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Findings in Newborns of Cocaine-Abusing Mothers

REFERENCE: Rogers, C., Hall, J., and Muto, J., **"Findings in Newborns of Cocaine-Abusing Mothers,"** *Journal of Forensic Sciences*, JFSCA, Vol. 36, No. 4, July 1991, pp. 1074–1078.

ABSTRACT: Cocaine has recently been shown to affect the outcome of pregnancy when taken by pregnant women. The authors measured fetal concentrations of cocaine and benzoylecgonine and reviewed autopsy and historical data for 62 successive infants who died at less than two days of age and were seen at the Los Angeles County Office of the Chief Medical Examiner-Coroner. Of 43 infants without an obvious cause of death at autopsy, cocaine or benzoylecgonine or both were present in 40%. None of the parameters studied predicted which infants would show cocaine or benzoylecgonine. We conclude that cocaine and benzoylecgonine concentrations should be measured on all infants who die at less than two days of age when the cause of death is not evident at gross autopsy.

KEYWORDS: pathology and biology, cocaine, infants, pregnancy, fetuses

In recent years, a decrease in the price of cocaine in Los Angeles County has led to its widespread availability. This has resulted in a sharp increase in cocaine-related morbidity and, inevitably, in an increase in the number of pregnant women using cocaine.

The effects of cocaine in pregnancy include an increased incidence of stillbirth related to abruptio placentae and placenta previa [*1–3*]; a reduction in birth weight, birth length, and Apgar scores [*2,4*]; and an increase in birth defects [*1,5–7*], including genitourinary tract malformations, ileal atresia, and perinatal cerebral infarction. In animal trials, cocaine causes increased uterine vascular resistance and fetal hypoxemia [*8*]. Finally, cocaine use in pregnancy reportedly causes behavioral changes in neonates [*5*]. The long-term effects of maternal cocaine abuse on infants are unknown, as most studies were published after 1986.

In the forensic scientist's practice, unexpected fetal death is common. The authors of this paper examined medical history and autopsy data from 62 successive cases of infant death to determine whether there were differences between those with cocaine present and those without cocaine. In addition, we measured the concentrations of cocaine and benzoylecgonine in the infants.

Methods

The infants autopsied at the Los Angeles County Office of the Chief Medical Examiner-Coroner were included in the study if they were either stillborn or had died at less than

Presented at the 42nd Annual Meeting of the American Academy of Forensic Sciences, Cincinnati, OH, 19–24 Feb. 1990. Received for publication 5 June 1990; revised manuscript received 29 Oct. 1990; accepted for publication 30 Oct. 1990.

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two days of age. Infants were excluded from study if the cause of death was evident at gross or microscopic autopsy. In a one-year period, 62 successive infants were studied. Four infants with congenital anomalies, 6 with congenital infections, and 9 with maternal or fetal trauma were excluded, leaving 43 infants for whom the cause of death could not be determined at autopsy.

For the remaining infants, the interval between death or stillbirth and autopsy varied from 14 to 423 h. In most cases, a detailed maternal history and the placenta were not available for study. Available tissues were taken for toxicology study: these included blood (29 cases), liver (7 cases), brain (5 cases), spleen (1 case), and kidney (1 case) tissue. The blood specimens were preserved with sodium fluoride.

Blood or tissue homogenates were screened by radioimmunoassay (cocaine metabolite kit, Diagnostic Products Corp.) for cocaine (sensitivity, 0.03 μg/mL) and benzoylecgonine (sensitivity, 0.05 μg/mL) and were considered positive for study purposes if either cocaine or benzoylecgonine were present. An initial 1:2 dilution of blood or tissue homogenate was made with a 3.5% zinc sulfate precipitating reagent (15 g of zinc sulfate, 2.5 g of 5-sulfosalicylic acid, 200 mL of water, and methanol to make 500 mL). One hundred microlitres of precipitant was used for the assay, and positive cases were compared with a 0.05-μg/mL cocaine standard.

All positive results were confirmed and quantitated by gas chromatography/mass spectrometry (GC/MS). Two millilitres of sample were mixed with deuterated cocaine and benzoylecgonine, buffered with a phosphate buffer, and eluted through XAD-2 solid-phase extraction columns. The extracts were derivatized with *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide and injected into a gas chromatograph/mass spectrometer equipped with a 15-m DB-5 column.

