PERINATAL JOURNAL

Research Article

Perinatal Journal 2013;21(3):119-123

The effect of maternal smoking during pregnancy on Doppler parameters

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Abstract

Objective: It is suggested that smoking has adverse effects on placenta development by decreasing placental vascularization. Cigarette exposure is associated with intrauterine and perinatal death, preterm labor, ablatio placenta, placenta previa and intrauterine growth retardation. The aim of this study is to investigate the effect of smoking on fetal Doppler ultrasound waveforms and its pathophysiological relationship with fetal birth weight.

Methods: The study was conducted in Gynecology and Obstetrics Department of Dokuz Eylül University between January 13th and 24th April 2011. One hundred nineteen singleton pregnancies were included to the study. Group 1 consisted of 22 patients who were smoking 4-10 cigarettes daily. Group 2 consisted of 97 non-smoker patients before and during their pregnancies. Patients' maternal uterine, fetal umbilical and fetal middle cerebral arteries Doppler measurements were done on 37th week of gestation.

Results: Weight gain in the Group 1 was statistically higher than non-smoking patients. There were statistically significant changes in fetal Doppler measurements, but no difference was found in maternal Doppler waveforms between the two groups. Maternal uterine artery Doppler waveforms were similar in both groups; in fact fetal umbilical artery and middle cerebral artery waveforms were statistically higher for Group 1.

Conclusion: Cigarette contains nicotine, carbon monoxide and thousands of other toxic chemicals. Carbon monoxide reduces the oxygen transfer to the fetus. Chronic tobacco use decreases placental blood flow, hypoxic pathologic environment occurs, and changes appear on fetal Doppler ultrasound waveforms.

Key words: Doppler ultrasound, intrauterine growth retardation, smoking.

Maternal sigara kullamının Doppler ölçümleri üzerine etkisinin araştırılması

Amaç: Sigaranın, plasental vaskülarizasyonu azaltarak, plasental gelişim üzerine olumsuz etki oluşturduğu öne sürülmektedir. Sigara kullanımı, intrauterin ve perinatal ölüm, preterm eylem, ablasyo plasenta, plasenta previa ve intrauterin gelişme geriliği ile ilişkili bulunmuştur. Bu çalışmadaki amacımız sigara kullanımının fetal doğum ağırlığı ile olan patofizyolojik ilişkisi ve fetal Doppler akımları üzerine etkisini incelemektir.

Yöntem: Çalışmaya Dokuz Eylül Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Anabilim Dalı Obstetrik polikliniğine 13 Ocak 2011 - 24 Nisan 2011 tarihleri arasında başvuran toplam 119 tekil gebeliği olan hasta alındı. Sigara kullanım miktarı 4-10/gün olan toplam 22 hasta Grup 1 olarak çalışmaya dahil edildi. Gebeliği sırasında ve gebelikten önce hiç sigara kullanmamış olan 97 hasta ise Grup 2 olarak çalışmaya dahil edildi. Bütün gebelerin 37. gestasyonel haftada maternal uterin arter, umbilikal arter ve orta serebral arter Doppler değerlendirilmesi yapıldı.

Bulgular: Günde 4-10 arasında sigara kullanımı olan gebelerde, hiç kullanmayanlara göre gebelikte kilo alımı anlamlı şekilde daha fazla bulunmuştur. Sigara kullanımının maternal Doppler akımları üzerine etkisi görülmezken, fetal Doppler akımlarındaki etkilenme iki grup arasında anlamlı olarak farklı bulunmuştur. Her iki grup için uterin arter Doppler akımları benzer iken, umbilikal arter ve orta serebral arter Doppler akımlarında Grup 1'de anlamlı olarak daha yüksek değerler kaydedilmiştir.

Sonuç: Sigara; nikotin, karbon monoksit ve binlerce toksik kimyasal bileşik içermektedir. Sigaradaki karbon monoksit, fetuse oksijen transportunu azaltmaktadır. Kronik tütün kullanımı ile plasental kan akımı azalmakta; patolojik hipoksik ortam meydana gelmekte ve fetal Doppler akımlarında değişiklikler oluşmaktadır.

Anahtar sözcükler: Doppler ultrason, intrauterin gelişme geriliği, sigara.

