Maternal Cocaine Use During Pregnancy: Effect on the Newborn Infant

Anthony J. Hadeed, MD, and Sharon R. Siegel, MD

From the Department of Pediatrics, University of Southern California, School of Medicine, Los Angeles, California

ABSTRACT. The newborn infants of 56 mothers who used cocaine were prospectively studied in to determine the effects of cocaine. There were no differences with respect to maternal preeclampsia or cesarean section rate. Meconium-stained amniotic fluid was increased (10 of 56 cases [17.8%]) compared with the control group (3 of 56 cases [5.3%]) (χ² = 4.2, P < .05). Fetal distress recorded with fetal monitoring and Apgar scores at 1 and 5 minutes were similar. The weight, length, and head circumference growth curves of the infants born to cocaine-using mothers were shifted below the 25th percentile. Microcephaly was present in 12 of 56 (21.4%) infants whose mothers used cocaine during pregnancy (χ² = 5.96, P < .01), and 15 of 56 (26.7%) had intrauterine growth retardation (χ² = 9.53, P < .01) compared with the control infants (2 of 5 [3.5%] and 3 of 56 [5.3%], respectively). There was no increase in teratogenicity. Neither narcotic withdrawal symptoms nor illness could distinguish the infants born of cocaine-using mothers from the control infants. In conclusion, cocaine use during pregnancy results in newborn infants with growth retardation and microcephaly. Pediatrics 1989;84:205–210; cocaine, intrauterine growth retardation, pregnancy, microcephaly.

Cocaine, derived from the Erythroxylon plants in South America is imported as a salt and sold illegally in the United States in white powder form as “snow,” “coke,” “gold dust,” and “lady” and varies greatly in purity. By 1985, approximately 25 million Americans had used cocaine and about 5 million use it regularly. Cocaine use is increasing among women. In Detroit and its suburbs, an estimated 10% of pregnant women used cocaine (Pediatric News, February 1986, p 64).

The complications of cocaine usually occur within 12 hours. Abruptio placenta and still birth have been reported immediately after intravenous injection and intranasal administration of cocaine. Bingol et al found a symmetrical intrauterine growth retardation and congenital malformations involving bony skull defects in the babies born to mothers using cocaine during pregnancy, whereas others found no evidence of intrauterine growth retardation or teratogenicity.

The purpose of this prospective study was to further elucidate the morbidity and mortality to the offspring of mothers who used cocaine during pregnancy.

METHODS

Study Site and Population

This prospective study took place between 1984 and 1987 at Hollywood Presbyterian Medical Center in Los Angeles, California. The medical center provides care for an ethnically and economically diverse population. The pregnant women receiving government subsidized medical care were enrolled in the study before giving birth. Patient histories were obtained by the obstetrical nurses and pediatric housestaff.

Laboratory Procedures

Urine samples were obtained immediately after birth from the newborn infants of these mothers. Urine toxicologic assays were performed for cocaine, opiates, methadone, quinine, barbiturates, phencyclidine, and tricyclic drugs.

Study Groups

The infants with urine toxicologic screen findings positive for only cocaine, and no history of other drug and alcohol abuse were called group 1 (n = 56). The infants with a similar maternal history, but negative urine toxicologic screen results and no

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history of drug and alcohol abuse were called control group 2 (n = 56). Those infants with a urine toxicologic screen positive for other drugs (with or without cocaine) or alcohol were excluded. The study groups were enrolled concurrently during the 3-year period.

The gestational age was carefully assessed from the history of the last menstrual period and Ballard score\(^6\) by the pediatric houseofficer under the supervision of the neonatologist. The physicians were unaware of which infants were in the cocaine or control groups at the time of evaluation.

Prematurity was defined as less than 37 gestational weeks. Infants were weighed on a Kentec scale immediately after birth. Maximal occipitofrontal head circumference and crown to heel length were determined. All measurements were plotted on a standard Colorado intrauterine growth chart.\(^{10,11}\) Infants with a head circumference less than the 10th percentile for gestational age were classified as having microcephaly.