In most cases, the fetal material was also examined for opiates and phencyclidine by radioimmunoassay, with GC/MS confirmation, and for ethanol by gas chromatography. Screening was done only for cocaine, benzoylecgonine, opiates, phencyclidine, and ethanol.

Autopsy records for each case were reviewed to determine the estimated gestational age (by cerebral configuration). In addition, the available history was reviewed to determine whether the infant was born in a hospital, whether it was stillborn, and whether the mother received prenatal care. In cases where other drug screening was done, the presence or absence of opiates, phencyclidine, and alcohol was noted.

Data from positive cases were compared with those from negative cases using either the two-tailed Student's *t* test or the chi-square test.

Results

The group with cocaine or benzoylecgonine present contained 17 infants (40% of the total). Table 1 shows data for these infants compared with those for infants with neither cocaine nor benzoylecgonine present. None of the history or gross autopsy findings studied was significantly associated with the presence of cocaine.

Figure 1 shows blood concentrations of cocaine and benzoylecgonine in nine infants with cocaine or benzoylecgonine present. The mean cocaine concentration was 0.60 μg/mL (range, 0 to 4.20 μg/mL), and the mean benzoylecgonine concentration was 1.97 μg/mL (range, 0.10 to 4.30 μg/mL). Most concentrations were below the range usually considered fatal for adults. One stillborn infant, however, did have a blood cocaine level of 4.20 μg/mL and a benzoylecgonine level of 3.70 μg/mL. This infant, born at 30 weeks' gestation, showed no evidence of malformation or placental abnormalities.

Cocaine or benzoylecgonine was present in the liver in five infants (mean cocaine, 0.18 μg/mL; range, 0 to 0.27 μg/mL; mean benzoylecgonine, 1.79 μg/mL; range, 0.25 to 1.90 μg/mL), and in the brain in three infants (mean cocaine, 0.02 μg/mL; range, 0 to 0.03 μg/mL; mean benzoylecgonine, 0.50 μg/mL; range, 0.08 to 0.72 μg/mL).

TABLE 1—*Comparison of infants with and without cocaine/benzoylecgonine present.*[a]

	Cocaine/Benzoylecgonine		
	Present	Absent	*P*
Number of cases	17	26	
Mean estimated gestational age, weeks	25	28	NS[b]
Death in hospital, %	47	63	NS
Prenatal care, %	18	12	NS
Stillbirth, %	88	81	NS
Opiates present, %	6	4	NS
Phencyclidine present, %	0	0	NS
Ethanol present, %	0	0	NS

[a]$N = 40$.
[b]NS = not significant ($P > 0.05$).

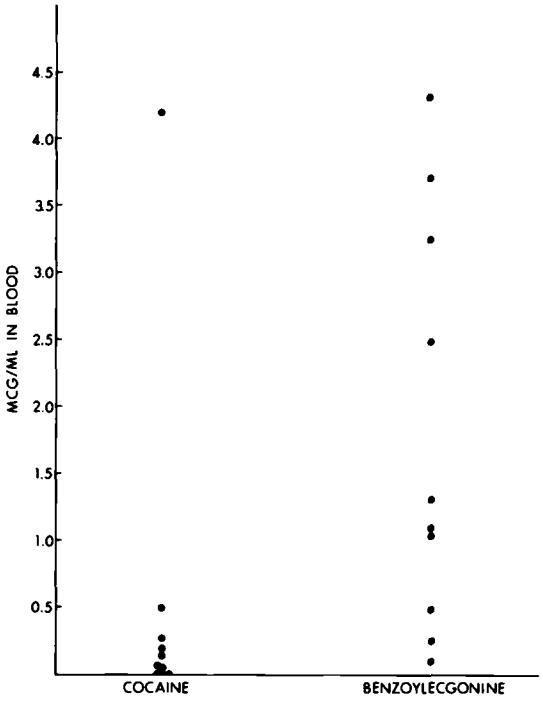

FIG. 1—*Concentrations of cocaine and benzoylecgonine in fetal blood.*

Discussion

Cocaine and benzoylecgonine are commonly associated with unexpected fetal death in Los Angeles County. One or both of these was present in 40% of the otherwise unexplained deaths in this study. This figure is probably an underestimate, as some mothers may have used cocaine well before delivery, allowing cocaine and benzoylecgonine to disappear from the fetal tissues. The fetal cocaine levels reported in this study may also be underestimates, as cocaine may be hydrolyzed to benzoylecgonine or ecgonine methyl ester after death.

