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The effect of passive and active exposure to tobacco smoke on lipid profile parameters and the activity of certain membrane enzymes in the blood of women in the first trimester of pregnancy

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ABSTRACT

The effect of tobacco smoke on lipid peroxidation, the lipid profile and membrane-bound enzymatic activity in the first trimester of pregnancy was investigated.

In the plasma of women with active exposure to tobacco smoke, we have found increased lipid peroxidation and higher total concentrations of cholesterol, triglycerides and low-density lipoproteins in the blood, as well as a decreased concentration of high-density lipoproteins. A higher concentration of low-density lipoproteins and a lower concentration of high-density lipoproteins were also found in the plasma of passive smokers. In contrast, women who smoked before pregnancy had only a higher low-density lipoprotein concentration. In the group of active and passive smoking women, lower arylesterase and phosphotriesterase activities of paraoxonase were observed, while the lactonase activity of paraoxonase decreased only in the group of active smoking women. In women with active exposure to tobacco smoke, a higher activity level of alanine aminopeptidase and γ-glutamyltransferase in the plasma was found.

It is important to monitor the lipid profile during pregnancy, especially when exposure to tobacco smoke occurs.

1. Introduction

Tobacco smoking is a serious health problem and the most important avoidable cause of death in the world (Pasupathi et al., 2009). Tobacco use during pregnancy exerts a toll on the fetus at all stages of prenatal development (Milnerowicz-Nabzdyk et al., 2017). Both active and passive smoking during pregnancy have various negative consequences (Milnerowicz-Nabzdyk and Bizoń, 2015). During exposure to tobacco smoke, the body undergoes a slow process of intoxication by cadmium (Cd), which is among the most toxic metals (Milnerowicz et al., 2001). Cadmium is well recognized for its adverse influence on the enzymatic systems of cells (Jaishankar et al., 2014). One of the enzymes affected by Cd is paraoxonase (PON), an enzyme that has two calcium (Ca) binding sites: one which is important for the stability of the enzyme and the other which is important for catalytic activity (Ceron et al., 2014). Paraoxonase has three sub-types: PON1, PON2 and PON3 (Costa et al., 2014; Elkiran et al., 2007). The various hydrolytic activities of PON1 can be broadly grouped into three categories–namely, arylesterase, phosphotriesterase and lactonase (Aggarwal et al., 2016). PON2 (43 and 55 kDa) and PON3 (about 40 kDa) are characterized mainly by lactonase activity (Costa et al., 2014). It has been proposed that the histidine residue at position 115 plays an important role in carrying out the lactonase and arylesterase activities of the enzyme (Aggarwal et al., 2016). PON1 is closely associated with HDL and protects against LDL oxidation (Gu et al., 2016). It has been shown that passive and active exposure to tobacco smoke can reduce PON-1 activity (Kahraman et al., 2017; Milnerowicz et al., 2015). There are several hypotheses for the reason behind this decrease. One is that Cd can bind to the free thiol group of PON located at residue 284 (Cys 284) or displace Ca ions from the active center, after which the hydrolytic activity and antioxidant function of PON are reduced (Li et al., 2009).

Exposure to tobacco smoke also influences lipid profile parameters. Smokers have significantly higher serum total cholesterol (TC), triglycerides (TG) and low-density lipoprotein (LDL) levels, while their high-density lipoprotein (HDL) levels are lower than in non-smokers (James et al., 2000; Nishio and Watanabe, 1997). Passive smoking is additionally associated with an approximately 30% increase in the risk of coronary artery disease (Ambrose and Barua, 2004). Both passive and active exposure to tobacco smoke increases the oxidative modification of lipids, proteins and DNA. One of the useful markers of lipid peroxidation is malondialdehyde (MDA). MDA appears to be the most

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Table 1
Characteristics of studied groups including age, BMI value, parity and gestational age.

Studied parameters	NS	PS	BS	AS
Age [years] X ± SD	36.4 ± 3.3	36.8 ± 2.3	36.4 ± 2.1	34.7 ± 4.4
BMI [kg/m^2] X ± SD	24.1 ± 3.9	22.9 ± 3.3	24.1 ± 3.4	25.9 ± 3.5
Parity [number] X ± SD	2.4 ± 1.3	2.9 ± 1.6	2.5 ± 1.7	2.7 ± 1.1
Gestational age [week] X ± SD	12.8 ± 0.6	12.5 ± 0.5	12.8 ± 0.5	12.8 ± 0.6

Legend:
NS – non-smoking pregnant women, PS – passively smoking pregnant women, BS – smoking before pregnancy women, AS – actively smoking pregnant women; BMI – body mass index

mutagenic product of lipid peroxidation (Ayala et al., 2014). Alanine aminopeptidase (AAP) (EC 3.4.11.2) and γ-glutamyltransferase (GGT) (EC 2.3.2.2), membrane-bound enzymes with a lipid in their membranes, have been singled out as the markers of Cd exposure (Milnerowicz et al., 2001). Determining the activity of these enzymes in amniotic fluid, for example, has been found to be very useful in prenatal clinical diagnostics (Milnerowicz et al., 2001). Additionally, GGT activity, apart from MDA, is a useful marker of oxidative stress (Lim et al., 2004).

