Environmental Research 151 (2016) 321–338

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Tobacco smoking and breastfeeding: Effect on the lactation process, breast milk composition and infant development. A critical review

Marta Napierala [a], Jan Mazela [b], T. Allen Merritt [c], Ewa Florek [a,*]

[a] Laboratory of Environmental Research, Department of Toxicology, Poznan University of Medical Sciences, 30 Dojazd Street, 60-631 Poznan, Poland
[b] Department of Neonatal Infection, Poznan University of Medical Sciences, 33 Polna Street, 60-535 Poznan, Poland
[c] Children's Hospital, School of Medicine, Loma Linda University, Loma Linda, CA 92354, USA

ARTICLE INFO

Article history:
Received 7 April 2016
Received in revised form
3 July 2016
Accepted 2 August 2016

Keywords:
Infant
Human milk
Smoking women
Breast milk composition
Lactation

ABSTRACT

Approximately 10% of women report smoking during pregnancy. The number of breastfeeding women who relapse back to smoking is even greater. Smoking may cause adverse changes to the milk's composition by not only reducing its protective properties, but also by affecting the infant's health. The pathophysiological mechanisms underlying these adverse effects are not entirely known.

This article is a review of previous reports about the effects of smoking on the lactation process, breast milk composition and infant development. A systematic search for English language articles published until 2015 was made, using a MEDLINE data. The key search terms were "smoking and breastfeeding", "smoking and lactation", "smoking and milk composition", "nicotine and breast milk".

Studies have shown that nicotine levels in breast milk of women who smoke are three times higher than those in the plasma levels. Breast milk volume is reduced and the duration of lactation period is shorter. Smoking causes adverse changes to the milk's composition by not only reducing its protective properties, but also affecting infants' response to breastfeeding and to breast milk.

Contents

1. Introduction

Smoking is one of the most serious contemporary threats of civilization. Exposure to environmental tobacco smoke (ETS) has been linked to a number of health effects. ETS exposure is associated with adverse impacts on male and female reproduction, perinatal and postnatal manifestations of developmental toxicity, respiratory diseases, cardiovascular diseases and cancers (Haroun et al., 1999).

Over 5300 compounds have been identified in tobacco smoke. ETS or secondhand smoke, means exposure to a mixture of compounds from the smoke of burning tobacco products and smoke exhaled by the smoker. Classes of compounds include carbon and nitrogen oxides, amides, imides, lactams, lactones, aldehydes, ketones, carboxylic acids, alcohols, phenols, esters, amines, N-nitrosamines, N-heterocyclics, nitriles, nitro compounds, anhydrides, carbohydrates, ethers, hydrocarbons and metals (IARC, 2012). The principal tobacco alkaloid and major psychoactive component in smoke is nicotine. It is responsible for the addictive properties of

* Correspondence to: Head of Laboratory of Environmental Research, Department of Toxicology, University of Medical Sciences, 30 Dojazd Street, 60-631 Poznan, Poland.
E-mail address: eflorek@ump.edu.pl (E. Florek).

http://dx.doi.org/10.1016/j.envres.2016.08.002
0013-9351/

tobacco smoke (Hukkanen et al., 2005). There are over 70 carcinogens in tobacco smoke that have been evaluated by the International Agency for Research on Cancer – IARC (IARC, 2004). Sixteen of them (among others: N′-nitrosonornicotine, 2-naphthylamine, formaldehyde, benzene, arsenic, beryllium, nickel compounds, chromium VI, cadmium, polonium-210) are classified as Group 1 - carcinogenic to humans. Moreover, there are other carcinogens in tobacco smoke that have not been evaluated by the IARC Monographs program (IARC, 2012).

In spite of documented evidence on the harmful effects of smoking on the fetus and infants, a considerable number of women continue to smoke during pregnancy and lactation. In the United States (US), 10.7% of pregnant women smoke (Centers for Disease Control and Prevention, 2012). It is estimated that in Europe this problem also affects more than 1 in 10 pregnant women (Euro-Peristat, 2013). As there is a tendency to quickly return to tobacco smoking after an interval of smoking cessation during pregnancy with 50–80% relapsing to smoking within six months after delivery. The US Surgeon General (SG), the American Academy of Pediatrics (AAP) and the World Health Organization (WHO) have recommended exclusive breastfeeding (with the exception of infants of HIV positive mothers) during the first 6 months (Centers for Disease Control and Prevention, 2002; Butte et al., 2002; Gartner et al., 2005). Thus the number of women smoking while breastfeeding represent a significant population of women and infants at risk.

Breast milk of mothers who smoke is a significant contributor to infant exposure to ETS constituents. Women who are less educated, have lower socioeconomic status and who began smoking at a younger age may not recognize or be aware of the adverse effects of tobacco smoking on fetal development, low birth weight, premature infants and increased complications of pregnancy such as placental abruption (Centers for Disease Control and Prevention, 2012; Euro-Peristat, 2013).

