

TÜTÜN VE ÇOCUK GÖĞÜS HASTALIKLARI

26. BÖLÜM

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Giriş

Akciğerlerin gelişimi, intrauterin dönemde embriyogenetik ile başlayıp çocukluk döneminde de devam etmektedir (1,2). Doğumdan sonra akciğer gelişiminin büyük bölümü ilk iki yıl içerisinde olmakla birlikte, alveollerin gelişim sürecinin 15 yaş sonrasına kadar devam ettiği bilinmektedir (3). İtrauterin dönemde ve doğum sonrası, tütün dumanı ve nikotine maruz kalmanın akciğerlerin gelişimini olumsuz etkilediği, alt solunum yolu enfeksiyonu gelişme riskini artırıldığı, vizing (hışılıtlı) sıklığını artırıldığı ve kronik akciğer hastalığı olan çocukların solunum semptomlarını tetiklediği gösterilmiştir (4-8).

Tütün dumanı, sağlık için zararlı etkileri olan 4000'den fazla kimyasal madde içermektedir (9). Özellikle nikotin, karbonmonoksit, akrolein, polisiklik aromatik hidrokarbonlar, aromatik aminler ve N-nitrozaminler gibi karsinojenler, fetal yaşamda ve doğum sonrası organların hızlı gelişme döneminde akciğerlerde ve beyinde olumsuz etkilere yol açabilmektedir (4). Tütün dumanındaki birincil bağımlılık yapan madde olan nikotinin plasentayı geçtiğine dair görüşler, gebelerde amniyon sıvısında ve yenidoğan bebeklerde kanda saptanan yüksek kotinin düzeyleri ile kanıtlanmıştır (10,11). Nikotin ayrıca sigara içen

annelerde anne sütünde de gösterilmiştir (12). Anneden indirek tütün dumanı maruziyeti yanında, çocuklar doğum sonrası dönemden başlayıp tüm yaşamları boyunca sekonder (ikincil) tütün dumanına veya üçüncü tütün dumanına da maruz kalabilirler. Bu durum çevresel tütün dumanı maruziyeti olarak tanımlanmaktadır. İkincil duman, sigara içenlerin dışarı verdikleri ana duman ve yanmış sigaradan çevreye yayılan dumanın bir karışımıdır. Son zamanlarda tanımlanan, üçüncü duman maruziyeti, özellikle iç ortamlarda, tütün dumanı ve nikotin maruziyeti olarak kabul edilmektedir. Üçüncü duman maruziyeti, tütün dumanı bileşenleri yüzeylerde biriktiğinde ortaya çıkar ve bu kimyasallar tozlara yapışarak havaya yeniden yayılabilir veya ortamdaki diğer kimyasallarla reaksiyona girebilir (13). Bunun sonucunda gelişen oksidasyona bağlı, üçüncü duman maruziyeti ikincil duman maruziyetine kıyasla daha fazla toksisiteye neden olabilir. Ayrıca, bebekler ve küçük çocuklar iç ortamlarda daha fazla zaman geçirmeleri, solunum hızlarının yüksek olması, ellerini daha sık ağızlarına götürmeleri nedeniyle büyük çocuklara göre ikincil ve üçüncü duman maruziyetine bağlı daha yüksek risk altındadırlar. Dünyada çocukların %40-50'sinin ikincil tütün dumanına maruz kaldığı ve özellikle de bu maruziyetin anne, baba ve diğer ev içi aile bireylerine bağlı olduğu bilinmektedir.

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Sonuç

Çocuklarda tütün dumanına intrauterin dönemde ve doğumdan sonra maruziyetin uzun önemli etkilerini değerlendirmek için yeni çalışmalar ihtiyaç bulunmaktadır, ancak özellikle intrauterin tütün dumanı maruziyetinin akciğer gelişimini olumsuz etkilediği, epigenetik faktörler ve genetik polimorfizmlerin akciğer hastalığı gelişmesi için risk faktörü olacağı akılda tutulmalıdır. Tüm bunlara ek olarak özellikle ergenlik döneminde artan elektronik sigara kullanımı nedeniyle, elektronik sigaraların akciğer gelişimi ve solunum fonksiyonlarına etkisinin değerlendirilmesi için uzun süreli araştırmalara ihtiyaç bulunmaktadır.

