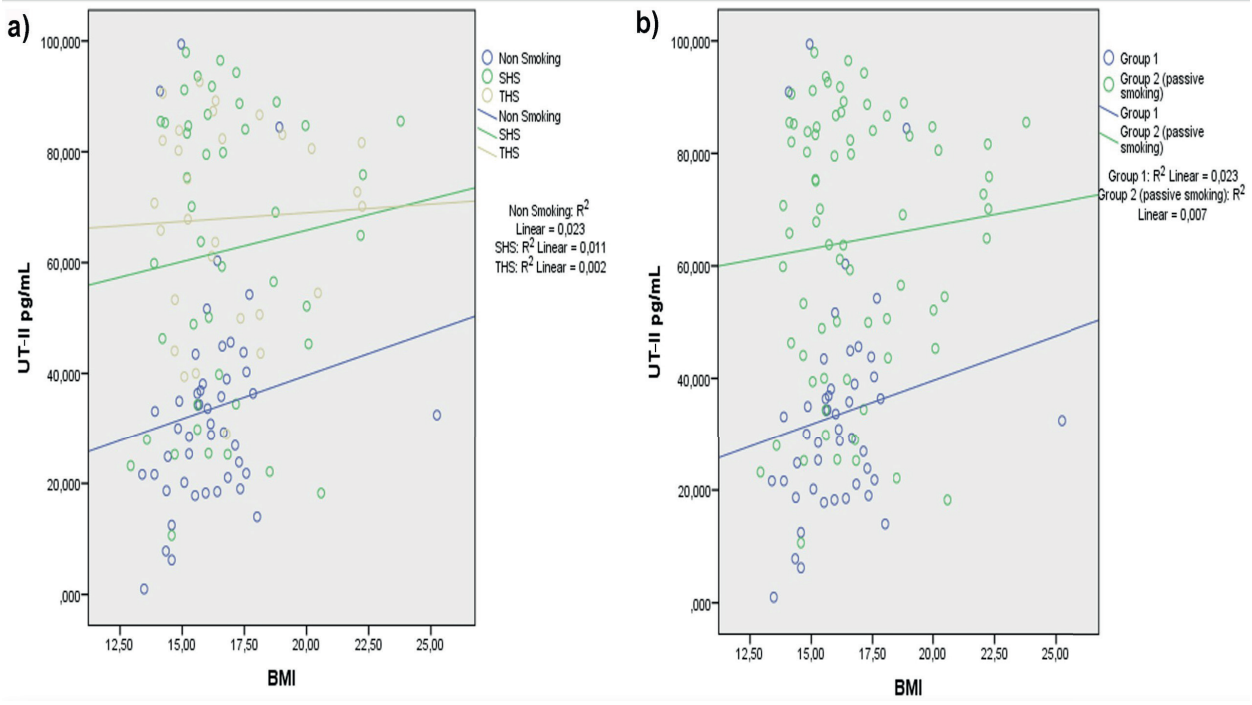

Figure 2. Comparison of positive correlation of UT-II levels and BMI and a) there was no significance between SHS and THS (p=0.604), b) but there was significance between non smoking group (Group 1) and passive smoking group (Group 2) (p=0.001) (SHS: second hand smoking, THS: third hand smoking, BMI: body mass index).

chemicals contained in cigarette smoke. In a study conducted in 2014, decreased Ca^{+2} $ATPase_2$ expression in the myocardial endoplasmic/sarcoplasmic reticulum was associated with increased UT-II expression in obese mice with metabolic syndrome (You et al. 2014). In another study, it was reported that the UT-II molecule plays a regulatory role in respiratory physiology and may be involved in the pathophysiology of asthma and pulmonary hypertension through airway smooth muscle cell proliferation (Zhang et al. 2012). UT-II levels were also found to be high in children with autism spectrum disorder (Uğur et al. 2018). Although there is insufficient evidence regarding the relationship between smoking exposure and otitis media, we can see that smoking or passive smoking is a common risk factor for all of these diseases that have been associated with UT-II.