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Received: June 13, 2013; **Accepted:** August 17, 2013

Available online at:
www.perinataljournal.com/20130213004
doi:10.2399/prn.13.0213004
QR (Quick Response) Code:

Introduction

Smoking is a modifiable risk which has an influence on gestational complications and neonatal growth. Smoking rate among women in the reproductive age range is reported as 11.6% for Turkey according to 2008 data.[1] Although this rate seems to be decreasing in recent years, it is reported as 22% in the USA.[2] Only 18-25% of smoker women quit smoking when their pregnancies are confirmed.[1,2]

Many chemical materials in cigarette affect human health negatively.[3] Maternal smoking habit causes gestational complications and affects baby growth negatively.[2,3] Although the relationship of maternal smoking with low birth weight and preterm labor has been shown, the mechanism causing this relationship is still controversial.[4,5] It is suggested that cigarette and the chemical materials in cigarette decrease placental vascularization and have a negative effect on placental growth.[6] The etiology of preterm labor and intrauterine growth retardation is multifactorial; however, it has been shown in the prospective study of Larsen et al. that smoking is the major factor causing the highest decrease in fetal growth percentile curves.[7,8]

Smoking has been found to be associated with increased miscarriage risk, intrauterine and perinatal death, preterm labor, ablation placenta, placenta previa and intrauterine growth retardation. Besides, it has been shown that smoking decreases preeclampsia risk by decreasing thromboxane A2 synthesis. It has been also found that sudden infant mortality rate in smoker pregnants increased 3 times more than non-smoker pregnants.[9]

Cigarette includes nicotine, carbon monoxide and thousands of toxic chemical compounds. These toxic substances in cigarette are associated with gestational complications. Carbon monoxide in cigarette decreases oxygen transfer to fetus, and nicotine causes decreases in uterine blood flow.[9]

Our aim in this study is to investigate the effect of smoking on fetal Doppler ultrasound waveforms and its pathophysiological relationship with fetal birth weight.

Methods

The study included 119 women with singleton pregnancy who applied to Gynecology and Obstetrics Department of Dokuz Eylül University between January 13th and 24th April 2011. The patients with pregnancy-induced hypertensive diseases (preeclampsia, eclampsia), chronic hypertension, gestational diabetes, morbid obesity, drug use, comorbid disease or with multiple pregnancies were excluded from the study. Group 1 included 22 patients who were smoking 4-10 cigarettes daily, and Group 2 included 97 patients who were non-smokers before and during their pregnancies.

Gestational ages of the patients were determined according to the first day of their last menstrual periods. In doubtful cases, gestational week was determined by ultrasonographic examination. Weights, heights and body mass index (BMI; kg/m^2) of all patients were calculated. Maternal and fetal Doppler measurements of all patients were done and recorded on 37 weeks of gestation. Pulsatility index (PI), resistance index (RI) and systole diastole (S/D) flow rates were recorded in maternal uterine artery (UtA) measurements. After bilateral maternal uterine artery measurements were done, half of the total of right and left uterine artery Doppler measurements was calculated and a single value was recorded. Pulsatility index (PI), resistance index (RI) and systole diastole (S/D) flow rates were recorded in fetal umbilical artery (UmbA) measurements. Similarly, middle cerebral artery (MCA) Doppler examination was conducted. Resistance index (RI), pulsatility index (PI), peak systolic velocity (PSV) and systole diastole (S/D) flow rates of middle cerebral artery were examined.

C-reactive protein (CRP; 0.1-8.2 mg/L), total cholesterol (T. chol; 0-200 mg/dl), triglyceride (Trig; 0-200 mg/dl), high density lipoprotein (HDL; 40-60 mg/dl), low density lipoprotein (LDL; 0-130 mg/dl) levels were checked through blood samples collected from the patients at the same period.

The statistical analysis of data was performed by SPSS (Statistical Package for Social Sciences) version 15 (SPSS Inc., Chicago, IL, USA). Continuous variables were given as mean±standard deviation (SD) with the lowest and the highest values in parenthesis. It was found out that all data are non-parametric and Mann-Whitney U and χ^2 tests were used for comparison of both groups. $p<0.05$ was considered statistically significant for all tests.

