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Smoking and Pregnancy

Vol 6 #4, March 1998

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Approximately 15% of women smoke cigarettes during pregnancy (Werler, 1997). Over the years, studies have associated smoking with various adverse pregnancy outcomes; many of these associations have, however, been controversial. This RISK//NEWSLETTER will address the effects of maternal cigarette smoking on pregnancy and on the neonate.

BACKGROUND INFORMATION

Cigarette smoke contains several hundred components. Of these, nicotine and carbon monoxide appear to have the most significant effects on a developing fetus. Nicotine is vasoconstrictive; it constricts the utero-placental arteries, reducing blood flow to the fetus. Women who smoke more than 10 cigarettes a day have more significant reductions in placental perfusion (Philipp et al., 1984). This reduced blood flow results in low birth weight and other adverse fetal outcomes. Carbon monoxide also affects fetal development by reducing the delivery of oxygen to fetal tissues. This elevates fetal carboxyhemoglobin, since carbon monoxide binds to fetal hemoglobin, decreases oxygen binding and results in reduced levels of oxygen and potentially fetal hypoxia.

Confounding factors such as maternal age, previous pregnancy history, other drug and alcohol use, and socioeconomic status make it difficult to determine exact risks associated with maternal smoking. However, the impact of maternal smoking on growth restriction, fertility, miscarriage, placentation, infant mortality, malformations, and developmental delay has been investigated and will be discussed.

GROWTH RESTRICTION

The most recognized effect of maternal smoking is the increased risk for intrauterine growth retardation and low birth weight. Smoking reduces uterine blood flow and consequently slows intrauterine growth. Most studies report a dose-related increased risk for low birth weight and small for gestational age infants of approximately 2-3 fold (Cnattingius et al., 1993). Smoking throughout pregnancy reduces birth weight an average of 200g (Werler, 1997). However, women who stop smoking preconceptionally or during pregnancy, even as late as the eighth month, have infants with birth weights within the range of infants of nonsmokers (Rush and Cassano, 1983). Therefore, women who quit smoking during a pregnancy can significantly reduce the risk of growth retardation.

ADVERSE PREGNANCY OUTCOMES

Fertility

Fertility is typically studied by measuring the time to conception. Smokers exhibit a dose-related decrease in fertility; one study estimates the fertility of light smokers (less than or equal to 20

cigarettes/day) is 75 percent, while the fertility of heavy smokers (greater than 20 cigarettes/day) is around 57% that of nonsmokers (Baird and Wilcox, 1985). Smokers are also two to three times more likely to take more than one year to conceive (Bolumar et al., 1996)

Spontaneous Abortion

It is difficult to evaluate the effects of maternal smoking on miscarriage, primarily because of the inherent difficulty in measuring the general population's rate of spontaneous abortions. While a dose-related association may exist (Harlap and Shiono, 1980), most studies have reported non-significant results. In general, maternal smoking is associated with a slightly increased risk, if any, for spontaneous abortions; this is most apparent in heavy smokers.

Placental Abruptio and Placenta Previa

Maternal smoking increases the risk for abnormal placentation, including abruptio and placenta previa. It is difficult to estimate the exact risk, however, because most studies do not show odds ratios greater than 2, and confounding factors are involved (Ananth et al., 1996). One study suggested the risk for placental abruptio increases by 20% with each additional half pack of cigarettes smoked daily (Raymond and Mills, 1993). Maternal smoking may also slightly increase the risk for placenta previa (odds ratios range from 1.3-2.6); women who smoke 16-20 cigarettes per day increase their risk for placenta previa by 80% (Ananth et al., 1996).

Several potential mechanisms for placental abruptio and placenta previa have been described. The placentas of women who smoke have been shown to be enlarged with an increased surface area and lesions characteristic of underperfusion of the uterus. There is also an increased frequency of hypoxia in smokers (Ananth et al., 1996). Abnormal placentation is associated with an increase in perinatal mortality, which is elevated among smokers compared to non-smokers (Raymond and Mills, 1993).

Perinatal Mortality

Smoking has been associated with a 30% increase in perinatal mortality, largely due to the increases in intrauterine growth retardation, low birth weight, abnormal placentation, and preterm delivery (Werler, 1997). These effects are dose related (Kleinman, 1988). Contrary to our expectations, the perinatal mortality rates among low birth weight infants are lower for smokers than for nonsmokers; the opposite is true for heavy infants. This occurs because of the skewed birth weight distribution in smokers. However, standardizing the distribution by weight demonstrates higher perinatal mortality risks for smokers at all weights (Wilcox, 1993). When women stop smoking, however, the frequency of perinatal mortality becomes almost equivalent to that of nonsmokers (Naeye, 1980).