Exposure to tobacco smoke and the presence of lipid disorders are inadvisable during pregnancy, especially in the first trimester, when the organs are formed and the development of the placenta begins (Burton and Jauniaux, 2015; Yamada et al., 2010). In our earlier studies, we have observed the adverse effects of exposure to tobacco smoke on the trophoblast volume (Milnerowicz-Nabzdyk et al., 2017); oxidative stress and antioxidant status (Bizoń et al., 2011); the morphometry of the fetus (Milnerowicz-Nabzdyk and Bizoń, 2015); and vascular flows in pregnancies complicated by intrauterine growth restrictions (Milnerowicz-Nabzdyk and Bizoń, 2014). Exposure to tobacco smoke is also associated with oligohydramnios and premature rupture of the membranes (Milnerowicz et al., 2001, 2000).

Until now, there has been no data about the influence of tobacco smoke in women in the first trimester of pregnancy on lipid peroxidation, the lipid profile, or PON, GGT, AAP activities. We have analyzed these parameters in the blood of pregnant women in the first trimester who experienced passive and active exposure to tobacco smoke before or during pregnancy (Li et al., 2009).

2. Materials and methods

2.1. Materials

The study population consisted of 138 pregnant women who attended their first antenatal visit (11–14 weeks of pregnancy) at the outpatient clinic of the second Department and Clinic of Gynecology and Obstetrics, Wroclaw Medical University, Poland. The study was approved by the Local Bioethics Committee of Wroclaw Medical University (KBN-152/2015). All participants were informed about the purpose of the study and requested to participate after giving written consent.

Samples were divided into four groups: non-smoking (NS) pregnant women (n = 88), passive smoking (PS) pregnant women (n = 19), smoking before (BS) pregnancy (n = 18) and women actively smoking (AS) during the first trimester of pregnancy (n = 13) (Table 1).

No subjects had any complications during pregnancy and all qualified for prenatal examination due to the mother's age (≥35 years). Data on maternal characteristics, including age, BMI, parity, and gestational age at blood sampling, are presented in Table 1. The intensity of cigarette smoking was assessed during a direct personal interview and the smoking status was verified by checking cadmium (Cd) and cotinine concentrations in the plasma (Table 2).

Venous blood was collected from pregnant women in the morning, after 12 h' fasting. Whole blood samples were drawn into trace element-free tubes containing heparin (Cat. No: 03.1631.001, Sarstedt, Germany) and were centrifuged at 2500 × g for 15 min to separate the plasma from the buffy coat and the erythrocyte pellet. Plasma was frozen at −30 °C until used.

To determine the Cd concentration, whole blood was collected into separate trace element-free tubes containing heparin (Cat. No: 06.1666.001, Sarstedt, Germany) and was frozen at −30 °C until assayed.

2.2. Methods

2.2.1. The measurement of Cd and cotinine concentration as markers of exposure to tobacco smoke

The concentration of Cd in whole blood was determined by atomic absorption spectrometry (AAS) using SOLAAR M6, Thermo Elemental Co by GFAAS, with an absorbency measurement at 228.8 nm wavelength, using the Zeeman background correction. The reference materials BCR-194, -195, -196 by IRMM, UE were used.

The concentration of cotinine in plasma was assayed using the commercial Cotinine ELISA test (Cat. No: 40-101-325056, GenWayBiotech, Inc., USA).

2.2.2. The measurement of MDA as a marker of lipid peroxidation and oxidative stress

The MDA concentration in plasma was determined using a commercial available kit (Lipid Peroxidation (MDA) Assay Kit, Cat. No: MAK085, Sigma-Aldrich, Germany).

Table 2
Effect of tobacco smoking on cadmium, cotinine, and malondialdehyde concentrations and alanyl aminopeptidase (AAP) and γ-glutamyltransferase (GGT) activities.

Studied parameters	NS	PS	BS	AS
Cd [μg/l] X ± SD	0.3 ± 0.1	0.3 ± 0.1	0.7 ± 0.4[a]	1.0 ± 0.5[a,b]
Cotinine [ng/ml] X ± SD	0.4 ± 0.2	1.2 ± 0.5[a]	0.7 ± 0.7	120.5 ± 73.3[a]
MDA [μmol/ml] X ± SD	0.5 ± 0.1	0.7 ± 0.2 [a]	0.7 ± 0.2[a]	0.8 ± 0.1[a]
AAP [μmol/ml] X ± SD	40.7 ± 20.9	47.2 ± 19.1	47.7 ± 21.1	49.0 ± 13.6[a]
GGT [μmol/ml] X ± SD	17.7 ± 10.4	25.5 ± 18.1[a]	20.4 ± 12.3	23.4 ± 16.9[a]

Legend:
NS – non-smoking pregnant women, PS – passively smoking pregnant women, BS – smoking before pregnancy women, AS – actively smoking pregnant women; BMI – body mass index; Cd – cadmium
[a] Statistically significant (p < 0.05) when compared to group NS.
[b] Statistically significant (p < 0.05) when compared to group PS.