Quantity and Timing of Maternal Prenatal Smoking on Neonatal Body Composition: The Healthy Start Study

Curtis S. Harrod, MPH, PhD[1], Regina M. Reynolds, MD[1,2], Lisa Chasan-Taber, ScD[3], Tasha E. Fingerlin, PhD[1], Deborah H. Glueck, PhD[4], John T. Brinton, MS, PhD[4], and Dana Dabelea, MD, PhD[1]

Objective To examine the dose-dependent and time-specific relationships of prenatal smoking with neonatal body mass, fat mass (FM), fat-free mass (FFM), and FM-to-FFM ratio, as measured by air-displacement plethysmography (PEA POD system).

Study design We analyzed 916 mother–neonate pairs participating in the longitudinal prebirth cohort Healthy Start study. Maternal prenatal smoking information was collected in early, middle, and late pregnancy by self-report. Neonatal body composition was measured with the PEA POD system after delivery. Multiple general linear regression models were adjusted for maternal and neonatal characteristics.

Results Each additional pack of cigarettes smoked during pregnancy was associated with significant decreases in neonatal body mass (adjusted mean difference, −2.8 g; 95% CI, −3.9 to −1.8 g; $P < .001$), FM (−0.7 g; 95% CI, −1.1 to −0.3 g; $P < .001$), and FFM (−2.1 g; 95% CI, −2.9 to −1.3 g; $P < .001$). Neonates exposed to prenatal smoking throughout pregnancy had significantly lower body mass ($P < .001$), FM ($P < .001$), and FFM ($P < .001$) compared with those not exposed to smoking. However, neonates of mothers who smoked only before late pregnancy had no significant differences in body mass ($P = .47$), FM ($P = .43$), or FFM ($P = .59$) compared with unexposed offspring.

Conclusion Exposure to prenatal smoking leads to systematic growth restriction. Smoking cessation before late pregnancy may reduce the consequences of exposure to prenatal smoking on body composition. Follow-up of this cohort is needed to determine the influence of catch-up growth on early-life body composition and the risk of childhood obesity. *(J Pediatr 2014;165:707-12)*.

Between 2000 and 2010, the prevalence of prenatal smoking decreased only slightly, from 13.3% to 12.3%.[1] Exposure to prenatal smoking is associated with numerous adverse outcomes, such as growth restriction,[2-4] medically indicated and spontaneous preterm birth,[5,6] and abortion.[7] There also are associations between intrauterine tobacco exposure and later-life morbidities, including asthma[8] and childhood overweight and obesity.[9-12] Fetal growth restriction leads to compensatory acceleration in the rate of growth early in life, also known as catch-up growth.[13] Offspring that demonstrate postnatal catch-up growth are at increased risk for later chronic diseases.[14,15] It has been theorized that catch-up growth as a result of exposure to prenatal smoking may be responsible for these long-term adverse effects.

The current knowledge base is limited regarding the relationships between the quantity and timing of prenatal smoking and measures of neonatal body composition: fat mass (FM), fat-free mass (FFM), and the FM-to-FFM ratio (F:FFM). In general, previous studies of prenatal smoking[16-21] have analyzed growth restriction using birth weight and indirect measures (eg, skinfold thickness) for neonatal body composition. Only 1 previous study directly measured neonatal body composition,[2] but using a less accurate measure relative to newer body composition systems.[22] Using birth weight or indirect measures of body composition provide be a biased representation of body composition. Understanding how neonatal body composition is affected by prenatal smoking may lead to a better understanding of the fetal programming effects.

The aims of the present study were to assess the dose-dependent and time-specific associations of intrauterine tobacco exposure and neonatal body composition. We hypothesized that exposure to prenatal smoking would be associated with an overall reduction in neonatal body mass, accounted for primarily by a reduction in FFM and a comparable proportionate reduction in FM, resulting in a similar F:FFM. Furthermore, we hypothesized that these relationships would be dose-dependent and time-specific, with growth restriction attributed mainly to smoking during late pregnancy.

BMI	Body mass index
F:FFM	Fat mass to fat-free mass ratio
FFM	Fat-free mass
FM	Fat mass
SGA	Small for gestational age

From the [1]Department of Epidemiology, Colorado School of Public Health; [2]Department of Neonatology, Children's Hospital, Aurora, CO; [3]Department of Epidemiology, University of Massachusetts, Amherst, MA; and [4]Department of Biostatistics, Colorado School of Public Health, Aurora, CO

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Methods

Healthy Start is an ongoing prospective prebirth cohort study in Colorado that enrolls ethnically diverse pregnant women and follows them until delivery. The study was approved by the Colorado Multiple Institutional Review Board. Participants are recruited primarily at the prenatal obstetrics clinics located at the University of Colorado Hospital Outpatient Pavilion within the Anschutz Medical Campus of the University of Colorado Denver. Women with expected multiple births or previous stillbirth, aged <16 years at consent, or at >24 weeks gestation at the time of the baseline research visit were not eligible. Participants who withdrew consent before delivery or if their index pregnancy resulted in fetal death or a very preterm birth (ie, <32 weeks gestation) were excluded from the analyses.