Infants with weights less than the 10th percentile were classified as having intrauterine growth retardation. All infants with intrauterine growth retardation were clinically assessed for stigmas of dysmorphism and intrauterine viral, protozoan, and spirochetal infections. Those suspected of having infection underwent the following tests: IgM, TORCH titers, urine cytologic determination, and roentgenographic examination of skull and long bones; those suspected of having chromosome aberrations received a genetic consultation and chromosome analysis. A maternal history was obtained for hypertension, chronic kidney, heart, and endocrine diseases and alcohol use. The infants with these documented causes for intrauterine growth retardation other than cocaine were excluded. All of the infants were observed daily after birth by neonatal nurses and pediatric housestaff unaware of the infants background; observations were recorded on neonatal abstinence syndrome score sheets, which provide a systematic assessment of central nervous system characteristics exhibited during narcotic withdrawal.\(^{12}\)

Statistics were performed by Student’s t test and \(\chi^2\) analysis.

RESULTS

The maternal backgrounds of the cocaine (n = 56) and control (n = 56) groups are shown in Table 1. There were no differences in age, parity, cigarette smoking, socioeconomic status, or ethnicity between the two groups.

Mothers who used cocaine had an increased history and obstetrical record documentation of spontaneous abortions and abruptio placentas associated with three stillborn infants compared with the control group (Table 2). Mothers who used cocaine during pregnancy had an increased number of instances of meconium-stained amniotic fluid compared with the control group. There was no statistically significant difference between groups for preeclampsia or cesarean section rate or for fetal distress documented with fetal monitoring (severe variable or late deceleration pattern) or Apgar scores at 1 and 5 minutes.

The full-term newborn infants (±37 weeks’ gestation) born to mothers taking cocaine were smaller with respect to weight, length, and head circumference than the control infants (Table 3). Intrauterine growth retardation (<10th percentile for gestational age) and microcephaly <10th percentile for gestational age) were present more often in preterm and full-term infants born to cocaine-using mothers than in the control group (Table 3). There were no statistically significant differences between the groups with respect to congenital malformations or prematurity rate.

In Fig 1, the weight distribution of the group 1 infants is shifted, with 27 of 56 (48%) infants below the 26th percentile. In Fig 2, the head circumference distribution of group 1 infants is shifted, with 35 of 56 (62.5%) below the 26th percentile.

During routine newborn care by the pediatric housestaff under the supervision of the neonatologist, both groups of infants had similar symptoms and illnesses (Table 4). There was no statistically significant difference between groups with respect to respiratory distress syndrome, a disease of prematurity.

DISCUSSION

Cocaine is absorbed through the mucous membranes. After entrance into the circulation, it is rapidly metabolized through plasma and hepatic cholinesterases, with a plasma half-life of 4 to 6 hours.\(^{13}\) Its metabolites can be found in the urine for as long as a week after its use. Cocaine is a highly water and lipid soluble, low molecular weight substance, 8.7% protein bound, passing the placenta by simple diffusion.\(^1\) It is a weak base with a \(pK_a\) of 5.6 and may concentrate in the fetus because of the lower pH of fetal blood. Because the plasma cholinesterase concentration is much less in the fetus and decreases during pregnancy, the metabolism would be slower, and both the pregnant woman and fetus may be more sensitive to smaller doses of cocaine.\(^{14}\) Cocaine is found in low concentrations in fetal tissues after administration to pregnant mice.\(^{15}\)
TABLE 1. Maternal Background*

<table>
<thead>
<tr>
<th></th>
<th>Cocaine Users (n = 56)</th>
<th>Control Women (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean y ± SD)</td>
<td>25.8 ± 4.7</td>
<td>24.7 ± 4.9</td>
</tr>
<tr>
<td>Primiparous (No.)</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Multiparous (No.)</td>
<td>50</td>
<td>43</td>
</tr>
<tr>
<td>Smoke ≥½ pkg of cigarettes/d (No.)</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Race/ethnicity (No.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>29</td>
<td>31</td>
</tr>
<tr>
<td>White</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Hispanic</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Low income (No.)</td>
<td>56</td>
<td>56</td>
</tr>
</tbody>
</table>

* No differences between groups were statistically significant.

