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Intrauterine Growth of Infants Exposed to Prenatal Methamphetamine: Results from the Infant Development, Environment, and Lifestyle (IDEAL) Study

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Abstract

Previous studies suggest prenatal methamphetamine (MA) exposure inhibits fetal growth. We examined neonatal growth effects of prenatal MA exposure in a prospective cohort study. After adjusting for covariates, exposed neonates had a higher incidence of being small for gestational age (SGA) than unexposed neonates.

Keywords

drug; amphetamine; antenatal; small for gestational age

Methamphetamine is one of the primary illicit drugs of dependence in the United States, and its use among women continues to be a serious problem. Early studies have reported an association between prenatal MA exposure and decreased newborn growth. A study of 91 mother-infant pairs with positive urine toxicology screens at delivery reported that MA/cocaine-exposed neonates had lower birth weights, smaller head circumferences and were more likely to be small for gestational age (SGA) than comparison neonates.[1] Growth deficits have also been reported in 65 MA-exposed children as old as 4 years.2 These previous reports were limited by small sample size, no adjustment for confounding factors, retrospective analysis1, no comparison group2, and reliance on hospital records1 or maternal

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self-report alone.[2] The Infant Development, Environment, and Lifestyle (IDEAL) study addresses some of these limitations. The IDEAL study is a prospective, longitudinal study of prenatal methamphetamine exposure and child outcome. Preliminary growth data from the IDEAL study after one year of recruitment reported a decreased birth weight and increased incidence of SGA in methamphetamine-exposed newborns.[3] We report the results from the complete data set.

METHODS

Detailed methods for the IDEAL study have been previously reported.[3] Briefly, recruitment occurred over a two-year period at four clinical sites with known high prevalence of methamphetamine use. The study was approved by the Institutional Review Boards at all participating sites. The National Institute on Drug Abuse Certificate of Confidentiality assured confidentiality of maternal drug use but any evidence of child abuse or neglect was reportable to protective services.

During the recruitment period, 34,833 mother-infant pairs were screened. Of the screened population, 26,999 were available to be approached, of which 17,961 (67%) were eligible for the study. Of the eligible population, 21% (3705) mother-infant pairs were consented for participation. Meconium tests were performed on all consented infants. Among the consented, 204 were exposed to methamphetamine and 3,501 were unexposed to methamphetamine. Eight subjects in the exposed group denied use of methamphetamine and were identified as exposed by toxicology screening. Both groups included prenatal alcohol, tobacco and marijuana use, but excluded use of cocaine-only, opiates, LSD, or PCP.

After informed consent was obtained, a maternal interview was conducted using the Lifestyle Interview (LI)4, 5 to determine prenatal drug use and sociodemographic information. Socioeconomic status (SES) was determined using Hollingshead V, an index that ranks SES based on occupation and years of education6. Birth weight and gestational age information was obtained. Alexander algorithm was used to calculate SGA7. Gestational age was determined by the estimated date of confinement for women with good prenatal care. In the few instances where there was a discrepancy between the postnatal gestation assessment and obstetrical dating, the postnatal examination by the subjects' physician trained in these examinations was used. For women with no or inadequate prenatal care, the postnatal examination by the patient's physician was used for gestational dating. Birth length and head circumference were not available for some of the non-exposed subjects and were not included in the analysis.

Meconium was collected from all neonates and screened using an enzyme multiplied immunoassay test (EMIT). Confirmation of drug or metabolite presence was performed by gas chromatography-mass spectrometry (GC/MS). Exposed subjects were identified by maternal report of methamphetamine use during pregnancy and/or GC/MS confirmation. Unexposed subjects were defined as denial of methamphetamine use and a negative EMIT for amphetamine and metabolites.

Initial comparisons of demographic and clinical characteristics by exposure were examined in unadjusted analyses using one-way analysis of variance for continuous variables and chi-square tests for categorical variables. The relationship of exposure and birth weight was examined using multiple linear regression. The relationship between methamphetamine exposure and the incidence of SGA was examined using multivariate logistic regression analysis. Covariates were selected on the basis of conceptual reasons, published literature, and maternal and neonatal characteristics shown in Tables I and II that differed between groups if not highly correlated with other variables. The covariates used in the final analysis

were sex, prenatal care, household income, socioeconomic status (SES), mother's weight gain, mother's age, partner status, race, and prenatal tobacco, alcohol and marijuana use. Cocaine exposure was also analyzed, but was not significant when comparing birth weights of the cocaine and methamphetamine exposed to methamphetamine exposed only, or in the regression models. Additionally, the birth weight analysis also adjusted for gestational age in weeks. Significance was accepted at $p<.05$.