None of the autopsy or history variables which we examined predicted the presence of cocaine or benzoylecgonine in the infant. Some associations may have been missed in this study because of the relatively small sample size. Nevertheless, there is no obvious way to predict the results of toxicology testing from the autopsy findings or history. In the authors' practice, therefore, we test for cocaine and benzoylecgonine in every infant dying at less than two days of age when the cause of death is not obvious at autopsy.

In one case, the fetal cocaine level was well into the range considered fatal for adults. The absence of findings such as malformations or abruptio placentae in this case suggests that the fetus may instead have died of acute cocaine overdose. It is of interest that the mother in this case did not die of cocaine overdose.

A single reported case of acute cocaine overdose in a pregnant woman [*9,10*] showed a maternal blood cocaine level about nine times higher than the fetal blood level. The low concentrations of cocaine observed in fetuses may reflect increased uterine and placental vascular resistance, as has been observed in animal studies [*8*], or may be related to low maternal cocaine levels at the time of fetal death.

There is little information, however, on fetal cocaine levels when the mother uses cocaine chronically. Infants may eliminate cocaine slower than adults [*11*], which suggests that a fetus could accumulate cocaine if the mother took repeated small doses. Additional studies are necessary to clarify the effects of chronic maternal cocaine use on the fetus.

Cocaine abuse has reached epidemic levels in many cities. In such areas, cocaine is an important cause of stillbirth and perinatal mortality, particularly in cases seen by the medical examiner.

References

[*1*] Bingol, N., Fuchs, M., Diaz, V., Stone, R. K., and Gromisch, D. S., "Teratogenicity of Cocaine in Humans," *Journal of Pediatrics*, Vol. 110, No. 1, Jan. 1987, pp. 93–96.

[*2*] Little, B. B., Snell, L. M., Klein, V. R., and Gilstrap, L. C., "Cocaine Abuse During Pregnancy: Maternal and Fetal Implications," *Obstetrics and Gynecology*, Vol. 73, No. 2, Feb. 1989, pp. 157–160.

[*3*] Acker, D., Sachs, B. P., Tracey, K. J., and Wise, W. E., "Abruptio Placentae Associated with Cocaine Use," *American Journal of Obstetrics and Gynecology*, Vol. 146, No. 2, May 1983, pp. 220–221.

[*4*] MacGregor, S. N., Keith, L. G., Chasnoff, I. J., Rosner, M. A., Chisum, G. M., Shaw, P., and Minogue, J. P., "Cocaine Use During Pregnancy: Adverse Perinatal Outcome," *American Journal of Obstetrics and Gynecology*, Vol. 157, No. 3, Sept. 1987, pp. 686–690.

[*5*] Chasnoff, I. J., Griffith, D. R., MacGregor, S., Dirkes, K., and Burns, K. A., "Temporal Patterns of Cocaine Use in Pregnancy: Perinatal Outcome," *Journal of the American Medical Association*, Vol. 261, No. 12, March 1989, pp. 1741–1744.

[*6*] Chasnoff, I. J., Chisum, G. M., and Kaplan, W. E., "Maternal Cocaine Use and Genitourinary Tract Malformations," *Teratology*, Vol. 37, No. 3, March 1988, pp. 201–204.

[*7*] Chasnoff, I. J., Bussey, M. E., Savich, R., and Stack, L. M., "Perinatal Cerebral Infarction and Maternal Cocaine Use," *Journal of Pediatrics*, Vol. 108, No. 3, March 1986, pp. 456–459.

[*8*] Woods, J. R., Plessinger, M. A., and Clark, K. E., "Effect of Cocaine on Uterine Blood Flow and Fetal Oxygenation," *Journal of the American Medical Association*, Vol. 257, No. 7, Feb. 1987, pp. 957–961.

[9] Mittleman, R. E., Cofino, J. C., and Hearn, W. L., "Tissue Distribution of Cocaine in a Pregnant Woman," *Journal of Forensic Sciences*, Vol. 34, No. 2, March 1989, pp. 481–486.
[10] Mittleman, R. E., Cofino, J., and Hearn, W. L., "Addendum on 'Cocaine in a Pregnant Woman'," *Journal of Forensic Sciences*, Vol. 34, No. 4, July 1989, p. 807.
[11] Chasnoff, I. J., Lewis, D. E., Griffith, D. R., and Willey, S., "Cocaine and Pregnancy: Clinical and Toxicological Implications for the Neonate," *Clinical Chemistry*, Vol. 35, No. 7, July 1989, pp. 1276–1278.

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