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Effects of maternal nicotine on breastfeeding infants

Efeitos da nicotina materna na criança em amamentação

Efecto de la nicotina en el niño en amamantación

Cândida Caniçali Primo¹, Priscilla Bôa F. Ruela², Léia Damasceno de A. Brotto³, Telma Ribeiro Garcia⁴, Eliane de Fátima Lima⁵

ABSTRACT

Objective: To assess scientific evidence about the effects of maternal nicotine on infant by an integrative review.

Data sources: Studies published in Portuguese, English and Spanish, from 1990 to 2009, with abstracts available in the Latin American Health Sciences Literature (Lilacs) and Medical Literature Analysis and Retrieval System On-Line (Medline) databases. The descriptors were: “breastfeeding”, “lactation” and “smoking”.

Data synthesis: The main identified effects of nicotine on infants were: changes in sleep and wakefulness patterns; reduction of iodine supply; histopathological damage on liver and lung; intracellular oxidative damage; reduction of pancreatic β cells; and decreased glucose tolerance.

Conclusions: It is recommended to inform mothers about harmful chemicals contained in cigarettes that can be secreted into breast milk. They should be strongly encouraged to stop smoking during lactation.

Key-words: breast feeding; lactation; smoking.

RESUMO

Objetivo: Avaliar as evidências científicas sobre efeitos da nicotina materna na criança em amamentação, a partir de uma revisão integrativa.

Fontes de dados: Artigos publicados em português, inglês e espanhol, de 1990 a 2009, com resumos disponíveis nas bases Literatura Latino-Americana em Ciências da Saúde

(Lilacs) e *Medical Literature Analysis and Retrieval System On-Line* (Medline). Utilizaram-se os descritores: “aleitamento materno”, “lactação” e “tabagismo”.

Síntese dos dados: Os principais efeitos da nicotina encontrados para a criança foram alterações nos padrões de sono e vigília; redução da oferta de iodo; danos histopatológicos no fígado e no pulmão; danos oxidativos intracelulares; redução de células β do pâncreas; e diminuição da tolerância à glicose.

Conclusões: Recomenda-se que as mães sejam informadas sobre os produtos químicos prejudiciais contidos no cigarro, os quais passam para o bebê por meio do leite materno, devendo ser fortemente encorajadas a não fumar durante a lactação.

Palavras-chave: aleitamento materno; lactação; hábito de fumar.

RESUMEN

Objetivo: Evaluar las evidencias científicas sobre efectos de la nicotina materna en el niño en amamantación, a partir de una revisión integrativa.

Fuentes de datos: Artículos publicados en portugués, inglés y español, de 1990 a 2009, con resúmenes disponibles en las bases Literatura Latinoamericana en Ciencias de la Salud (Lilacs) y *Medical Literature Analysis and Retrieval System On-Line* (Medline). Se utilizaron los descriptores: «lactancia materna», «lactancia» y «tabaquismo».

Síntesis de los datos: Los principales efectos de la nicotina encontrados fueron alteraciones en los estándares de sueño y vigilia; reducción de la oferta de yodo; daños histopatológicos en el hígado y en los pulmones; daños

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oxidativos intracelulares; reducción de células β del páncreas y reducción de la tolerancia a la glucosa.

Conclusiones: Se recomienda que las madres sean informadas sobre los productos químicos perjudiciales contenidos en los cigarrillos, que pasan para el bebé mediante la lactancia materna, debiendo ser fuertemente motivadas a no fumar durante la gestación y lactancia.

Palabras clave: lactancia materna; lactancia; hábito de fumar.

Introduction

Breastfeeding is recognized as the most appropriate way of providing ideal food to meet the nutritional needs of all children and promoting optimal growth and development. More than 200 substances are found in breast milk composition, among which the following stand out: water, carbohydrates, proteins, lipids, minerals and vitamins, as well as cellular immunological components (macrophages, lymphocytes, neutrophils, and epithelial cells) and soluble components (immunoglobulins A, G, M, D and E, complement system, interleukins 6, 8 and 10, cytokines, bifid factor, resistance factor, lactoferrin, antioxidants, and hormones such as insulin, erythropoietin, bombesin, thyroxine, among others)⁽¹⁾.