Preterm Delivery

Several studies have reported a slight increase in the risk for preterm delivery (less than 37 weeks gestation) in women who smoke more than one pack per day (OR 1.2; 95% C.I. 1.1-1.4). The risk for very preterm birth, less than 33 weeks gestation (OR 1.6; 95% C.I. 1.2-2.3) also appears increased (Shiono et al., 1986). Additionally, Shiono et al. found a 2-fold increase in premature rupture of membranes at less than 33 weeks.

Sudden Infant Death

Maternal cigarette smoking may also increase the risk for Sudden Infant Death (SIDS). One study demonstrated a dose-related effect, with a 2-3 fold increased risk for SIDS (before 6 months) and a 3-4 fold increased risk for early SIDS (before 2 months) in the offspring of smokers (Haglund et al., 1990). It is often difficult, however, to separate the effects of cigarette smoke in utero and after birth, making it complicated to measure exact risks.

Congenital Malformations

There has been much debate in the literature concerning the association between maternal smoking and congenital malformations. Every pregnant woman has a 3-4% risk of having a baby with a birth defect. Overall, most studies indicate that maternal smoking does not increase this risk for congenital malformations, despite some studies showing slightly increased risks for cardiac defects, neural tube defects, and vascular disruptions (Werler, 1997).

A theoretical risk exists for vascular defects since smoking has vasoconstrictive effects. The larger studies have suggested a slight, but still non-significant risk for gastroschisis (OR 1.2; 95% C.I. .6-2.2) and no dose-response effect has been established (Werler et al., 1992). However, maternal age is a likely confounding factor since younger women have an increased risk for gastroschisis and more younger women smoke. Controlling for age reduces these risk estimates. Limb reduction defects, which also arise from a vascular disruption, have yielded controversial results as well. Currently, more research is needed to determine whether or not an association exists between vascular defects and maternal smoking.

Recently, an association between smoking and oral clefts has been reported (Hwang et al., 1995; Shaw et al., 1996). Several earlier studies reported an increased risk for oral clefts in the offspring of smokers. Recent studies have examined the interaction between the rare TGF α TaqI allele, maternal smoking, and oral clefting. Two separate studies have reported significantly increased risks for oral clefts in infants with the TGF α allele whose mothers smoked. Shaw et al. reported a 4-fold increased risk for cleft palate alone and a 2-fold increased for cleft lip with or without cleft palate (Shaw et al., 1996). Hwang et al. reported a 5-fold increased risk for cleft palate in infants with the TGF α allele and in utero exposure to smoke (Hwang et al., 1995). However, these associations require more research for confirmation. It is currently premature to counsel patients about these risks.

Cognitive Development

The many confounding factors create difficulty in assessing the impact of exposure to cigarette smoke in utero on cognitive function. It is also difficult to separate the effects of passive exposure to smoke after birth from the in utero effects. Some studies have reported a slight decrease in cognitive function including lower IQ scores, hyperactivity and shorter attention spans. One study compared siblings in which the mother had smoked during one pregnancy and not the other. Exposed siblings had slightly lower spelling, reading and achievement test scores by 3-4%; behavioral problems were also 2% more frequent in the exposed siblings (Naeye and Peters, 1984). Additionally, among the offspring of heavy smokers, the children with hyperactivity and short attention spans had increased hemoglobin levels and lower birth weights. Fetal hypoxia may be the underlying cause. Because of the difficulty in controlling for confounding factors, these associations remain unclear.

Nicotine Replacement Therapy

Recently, various nicotine replacement therapies, including transdermal nicotine (the "patch") and nicotine chewing gum, have gained popularity. The risks of using these therapies during pregnancy have not as yet been elucidated. Theoretically, nicotine replacement therapies are likely to represent less risk to the fetus. Unlike cigarette smoke which contains hundreds of chemicals, including nicotine and carbon monoxide, these therapies contain only nicotine, eliminating any effects of carbon monoxide. Also, the daily dose of nicotine from transdermal therapy or chewing gum is typically less than the dose from smoking one pack of cigarettes. Although it appears as though these therapies would represent less of a risk to the fetus than smoking one pack or more per day, the risks associated with smoking are not completely eliminated (Benowitz, 1991). Research examining the effects of nicotine replacement therapy on pregnancy is needed for confirmation.

Summary

Maternal smoking during pregnancy has been associated with a dose-dependent increase in the risk for low birth weight, IUGR, abnormal placentation, and perinatal mortality. Possible associations have been reported with decreased fertility, oral clefting, SIDS, and impaired cognitive development. These risks, however, have not been confirmed and are therefore less defined. Although decreasing the number of cigarettes smoked per day can decrease these risks, it is important to encourage women to quit smoking during pregnancy in order to completely eliminate these risks.

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