

Doppler measurements of feto-placental blood stream in pregnant smokers

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Abstract

Introduction: Doppler analysis of the feto-placental and fetal circulation give dynamic information on the condition of the bloodstream during pregnancy, and early detection of fetal hypoxia. The objectives of the study were: testing whether there is influence of smoking on feto-placental circulation; determining whether there is a link to a number of smoked cigarettes during the day; assessing the benefits of Doppler ultrasonographic screening in detection of fetal hypoxia in pregnant women who smoke during pregnancy.

Methods: 300 pregnancies were included in the prospective research. With regard to a number of smoked cigarettes the pregnant women were divided into three groups: I. the first group (moderate smokers) consisted of 100 pregnant women who smoked up to 15 cigarettes a day during pregnancy; II. the second group (heavy smokers) 100 pregnant women who smoked more than 15 cigarettes a day during pregnancy and III. the third group (control group) 100 pregnant women who did not smoke during pregnancy. All pregnant women underwent Doppler measurements of blood circulation (determination of resistance index – RI) in the umbilical artery, fetal aorta and middle cerebral artery.

Results: The intensity of smoking has influence to circulation because RI in the umbilical artery and fetal aorta is increased and RI is decreased in the middle cerebral artery in pregnant women heavy smokers in comparison to pregnant women moderate smokers.

Conclusion: Doppler sonography of the blood vessels could have an important role in detection of hypoxia and monitoring of the condition of the fetus of pregnant women who smoked during pregnancy.

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Keywords: Doppler, cigarette smoking, fetus, cerebral blood flow, placenta

Introduction

Tobacco smoking is one of the biggest threats to human health which could be prevented and stopped. Tobacco and its ingredients are identified as the main cause of morbidity and mortality of human starting from conception and to late age (1). Smoking has multiple influences on reproduction health. Tobacco smoking during pregnancy is connected to increased number of miscarriages, preterm births, more frequent bleeding during pregnancy, increased percentage of placenta previa and ablation of the placenta, horioamnionitis and preterm rupture of membranes (2). There is also fetal growth retardation,

which results in birth of children with decreased birth weight and length (3). More frequently they have hypoglycemia, disturbed regulation of body temperature, and due to sensitivity of blood vessels, cerebral hemorrhage is more frequent and subsequently neurological defects (4). Children of mothers who smoke have in their early age respiratory and neurological complications more often, they are hospitalized more frequently and placed in the intensive care unit (5). Tobacco smoke contains 4000 chemical ingredients, of which some 30 are linked to different harmful impact to human health. Nicotine from the tobacco smoke influences the blood vessels causing vaso-constriction (due to increased quantity of released catecholamine), and decreases uteri-placental perfusions. In addition to nicotine tobacco smoke contains other vasoactive substances: endothelin, corticotrophin releasing factor, sodium-nitropruside, cadmium and prostaglandin. All these substances

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cause mechanical changes to villous arteries, and that causes functional changes i.e. decrease of blood circulation through fetoplacental unit (6). It has been almost 30 years since the first Doppler analysis of fetoplacental circulation and until today thanks to this method knowledge about circulatory changes in fetuses during physiological and pathological pregnancy is significantly complemented (7). Today it is well known that certain Doppler registered changes of umbilical circulation and some fetal arteries in risky pregnancies are directly linked to high perinatal mortality (20-100%) and morbidity (8). Doppler measurements enable non-invasive estimation of the hypoxemia that is hypoxia (9). Due to big significance attached to harmful impact of smoking tobacco during pregnancy in the world the objective of the study was: 1. Research whether there is impact of smoking tobacco during pregnancy to hemodynamic changes to fetoplacental blood stream, 2. Determine whether these changes are linked to a number of smoked cigarettes during a day and 3. Estimate benefits of Doppler-ultrasound screening in such pregnancies.