Breastfeeding is beneficial to the child, to the mother, to the family, and also to society. As for the child, the following aspects stand out: reduction of infant mortality, especially from diarrhea and respiratory infections; reduction of allergic manifestations; improvement in neuropsychomotor development; reduction of the incidence of chronic diseases, such as arterial hypertension, diabetes mellitus, Crohn disease, ulcerative colitis, celiac disease, autoimmune diseases, and lymphoma; protective action against dental problems such as dental occlusion, mouth breather syndrome, and speech articulation disorders⁽²⁾.

For the mother, the act of breastfeeding accelerates the process of uterine involution, due to the release of oxytocin; reduces postpartum bleeding and thus the chances of developing anemia; decreases the occurrence of diabetes mellitus, of cancers (breast, ovarian and uterine) and of bone fractures due to osteoporosis; promotes mother-child bonding; has a contraceptive effect on newly delivered mothers, increasing the time interval between pregnancies; and promotes greater postpartum weight loss in women who breastfeed exclusively for six months or more. For the family, it saves money, avoiding expenses with infant formulas, feeding bottles, and

medication for the baby, since exclusively breastfed babies will be healthier^(1,2).

Although being aware of the many benefits of breastfeeding, experts are concerned about maternal smoking when it comes to the children, since they may be exposed both to cigarette smoke (second-hand smoker) and to nicotine transferred via breast milk. The consequences of passive exposure to smoke for children are well defined in the literature: worsening and development of allergic diseases, such as rhinitis and asthma⁽³⁾, onset of chronic respiratory illnesses⁽⁴⁾, increased duration and frequency of upper and lower airway infections⁽⁵⁾, and greater frequency of hospitalizations⁽⁶⁾.

However, the possible effects on the child, resulting from the transfer of the harmful components of cigarettes via breast milk, such as cyanide, aluminum, dichlorodiphenyltrichloroethane (DDT), arsenic, ammonia, formaldehyde, benzene, lead, hydrogen, carbon monoxide and dioxide, and especially nicotine⁽⁷⁾, are not well elucidated yet, with little evidence showing adverse effects on breastfed infants⁽⁸⁾.

Studies indicate the risks arising from maternal smoking: reduction of basal prolactin levels and consequent decrease in milk supply^(8,9), changes in milk composition and flavor⁽¹⁰⁾, and trend to early weaning^(9,11). In addition, more recent statistics indicate that 12–15% of women continue to smoke during pregnancy⁽⁸⁾. However, a study conducted in southern Brazil found a smoking prevalence of 23.5% during pregnancy⁽¹¹⁾.

In view of the foregoing, this study aimed to assess evidence available in the literature about the effects of nicotine on breastfed infants.

Method

This is an integrative review that allows for the synthesis of relevant studies published on the topic, as well as promoting improvement in clinical practice and decision-making. It consisted of the following steps: identification of the theme and formulation of the research question; establishment of the objective of the review; establishment of inclusion and exclusion criteria for selection of articles; definition of the information to be extracted from the selected articles; evaluation of the studies included in the integrative review; interpretation and presentation of research results⁽¹²⁾.

The leading question was: what evidence is available in the literature about the effects of maternal nicotine on breastfed infants? A bibliographical survey was performed in the Latin American Health Sciences Literature (Lilacs) and Medical

Literature Analysis and Retrieval System On-Line (Medline) databases. The descriptors used were: “breastfeeding”, “lactation” and “smoking”. Inclusion criteria were: articles published in Portuguese, English and Spanish, from 1990 to 2009; abstracts available in the databases; published studies whose methodology allowed us to obtain evidence, i.e., randomized controlled clinical trials in animals or studies with experimental or quasi experimental design in humans. Due to the low number of articles on the topic in human beings, it was necessary to include studies conducted in animals. It is also important to highlight that, although the study period covers the 1990's, no articles addressing the objective of this review were found in this period.

A total of 1,605 articles were identified in the two databases. After reading of the abstracts, 31 studies on the topic were selected and, among these, five dealt specifically with the effect of maternal nicotine on breastfed infants or offspring of animals, meeting the inclusion criteria. Of the articles selected, two of them were found in the Lilacs database and three in the Medline database.