Table II. Evaluation of serum UT-II levels of children exposed to passive smoking according to according to the age, gender, BMI (body mass index) and amount of cigarettes per day, smoking, number of smokers and condition of mother's smoking.

Headings	Groups	UT-II pg/mL (mean±std)	UT-II pg/mL median(min-max)	*p value*
Age (year)	2-6 (n:75) 7-11 (n:37) 12-16 (n:8)	51.19±28.59 51.32±22.73 67.98±23.54	44.91(0.99-97.95) 46.30(20.18-99.44) 78.22(19.02-85.53)	0.341[k]
Gender	Female (n:53) Male (n:67)	53.16±25.06 51.70±28.17	49.95(13.99-92.65) 46.30(0.99-99.44)	0.767[t]
BMI	<25 percentile (n:27) 25-75 percentile (n:66) >75 percentile (n:27)	46.20±32.29 54.12±24.88 52.35±2674	33.13(0.99-99.44) 45.12(17.79-97.95) 54.52(13.99-94.32)	0.288[k]
Passive smoking groups	Group 1 (n:47) Group 2 (n:73)	33.47±19.71 64.50±23.47	30.86(0.99-99.44) 70.11(10.62-97.95)	***0.001*[t]**
Cigarette count	1-9 cigarette/day (n:16) 10-20 cigarette/day (n:22) >20 cigarette/day (n:35)	46.86±22.16 67.45±18.92 70.7±23.17	46.48(18.25-89.00) 71.44(25.45-93.65) 80.58(10.62-97.95)	***0.003*[k]**
Second (SHS) and Third (THS) hand smoking groups	SHS (n:44) THS (n:29)	68.00±18.06 62.19±26.38	67.00(10.62-97.52) 70.74(28.99-92.65)	0.604[m]
Smoking person count in childrens' home	Only 1 person smoking (n:45) >1 person smoking (n:28)	65.43±21.46 62.99±26.72	69.08(18.25-97.95) 77.49(10.62-93.65)	0.905[m]
Mother smoking	Mother smoking (n:27) Mother non smoking (n:93)	62.13±26.01 49.50±26.40	75.10(18.25-91.17) 43.82(0.99-99.44)	***0.046*[m]**
Smoking in pregancy	Smoking (n:15) Non smoking (n:105)	65.44±25.35 50.48±26.52	75.35(23.20-93.65) 44.91(0.99-99.45)	0.063[m]

[t]Student T Test, [k]Kruskal Wallis Test, [m]Mann Whitney U Test, std=standart deviation, min=minimum, max=maksimum, p<0.05 is significant.

Passive smoking has two components: second-hand smoking (SHS) and third-hand smoking (THS). SHS is defined as the smoke from burning tobacco products. THS refers to the chemical residual of tobacco smoke contamination that clings to furniture, such as carpets and curtains and to hair, skin, and other materials after the cigarette is extinguished (Ferrante et al. 2013, Roberts et al. 2017). Second-hand tobacco smoking (SHS) is exposure to smoke due to proximity to a person who is actively smoking, and third-hand tobacco smoking (THS) is exposure to compounds that remain in the air and on surfaces such as clothing and furniture after someone has finished smoking rather than being exposed to the smoke itself (Matt et al. 2011, Roberts et al. 2017). This study found that 60.8% of the children had family members who smoked when the child was present in the same area. There was no significant difference between the type of smoking and serum UT-II levels. This implies that THS could be as harmful as SHS. In other words, it indicates that whether the child is present in the same area when a family member is smoking is not important if smokers live with the child. Although there are many articles on SHS, THS is still a new topic and needs further study. However, it has been emphasized that THS is as impactful and harmful as SHS (Acuff et al. 2016, Holitzki et al. 2017, Kuo & Rees 2019). It is thought that children are exposed to carcinogenic substances through the mouth, hands and skin and are especially exposed when they are on the lap of a smoking parent because they come into contact with the parts of the parents' clothes onto which cigarette particles fall (Ferrante et al. 2013, Acuff et al. 2016). The concept of THS has gained importance in the literature in recent years, and THS has been identified as the reason why the desired health results have not been achieved despite the enactment of prohibitory policies (Ferrante et al. 2013). In our study, SHS and THS had similar effects on serum UT-II levels because there was no significant difference in UT-II levels between the THS- and SHS-exposed groups, but both groups had significantly different UT-II levels than those of the children with no passive smoking exposure.