Methods

Study design

The prospective research was carried out at the Gynecology-obstetrics clinic UKC Tuzla in the period of 2001-2005 years. Criteria for inclusion into the study were: singleton pregnancy; pregnant women who smoked during pregnancy, without other risk factor or disease which could influence course or outcome of pregnancy; age of pregnant women from 25th to 35th years; exact gestation age of pregnancy (determined according to the last period, which was later confirmed by ultrasound examination). In comparison to the number of smoked cigarettes during a day the examinees were divided into three groups (as recommended by WHO, 1992):

1. The first group (moderate smokers) consisted of 100 pregnant women who smoked up to 15 cigarettes a day during pregnancy
2. The second group (heavy smokers) consisted of 100 pregnant women who smoked more than 15 cigarettes a day during pregnancy
3. The third group (control group), consisted of 100 pregnant women who did not smoke during pregnancy

Procedure

We got information on smoking habits by questionnaire, which is an integral part of the history of disease. Doppler measurement of blood circulation by apparatus Kretz technik, Voluson 530 D with semi convex 3,5 MHz tube was carried out for pregnant women from all groups. Analysis of blood circulation using Doppler effect was done by analyzing sonogram of umbilical artery, fetal aorta and middle cerebral artery. For the analysis of sonogram resistance index – RI (10) was used. Measured mean of resistance index was compared with mean for the respective gestation of the normal pregnancy (11). Pathological index of resistance in the umbilical artery and aorta is defined as increase of mean for two standard deviations (+2SD), and pathological resistance index in middle cerebral artery as decrease of mean values (-2SD), in comparison to gestation.

Statistical analysis

Derived values were processed by standard statistical methods such as calculation of mean and standard deviation. While comparing derived results Student *t-test* was used. Statistical significance of distinction was determined on the risk level less than 5%.

Results

Results of Doppler measurement of resistance index in the umbilical artery (grouped by weeks of pregnancy) are shown in the Table 1. Mean difference of resistance index in the umbilical artery between heavy smokers, moderate smokers and control group, is statistically significant in the gestation age from 32nd to 41st week of pregnancy ($p < 0.05$) (Table 1). For the complete number of moderate smokers we calculated mean resistance index ($= 0.68 \pm 0.05$), in

TABLE 1. Resistance index in umbilical artery

Week of pregnancy	Moderate smokers (N=100) $\bar{x} \pm SD$	Heavy smokers (N=100) $\bar{x} \pm SD$	Control group (N=100) $\bar{x} \pm SD$
28-31	0.78±0.005	0.79±0.01	0.70±0.01
32-35	0.70±0.03	0.76±0.03	0.64±0.03
36-37	0.67±0.04	0.76±0.03	0.64±0.03
38-41	0.66±0.04	0.75±0.02	0.63±0.02

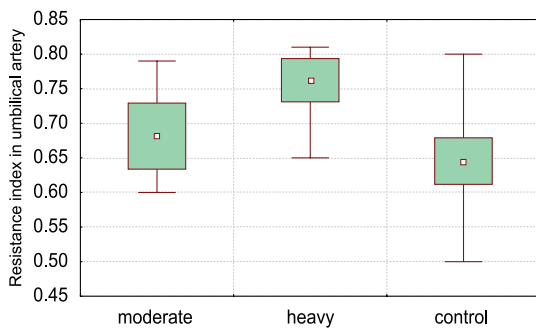


FIGURE 1. Mean, standard deviation, and upper and lower limits of data of resistance index values in umbilical artery in moderate, heavy and non-smokers (control) groups of pregnant women

