Effects of Maternal Smoking on Placental Structure and Function


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The adverse effect of maternal smoking on fetal birth weight is a well-established fact, but the role of the placenta in this phenomenon is not fully understood. During the last 4 years, we have determined the effects of smoking on placental structure and function in Aberdeen women. Mothers were interviewed and completed a questionnaire at their first antenatal clinic and again at their clinic at the 34th week of gestation. The questionnaires established smoking habit (including brand of cigarette smoked) and also determining factors that might confound the study, such as intake of alcohol and caffeine and exposure to environmental tobacco smoke. Medical records were kept, and only healthy subjects with normal uncomplicated pregnancies were included. Plasma cotinine was estimated from a blood sample taken at the 34th-week clinic (all procedures on this project had prior approval of the local ethics committee), and this was used as an objective measure of smoking habit. At delivery, maternal and fetal blood samples were taken and randomized samples of placental tissue were obtained for morphometry, enzyme and heavy metal analysis, and transport studies. Data are presented as the mean ± standard error of the mean. Birth weights of the children born to smokers were 3421 ± 59 g (n = 56), and to nonsmokers they were 3534 ± 75 g (n = 37).

EXPOSURE TO SMOKING

Fifty-eight percent of the patients recruited declared themselves to be smokers. Patient-declared smoking rate correlated significantly with plasma cotinine level, assayed by high-performance liquid chromatography (n = 86; p < .001, Spearman rank correlation analysis).

Smoking caused a marked induction in the activity of the cytochrome P450-dependent enzyme ethoxyresorufin-O-de-ethylase (EROD). Activity measured as the mean
rate of resorufin production from ethoxyresorufin in placental microsomes was 58.9 ± 12.9 pmol/mg/min in smokers (n = 24) and 5.2 ± 2.8 pmol/mg/min in nonsmokers (n = 14; p < .001, unpaired t test). We did not observe any correlation between quinone reductase activity and smoking (quinone reductase activity has been shown to be induced in vitro in first-trimester placental tissue by benzo[α]pyrene, a major component of cigarette smoke).

Cadmium is present in tobacco and may interfere with zinc metabolism. The cadmium and zinc content of the placental tissue was measured by inductively coupled plasma mass spectrometry. Smokers showed a significantly higher tissue cadmium content than nonsmokers (24 smokers, 24 nonsmokers; p < .03, paired Student's t test), and tissue cadmium content correlated with declared smoking rate (n = 48; p < .01, Spearman rank correlation analysis). There was, however, no correlation with smoking for tissue content of zinc or for placental metallothionein content (measured by the silver saturation method).

MORPHOMETRY

Systematic random samples of placental tissue were taken and fixed by immersion in 10% vol/vol formaldehyde. Fifteen classes of morphometric measurements, including surface areas, volumes, and thicknesses of placental tissue components, were examined, but only three of these showed changes correlated with smoking. The fractional volume of the chorionic villi occupied by stromal tissue was 48 ± 1.7% in nonsmokers (n = 11) and 52 ± 0.8% in smokers (n = 27; p < .05, unpaired Student’s t test), and in the same samples stromal arithmetic mean thickness increased from 12 ± 0.4 μm to 13 ± 0.3 μm (p < .01, unpaired Student’s t test). These two changes partly reflected a reduction in fetal capillary volume associated with smoking. This was 44 ± 6.3 cm³ in mothers who smoked five cigarettes a day or less (n = 17), and 28 ± 2.6 cm³ in mothers who smoked more than five cigarettes a day (n = 13; p < .05, unpaired Student’s t test).

TRANSPORT STUDIES

The surface of the placenta in contact with maternal blood, the microvillous border, may provide the rate-determining step for the maternofetal transport of a number of different nutrients. We examined uptake of zinc and alanine by microvillous border vesicles prepared from our samples of placental tissue. No difference was observed between smokers and nonsmokers regarding zinc uptake, but there was a significant increase in the sodium-dependent component of alanine uptake of smokers (n = 17) compared with nonsmokers (n = 15; p < .01, two-way analysis of variance). Analysis using the Michaelis-Menten equation indicated that this increase was primarily the consequence of a change in maximal uptake rather than an increase in affinity. There was no association with smoking regarding sodium-independent uptake of alanine.
CONCLUSION

EROD activity and morphologic studies clearly indicate that smoking has significant effects on the placenta. The consequences of these effects on fetal development are less easily established. Maternal smoking reduces the fetal capillary volume within the placenta, which could have a detrimental effect on transport function, as it increases the diffusion distance between maternal and fetal blood. We have estimated the diffusive conductance of oxygen in the placenta from our morphometric data. Although our results seemed to show a 13% lower conductance in smokers compared with nonsmokers, this difference was too small to reach statistical significance. It is also possible that the placenta has the capacity to compensate for some of the effects of smoking. Our results show that cadmium derived from cigarette smoke is bound by placental tissues. Work on experimental animals has indicated that by binding cadmium, the placenta can act as a barrier protecting the fetus from environmental sources of this element. The induction of sodium-dependent alanine transport could also represent a change in placental function that would compensate for an adverse maternal environment produced by cigarette smoking. There remains a need to establish better the relative importance of these various factors on fetal growth.

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