Prevalence of prenatal exposure to cocaine in a sample of newborns from a university teaching hospital

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Abstract

Objective: to assess the prevalence of prenatal exposure to cocaine in a sample of newborns using two methods: fluorescence polarization immunoassay and interview with the mother.

Methods: this cross-sectional study was carried out in a university teaching hospital. The population included all live births between March 23, 1999 and June 01, 1999 (n=847). Exposure was determined by a benzoylecgonine-positive meconium specimen and/or by a positive interview with the mother.

Results: the prevalence of prenatal exposure to cocaine in this sample was 2.4% (16 cases) according to the interviews, and 3.4% (25 cases) according to the meconium analysis. A rate of 4.6% (34 cases) was found when both methods were associated.

Conclusions: we observed that the meconium test was more effective than the maternal interview for the diagnosis of prenatal exposure to cocaine. The meconium analysis enhanced diagnostic chances by 53.4%, compared to 26% in the case of maternal interview.


Introduction

In the United States, in the late 1970s, the use of cocaine started to be noticeable in both urban and rural areas. During the 1980s, there was the crack epidemic and the first reports of child abuse, negligence, and abandonment by parents who used drugs and of use of cocaine and other drugs during gestation.1

Development of the central nervous system (CNS) begins on the 28th day after conception and continues throughout gestation and childhood. In this sense, the CNS has a biological and continuous vulnerability to toxic insults. Cocaine can affect formation and remodeling of the brain by its actions on neurotransmitters. Cocaine can simulate the action of neurotransmitters or change neurotransmitter system activity; this results in abnormalities in brain development and in the architecture of the cortex, especially with lack of discernible cortical lamination suggesting neuronal differentiation and migration disorders.2

Rare, though severe, teratogenic effects have been described in fetuses exposed to cocaine, including urogenital abnormalities, distal deformities, gastroschisis, cardiac

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defects, and CNS malformations. Moreover, there are reports of neuronal migration and prosencephalic development disorders such as corpus callosum agenesis, absence of pellucid septum, septo-optic dysplasia, schizencephaly, optic nerve hypoplasia, dysgenesis and coloboma of the retina. Until the present moment, the basal mechanism, or mechanisms, that cause these teratogenic effects are not understood; however, it is suggested that hypoxemia, alterations in the synthesis of deoxyribonucleic acid (DNA) in certain regions of the brain, and the alterations in neurotransmitters may be involved.3-8

One of the most important studies on prenatal drug exposure is being carried out nationwide in the United States; the study is organized by the National Institute of Child Health and Human Development, called Maternal Lifestyles Study (MLS). Ten percent of the population of babies were exposed to the drugs studied (cocaine or opiates). The prevalence of prenatal exposure to cocaine was 5.4%.7

A study carried out in the city of Porto Alegre, southern Brazil, showed that inhaled cocaine is the third most widely used drug, after alcohol and marijuana; in this group, injected cocaine was the fifth most widely used drug.9 However, after an extensive review of the literature, we did not find studies describing prevalence of prenatal exposure to cocaine in Brazil and South America.

Exposure to drugs can be assessed by direct methods, called biological markers, and by indirect methods, such as questionnaires and statistical models. Both these types of methods present advantages and limitations, in this sense, a combination of both would be ideal for better assessment of the exposure.10

Biochemical markers of exposure to cocaine - benzoylecgonine (BE), ecgonine, and ecgonine methyl ester - are the main metabolites. Cocaine and its metabolites have been commonly described in serum, urine, meconium, hair, saliva, fluid, amniotic fluid, sweat, and gastric fluid of patients.10 Studies have demonstrated the presence of cocaine metabolites in the meconium of fetuses at 17 weeks gestation.11,12

Techniques used in toxicologic analysis include colorimetric tests, such as color or spot tests and ultraviolet spectrophotometry; immunoassays, such as enzyme-multiplied immunnoassay technique (EMIT), radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA), and fluorescence polarization immunoassay (FPIA); and chromatography, such as thin-layer chromatography (TLC), gas chromatography-mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), fluorometry, and infrared spectroscopy. Tests vary from being rapid, easy, and low-cost such as FPIA to more complex, high-cost such as GC-MS, which is not used as a screening method.10,13,14

Ostrea et al. described, initially, the adaptation of the meconium for radioimmunoassay; subsequently, the authors described an 80% positivity of cocaine metabolites using FPIA, in the meconium of newborn infants from drug-dependent mothers, compared to 30% using urine. The EMIT was inferior than FPIA for the detection of cocaine in meconium.15-25

The FPIA is less sensitive than other methods such as EMIT and RIA, but it is adequate for most tested drugs; the RIA, however, cannot be used for screening methods since it involves separate extractions for each drug using acidic water.22

The most widely described method in the literature for prenatal exposure to cocaine is testing urine from the newborn. The problem is that urine tests detect only recent use of cocaine, since the drug is excreted by the fetus 1 to 2 days after use by the mother; thus, they allow for an increase in false negatives.15,26 In this sense, FPIA of meconium detected different metabolites whereas FPIA of urine detected only the highest concentration metabolite.16

Studies on the prevalence of prenatal exposure to drug abuse should, ideally, include interviewing, since it is the only method that allows for information on the initial and critical stages of gestation, along with dosing drug metabolites in bodily fluids. These two methods should be included because studies have indicated high rates of omission of information in interviews, since they deal with illicit drugs.27,28 We chose, thus, to apply testing of meconium of newborn infants considering that this method allows for a longer interval between use of the drug and diagnosis, combined with interviewing.