This article is a review of previous reports on the impact of smoking on the lactation process, breast milk composition and infant development. A systematic search for English language articles published until 2015 was made, through a MEDLINE search using the terms “smoking and breastfeeding”, “smoking and lactation”, “smoking and milk composition”, “nicotine and breast milk”. Additional studies were identified through a search of the Cochrane and Scopus database, through discussions with experts, and by hand-searching of reference lists from major review articles. This review aims to describe the literature available with particular reference to the impact of tobacco smoking during breastfeeding and nicotine consumption on the lactation process, milk changes in composition and dangers/risks on the well-being and health status of children as well as to discuss the necessary future directions of research in this matter.

2. Nicotine and cotinine in breast milk

Simultaneous maternal smoking and breastfeeding significantly increases absorption of nicotine by the infant compared to this only being exposed to tobacco smoke (Luck and Nau, 1985; Dahlström et al., 1990; Schulte-Hobein et al., 1992). Studies of pharmacokinetics of nicotine have shown that its half-life in milk ($t_{1/2}=97\pm20$ min) is longer than the half-life in serum ($t_{1/2}=81\pm9$ min); however, the difference between these two values was not statistically significant (Luck and Nau, 1985). When consumed enterally (as in breastfeeding or being fed expressed breast milk), nicotine is absorbed by the digestive system of the baby where it is metabolized in the liver to cotinine (Labrecque et al., 1989). Thus both nicotine and cotinine are present in the blood and can exert circulatory effects on the infant including an increased baseline heart rate (Sherman et al., 2002). Time of nicotine elimination in the newborn is three to four times longer than that in adults, while in the case of cotinine is similar (Dempsey et al., 2000; Benowitz et al., 2009).

The milk/serum concentration ratio for nicotine is, on average, 2.92 ± 1.09, while for cotinine it is 0.78 ± 0.19 (Luck and Nau, 1985). These differences are explained by pH (average: breast milk pH$=7.06\pm0.16$ vs. serum pH$=7.40\pm0.03$) (Luck and Nau, 1985; Dahlström et al., 1990; Chilmonczyk et al., 1990). However, in human milk, pH variation: from 6.65 to 7.45, can lead to nicotine level changes in breast milk. The lower the milk's pH, the higher the nicotine concentration has been observed (Luck and Nau, 1985).

Cotinine is nicotine's major metabolite with a longer half-life (20 h vs. 2 h for nicotine); therefore, cotinine concentrations are more frequently used as a biomarker of exposure to tobacco smoke. The concentration of cotinine in breast milk is “dose dependent” based on the number of cigarettes smoked (Woodward et al., 1986; Mascola et al., 1998). Several studies confirmed that infants of smoking and breastfeeding mothers have cotinine urine levels two to ten times higher than that in formula-fed babies exposed only to second-hand smoke (SHS) (Schulte-Hobein et al., 1992; Labrecque et al., 1989; Chilmonczyk et al., 1990; Mascola et al., 1998).

Age, sex, race, use of xenobiotics and disease states have been reported to affect nicotine metabolism among people (Benowitz et al., 2009; Avila-Tang et al., 2013). Approximately 75% of nicotine is converted to cotinine in human liver (Avila-Tang et al., 2013). In adults, the metabolism of nicotine and cotinine takes place mainly due to cytochrome P450 2A6 enzyme (CYP2A6). In addition, during pregnancy, there is a marked acceleration in metabolism of both nicotine (60% increase) and cotinine (140% increase), compared to the postpartum levels (Dempsey et al., 2002). Prolonged elimination of nicotine (not cotinine) among the newborn compared with that in the adult may be a result of different newborn CYP2A6 activity (Dempsey et al., 2000). In the case of children aged 2–84 months with normal-activity CYP2A6*1/*1 genotypes, faster metabolism was manifested by a shorter half-life of cotinine, than in those with one or two reduced-activity variant alleles (Dempsey et al., 2013).

In reference to the studies on animal models: many animals contrary to humans metabolize nicotine more rapidly (Hukkanen et al., 2005). Although the mouse CYP2A5 is a homolog of human CYP2A6, in the rat, CYP2A6 is inactive and CYP1B1/2 is responsible for nicotine metabolism (Matta et al., 2007). In addition, rats being much smaller than humans and have a faster rate of metabolism. Therefore, rats eliminate most toxicants much more rapidly. This makes the rat less a suitable model for investigations focusing on human nicotine metabolism. Plasma nicotine half-life in rodents is generally shorter than in humans (6–7 min in the mouse; 45 min in the rat vs. 2 h in the human) (Matta et al., 2007). These differences needs to be taken into account in the selection of dose levels. Higher daily doses of nicotine in rodent models have to be used to achieve the blood nicotine concentrations comparable to those seen in smokers (Hukkanen et al., 2005; Matta et al., 2007).

Nicotine replacement therapies (NRT), such as chewing gums or nicotine patches, are formulated to aid those seeking to stop smoking, and they are potentially beneficial in reducing harmful effects of exposure to environmental tobacco smoke components (Ilett et al., 2003). However, some reports showed that children's learning and memory deficits have been associated with maternal nicotine use (Narayanan et al., 2002; Mahar et al., 2012; Nakauchi et al., 2015). Moreover, nicotine absorption and kinetics from gums and patches are different than absorption from inhaling cigarette smoke. Prolonged use of nicotine replacement therapy (particularly in initial phase when doses are higher) may lead to an