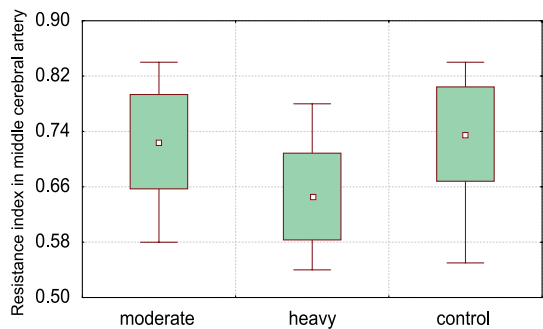


FIGURE 2. Mean values, standard deviations, and upper and lower values of resistance index in middle cerebral artery in moderate, heavy and non-smokers (control) groups of pregnant women

heavy smokers that value is ($=0.76 \pm 0.03$), and in the control group ($=0.64 \pm 0.03$). Comparing the mean and standard deviations of resistance index in the umbilical artery, we found that all three groups are statistically significantly different ($p < 0.05$). The results given of complete series of resistance index in the umbilical artery in moderate smokers, heavy smokers and control group are shown in Figure 2. Figure 1. Graphic display of mean, standard deviation, and upper and lower limits of data of resistance index values in umbilical artery of examinee groups of pregnant women In Table 2. Results of measured and calculated mean of resistance index are shown (for the respective gestation) in fetal aorta. We see from the shown table that mean values of resistance index in fetal aorta in fetuses of heavy smokers in comparison to control group are significantly higher for the gestation ($p < 0.05$). The group of moderate smokers has higher mean values of resistance index in fetal aorta in comparison to control group in gestation age from 28th to 37th week ($p < 0.05$). Group of moderate and heavy smokers statistically significantly differ in gesta-

tion from 36th to 41st week of pregnancy (Table 2). In Table 3. Resistance index values in middle cerebral artery are shown (for certain gestation age). Between the group of heavy smokers fetuses and control group resistance index values differ for gestation age from 32nd to 41st week of pregnancy. Lower values of resistance index in middle cerebral artery in fetuses of moderate smokers in comparison to control group are considerably lower in gestation age from 32nd to 41st week ($p < 0.05$). Comparing the group of heavy and moderate smokers significant difference in resistance index values in middle cerebral artery is present in all examined pregnancy periods, and in the gestation age from 38th to 41st week on the significance level $p < 0.01$ (Table 3). In Figure 2 mean values and standard deviations of resistance index in the middle cerebral artery for complete series of fetuses of moderate smokers, heavy smokers and control group regardless of gestation age are shown. There is significant statistical difference between three groups ($t_1=2.51$; $t_2=1.99$; $t_3=2.05$; $p < 0.05$) (Figure 2). Figure 2. Mean values, standard deviations, and

TABLE 2. Resistance index in fetal aorta

Week of pregnancy	Moderate smokers (N=100) $\bar{x} \pm SD$	Heavy smokers (N=100) $\bar{x} \pm SD$	Control group (N=100) $\bar{x} \pm SD$
28-31	0.87	0.87	0.79
32-35	0.86±0.01	0.87±0.01	0.74±0.01
36-37	0.79±0.02	0.84±0.02	0.77±0.02
38-41	0.79±0.03	0.87±0.01	0.79±0.03

TABLE 3. Resistance index in the middle cerebral artery

Week of pregnancy	Moderate smokers (N=100) $\bar{x} \pm SD$	Heavy smokers (N=100) $\bar{x} \pm SD$	Control group (N=100) $\bar{x} \pm SD$
28-31	0.80±0.01	0.77	0.81±0.01
32-35	0.78±0.03	0.70±0.02	0.77±0.05
36-37	0.74±0.04	0.65±0.01	0.75±0.04
38-41	0.65±0.04	0.57±0.01	0.68±0.06

upper and lower values of resistance index in middle cerebral artery in examined groups of pregnant women.