Results

Five articles⁽¹³⁻¹⁷⁾ that met the pre-established inclusion criteria were identified and analyzed. The analysis and subsequent synthesis of the articles included in this review allowed for the elaboration of two charts, covering the following items: title of the article, with reference to its publication in the literature; objective(s) of the study; results and conclusions and/or recommendations. Chart 1 shows the two

studies involving human beings; Chart 2, the three studies involving animals.

Discussion

Nicotine secreted into breast milk has a potential to cause severe adverse effects on the newborn⁽⁹⁾, which depends on the number of cigarettes consumed by the mother per day and also on the time interval between the last inhaled cigarette and the beginning of breastfeeding⁽¹⁸⁾, because the half-life of nicotine in breast milk is of approximately two hours⁽¹⁹⁾. Nicotine is rapidly absorbed by the intestine of the infant and may be accumulated in some tissues, causing episodes of apnea, restlessness and even vomiting⁽²⁰⁾, because there is no knowledge of the exact period when infants develop the ability of completely metabolizing nicotine. It is known that, in an aqueous solution, nicotine is widely metabolized by the liver before reaching systemic circulation⁽¹⁸⁾, which, besides causing concern, deserves further studies^(14,16).

When investigating urinary cotinine levels in infants of smoking mothers and the contribution of breastfeeding to these values, researchers found that breastfeeding increases considerably the exposure to tobacco products, especially nicotine. This same study states that it is possible that the adverse effects of smoking on children, attributed only to environmental exposure to tobacco smoke by inhalation, are greatly influenced by breastfeeding, i.e., these effects are a consequence both of exposure by environmental inhalation and of exposure via breast milk⁽¹⁸⁾.

Chart 1 - Synthesis of the articles included in the integrative review – studies in human beings

Title of the article	Objective(s)/method	Results	Conclusions/ recommendations
Breastfeeding and smoking: short-term effects on infant feeding and sleep ⁽¹³⁾	To determine how breastfeeding from a mother who smokes affects infants in the short term. Experimental study.	Children spent less time sleeping immediately after their mothers smoked (53.4 minutes), compared with the day when their mothers abstained from smoking (84.5 minutes).	An acute episode of smoking by lactating mothers alters the sleep/wake patterns of breastfed infants.
Iodine nutrition in breast-fed infants is impaired by maternal smoking ⁽¹⁴⁾	To assess the risk of iodine deficiency in breastfed infants associated with maternal smoking. Experimental study.	Smoking was associated with reduction of breast milk iodine content to nearly a half. Serum thiocyanate levels were higher in mothers who smoke.	It is recommended that breastfeeding mothers should not smoke, but if they do, additional iodine supplementation is suggested.

Studies indicate that the amount of nicotine found in breast milk is 2.9 times greater than that found in maternal blood plasma⁽²¹⁾ and that the amount of cotinine, the major metabolite of nicotine, present in the urine of infants breastfed by smoking mothers was on average ten times higher than that found in bottle-fed children whose mothers smoke. Urinary cotinine levels in infants breastfed by smoking mothers is similar to those found in adult smokers⁽¹⁸⁾.

As for the objective of this review, it was observed that the effects of maternal nicotine on infants are multiple, such as changes in sleep and wake patterns; reduction of iodine supply to the infant through breast milk, leading to an increased risk of deficiency of iodine and thyroid stimulating hormone (TSH); damage to the liver and lung, besides showing significantly higher levels of superoxide dismutase (SOD), minor catalase (CAT) and malondialdehyde (MDA); reduction of pancreatic β cells responsible for insulin production and thus decrease in glucose tolerance; high body weight after weaning; hyperleptinemia; lower amount of type-1 deiodinase in the liver. Generally speaking, articles recommend breastfeeding mothers to quit smoking.

As for changes in sleep and wake patterns⁽¹³⁾, a considerable change was observed in sleep and wake patterns when children were breastfed immediately after their mother smoked, with a variation from 53.4 minutes when their mothers smoked to 84.5 minutes when they did not. The authors attribute the reduction of the amount of time spent in active and quiet sleep to an acute episode of smoking by mothers. The study indicates that an acute episode of smoking significantly alters the sleep and wake patterns of breastfed infants. Corroborating these findings, another study observed that infants of smoking mothers have sleeping disorders⁽¹⁰⁾. It is also known that the inhaled nicotine causes problems for the infant, speculating that it could lead to irritability, excessive crying, lassitude, colic and pallor^(5,7-10).