KAYNAKLAR

- Gibbs K, Collaco JM, McGrath-Morrow SA. Impact of Tobacco Smoke and Nicotine Exposure on Lung Development. *Chest*. 2016;149(2):552-561. doi:10.1378/chest.15-1858
- Smith LJ, McKay KO, van Asperen PP, et al. Normal development of the lung and premature birth. *Pediatr Respir Rev*. 2010;11(3):135-142. doi:10.1016/j.prrv.2009.12.006
- Herring MJ, Putney LF, Wyatt G, et al. Growth of alveoli during postnatal development in humans based on stereological estimation. *Am J Physiol Lung Cell Mol Physiol*. 2014;307(4):L338-L344. doi:10.1152/ajplung.00094.2014
- Maritz GS, Harding R. Life-long programming implications of exposure to tobacco smoking and nicotine before and soon after birth: evidence for altered lung development. *Int J Environ Res Public Health*. 2011;8(3):875-898.
- den Dekker HT, Sonnenschein-van der Voort AM, de Jongste JC, et al. Tobacco smoke exposure, airway resistance, and asthma in school-age children: the Generation R Study. *Chest*. 2015;148(3):607-617.
- Collaco JM, Aherrera AD, Breysse PN, et al. Hair nicotine levels in children with bronchopulmonary dysplasia. *Pediatrics*. 2015;135(3):e678-e686.
- Lodge CJ, Zaloumis S, Lowe AJ, et al. Early-life risk factors for childhood wheeze phenotypes in a high-risk birth cohort. *J Pediatr*. 2014;164(2):289-294.
- Wilson KM, Pier JC, Wesgate SC, et al. Secondhand tobacco smoke exposure and severity of influenza in hospitalized children. *J Pediatr*. 2013;162(1):16-21.
- Moritsugu KP. The 2006 Report of the Surgeon General: the health consequences of involuntary exposure to tobacco smoke. *Am J Prev Med*. 2007;32(6):542-543.
- Luck W, Nau H, Hansen R, et al. Extent of nicotine and cotinine transfer to the human fetus, placenta and amniotic fluid of smoking mothers. *Dev Pharmacol Ther*. 1985;8(6):384-395.
- Jauniaux E, Gulbis B, Acharya G, et al. Maternal tobacco exposure and cotinine levels in fetal fluids in the first half of pregnancy. *Obstet Gynecol*. 1999;93(1):25-29.
- Schulte-Hobein B, Schwartz-Bickenbach D, Abt S, et al. Cigarette smoke exposure and development of infants throughout the first year of life: influence of passive smoking and nursing on cotinine levels in breast milk and infant's urine. *Acta Paediatr*. 1992;81(6-7):550-557.
- Ferrante G, Simoni M, Cibella F, et al. Third-hand smoke exposure and health hazards in children. *Monaldi Arch Chest Dis*. 2013;79(1): 38-43.
- Brehm JM, Ramratnam SK, Tse SM, et al. Stress and bronchodilator response in children with asthma. *Am J Respir Crit Care Med*. 2015;192(1):47-56.
- Chhabra D, Sharma S, Kho AT, et al. Fetal lung and placental methylation is associated with in utero nicotine exposure. *Epigenetics*. 2014;9(11):1473-1484.
- Tong VT, Dietz PM, Morrow B, et al. Trends in smoking before during, and after pregnancy—Pregnancy Risk Assessment Monitoring System, United States, 40 sites, 2000-2010. *MMWR Surveill Summ*. 2013;62(6):1-19.
- Neuman A, Hohmann C, Orsini N, et al. Maternal smoking in pregnancy and asthma in preschool children: a pooled analysis of eight birth cohorts. *Am J Respir Crit Care Med*. 2012; 186:1037-1043.
- Smedberg J, Lupattelli A, Mardby AC, Nordeng H. Characteristics of women who continue smoking during pregnancy: a cross-sectional study of pregnant women and new mothers in 15 European countries. *BMC Pregnancy Childbirth*. 2014; 14:213.
- Caleyachetty R, Tait CA, Kengne AP, Corvalan C, Uauy R, Echouffo-Tcheugui JB. Tobacco use in pregnant women: analysis of data from Demographic and Health Surveys from 54 low-income and middle-income countries. *Lancet Glob Health*. 2014; 2:e513-e520.
- Ben-Yehudah A, Campanaro BM, Wakefield LM, et al. Nicotine exposure during differentiation causes inhibition of N-myc expression. *Respir Res*. 2013;14:119.
- Sekhon HS, Jia Y, Raab R, et al. Prenatal nicotine increases pulmonary alpha7 nicotinic receptor expression and alters fetal lung development in monkeys. *J Clin Invest*. 1999;103(5):637-647.
- Singh SP, Gundavarapu S, Pena-Philippides JC, et al. Prenatal secondhand cigarette smoke promotes Th2 polarization and impairs goblet cell differentiation and airway mucus formation. *J Immunol*. 2011;187(9):4542-4552.
- Huang LT, Chou HC, Lin CM, et al. Maternal nicotine exposure exacerbates neonatal hyperoxia-induced lung fibrosis in rats. *Neonatology*. 2014;106(2):94-101.
- Shorey-Kendrick LE, Ford MM, Allen DC, et al. Nicotinic receptors in non-human primates: analysis of genetic and functional conservation with humans. *Neuropharmacology*. 2015;96(Pt B): 263-273.
- Lavezzi AM, Corna MF, Alfonsi G, et al. Possible role of the alpha7 nicotinic receptors in mediating nicotine's effect on developing lung - implications in unexplained human perinatal death. *BMC Pulm Med*. 2014;14:11.
- Scott JE. The pulmonary surfactant: impact of tobacco