Discussion

From the first trimester and to the end of pregnancy fetoplacental circulation is developed and functions as low resistance circulation system, in which low vascular resistance allows constant and good vascularization of fetoplacental unit. There is relatively high resistance only in cerebral blood circulation, which is interpreted as protective mechanism, because in such a way there is physiological vascular reserve for vasodilatation in order to provide better circulation for brain in case of hypoxia. Doppler record of blood circulation through umbilical artery (AU) is characteristic for blood vessels of low vascular resistance, with considerable decrease of resistance as the pregnancy progresses, which is consequence of increase of growth of placenta and expansion of its blood vessels, and increase of fetal minute cardiac volume (9). Campbell (12) examined relation between the resistance in umbilical artery and number of small arteries and arterioles in tertiary villis. He determined that in increased resistance in AU this number is significantly reduced because of their obliteration. All pathological conditions which change placenta blood vessels (sclerosis, degeneration, obliteration, thrombosis) influence the diastolic circulation in umbilical arteries, which reflects in increased values of resistance index. Decreased uteroplacental perfusion leads to placental ischemia and it leads to vasoconstriction and obliteration of blood vessels. Smoking during pregnancy is understood as antepartal (maternal) cause of fetal hypoxia and fetoplacental respiratory insufficiency. Carboxyhemoglobinemia and chronic hypoxemia influence in chronic placental hystoarchitecture, vasoconstriction fetoplacental circulation and disturbance of intermedial metabolism (13). Some researchers have examined changes in blood circulation in UA and MCA before and after smoking one cigarette. They did not found acute hemodynamic resistance changes in fetus, indicating significance of chronic tobacco use and chronic changes of small placental blood vessels (14, 15). Sindberg obtained the same results (16) and concluded that after smok-

ing one cigarette there is increase in central circulation, but peripheral resistance is unchanged. Our results indicate that there is significant difference between the group of pregnant moderate smokers and control group, for gestation age from 32nd to 41st week of pregnancy. Smoking of up to 15 cigarettes a day has influence to blood circulation through umbilical artery both in preterm and also term pregnancies, which results in lower perfusion and thereby oxygen and nutrients transport to fetus. In pregnant heavy smokers in comparison to control group increased values of RI in UA are found in gestation age 32nd to 41st week, which is in line with results of other authors (17, 18, 19). Increased resistance in umbilical artery in heavy smokers reflects disturbed vascular tone and sclerosis of placental blood vessels. Increased RI in UA in heavy smokers in comparison to control group indicates possibility for development or existence of intrauterine fetal hypoxia and all consequences it entails. Also there is increased resistance index in heavy smokers in comparison to the group of moderate smokers, which is in line with Ates claims (19) that only in chronic and intensive use of tobacco there is increased vascular resistance in placenta and umbilical cord. Vascular resistance is in irreversible relation with blood circulation through the respective organ (20). The increased resistance in UA indicates compromised fetoplacental bloodstream, which results in a number of complications in fetus: lower birth weight, intrauterine retardation, poorer vitality at birth and etc. Wang and authors (21) published that stagnation in the growth of fetus while smoking during pregnancy is linked to vascular changes in fetoplacental microcirculation. Based on significant increase of RI in umbilical artery in pregnant women, both moderate and heavy smokers in comparison to the control group, we conclude that smoking tobacco during pregnancy influences blood circulation in UA, regardless of pregnancy gestation. Due to disturbed blood circulation fetuses of pregnant smokers are endangered, because they are without an adequate support for normal growth and development. In compromised fetoplacental circulation (in chronic tobacco smoking), in fetal aorta similar like in UA resistance of blood stream is increased, which also has predictive values to eventual out-