The proportion of children whose mothers smoked was 37% in our study, and the proportion of those whose mothers smoked during pregnancy was 10.9%. These rates were similar to those reported by other studies conducted in our country (Karcaaltincaba et al. 2009, Çınar et al. 2015). We categorized the group that was exposed to passive smoking according to the number of smokers in the home and whether their mothers, who were assumed to be the main caregivers, smoked. While there was no significant relationship between the number of smokers and serum UT-II levels, when the mother was evaluated on the status of smoking, it was determined that the serum UT-II level was significantly high in the children of the smoker mothers. Considering that the person care giving and spending the most time with the child to be his/her mother, it can be predicted that the mother's smoking is more critical. Not surprisingly, exposure to passive smoke was significantly higher among children living in rural zones and those with fathers with low educational levels. Studies have reported that smoking was correlated with low education levels and that people did not have sufficient knowledge of the harms of cigarette smoke (Vardavas et al. 2010, de Carvalho Ribeiro et al. 2015). We know that it is very important as a general health policy to increase the level of education and to provide adequate information about the subject. In addition, we believe that new studies that strengthen the relationship between UT-II and passive smoking will be as

valuable as improved education in preventing the harm of passive smoking.

Limitations

These findings show the importance of the concept of THS. However, the facts that the participants do not represent the whole population and that the study did not consider the amount of time the parents spent with their children or the possibility that the caregiver may be somebody other than the parents constituted limitations of our study. The cross-sectional nature of the study was another limitation. The time that only two months may be short to reflect the truth was another limitation. Although UT-II is a vasoconstrictor agent, we did not measure blood pressure in the two groups. The study was limited in that the children's blood pressure measurements were not assessed but we know that kidney diseases are the major cause of childhood hypertension and we excluded children with chronic kidney disease.

CONCLUSIONS

UT-II levels increase as a result of exposure to cigarette smoke and according to the level of exposure. First, public health measures, training programmes, and protective methods should be developed to prevent exposure to smoke among children. These studies will inform the development of new pharmacological agents to prevent smoking-induced diseases in children exposed to cigarette smoke. There is also a need for multidisciplinary, molecular and genetic studies on how children exposed to passive smoke are affected through the UT-II pathway. Our study, which draws attention to this issue, has paved the way for future studies.

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REFERENCES

ACUFF L, FRISTOE K, HAMBLEN J, SMITH M & CHEN J. 2016. Third-Hand Smoke: Old Smoke, New Concerns. J Community Health 41: 680-687.

ASMA S, SONG Y, COHEN J, ERIKSEN M, PECHACEK T, COHEN N, ISKANDER J & CENTERS FOR DISEASE CONTROL AND PREVENTION. 2014. CDC Grand Rounds: global tobacco control. MMWR Morb Mortal Wkly Rep 63: 277-280.

BANDERALI G, MARTELLI A, LANDI M, MORETTI F, BETTI F, RADAELLI G, LASSANDRO C & VERDUCI E. 2015. Short and long term health effects of parental tobacco smoking during pregnancy and lactation: a descriptive review. J Transl Med 13: 327.

BOZKURT E, MUHAFIZ E, YAYLA M & CINAR I. 2021. The Relationship of the Urotensin-2 Level in the Aqueous Humor with Systemic Diseases and Pupil Size: Comparative Study. J Ocul Pharmacol Ther 37: 45-51.