Results

Comparison of overall characteristics of both groups is given in **Table 1**. Mean age of Group 1 was found to be 29.8±4.2 (range: 23-38) years while it was 29.2±4.8

(range: 19-40) years and it was considered similar for both groups (p=0.546). Statistically no difference was observed between groups in terms of parity (2.1±1.7 and 2.3±1.5; p=0.623). For the comparison of BMI, it was found to be 27.1±2.0 (range: 23.0-30.7) kg/m^2 for Group 1 and 27.2±2.6 (range: 21.1- 30.8) kg/m^2 for Group 2 (p=0.524). Weight gain was found as 17.3±2.8 (range: 13.5-24.0) kg for Group 1 and 13.6±4.5 (range: 4.0-24.0) kg for Group 2. Weight gain was significantly high in pregnants who were smoking 4-10 cigarettes daily compared to non-smokers (p=0.000).

Additionally, statistically no significant difference was found at total cholesterol and LDL levels of groups in terms of lipid parameters (p=0.803 and p=0.240, respectively). On the other hand, HDL level was significantly low for Group 1 (p=0.001). HDL level was recorded as 52.8±7.4 (range: 42.0-68.0) mg/dl for Group 1 and as 62.4±12.9 (range: 41.0-94.0) mg/dl for Group 2. Triglyceride level was found statistically higher in Group 1 compared to Group 2 (p=0.028). Triglyceride level was found as 278.4±97.9 (range: 128.0-428.0) mg/dl for Group 1 one and 236.5±82.9 (range: 117.0-567.0) mg/dl for Group 2. When groups were compared for CRP level, it was found as 6.7±4.2 (range: 2.7-17.1) mg/L for Group 1 while it was 6.11±6.07 (range: 0.5-37.6) mg/L in Group 2. This result was not considered as statistically significant (p=0.258). Compared data of both groups in terms of fetal gender are given in **Table 1.** Fetal gender of Group 1 consisted of 44.5% female and 54.5% male while it was 54.6% female and 45.4% male for Group 2 (p=0.436).

In addition to these results, comparison of maternal and fetal Doppler waveforms for Group 1 and Group 2 is shown in **Table 2.** Statistically no significant difference was found when UtA PI, RI and S/D flows were compared between groups (p=0.432, p=0.317 and p=0.472, respectively). For Group 1, UmbA S/D rate was found as 2.6±0.5 (range: 1.8-3.3), UmbA RI as 0.6±0.1 (range: 0.4-0.7) and UmbA PI as 0.9±0.2 (range: 0.6-1.5). For Group 2, UmbA S/D rate was found as 2.3±0.4 (range: 1.1-3.4), UmbA RI as 0.6±0.1 (range: 0.4-0.7) and UmbA PI as 0.8±0.1 (range: 0.5-1.1). Umbilical artery Doppler flows was found to be statistically significant between two groups (p= 0.010 for UmbA S/D; p=0.008 for UmbA RI; p=0.016 for UmbA PI). UmbA Doppler flows found to be statistically significant are not different clinically. When Doppler MCA values were compared between groups, it was found that MCA S/D was 2.6±0.5 (range: 1.8-3.3), MCA RI was 0.8±0.1 (range: 0.7-0.9), MCA PI was 1.7±0.3 (range: 1.2-2.2) and MCA PSV was 61.8±12.2 (range: 42.3-82.5) for Group 1 while MCA S/D was 4.2±1.2 (range: 2.0-7.4), MCA RI was 0.7±0.1 (range: 0.5-0.9), MCA PI was 1.5±0.3 (range: 0.7-2.1) and MCA PSV was 57.4±12.4 (range: 37.5-99.9) for

Table 1. Data of the pregnants included to the study.

	Group 1 N=22	Group 2 N=97	P*
Age	29.82±4.22	29.16±4.75	0.546
Parity	2.1±1.7	2.3±1.5	0.623
BMI (kg/m^2)	27.10±2.00	27.24±2.64	0.524
Weight gain (kg)	17.29±2.81	13.56±4.53	0.000
T. cholesterol (mg/dl)	246.00±48.78	242.10±38.02	0.803
Triglyceride (mg/dl)	278.36±97.96	236.49±82.91	0.028
HDL (mg/dl)	52.82±7.36	62.41±12.93	0.001
LDL (mg/dl)	148.18±42.68	145.09±61.98	0.240
CRP (mg/L)	6.62±4.22	6.11±6.07	0.258
Newborn weight (g)	3328.18±231.05	3379.12±356.45	0.334
Baby's gender:			
Female (n, %)	10 (%44.5)	53 (%54.6)	0.436
Male (n, %)	12 (%54.5)	44 (%45.4)	

*p<0.05 was considered as significant.