As for iodine supply through breast milk⁽¹⁴⁾, it was described that breast milk iodine content was reduced in smoking mothers (26.0g/L) compared with nonsmoking mothers (53.8g/L); therefore, the amount of iodine found in the urine of infants was also similar to that of mothers: babies of smoking mothers had 33.3 *versus* 50.4g/L for children

Chart 2 - Synthesis of the articles included in the integrative review – studies in animals

Title of the article	Objective(s)/ Method	Results	Conclusions/ Recommendations
Effects of maternal nicotine exposure during lactation on breast-fed rat pups ⁽¹⁵⁾	To investigate the effects of maternal nicotine exposure on rat pups during lactation. Experimental study.	Maternal nicotine exposure causes detrimental histopathological changes in the lung and liver of lactating offspring and induces oxidative stress.	It recommended to inform mothers about harmful chemicals in cigarettes, which are secreted into breast milk, and to encourage them to stop smoking during pregnancy and lactation.
Fetal and neonatal nicotine exposure and postnatal glucose homeostasis: identifying critical windows of exposure ⁽¹⁶⁾	To identify critical windows of fetal and neonatal exposure to maternal nicotine on the development of pancreatic β cell and glucose intolerance in the offspring of rats. Experimental study.	Continued exposure to nicotine from conception through lactation results in permanent β -cell loss and subsequent impaired glucose tolerance. There may be a recovery with smoking cessation.	Smoking cessation is recommended during pregnancy and lactation as a way of preventing possible permanent damage to β cells.
Short- and long-term effects of maternal nicotine exposure during lactation on body adiposity, lipid profile, and thyroid function of rat offspring ⁽¹⁷⁾	To evaluate the short- and long-term consequences of maternal nicotine exposure, during lactation on a rat offspring at different ages. Experimental study.	Nicotine causes a neonatal thyroid dysfunction neonatal and programs for significant adiposity, hyperleptinemia, and secondary hypothyroidism in adulthood.	It is concluded that lactation is a critical period in which nicotine may program for obesity, with hypothyroidism being a possible contributing factor.

of nonsmoking mothers. The transfer of iodine into breast milk was negatively correlated to cotinine concentration in mother's urine. Cotinine is the most precise indicator of smoking status (half-life of approximately 20 hours). For the authors, this reduction of breast milk iodine content exposes the infant to an increased risk of iodine deficiency and may lead to physiological disorders in the child, since, during the period of breastfeeding, thyroid function of the infant depends on iodine in maternal milk. Another finding was that smoking mothers had significantly higher serum levels of thiocyanate, which may competitively inhibit the sodium-iodide symporter (secondary active transport, when two substances are transported in the same direction) responsible for iodide transport in the lactating mammary gland.

A study in rats⁽¹⁷⁾ found that maternal nicotine exposure imprints a neonatal thyroid dysfunction and possible secondary hypothyroidism in adulthood. This hypofunction was confirmed by the lower liver deiodinase 1 (or iodine peroxidase) activity in offspring exposed to nicotine at 15 and 180 days of life, since this enzyme activity is considered a marker of thyroid status, which is decreased in hypothyroidism and increased in hyperthyroidism. It was also observed that maternal nicotine exposure did not alter offspring body weight gain during lactation. However, after weaning, offspring exposed to nicotine showed higher body weight compared with the control offspring. The treatment with nicotine also caused hyperleptinemia at all ages tested (15, 21, 90 and 180 days), with significant increase at 180 days of life, i.e., in adulthood. During exposure in lactation (under 15 days of age) and in adulthood (180 days), the group exposed to nicotine showed higher total adiposity (27 and 33%). In addition, it presented increased total body protein and visceral fat compared with controls. Lipid profile was not changed in adulthood.

Corroborating the results of both articles that addressed the negative effects of nicotine, with reduction of iodine supply to the infant through breast milk^(14,17), another research indicates decreased iodine supply in breast milk as a problem arising from smoking⁽⁹⁾.