CAO S, YANG C, GAN Y & LU Z. 2015. The Health Effects of Passive Smoking: An Overview of Systematic Reviews Based on Observational Epidemiological Evidence. PLoS ONE 10: e0139907.

ÇINAR N, TOPAL S & ALTINKAYNAK S. 2015. Gebelikte Sigara Kullanımı ve Pasif İçiciliğin Fetüs ve Yenidoğan Sağlığı Üzerine Etkileri. J Hum Rhythm 1: 52-57.

DE CARVALHO RIBEIRO FA, DE MORAES MK, DE MORAIS CAIXETA JC, DA SILVA JN, LIMA AS, PARREIRA SL & FERNANDES VL. 2015. [Perception of parents about second hand smoke on the health of their children: an ethnographic study]. Rev Paul Pediatr 33: 394-399.

DREXLER H & HORNIG B. 1999. Endothelial dysfunction in human disease. J Mol Cell Cardiol 31: 51-60.

FERRANTE G, SIMONI M, CIBELLA F, FERRARA F, LIOTTA G, MALIZIA V, CORSELLO G, VIEGI G & LA GRUTTA S. 2013. Third-hand smoke exposure and health hazards in children. Monaldi Arch Chest Dis 79: 38-43.

GOLBIDI S, EDVINSSON L & LAHER I. 2020. Smoking and Endothelial Dysfunction. Curr Vasc Pharmacol 18: 1-11.

GOLD SJ, THOMPSON JP, WILLIAMS JP, HELM EE, SADLER J, SONG W, NG LL & LAMBERT DG. 2007. Does cigarette smoking increase plasma urotensin II concentrations? Eur J Clin Pharmacol 63: 253-257.

GULER EM, GOKCE M, BACAKSIZ A & KOCYIGIT A. 2020. Urotensin-II, oxidative stress, and inflammation increase in hypertensive and resistant hypertensive patients. Clin Clin Exp Hypertens 43(3): 211-216.

HOLITZKI H, DOWSETT LE, SPACKMAN E, NOSEWORTHY T & CLEMENT F. 2017. Health effects of exposure to second- and third-hand marijuana smoke: a systematic review. CMAJ Open 5: E814-E822.

HWANG SH, HWANG JH, MOON JS & LEE DH. 2012. Environmental tobacco smoke and children's health. Korean J Pediatr 55: 35-41.

JING W, WANG W & LIU Q. 2019. Passive smoking induces pediatric asthma by affecting the balance of Treg/Th17 cells. Pediatr Res 85: 469-476.

JONES LL, HASSANIEN A, COOK DG, BRITTON J & LEONARDI-BEE J. 2012. Parental Smoking and the Risk of Middle Ear Disease in Children: A Systematic Review and Meta-analysis. Arch Pediatr Adolesc Med 166: 18-27.

JUNG Y, LEE AM, MCKEE SA & PICCIOTTO MR. 2017. Maternal smoking and autism spectrum disorder: meta-analysis with population smoking metrics as moderators. Sci Rep 7: 4315.

KARCAALTINCABA D, KANDEMIR O, YALVAC S, GUVEN ES, YILDIRIM BA & HABERAL A. 2009. Cigarette smoking and pregnancy: results of a survey at a Turkish women's hospital in 1,020 patients. J Obstet Gynaecol 29: 480-486.

KUO HW & REES VW. 2019. Third-hand smoke (THS): What is it and what should we do about it? J Formos Med Assoc 118: 1478-1479.

LI JSM, PEAT JK, XUAN W & BERRY G. 1999. Meta-analysis on the association between environmental tobacco smoke (ETS) exposure and the prevalence of lower respiratory tract infection in early childhood. Pediatr Pulmonol 27: 5-13.