A total of 1092 mother–neonate pairs who were enrolled in the study and delivered between March 19, 2010, and November 1, 2013, were eligible to participate in this study. The women were invited to participate in 3 research visits, with the first visit during early pregnancy (median, 17 weeks), the second visit during mid-pregnancy (median, 27 weeks), and the third visit after delivery (median, 1 day).

Exposure: Prenatal Smoking

Information about prenatal smoking was ascertained through interview-administered questionnaires at each of the 3 prenatal research visits. Data were collected on the quantity and duration of early, mid, and late pregnancy smoking. The duration of weekly exposure to secondhand smoke during these periods was assessed as well. Subjects reported the average number of cigarettes per day generally smoked, and interviewers recorded the value within a prespecified range (ie, <1 cigarette/day, 1-4 cigarettes/day, 5-14 cigarettes/day, 15-24 cigarettes/day, or ≥25 cigarettes/day). For analytic purposes, the center of each range was taken and used to estimate total packs smoked during pregnancy. Duration of prenatal smoking was calculated based on the sum of the differences between dates of: (1) conception and the first prenatal research visit (ie, early pregnancy); (2) the first and second prenatal research visits (ie, mid-pregnancy); and (3) the second prenatal research visit until date of delivery (ie, late pregnancy). The quantity of prenatal smoking reported at a specific research visit was used in conjunction with the interval between visits. For smokers who missed the mid-pregnancy visit (n = 21), the mean number of cigarettes smoked per day during their 2 completed visits was used to estimate the quantity of prenatal smoking, and the observed median time (65 days) from our cohort between the early and mid-pregnancy visits was used to determine the interval.

The associations of total packs smoked during pregnancy and time-specific relationships on neonatal body mass, FM, FFM, and F:FFM were tested separately. Time-specific analyses compared: (1) neonates of mothers who smoked throughout pregnancy relative to nonsmokers; (2) neonates of mothers who smoked before late pregnancy relative to nonsmokers; and (3) in an exploratory analysis, neonates of mothers who smoked throughout pregnancy relative to those who stopped before late pregnancy.

Outcomes: Neonatal Body Mass and Composition

The PEA POD system (COSMED, Rome, Italy) is a 2-compartment module that measures neonatal body mass, FM (ie, adipose tissue), and FFM (ie, water, bone, and nonbone mineral and protein) in both absolute and proportionate terms. The ratio of absolute measures for FM and FFM was used to calculate F:FFM. To measure these variables, the PEA POD system uses a densitometric technique based on air displacement plethysmography.[22] This technique is reliable and valid for measuring neonatal body composition.[22-25]

Trained clinical personnel measured each neonate twice using PEA POD, and then a third time if %FM differed by >2%. Neonatal body composition was generally measured within 24 hours after delivery (median, 1 day). To reduce measurement error for each outcome, the mean of the 2 closest measures was taken.

Covariates

Covariate information was collected on mother–neonate pairs during research visits and through medical record abstraction. Maternal age at delivery was calculated based on offspring delivery date and maternal date of birth. Data on education, gravidity, household income, and race/ethnicity were collected through research questionnaires. Maternal prepregnancy weight from research visits and medical records and maternal height measured at the baseline research visit were used to calculate prepregnancy body mass index (BMI). Weight during pregnancy was measured at the research visits and also abstracted from medical records (median, 12 measurements per participant). Total gestational weight gain was estimated using mixed models predicting gestational weight gain at 39 weeks gestation (ie, the mean gestational age of the cohort). Maternal physical activity levels were ascertained through a validated Pregnancy Physical Activity Questionnaire[26,27] during each research visit. Gestational age at delivery was estimated using ultrasound data, self-reported last menstrual period, or both. Neonatal birth weight and length were obtained during the delivery visit and from medical records. Using US national reference data,[28] small for gestational age (SGA) status was defined as a birth weight below the 10th percentile for gestational age, given the sex of the offspring.

Data Analyses

All statistical analyses were conducted using SAS 9.3 (SAS Institute, Cary, North Carolina). Relationships between prenatal smoking and continuous and categorical maternal and neonatal characteristics were analyzed with the t test and χ^2 test, respectively. Simple linear models were first tested, and multiple linear regression models (SAS PROC GLM) were then constructed. Standard confounders of the relationship between prenatal smoking and offspring growth