As for increase in body weight after maternal nicotine exposure⁽¹⁷⁾, the authors state that maternal smoking during lactation is a risk factor for obesity, because it contributes to the possibility of developing hypothyroidism. Epidemiological studies also indicate that maternal smoking may be related to childhood obesity, but all the related factors have not been elucidated yet^(22,23). As for hyperleptinemia, a significant increase was observed in adulthood,

as well as a decrease in thyroid hormones⁽¹⁷⁾. Confirming these findings, a study describes that leptin is responsible for regulating food intake, increase in energy expenditure, neuroendocrine function and for helping in glucose and fat metabolism, besides reporting that the decrease in thyroid hormones leads to an increase in leptin levels⁽²⁴⁾.

When investigating the effects of maternal nicotine during lactation of rat pups⁽¹⁵⁾, experts observed histopathological changes in the liver of the nicotine-exposed group, with portal inflammatory infiltrate, degeneration of hepatocytes, and focal necrosis in the parenchyma. Thickening of alveolar walls because of interstitial inflammation was noted in the lungs. In the experimental group, SOD levels were significantly lower compared with the control group (smokers: 24.82U/mg; nonsmokers: 34.89U/mg), as well as CAT levels (smokers: 532.32.10⁴U/mg; nonsmokers: 712.22.10⁴U/mg), but MDA levels were significantly higher compared with the control group (smokers: 3.87mmol/mg; nonsmokers: 2.42mmol/mg). These results indicate that nicotine maternal exposure induces oxidative stress and causes histopathological impairment in the lung and liver of lactating offspring, since enzymes such as SOD and CAT, which act by sweeping away free radicals, are found at decreased levels; MDA, an important parameter of intracellular oxidative stress, is found to be high.

It was also demonstrated that nicotine exposure during pregnancy and lactation resulted in the permanent loss of pancreatic β cells and subsequent impaired glucose tolerance⁽¹⁶⁾. However, using nicotine only during lactation or only during pregnancy did not result in permanent damage, because animals exposed to nicotine only during pregnancy had reduced β cell mass at birth. Exacerbated proliferation following nicotine weaning led to recovery to 98% with regard to controls (9.66mg compared with 9.83mg). As for glucose homeostasis, the group exposed to nicotine during pregnancy and lactation had a greater response to the administered glucose load than the control group, showing decreased glucose tolerance at 26 weeks of age. This result is comparable to type-2 diabetes model in humans. According to the authors, it is essential to consider the developmental differences between species, because in rats pancreatic development occurs both prenatally and postnatally, whereas, in humans, the majority of development is completed before term birth. These authors reaffirm the importance of quitting smoking during pregnancy and lactation as a way of preventing permanent damage that is likely to occur as a consequence of this habit.

Generally speaking, studies recommend that mothers should be informed about harmful chemicals contained in cigarettes that can be secreted into breast milk and should be strongly encouraged to stop smoking during pregnancy and lactation. There is evidence proving the protective effect of breastfeeding on the incidence of respiratory diseases, even in children of smoking mothers⁽²⁵⁾. Because the benefits of breast milk outweigh the risks of nicotine exposure, mothers should be advised to stop smoking during breastfeeding⁽¹³⁾.

Finally, this integrative review allows us to conclude that there is scientific evidence about the adverse effects of maternal nicotine on breastfed infants. These effects are of different nature, such as changes in sleep and wake patterns; reduction of iodine supply to the infant through breast

milk, with increased risk of iodine and TSH deficiency; histopathological damage in the liver and lung; intracellular oxidative damage; reduction of pancreatic β cells; decreased glucose tolerance; increased body weight after weaning from maternal addiction, and hyperleptinemia.

Given the negative effects of the nicotine present in breast milk on the infant, it is recommended that mothers should be informed about all the harmful chemicals contained in cigarettes that can be secreted into breast milk. They should be strongly encouraged to stop smoking during pregnancy and lactation. More investigations are needed to analyze the physiological effects of tobacco smoke and nicotine during breastfeeding in terms of breast milk production, neonatal hormone levels, child's weight gain, child's behavior, and breastfeeding time.

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