RESULTS

The maternal characteristics are shown in Table I. Mothers in the methamphetamine group were younger and more likely to have a lower SES, no partner, receive Medicaid, and have fewer than 12 years of education than the unexposed group. The methamphetamine group had fewer prenatal care visits and began prenatal care at a later gestational age when compared with mothers unexposed to methamphetamine. Mothers in the methamphetamine group gained more weight than mothers that were unexposed to methamphetamine, and used more tobacco, alcohol, and marijuana during pregnancy than the unexposed mothers. We compared weight gain between mothers in the exposed group who reported methamphetamine use during the first or second trimester only (N=114, 55.9%) versus those also using in the third trimester (N=82, 40.2%). Those who quit using methamphetamine earlier in gestation gained 10.4 pounds more than those who continued to use throughout pregnancy ($P<.0001$). We did not find potentiation between methamphetamine exposure and maternal smoking. There was a low incidence of maternal complications that are known to cause SGA in the exposed group, with only three diagnosed with insulin-dependent diabetes, six with chronic hypertension, and 10 with preeclampsia. None of the mothers with diabetes or chronic hypertension delivered SGA infants. For those diagnosed with preeclampsia, two of the 10 delivered SGA infants.

The infants in the methamphetamine-exposed group were born slightly earlier than the unexposed group, but both groups had a term mean gestational age (Table II). Eight of the methamphetamine exposed newborns (8.8%) were less than 36 weeks' gestation and 130 were premature in the unexposed group (3.7%). Though no differences were found in birth weight (3313.35±36.95 vs. 3367.69±7.57 grams; mean±SEM exposed vs. comparison), the incidence of SGA was higher ($p<0.001$) in the exposed group than the unexposed group. After adjusting for covariates, the exposed group had an increased likelihood of being born SGA (OR=2.05, CI 1.24-3.37). There were no differences observed in birth weigh ($p=0.154$) after adjusting for covariates.

DISCUSSION

The IDEAL study is a prospective cohort study exploring the effects of prenatal methamphetamine exposure on fetal growth. Consistent with our previously reported findings in the partial cohort[3], we found that after adjusting for covariates, including prenatal drug use and lower SES, methamphetamine-exposed neonates had an increased incidence of being born SGA. In contrast to our previously reported findings, no differences in birthweight were noted after adjusting for covariates. The findings of increased risk of being born SGA are consistent with previous studies on newborns exposed to methamphetamine.[1, 2]

There are several proposed mechanisms for how methamphetamine causes fetal growth restriction including maternal vasoconstriction leading to restricted nutrient delivery to the fetus and fetal vasoconstriction and hypertension leading to decreased fetal oxyhemoglobin saturation.[8, 9] Of note, maternal weight gain was increased in the methamphetamine using mothers which likely reflects that many women try to abstain from methamphetamine once

they learn of their pregnancy. As methamphetamine is a known anorectic, overeating is often a consequence of abstaining from methamphetamine. Mothers in the exposed group who quit using methamphetamine in the first and second trimesters gained approximately 10 more pounds than those who used throughout pregnancy. These findings suggest the anorexic effects of methamphetamine are limited to continuous use and there may be a rebound in weight gain if mothers quit. Limitations of this study include that the significance of the timing and dosage of methamphetamine exposure during gestation on fetal growth was not explored and birth length, head circumference and obstetric complications were not available for the non-exposed subjects.

In summary, prenatal methamphetamine use is associated with fetal growth restriction. The increased incidence of SGA may have serious long term health risks in the exposed children including coronary heart disease, stroke, diabetes, and hypertension as adults.[10] Longitudinal studies will determine if these exposed infants are at increased risk for future growth abnormalities or other medical problems associated with being born SGA.