- co smoke and related compounds on surfactant and lung development. *Tob Induc Dis.* 2004;2(1):3-25. doi:10.1186/1617-9625-2-1-3.
27. Trachtenberg FL, Haas EA, Kinney HC, et al. Risk factor changes for sudden infant death syndrome after initiation of Back-to-Sleep campaign. *Pediatrics.* 2012;129(4):630-638.
 28. Mitchell EA, Milerad J. Smoking and the sudden infant death syndrome. *Rev Environ Health.* 2006;21(2):81-103.
 29. Cerpa VJ, Aylwin Mde L, Beltrán-Castillo S, et al. The alteration of neonatal raphe neurons by prenatal-perinatal nicotine. Meaning for sudden infant death syndrome. *Am J Respir Cell Mol Biol.* 2015;53(4):489-499.
 30. Pendlebury JD, Wilson RJ, Bano S, et al. Respiratory control in neonatal rats exposed to prenatal cigarette smoke. *Am J Respir Crit Care Med.* 2008;177(11):1255-1261.
 31. Eugenin J, Otarola M, Bravo E, et al. Prenatal to early postnatal nicotine exposure impairs central chemoreception and modifies breathing pattern in mouse neonates: a probable link to sudden infant death syndrome. *J Neurosci.* 2008;28(51):13907-13917.
 32. McEvoy CT, Spindel ER. Pulmonary Effects of Maternal Smoking on the Fetus and Child: Effects on Lung Development, Respiratory Morbidities, and Life Long Lung Health. *Paediatr Respir Rev.* 2017;21:27-33. doi:10.1016/j.prrv.2016.08.005.
 33. Duijts L, Jaddoe VW, van der Valk RJ, et al. Fetal exposure to maternal and paternal smoking and the risks of wheezing in preschool children: the Generation R Study. *Chest.* 2012;141(4): 876-885.
 34. Hayatbakhsh MR, Sadasivam S, Mamun AA, et al. Maternal smoking during and after pregnancy and lung function in early adulthood: a prospective study. *Thorax.* 2009;64(9):810-814.
 35. He QQ, Wong TW, Du L, et al. Environmental tobacco smoke exposure and Chinese schoolchildren's respiratory health: a prospective cohort study. *Am J Prev Med.* 2011;41(5):487-493.
 36. Kalliola S, Pelkonen AS, Malmberg LP, et al. Maternal smoking affects lung function and airway inflammation in young children with multiple-trigger wheeze. *J Allergy Clin Immunol.* 2013;131(3):730-735.
 37. Cunningham J, Dockery DW, Speizer FE. Maternal smoking during pregnancy as a predictor of lung function in children. *Am J Epidemiol.* 1994; 139:1139-1152.
 38. Dai X, Dharmage SC, Lowe AJ, et al. Early smoke exposure is associated with asthma and lung function deficits in adolescents. *J Asthma.* 2017;54(6):662-669.
 39. Dai X, Dharmage SC, Bowatte G, et al. Interaction of Glutathione S-Transferase M1, T1, and P1 Genes With Early Life Tobacco Smoke Exposure on Lung Function in Adolescents. *Chest.* 2019;155(1):94-102. doi:10.1016/j.chest.2018.08.1079.
 40. Milanzi EB, Koppelman GH, Smit HA, et al. Timing of secondhand smoke, pet, dampness or mould exposure and lung function in adolescence. *Thorax.* 2020;75(2):153-163. doi:10.1136/thoraxjnl-2019-213149.
 41. Thacher JD, Schultz ES, Hallberg J, et al. Tobacco smoke exposure in early life and adolescence in relation to lung function. *Eur Respir J.* 2018;51(6):1702111.