LI YY, SHI ZM, YU XY, FENG P & WANG XJ. 2016. Urotensin II-induced insulin resistance is mediated by NADPH oxidase-derived reactive oxygen species in HepG2 cells. World J Gastroenterol 22: 5769-5779.

LIBBY P. 2007. Inflammatory mechanisms: the molecular basis of inflammation and disease. Nutr Rev 65: S140-S146.

MANGRIO E, LINDSTROM M & ROSVALL M. 2010. Early life factors and being overweight at 4 years of age among children in Malmo, Sweden. BMC Public Health 10: 764.

MATT GE, QUINTANA PJ, ZAKARIAN JM, FORTMANN AL, CHATFIELD DA, HOH E, URIBE AM & HOVELL MF. 2011. When smokers move out and non-smokers move in: residential thirdhand smoke pollution and exposure. Tob Control 20: e1.

ROBERTS C, WAGLER G & CARR MM. 2017. Environmental Tobacco Smoke: Public Perception of Risks of Exposing Children to Second- and Third-Hand Tobacco Smoke. J Pediatr Health Care 31: e7-e13.

RONG X, WU HP, QIU HX, REN Y, ZHANG YH, CHEN Q, WU RZ & HU XT. 2012. Expression and role of urotensin II on the lung of patients with pulmonary hypertension with congenital heart disease. Zhonghua Er Ke Za Zhi 50: 689-691.

ROSS B, MCKENDY K & GIAID A. 2010. Role of urotensin II in health and disease. Am J Physiol Regul Integr Comp Physiol 298: R1156-1172.

SHIELS MS ET AL. 2014. Cigarette smoking and variations in systemic immune and inflammation markers. J Natl Cancer Inst 106(11): 1-8.

SUMBULOGLU K & SUMBULOGLU V. 2016. Biostatistics. Ankara, Hatiboglu Yayinlari.

TALHOUT R, SCHULZ T, FLOREK E, VAN BENTHEM J, WESTER P & OPPERHUIZEN A. 2011. Hazardous compounds in tobacco smoke. Int J Environ Res Public Health 8: 613-628.

UĞUR Ç, SERTÇELIK M, ÜNERI Ö, DINÇ GŞ, SEKMEN E & SOLMAZ E. 2018. Evaluation of serum urotensin-II levels of children with ADHD and autism spectrum disorder. Anatolian Journal of Psychiatry 2018: 80-86.

VARDAVAS CI ET AL. 2016. The independent role of prenatal and postnatal exposure to active and passive smoking on the development of early wheeze in children. Eur Respir J 48: 115-124.

VARDAVAS CI, PATELAROU E, CHATZI L, ROUMELIOTAKI T, SARRI K, MURPHY S, KOUTIS A, KAFATOS AG & KOGEVINAS M. 2010. Factors associated with active smoking, quitting, and secondhand smoke exposure among pregnant women in Greece. J Epidemiol 20: 355-362.

VAUDRY H ET AL. 2010. Urotensin II, from fish to human. Ann N Y Acad Sci 1200: 53-66.

YAYLA M, ÇETIN D, ÜSTEBAY S, BOZKURT HB, ERTEKIN Ö & ÜSTEBAY DÜ. 2019. Boy kısalığı olan çocukların serum ürotensin 2 düzeylerinin igf-1 ile ilişkisi. Genel Tip Dergisi 29(4): 194-200.

YOU Z, AL KINDI H, ABDUL-KARIM A, BARRETTE PO & SCHWERTANI A. 2014. Blocking the urotensin II receptor pathway ameliorates the metabolic syndrome and improves cardiac function in obese mice. FASEB J 28: 1210-1220.

ZHANG WX, LIANG YF, WANG XM, NIE Y, CHONG L, LIN L, CHEN C & LI CC. 2012. Urotensin upregulates transforming growth

factor-beta1 expression of asthma airway through ERK-dependent pathway. Mol Cell Biochem 364: 291-298.

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