Group 2. Comparison of MCA values showed that S/D, RI and PI values in Group 1 patients were statistically higher than the values of Group 2 patients; however, this difference is not clinically significant (p= 0.004, p=0.002 and p=0.008, respectively). Although MCA PSV rates were found to be higher in Group 1 patients, they were not considered as statistically significant (p=0.076).

Table 2. Comparison of Doppler findings between groups.

	Group 1 N=22	Group 2 N=97	P*
MCA-PSV	61.80±12.18	57.36±12.43	0.076
MCA-RI	0.79±0.06	0.74±0.07	0.002
MCA PI	1.66±0.29	1.45±0.29	0.008
MCA S/D	5.26±1.64	4.20±1.23	0.004
UmbA RI	0.60±0.07	0.55±0.06	0.008
UmbA PI	0.94±0.23	0.82±0.13	0.016
UmbA S/D	2.57±0.48	2.27±0.38	0.010
UtA RI	0.47±0.08	0.45±0.06	0.432
UtA PI	0.73±0.02	0.75±0,22	0.317
UtA S/D	2.06±0.71	2.11±0.79	0.472

*p<0.05 was considered as significant.

Discussion

In this paper, the impact of smoking on maternal and fetal Doppler flows and on fetal birth weight was studied. The relationship of smoking with low fetal birth weight is well-known. It was shown in the study conducted by Rizzo et al. in 2009 that chronic tobacco use does not affect placental volume and placental vascularization at first trimester although it causes decreases in fetal birth weight.[4] No intrauterine growth retardation was detected in any 22 patients included in our study. Unlike contemporary studies, it was proven in our study that smoking 4-10 cigarettes daily has no effect on fetal birth weight. It was shown in the study carried out by Vielwert et al. in 2006 that smoking 15 or more cigarettes daily is associated with decrease in growth rate (p=0.007) and low birth weight (p=0.002) at third trimester, and that fetal birth weight is not affected in pregnancies whose smoking is limited (less than 15).[6]

There are studies in the literature analyzing the relationship of smoking with weight gain and loss. Some studies evaluate weight changes and eating habits of individuals, who are severely smoking-addicted, during smoking cessation periods. In the study performed by Grebenstein in 2013, it was shown that nicotine is not associated with weight gain.[10] In our study, weight gain of smoker pregnants was found to be higher than non-smoker pregnants. Although currently there is no study analyzing the impact of smoking on weight gain during pregnancy, it can be asserted that they increase weight gain by considering psychologically that baby may be affected negatively. Therefore, additional studies are required to analyze these pregnants psychologically. Unlike our study, the study of Newnham et al. performed in 1990 suggested that both maternal and fetal weight gains are lower in smoker pregnants.[11]

Chronic tobacco exposure deteriorates vascularization in placental bed due to toxic chemical compounds. Reduction in intervillous area and decrease in capillary volume were observed in the histological examination of placentas of smoker pregnants. Decreased angiogenesis and increased resistance in placenta affect maternal and fetal Doppler flows.[6,11-13] In the results of our study, it was seen that UmbA and MCA Doppler flows are affected by smoking. Acute effect of nicotine on fetal UmbA flows was analyzed in the study conducted by Bruner and Forouzan in 1991 and diastolic flow loss was shown in UmbA.[12] In 1990, Newnham et al. examined the effects of smoking on pregnants at 24 weeks of gestation. In the result of Newnham et al.'s study, no difference was found between UmbA S/D rates of smoker and non-smoker pregnants. Newnham et al. assert that toxic chemicals in cigarette cause periodical changes on Doppler flows but they do not have chronic effects.[11] It was shown by the study of Rizzo et al. performed in 2009 that smoking during first trimester does not affect fetal Doppler flows.[4] There is no study examining the relationship of smoking with fetal and maternal Doppler flows particularly at third trimester. Therefore, affected UmbA and MCA Doppler flows recorded in our studies provide a new perspective to the literature.

Smoking activates immune system and creates a low systemic inflammatory response, and particularly causes increase in CRP values.[14] Humoral immune system is suppressed in pregnancy; on the other hand, CRP and sedimentation increases are known by acute phase reactants.[15] In our study, no high value was detected for CRP although they were close to upper limit, and it was found that there was no statistically significant difference in CRP levels of smoker pregnants compared to non-smoker pregnants.