 42. Fergusson DM, Horwood LJ, Shannon FT. Parental smoking and respiratory illness in infancy. *Arch Dis Child.* 1980;55(5):358-361.
 43. Haberg SE, Stigum H, Nystad W, et al. Effects of pre- and postnatal exposure to parental smoking on early childhood respiratory health. *Am J Epidemiol.* 2007;166(6):679-686.
 44. Singh SP, Gundavarapu S, Pena-Philippides JC, et al. Prenatal secondhand cigarette smoke promotes Th2 polarization and impairs goblet cell differentiation and airway mucus formation. *J Immunol.* 2011;187(9):4542-4552.
 45. Tebow G, Sherrill DL, Lohman IC, et al. Effects of parental smoking on interferon gamma production in children. *Pediatrics.* 2008;121(6):e1563-e1569.
 46. Wang L, Joad JP, Zhong C, et al. Effects of environmental tobacco smoke exposure on pulmonary immune response in infant monkeys. *J Allergy Clin Immunol.* 2008;122(2):400-406.
 47. Lanari M, Vandini S, Adorni F, et al. Prenatal tobacco smoke exposure increases hospitalizations for bronchiolitis in infants. *Respir Res.* 2015;16:152.
 48. Maedel C, Kainz K, Frischer T, Reinweber M, Zacharsiewicz A. Increased severity of respiratory syncytial virus airway infection due to passive smoke exposure. *Pediatr Pulmonol.* 2018;53(9):1299-1306.
 49. DiFranza JR, Masaquel A, Barrett AM, Colosia AD, Machadevia PJ. Systematic literature review assessing tobacco smoke exposure as a risk factor for serious respiratory syncytial virus disease among infants and young children. *BMC Pediatr.* 2012;12:81.
 50. Gilliland FD, Li YF, Peters JM. Effects of maternal smoking during pregnancy and environmental tobacco smoke on asthma and wheezing in children. *Am J Respir Crit Care Med.* 2001; 163:429-436.
 51. Silvestri M, Franchi S, Pistorio A, et al. Smoke exposure, wheezing, and asthma development: a systematic review and meta-analysis in unselected birth cohorts. *Pediatr Pulmonol.* 2015;50(4):353-362.
 52. Burke H, Leonardi-Bee J, Hashim A, et al. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics.* 2012;129:735-744.
 53. Lyell PJ, Villanueva E, Burton D, Freezer NJ, Bardin. Risk factors for intensive care in children with acute asthma. *Respirology* 2005;10:436-441.
 54. Vargas PA, Brenner B, Clark S, et al. Exposure to environmental tobacco smoke among children presenting to the emergency department with acute asthma: a multicenter study. *Pediatr Pulmonol.* 2007;42(7):646-655. doi:10.1002/ppul.20637
 55. Samir S, Colin Y, Thomas S. Impact of environmental tobacco smoke on children admitted with status asthmaticus in the pediatric intensive care unit. *Pediatr Pulmonol.* 2011;46(3):224-229. doi:10.1002/ppul.21355
 56. Yilmaz O, Turkeli A, Onur E, et al. Secondhand tobacco smoke and severity in wheezing children: Nasal oxidant stress and inflammation. *J Asthma.* 2018;55(5):477-482.
 57. Lang JE, Dozor AJ, Holbrook JT, et al. Biologic mechanisms of environmental tobacco smoke in children with poorly controlled asthma: results from a mul-