Our objective was to study the prevalence of prenatal exposure to cocaine in a population sample of newborns from the Hospital de Clínicas de Porto Alegre (HCPA).

Patients and methods

We chose the design of study on prevalence study. Positive cases of prenatal exposure to cocaine were determined according to meconium BE indicated by positive FPIA (greater than or equal to 10.26 ng/ml) and to positive answers to the questionnaire on use of cocaine at any moment during current gestation. Our study was carried out at the Obstetrics Center of the Neonatology Unit of the Hospital de Clínicas de Porto Alegre (HCPA). The analysis of meconium samples was carried out at HCPA’s research and radioimmunoassay laboratories.

To calculate sample size, we considered prevalence of cocaine use among pregnant women and the monthly average of births (300 births per month) at the HCPA. Based on minimal expected prevalence of 4.6% and 2% precision, the sample should include 421 newborn infants. Our population sample was calculated aiming at a 0.05 significance level. In order to increase the number of exposed and identified infants for follow-up in further studies, we analyzed as many meconium samples as the funding rendered possible.
The population included all newborn infants from the Obstetrics Center at the HCPA from March 23, 1999 to June 01, 1999 (n=847). The research included 739 newborn infants who fulfilled the criteria for inclusion in the study. The loss of 108 cases (12.8%) was due to meconium sample that could not be used, out of which 104 cases presented negative answers to the questionnaire, and four no interview at all. The parents of one newborn refused to participate in the study and did not answer the questionnaire.

The studied newborn infants and their family did not differ from the general population of the HCPA, according to a comparison with recent studies carried out at the same hospital.29,30,31. Age average and standard deviation of the 739 mothers included in the study was 25.4 ± 6.8 years; according to skin color, 73.9% of mothers were white. Also, 78.5% lived with a fixed partner, 50.6% had not finished elementary school, and 61.3% had monthly family income greater than or equal to three minimum wages (Brazilian minimum wage = ~ 100 US$). The study population did not differ, according to maternal and neonatal characteristics, from the lost cases.

After the elimination of the first meconium or, in case of loss of the first meconium, a second meconium was collected by the nurses directly from the diapers of newborn infants. Meconium flasks were enveloped in thermal bags and taken to the laboratory for processing. A researcher from the area of mental health was informed of the names of the puerpera of the previous day and, subsequently, went to the obstetrics center or the rooming-in wards. The researcher presented the informed consent form to the parents and, if they agreed to it, the mother would be interviewed with respect to use of cocaine or other drugs by answering the research protocol. Interview consisted of nonstandardized anamnesis on use and pattern of use of drugs in each trimester of the gestation. We employed a protocol similar to that of the MLS following the suggestion of one of the authors.10 Interviews were positive when there were reports of use of cocaine during current gestation. The nursing staff of the obstetrics center, of the maternity, and of the rooming-in ward were responsible for the collection of meconium; these staff members were supervised and oriented by the head nurse of each department.

At the laboratory, the labels of the flasks belonging to the one newborn whose parents did not consent to participate in the interview were removed; these meconium samples were screened anonymously. A part of the meconium sample was frozen and another processed according to meconium preparation technique described in other studies.21,24 BE levels were measured by fluorescence polarization immunoassay (FPIA) (TDX). Results were entered into a standard form.

Benzoyllecogine levels were measured using the TDx/TDXFLx Cocaine Metabolite Assay Kit standard curve. Test positivity for presence of BE was established at 10.26 ng/ml, according to the average values of 17 negative (4.69 ng/ml) meconium samples and two standard deviations (2.78). Data were processed and analyzed using EXCEL 1997, SPSS version 8, and EPI-INFO version 6.04C software.

All parents and guardians of newborn infants received oral and written information on the study objectives, as well on general aspects of the matter being studied. After the information was provided, we asked parents or guardians to sign the informed consent form. Parents and guardians were informed that exam results were not going to be used for reasons other than the study; moreover, in case results were made public, patients would remain anonymous. Our study was approved by the Research Ethics Committee of the HCPA of the Research and Graduate Studies Group (Grupo de Pesquisa e Pós-Graduação, GPPG #98145). The study was also approved methodologically and ethically according to the Guidelines and Norms on Research with Human Beings (Diretrizes e Normas Regulamentadoras de Pesquisa Envolvendo Seres Humanos) resolution # 196/96 of the National Health Council and to the Normative Resolutions of the GPPG/HCPA.