TABLE 2. Intrapartum/Postpartum Period*

<table>
<thead>
<tr>
<th></th>
<th>No. (%) of Cocaine Users (n = 56)</th>
<th>No. (%) of Control Group (n = 56)</th>
<th>χ² Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>1 (&lt;1)</td>
<td>1 (&lt;1)</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Total spontaneous abortion</td>
<td>14 (25)</td>
<td>4 (7.1)</td>
<td>6.6</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Meconium-stained amniotic fluid</td>
<td>10 (17.8)</td>
<td>3 (5.3)</td>
<td>4.2</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Abruptio placenta</td>
<td>6 (10.7)</td>
<td>1 (1.7)</td>
<td>3.8</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Severe variable, late deceleration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal distress</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean section/vaginal delivery</td>
<td>7 (12.5)</td>
<td>10 (17.8)</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Apgar score ≥4 at 1 min</td>
<td>3</td>
<td>2</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Apgar score ≤6 at 5 min</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE 3. Newborn Growth and Development

<table>
<thead>
<tr>
<th></th>
<th>Cocaine Group</th>
<th>Control Group</th>
<th>E Value</th>
<th>P Value</th>
<th>χ² Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls (No.)</td>
<td>32</td>
<td>29</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Infants ≥37 wk gestational age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (mean g ± SD)</td>
<td>2795 ± 448</td>
<td>3305 ± 345</td>
<td>5.93</td>
<td>&lt;.001*</td>
<td></td>
</tr>
<tr>
<td>Length (mean cm ± SD)</td>
<td>45 ± 2.1</td>
<td>50 ± 1.5</td>
<td>5.26</td>
<td>&lt;.001*</td>
<td></td>
</tr>
<tr>
<td>Head circumference (mean cm ± SD)</td>
<td>32 ± 1.3</td>
<td>34 ± 1.1</td>
<td>5.6</td>
<td>&lt;.001*</td>
<td></td>
</tr>
<tr>
<td>Gestational age ≤36 wk (No.)</td>
<td>13</td>
<td>8</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Head circumference &lt;10th percentile (No.)</td>
<td>12</td>
<td>2</td>
<td>&lt;.01†</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>Wt &lt;10th percentile (No.)</td>
<td>15</td>
<td>3</td>
<td>&lt;.01†</td>
<td>9.53</td>
<td></td>
</tr>
<tr>
<td>Congenital malformations (No.)</td>
<td>0</td>
<td>0</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

* Student's t test.
† x² test.

The mothers in each group were similar with respect to age and background. Approximately one half of the women were black, one fourth white, and one fourth Hispanic in the two groups (Table 1).

The mothers using cocaine (Table 2) had an increased history and documentation of abortions. The reason for the increased abortion rate is not known. The quantity and quality of cocaine and acute intoxication needs to be investigated at various time intervals during fetal development. The spontaneous abortions occurred between 10 and 20 weeks' gestation.

Historically, there was an increased number of abruptio placenta, resulting in three stillborn infants (Table 2). Abruptio placenta and stillbirths have been reported immediately after intravenous and intranasal administration of cocaine.\(^5^,^6\) Cocaine blocks uptake of catecholamines at the adrenergic nerve endings, producing sensitization of tissue to the action of catecholamines. There is an increased cardiac rate and body temperature and elevation in
blood pressure from sympathetically mediated tachycardia and vasoconstriction. The vasoconstriction at the uteroplacental complex and hypertension and tachycardia in the mother may contribute to the abruptio placenta.

Although cocaine causes hypertension and vasoconstriction, it did not induce preeclampsia during the pregnancy. There was an increased number of instances of meconium-stained amniotic fluid (Table 2) at birth in the infants of cocaine-using mothers but not an increased number of cases of pre- or postpartum meconium aspiration syndrome (Table 4) compared with the control infants. The increased sympathetic tone in the group 1 infants may result in intestinal release of meconium in utero. Cocaine given to pregnant ewes has produced dose-dependent increases in maternal blood pressure, decreases in uterine blood flow, and increased vascular resistance, resulting in marked fetal hypoxia, hypertension, and tachycardia. However, vasoconstriction of the uteroplacental complex in humans may not create hypoxia-induced meconium aspiration in utero or at the time of delivery. The similar number of fetal distress patterns with fetal monitoring and Apgar scores at 1 and 5 minutes in groups 1 and 2 suggest that hypoxia was not present more often during labor and delivery in the infants of cocaine-using mothers. Meconium-stained amniotic fluid and meconium aspiration syndrome has been reported in infants born to mothers addicted to such narcotics as methadone and heroin. Cocaine did not increase the need for cesarean section.