- ticenter clinical trial. *J Allergy Clin Immunol Pract.* 2013;1(2):172-180.
58. Feleszko W, Ruszczyński M, Jaworska J, et al. Environmental tobacco smoke exposure and risk of allergic sensitisation in children: a systematic review and meta-analysis. *Arch Dis Child.* 2014;99(11):985-992.
59. Strzelak A, Ratajczak A, Adamiec A, et al. Tobacco Smoke Induces and Alters Immune Responses in the Lung Triggering Inflammation, Allergy, Asthma and Other Lung Diseases: A Mechanistic Review. *Int J Environ Res Public Health.* 2018;15(5):1033.
60. Kopp BT, Ortega-García JA, Sadreameli SC, et al. The Impact of Secondhand Smoke Exposure on Children with Cystic Fibrosis: A Review. *Int J Environ Res Public Health.* 2016;13(10):1003.
61. Collaco JM, Vanscoy L, Bremer L, et al. Interactions between secondhand smoke and genes that affect cystic fibrosis lung disease. *JAMA.* 2008;299(4):417-424.
62. Sanders DB, Emerson J, Ren CL, et al. Early Childhood Risk Factors for Decreased FEV1 at Age Six to Seven Years in Young Children with Cystic Fibrosis. *Ann Am Thorac Soc.* 2015;12(8):1170-1176.
63. Kopp BT, Sarzynski L, Khalfoun S, et al. Detrimental effects of secondhand smoke exposure on infants with cystic fibrosis. *Pediatr Pulmonol.* 2015;50(1):25-34.
64. Cantin AM, Hanrahan JW, Bilodeau G, et al. Cystic fibrosis transmembrane conductance regulator function is suppressed in cigarette smokers. *Am J Respir Crit Care Med.* 2006;173(10):1139-1144.
65. Walsh SLF, Nair A, Desai SR. Interstitial lung disease related to smoking: imaging considerations. *Curr Opin Pulm Med.* 2015;21(4):407-416.
66. Sismanlar T, Aslan AT, Turktaş H, et al. Respiratory Bronchiolitis-Associated Interstitial Lung Disease in Childhood: New Sequela of Smoking. *Pediatrics.* 2015;136(4):e1026-e1029.
67. Zeilinger S, Kuhnel B, Klopp N, et al. Tobacco smoking leads to extensive genome-wide changes in DNA methylation. *PLoS One.* 2013;8(5):e63812.
68. Li YF, Langholz B, Salam MT, et al. Maternal and grandmaternal smoking patterns are associated with early childhood asthma. *Chest.* 2005;127(4):1232-1241.
69. Lerner CA, Sundar IK, Yao H, et al. Vapors produced by electronic cigarettes and e-juices with flavorings induce toxicity, oxidative stress, and inflammatory response in lung epithelial cells and in mouse lung. *PLoS One.* 2015;10(2):e0116732.
70. Brown A, Balk SJ. E-Cigarettes and Other Electronic Nicotine Delivery Systems (ENDS). *Curr Probl Pediatr Adolesc Health Care.* 2020;50(2):100761.
71. Hamberger ES, Halpern-Felsher B. Vaping in adolescents: epidemiology and respiratory harm. *Curr Opin Pediatr.* 2020;32(3):378-383.
72. Le Souëf PN. Pediatric origins of adult lung diseases. 4. Tobacco related lung diseases begin in childhood. *Thorax.* 2000;55(12):1063-1067.