Results

We studied the prevalence of cocaine use during current gestation. By interviewing 739 mothers, we were able to diagnose 16 mothers of newborn infants exposed to cocaine for a rate of 2.4%.

Testing of 738 meconium samples indicated 25 newborn infants exposed to the drug for a prevalence rate of 3.4%.

Seven of the cases were diagnosed by both the interview and positive meconium samples. There were 16 cases of positive meconium samples and negative answers to interviews. In other nine cases, the meconium samples were negative but the interviews were positive for use of cocaine. Thus, 34 patients were classified as exposed to cocaine, for an overall prevalence of 4.6% (95% CI 3.2 - 6.4).

Discussion

Epidemiological studies carried out in several countries since the 1980s have shown that prenatal exposure to cocaine not only occurs, but is also present in high prevalence rates. Depending on the methods and the study populations, there have been reports of prevalence rates as high as 50% of exposure of newborn infants to substance abuse.32

Our finding of 4.6% of prenatal exposure to cocaine in newborn infants from the HCPA is similar to those of urban populations from public hospitals in other countries. In this sense, if routine screening procedures are not carried out, the diagnosis of prenatal exposure to cocaine is elusive. On the one hand, the prevalence rate indicated by the interviews, despite being lower than that by the meconium testing, is higher than those commonly reported by other authors. This finding may be explained by the structured characteristic of the interviews, which did not present punitive aspects, and
by the fact that they were carried out by a certified mental health professional. On the other hand, however, conversely to the high prevalence rate observed in the interview, the analysis of meconium samples indicated lower prenatal exposure rates in comparison to that of other local studies using analysis of meconium. This difference is probably related to differences in the populations studied.\(^{33,35}\)

Nine infants born to substance-abusing mothers diagnosed by the interview presented negative meconium samples; this is probably due to use of the drug before the 16th week of gestation.

In countries that have documented use of cocaine during gestation for the past two decades, such as the United States, there are healthcare centers whose routine protocols include questioning patients on the use of psychoactive substances and testing bodily fluids of pregnant women, puerperae, and newborn infants. In general, these are not universal screening procedures, but rather of screening mothers who present characteristics of risk for substance abuse, such as low social and economic status, non-Caucasian, polydrug use, no fixed partners, no prenatal examinations, sexually-transmitted diseases, and so on. However, some authors have posited that these characteristics may be equivocal, since studies on substance abuse usually do not include mothers outside the referred attributes; in other words, research on prenatal substance exposure usually does not include subjects with higher family income and characteristics such as Caucasian, non-polydrug users, fixed partners, and frequent prenatal examinations.\(^{36}\) The ideal situation for this type of screening is still not well-established.

We did not follow the criteria for risk of prenatal substance exposure and the cases not included in the study due to loss did not differ from the study population.

Independently of pertinent comparisons, the prevalence rate of 4.6% on use of cocaine during gestation indicates that part of the mothers who deny use of the substance allow for an underestimation of prenatal exposure and of possible effects on newborn infants.

This is the first epidemiological survey on prenatal exposure to cocaine at our services, after approximately two decades of the first studies on the subject matter in other countries. Further studies, as that of Chasnoff et al. on the epidemiology of prenatal exposure in populations from private healthcare clinics (higher social and economical status) are still necessary.\(^{37}\)

In Brazil, studies on epidemiology and effects of use of cocaine during gestation are off to a late start in comparison to other countries. However, there may be positive aspects in this fact, especially that of not taking too much into account data from separated populations and of other methodology problems. It is also important to be extremely careful with the publishing of information in the media in order to avoid marginalization of children exposed to substance abuse during intrauterine life.

Despite the fact that effects of prenatal exposure to cocaine are not disastrous, they do exist, are severe, and, most of the time, are optimized by other risk factors that are difficult to change. The ideal approach to prenatal exposure to drugs is prevention. Prohibiting substance abuse, despite seeming to be the best solution, has not been effective and it seems that at least in the short run the problem will not cease to exist. In this sense, a number of children will still be exposed to substance abuse before this social problem is solved.

However, it is possible to offer mothers and infants the possibility of diagnosis and of handling the problem as a disease, avoiding criminalization. To label prenatally exposed children as permanently handicapped and with a negative future outlook is to deny the understanding that most effects of cocaine can be remedied, and deny the opportunity to treatment.\(^{37,38}\) Rather, it is known that development of exposed subjects depends on the environment in which the child is brought up as well as on early intervention.\(^{39}\)

There is evidence that women who use drugs during gestation and during critical development stages of their children most likely have a family history of substance abuse.\(^{35}\) Likewise, if the exposed babies of today are not identified and helped to avoid the early effects, they might help to perpetuate the condition of substance abuse. In conclusion, identifying infants exposed to substance abuse during intrauterine life is a form of future prevention.

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