Physiological metabolic adaptations occur during pregnancy. In the studies examining effects of pregnancy on lipid and lipid metabolism, it was found out that total cholesterol, triglyceride, LDL and HDL values are increased during pregnancy.[16] In our study, we examined the effect of smoking on lipid profile during pregnancy. It was shown by our study that smoking is significantly associated with decreased HDL levels and increased triglyceride levels. Carbon monoxide and nitrosamines in cigarette creates oxidative stress and it was proven that it is associated with the decrease in HDL levels and vascular endothelial damage.[17]

Conclusion

Consequently, our data show that smoking 4-10 cigarettes daily does not change maternal uterine artery flows while affecting fetal Doppler flows. It was proven by our study that there is no effect on fetal birth weight even though there are changes in fetal Doppler flows when smoking is limited to 4-10 times daily.

Conflicts of Interest: No conflicts declared.

References

1. Bilir N. Dünya'da ve Türkiye'de Tütün Kullanımı Etiyolojisi. Ankara: Hacettepe Üniversitesi Halk Sağlığı Anabilim Dalı; 2008.
2. Batech M, Tonstad S, Job JS, Chinnock R, Oshiro B, Merritt TA, et al. Estimating the impact of smoking cessation during pregnancy: the San Bernardino County experience. J Community Health 2013;4:1-10.
3. Huruba D, Sikolova V, Kunzova S, Kasikova K. The role of smoking in the epigenetic modification of phenotype: the latest knowledge about smoking-induced pathways. [Article in Czech] Cas Lek Cesk 2013;152:31-5.
4. Rizzo G, Capponi A, Pietrolucci ME, Arduini D. Effects of maternal cigarette smoking on placental volume and vascularization measured by 3-dimensional power Doppler ultrasonography at 11+0 to 13+6 weeks of gestation. Am J Obstet Gynecol 2009;200:415.e1-5.
5. Castles A, Adams EK, Melvin CL, Kelsch C, Boulton ML. Effects of smoking during pregnancy: five meta-analyses. Am J Prev Med 1999;16:208-15.
6. Vielwerth SE, Jensen RB, Larsen T, Greisen G. The impact of maternal smoking on fetal and infant growth. Early Hum Dev 2007;83:491-5.
7. Larsen T, Greisen G, Petersen S. Intrauterin growth correlation to postnatal growth-influence of risk factors and complications in pregnancy. Early Hum Dev 1997;47:157-65.
8. Guiot C, Gaglioti P, Oberto M, Piccoli E, Rosato R, Todros T. Is three dimensional power Doppler ultrasound useful in the assessment of placental perfusion in normal and growth restricted pregnancies? Ultrasound Obstet Gynecol 2008;31:171-6.
9. American College of Obstetricians and Gynecologists. ACOG committee opinion: smoking cessation during pregnancy. Obstet Gynecol 2010;116:1241-45.
10. Grebenstein PE, Thompson IE, Rowland NE. The effects of extended intravenous nicotine administration on body weight and meal patterns in male Sprague-Dawley rats. Psychopharmacology 2013;3:43-7.
11. Newnham JP, Patterson L, James I, Reid SE. Effects of maternal cigaratte smoking on ultrasonic measurements of fetal growth and on Doppler flow velocity waveforms. Early Hum Dev 1990;24:23-26.
12. Bruner JP, Forouzan I. Smoking and buccally administered nicotine. Acute effect on uterine and umbilical artery Doppler flow velocity waveforms. J Reprod Med 1991;36:436-40.
13. Campbell S. Placental vasculature as visualized by 3D power Doppler angiography and 3D color Doppler imaging. Ultrasound Obstet Gynecol 2007;309:17-20.
14. Yano Y, Hoshide S, Shimada K, Kario K. The impact of cigarette smoking on 24-hour blood pressure, inflammatory and hemostatic activity, and cardiovascular risk in Japanese hypertensive patients. J Clin Hypertens (Greenwich) 2013;15:234-40.
15. Rico-Rosillo MG, Vega-Robledo GB. Immunological mechanism involved in pregnancy. [Article in Spanish] Ginecol Obstet Mex 2012;80:332-40.
16. Lippi G, Albiero A, Montagnana M. Lipid and lipoprotein profile in physiological pregnancy. Clin Lab 2007;53:173-7.
17. Rao ChS, Subash YE. The effect of chronic tobacco smoking and chewing on the lipid profile. J Clin Diagn Res 2013;7:31-4.