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Smoking and pregnancy

Claudia Mehedintu[1,2], Oana Maria Ionescu[2], Mihaela Plotogea[1], Antoine Edu[1,2], Mihaela Bujor[1,2], Andreea Carp-Veliscu[2], Mihai Dumitrascu[1], Florica Sandru[1], Mona Khraibani[1]

[1]"Nicolae Malaxa" Clinical Hospital, Bucharest, Romania
[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

ABSTRACT

Smoking is one of the most harmful habits among adults. During pregnancy, the adverse effects go beyond the organism of the mother and it is considered to be a risk factor for miscarriage, stillbirth, placental abruption, preterm birth, low birthweight, morbidity and mortality. Through its numerous and dangerous compounds, tobacco smoking influence proteins and is leading to despaired fetal nourishment. Cigarette smoke toxicity is mainly driven by carbon monoxide, tar and nicotine.

Carcinogens have a high negative impact, causing both maternal and fetal anemia, as well as abnormal fetal growth and development, pathology that by itself is associated with an additional risk of preterm delivery and low birthweight. Having the capability to cross the placenta, nicotine along with the other compounds, can be fetotoxic, neurologic teratogen and impact brain development.

Smoking cessation outside or during pregnancy should be encouraged. Various medication and procedures have been proposed including in gestation. Some have proved to have positive effects, while others are not recommended during pregnancy or didn't show promising outcome. Still, pregnant women should be informed upon general and fetal risk that are associated with smoking and pregnancy need additional medical care due to related smoking complications.

Keywords: smoking, pregnancy, carbon monoxide, fetal anemia

INTRODUCTION

Cigarette smoking during pregnancy has serious impact on maternal and fetal health due to its compounds, including carbon monoxide, nicotine, tar, heavy metals like cadmium, with a strong negative impact in obstetrical area. Smoking in pregnancy has an adverse impact on maternal and fetal health increasing the risk for miscarriage, stillbirth, placental abruption, preterm birth, low birthweight, congenital abnormalities, ectopic pregnancy, morbidity and mortality. Emerging evidence suggest that in utero exposure to smoking has also long-term adverse effects such as impaired neurological development, endocrine dysfunction, oncogenesis, increased incidence of sudden infant death syndrome, hyperactivity disorder, poor academic performances, being more likely to become a smoker in adulthood [1-4]. Moreover, research shows that tobacco consume decreases woman's chances of completing a pregnancy to term without complications [5]. Placenta previa, restricted fetal growth, abortion and preterm labor are the most common complications that have been reported in smoking mothers [6-10].

SCIENTIFIC RESEARCH AND FINDINGS

Tobacco consumption during gestation leads to higher risks of pregnancy complications due to chronic exposure of the fetus to a toxic environment [10,11]. Smoking during pregnancy is associated with high risk of inappropriate placentation and disorders in development of the placenta that leads to both macroscopic and microscopic changes in placental morphology [10-12]. Many studies have reported that the intervillous space and the maternal blood flow to the placenta were decreased in

Corresponding author:
Mihaela Plotogea
email: nicole_plotogea@yahoo.co.uk

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pregnant mothers that smoke. It is considered that impaired differentiation of the cytotrophoblast [10,12,13] and inappropriate development of the syncytiotrophoblast in terms of smoking is the explanation of the placental malfunction [10,14]. Trophoblastic cells play a role in filtering the maternal blood, mechanism that guarantees a proper fetal nutrition. The chronic exposure of these cells to the toxins present in tobacco will make them inefficient to accomplish this important function in the long term [10,11]. Carbon monoxide causes hypoxemia that leads to compensatory placental hypertrophy; placentas have the tendency to extend to the cervical canal [15]. Placental invasion of the endometrium is mediated by the trophoblast during the placentation process [10,16,17]. Therefore, all these reported characteristics could lead to disorders of placental function, abnormal implantation and subsequently the trigger of pregnancy complications for smoking mothers [7,10,12,18].

Iron is an essential element in ensuring a proper fetal development and a healthy pregnancy outcome. The average demand for Fe during pregnancy is variable: from 6 mg per day in the first trimester, to 22 mg per day in the third trimester. Due to this increasing requirement of Fe, many pregnant women suffer from iron-deficient anemia, pathology that by itself is associated with an additional risk of preterm delivery and low birthweight [19-23]. The most important protein responsible for iron homeostasis is transferrin (Tf) [24]. Tf is a very heterogenous plasmatic glycoprotein transporting Fe; it has several isoforms depending on the number of terminal residues of sialic acid contained, with different biochemical properties. The impact of number of sialic acids residues on the function of this protein, including affinity of Tf receptors and Fe transport, is not fully understood. Tobacco smoking produces many abnormalities by including changes in glycan branching, as well as sialylation and galactosylation [25]. A shift toward higher sialylated Tf isoforms during pregnancy could be observed in smoker mothers, comparing to a non-smoking one, where the parameters of iron deposits are normal and the changes in Tf sialylation are balanced. A higher rate of distribution of 5- and 6-sialoTf and a lower rate of distribution of 4-sialoTf are observed in the case of low Fe deposits and may be responsible for an increased fetal demand for Fe. In women who smoke, the correlations between iron deposits and sialylation of transferrin are disrupted [26-29]. Severe anemia with maternal hemoglobin <6g/dL has been associated with inadequate fetal oxygenation that may lead to abnormal fetal heart rhythm, decreased amniotic fluid volume, fetal cerebral vasodilatation and even death [30]. Iron deficiency, in utero or in the first months of life, can also cause brain structural anomalies, as iron is an essential element for neurogenesis, neuronal and structural differentiation [31].