come of pregnancy (16). According to our research smoking of up to 15 cigarettes a day has influence on blood circulation through fetal aorta in comparison to the control group it is only in preterm pregnancy. That is, in moderate smokers preterm pregnancy is threatened, while term pregnancies have compensatory ability of the fetus response to hypoxia. A number of studies (22, 23) showed that increased RI in blood circulation in fetal aorta is connected to smoking cigarettes during pregnancy. Comparing the group of heavy smokers and the control group we found increased RI in fetal aorta in all gestation age, and we conclude that in heavy smokers both pre-term and term pregnancies are threatened. Difference between the group of moderate and heavy smokers is significant from 36th to 41st week of pregnancy. The higher vulnerability of term fetuses of heavy smokers in comparison to the control group, and also to the group of moderate smokers indicate that resistance of fetuses to harmful influence of tobacco depends less on gestation age and maturity and more on intensity of smoking. Comparing the mean values of RI for the whole series of studied groups, we found significant difference, and characterized smoking as significant factor which influences blood circulation in fetal structures, which is consistent with the results of other authors (24). The blood circulation in the central nervous system is subject to auto-regulation and depends on the oxygen concentration in the blood coming to brain. Metabolic activity of brain cells is the second important regulation factor of blood circulation. Vascular resistance in the middle cerebral artery (MCA) shows low values in the period from 15th to 20th week and after 36th week of pregnancy, that is periods when brain is most intensely developing (9). In some pathological conditions with increased resistance in fetoplacental circulation there is redistribution of bloodstream in fetus' vessels favoring central nervous system („brain-sparing effect“). In cerebral blood vessels vascular resistance is decreasing and diastolic flow is significantly increased. Decreased values of these indexes are in correlation with fetal hypoxia and acidosis (25). There are number of data in literature on decreased values of RI in MCA in pregnant women who smoke

during pregnancy (15, 17, 26). All authors point out significance of long that is more intensive smoking for occurrence of changes in blood vessels and disturbance of fetoplacental circulation. Our results are consistent with previous reports. The difference of mean of RI in MCA between fetuses of heavy smokers and the control group is significant in all studied gestation age. We conclude that fetuses of heavy smokers, decreased placental blood circulation and possible tissue hypoxia are compensated by centralization of blood. They are vulnerable group and have increased risk for inadequate growth and development regardless of gestation age. Smoking of up to 15 cigarettes a day also influences cerebral blood circulation, because the resistance indexes in fetuses of that group are significantly lower, in comparison to the control group (for each studied gestation period), and they also indicate fetus' ability to adjust to the insufficient support for normal growth and development. Although details of that circulation adjustment and their mechanisms are incomplete, it is possible that when partial oxygen pressure decreases and partial carbon monoxide pressure increases above acute level, the aortic and carotid chemo receptors are activated. That is probably the mechanism which regulates middle vasodilator response for guaranteeing adequate oxygenation of the fetal brain (27). Testing values of RI in MCA between fetuses of pregnant moderate and heavy smokers, we found significantly decreased resistance in heavy smokers, which we explain by stronger and longer disturbances of fetal circulation, as consequence of more intensive toxic activity of tobacco smoke. Significant difference is particularly important for gestation age from 38th to 41st week of pregnancy. In this period of pregnancy (around birth term), fetal intravenous sinusoids are the closest to the mother's blood, so the circulation disturbance i.e. reduction of the flow of oxygen and nutrients is reflected directly on the fetus (28). Greater vulnerability of term fetuses of heavy smokers in comparison to term fetuses of moderate smokers shows that intensity of smoking has big influence because other predisposing factors are excluded, such as prematurity and immaturity. Analysis of the cerebral blood circulation by method of colored Doppler in pregnant women who smoked during pregnancy in our study is

consistent with the results of other authors (27, 29). The comparative analysis of mean values of RI in MCA for the whole series of fetuses of the pregnant moderate smokers, heavy smokers and the control group we found the significant difference, which proves that smoking has influence on the cerebral blood circulation and that it is connected with fetal hemodynamic adjustments.

Conclusions

In this study, using the method of Doppler sonography we found that cigarettes smoking during pregnancy influences feto-placental circulation due to: increased resistance index in u umbilical artery and fetal aorta, and decreased resistance index in

the middle cerebral artery. Smoking interferes with physiological feto-placental circulation and influence fetus' supply by nutrients and oxygen. Negative effect of smoking to blood circulation is connected with intensity of smoking. Considering the good correlation of Doppler changes in the flow of certain fetal blood vessels with unfavorable perinatal outcome in pregnant women who smoked cigarettes during pregnancy, it is a method which contributes significantly to the ability to monitor these pregnancies. Our results which identify cigarettes smoking during pregnancy as risk factor for increased perinatal morbidity and mortality could help in health education of population and taking measures to combat tobacco smoking.

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