Abbreviations

MA	Methamphetamine
SGA	small for gestational age
IDEAL	Infant, Development, Environment and Lifestyle
LI	Lifestyle Interview
EMIT	Enzyme Multiplied Immunoassay Test
GC/MS	Gas Chromatography-mass Spectrometry
SES	Socioeconomic Status

Reference List

1. Oro AS, Dixon SD. Perinatal cocaine and methamphetamine exposure: maternal and neonatal correlates. J Pediatr Oct;1987 111:571–8. [PubMed: 3655989]
2. Eriksson M, Jonsson B, Steneroth G, Zetterstrom R. Cross-sectional growth of children whose mothers abused amphetamines during pregnancy. Acta Paediatr Jun;1994 83:612–7. [PubMed: 7919758]
3. Smith LM, LaGasse LL, Derauf C, Grant P, Shah R, Arria A, et al. The infant development, environment, and lifestyle study: effects of prenatal methamphetamine exposure, polydrug exposure, and poverty on intrauterine growth. Pediatrics Sep;2006 118:1149–56. [PubMed: 16951010]
4. Bauer CR, Shankaran S, Bada HS, Lester B, Wright LL, Krause-Steinrauf H, et al. The Maternal Lifestyle Study: drug exposure during pregnancy and short-term maternal outcomes. Am J Obstet Gynecol Mar;2002 186:487–95. [PubMed: 11904612]
5. Lester BM, Tronick EZ, LaGasse L, Seifer R, Bauer CR, Shankaran S, et al. The maternal lifestyle study: effects of substance exposure during pregnancy on neurodevelopmental outcome in 1-month-old infants. Pediatrics Dec;2002 110:1182–92. [PubMed: 12456917]
6. Hollingshead, AB. Four factor index of social status. Department of Sociology, Yale University; New Haven, CT: 2009.
7. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. Obstet Gynecol Feb;1996 87:163–8. [PubMed: 8559516]
8. Burchfield DJ, Lucas VW, Abrams RM, Miller RL, DeVane CL. Disposition and pharmacodynamics of methamphetamine in pregnant sheep. JAMA Apr 17;1991 265:1968–73. [PubMed: 2008026]

9. Stek AM, Baker RS, Fisher BK, Lang U, Clark KE. Fetal responses to maternal and fetal methamphetamine administration in sheep. Am J Obstet Gynecol Nov;1995 173:1592–8. [PubMed: 7503206]

10. Barker DJ, Osmond C, Simmonds SJ, Wield GA. The relation of small head circumference and thinness at birth to death from cardiovascular disease in adult life. BMJ Feb 13;1993 306:422–6. [PubMed: 8461722]

Table 1

Maternal Characteristics.

	Number (Percent) or Mean (STD)		
	Exposed (n=204)	**Unexposed (n=3,501)**	**P-value**
Race			<0.001
White	77 (37.7%)	1,615 (46.5%)	
Hispanic	47 (23.0%)	518 (14.9%)	
Pacific Islander	37 (18.1%)	337 (9.7%)	
Asian	28 (13.7%)	390 (11.2%)	
Black	9 (4.4%)	524 (15.1%)	
Other	6 (2.9%)	90 (2.6%)	
Maternal Age	25.8 (5.6)	26.9 (5.9)	0.010
Low SES (Hollingshead V)	68 (33.5%)	245 (7.0%)	<0.001
SES Hollingshead Social Position Index	24.7 (9.1)	37.6 (12.6)	<0.001
Income < $10,000	68 (37.6%)	387 (11.5%)	<0.001
No partner	115 (56.4%)	915 (26.2%)	<0.001
Medicaid recipient	185 (93.9%)	1781 (51.6%)	<0.001
Education < 12 years	93 (45.8%)	547 (15.7%)	<0.001
Prenatal care visits < 5	33 (17.5%)	66 (1.9%)	<0.001
GA 1st prenatal visit (wks)	14.6 (8.1)	9.3 (5.4)	<0.001
Pregnancy weight Gain (lbs)	41.9 (19.9)	33.7 (15.2)	<0.001
Maternal tobacco use	163 (79.9%)	706 (20.2%)	<0.001
Maternal alcohol use	78 (38.2%)	733 (20.9%)	<0.001
Maternal marijuana use	68(33.3%)	157 (4.5%)	<0.001

Table 2

Neonatal Characteristics.

	Number (Percent) or Mean (STD)		
	Exposed (n = 204)	**Unexposed (n= 3,501)**	**P-value**
Gestational age (wks)	38.6 (2.3)	39.1 (1.9)	<0.001
Male	110 (53.9%)	1,791 (51.2%)	0.452
Birth Weight (g)	3179.5 (608.7)	3368.8 (557.4)	0.154*
Small for gestational age (%)	35 (17.3)%	310 (8.9)%	0.005*

* P-values adjusted for covariates.