THE PATHOPHYSIOLOGY OF HARM FROM SMOKING

Cigarette smoke contains more than 4000 compounds including carbon monoxide, nicotine, tar, heavy metals, carcinogens with a high negative impact on the fetal growth and development [1].

Nicotine is the main addictive substance for a smoker. It is an alkaloid derived from tobacco that stimulates the parasympathetic nervous. It impacts the mother's organism and by crossing the placenta, it becomes also fetotoxic by being a great vasoconstrictor. In the fetal brain, nicotine has a neurologic teratogen effect by biding nicotinic acetylcholine neuroreceptors; it leads to a disruption in neurotransmitter function which causes an altered brain development [32-34].

Carbon monoxide, one of the gases produced by tobacco combustion, colorless and odorless, is inhaled during smoking. After absorption, it rapidly binds to hemoglobin, resulting carboxyhemoglobin. The iron atoms from hemoglobin composition, preferentially bind a carbon monoxide molecule at the expense of one oxygen molecule. Non-smoking pregnant women have an about 1% carboxyhemoglobin in their blood and pregnant smokers can reach even levels of 15% concentration of the same substance. The outcome of increased carboxyhemoglobin concentrations in pregnant women's blood is a left shift of the oxygen-hemoglobin dissociation curve, reflecting the higher affinity of hemoglobin for carbon monoxide. This left shift impairs oxygen delivery to the myometrium and fetoplacental unit, being associated with fetal growth restriction and preterm birth [1].

Tar is a toxic substance obtained from tobacco combustion that has the property to form a residue on the skin and the mucous membranes of smokers. It damages the respiratory tract through both physical and biochemical mechanisms. It contains many carcinogenic compounds, such as polycyclic aromatic hydrocarbons, aromatic amines and nitrosamines. The outcome is a global proinflammatory status with increased oxidative stress level [35].

Cadmium is one of the heavy metals contained in cigarette smoke that manifests its toxicity by accumulating in the placenta; it has been associated with intrauterine growth restriction [1].

The toxic and teratogenic effect of these compounds has been researched and studied more in animals and less in human beings. The effect of many other substances contained in cigarette smoke remains unclear [1].

SMOKING CESSATION

Addiction and dependence to cigarettes is a physiologic and psychologic process, so cessation techniques have to include psychosocial interventions and pharmacologic therapy. Quitting smoking during pregnancy comes with lots of benefits. There are pharmacological methods, nicotine replacement treatment and non-pharmacological ones [36].

Pharmacological methods are Bupropion and Varenicline. Bupropion is an antidepressant for whom there is limited data on use during pregnancy, but there is no known risk of fetal abnormalities or adverse effects on pregnancy [37]. Varenicline is a partial agonist for nicotinic receptors in the brain. Small studies evaluating its safety usage in pregnancy did not show teratogenicity [38,39].

The U.S. Preventive Services Task Force has concluded that there are insufficient evidences to assess the balance of benefits and risks of nicotine replacement products or other pharmaceuticals for smoking cessation during pregnancy [40]. Many of the studies performed in the United States have been stopped by data and safety monitoring committees, either because of adverse effects on pregnancy or lack of demonstration of effectiveness [39-42]. The use of nicotine replacement therapy should only be considered after a detailed discussion with the patient and requires close monitoring [42].

Non-pharmacological methods are represented by written and audio-video materials, but a Cochrane study revealed that the benefits of this method versus no involvement are small [43]. Individual telephone counseling represented by regular telephone calls lasting less than 5 minutes had a greater impact on pregnant light smokers (< 10 cigarettes per day) who have already tried individually to quit smoking during pregnancy [44-46].

Alternative therapies: hypnotherapy, acupuncture, acupressure, laser therapy, electrostimulation have been studied, but no evidence was found to be effective in smoking cessation therapy [45]. Acupuncture has not been proved completely ineffective, there are still studies ongoing on the subject [46].

CONCLUSIONS

Smoking in pregnancy is one of the biggest preventable risk factors for maternal and neonatal morbidity in pregnancy. The most harmful substances from cigarette smoking are carbon monoxide, tar, heavy metals and nicotine which may affect the pregnancy and contributes to many disorders in the offspring of smokers. Smoking cessation is a key part and a care bundle for decreasing pregnancy complications. Pregnant women should be advised of the risks associated with tobacco use and clinicians should provide smoking cessation advice and support. Individualized smoking cessation combined techniques are most likely to succeed.

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