Growth and development (Table 3, Figs 1 and 2) are affected by maternal cocaine use during pregnancy. The mean weight (P < .001), length (P < .001), and head circumference (P < .001) were smaller in the group 1 infants. The distribution of the weight and head circumference was shifted to the lower percentiles in the group 1 compared with the group 2 infants (Figs 1 and 2). Microcephaly (21.4%) and intrauterine growth retardation (20.7%) were both present significantly (P < .01) more often in the infants born to cocaine-using mothers than the control infants. Growth has been shown to be most limited in infants who are also microcephalic at birth. Maternal cigarette smoking affects fetal growth. There were no differences in the amount of smoking between groups 1 and 2 (Table 1). Cocaine is anorectic in

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**TABLE 4. Newborn Illnesses**

<table>
<thead>
<tr>
<th>Illness</th>
<th>Cocaine Group (n = 56)</th>
<th>Control Group (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jitteriness</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Meconium aspiration syndrome</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>6†</td>
<td>3‡</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hypotonia</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Poor feeding</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Infection</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

* Results are numbers of infants. No differences between groups were statistically significant.
† 13 infants were premature.
‡ 8 infants were premature.
chronic users and results in weight loss. The pregnant women in this study used cocaine or crack predominantly by smoking or intranasally during the entire pregnancy. Maternal weight gain, not known in this study, should also be evaluated as a possible mechanism contributing to infant growth retardation.

Studies of children with disruption of head and/or somatic growth due to various causes may have serious neurobehavioral impairments. Harvey et al. showed that term intrauterine growth-retarded babies with slow head growth in utero, starting before 26 weeks and continuing until near term, had delayed cognitive index, motor, perceptual performance, and motor ability at 3 to 7 years of age. Chasnoff et al. used the Brazelton Neonatal Behavioral Assessment Scale to test infants exposed to cocaine in utero. They found that the infants had significant depression of interactive behavior and a poor organizational response to environmental stimuli (state organization). Our study infants did not receive a neurobehavioral assessment by a neurologist or developmentalist. The neurobehavior of our group 1 infants receiving medical care by the neonatologist, pediatric housestaff, and neonatal nurses was not notably different from the control infants during their newborn hospital stay after birth.

Although there were more premature infants \( \leq 36 \) gestational weeks in the cocaine group vs the control group (23% compared with 14.2%) (Table 3), the difference was not statistically significant. This is in agreement with previous studies. Cocaine was not found to have teratogenic effects in this study (Table 3) as previously shown by Madden et al. Bingel et al. found an increased malformation rate in the form of bony skull defects, studying a cocaine and control group (50 vs 340 infants, respectively). An animal study in gravid mice showed that nontoxic doses of cocaine were teratogenic. Further studies using large, closely matched groups will provide more information about any teratogenicity associated with cocaine.

Approximately 85% of narcotic-addicted infants born to mothers using such drugs as heroin, methadone, morphine, and propoxyphene will have central nervous system symptoms and signs listed on a neonatal abstinence syndrome score sheet. Approximately 10% of our group 1 and group 2 infants (Table 4) had unexplained jitteriness that required no treatment and could have been due to neurologic immaturity.

Intrauterine growth-retarded infants have had higher mortality rates. Recently, in utero cocaine exposure has been linked to an increased incidence of sudden infant death syndrome. There was no increase in mortality in our group 1 infants in the early newborn period.

**SUMMARY AND IMPLICATIONS**

Results of this study indicate that cocaine use during pregnancy can cause newborn infant growth retardation and microcephaly. Historically, there was fetal mortality from spontaneous abortion and abruptio placenta. The neurobehavioral sequelae, growth pattern as a result of the intrauterine growth retardation and microcephaly, and future mortality of infants born to cocaine-using mothers requires long-term follow-up. These data suggest that it would be worthwhile to screen an infant born with intrauterine growth retardation and microcephaly for cocaine.

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J Pediatr. 1982;101:969–977

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For details, contact:
G.E. Moro, MD
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Telephone: (02) 7523251/2
Fax (02) 7523299

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