Maternal and Paternal Recreational Drug Use and Sudden Infant Death Syndrome

Hillary Klonoff-Cohen, PhD; Phung Lam-Kruglick, MA

Objective: To determine whether maternal or paternal use of cocaine, opiates, or marijuana during conception and pregnancy and postnatally increases the risk of sudden infant death syndrome (SIDS) during the first year of the infant’s life. This is an important issue and may prove useful in further decreasing the rate of SIDS.

Methods: A case-control study was conducted consisting of 239 infants who died of SIDS in southern California between 1989 and 1992, and 239 healthy infants who were matched on the basis of birth hospital, date of birth, age, and sex. Specific drug use at the period of conception, during pregnancy and breastfeeding, and in the presence or vicinity of the infant was ascertained by telephone for the white, African American, Hispanic, Asian American, and Pacific Islander case and control fathers and mothers.

Results: Maternal recreational drug use during pregnancy was not associated with the risk of SIDS after adjusting for maternal smoking during pregnancy (adjusted odds ratio [OR] = 2.0; 95% confidence interval [CI], 0.6-6.5). There were statistically significant differences between case and control fathers’ use of marijuana during conception (OR = 2.2; 95% CI, 1.2-4.2; P = .01), during pregnancy (OR = 2.0; 95% CI, 1.0-4.1; P = .05), and postnatally (OR = 2.8; 95% CI, 1.1-7.3; P = .04) and the risk of SIDS, while adjusting for paternal smoking and alcohol use.

Conclusions: There was no association between maternal recreational drug use and SIDS. Paternal marijuana use during the periods of conception and pregnancy and postnatally were significantly associated with SIDS. The role of paternal psychoactive drug use, especially the relationship between marijuana and SIDS, is an understudied area; however, before any definitive role for the father can be confirmed, these findings should be investigated and replicated in future studies.


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SUBJECTS AND METHODS

HYPOTHESIS

The objective of this study was to investigate whether maternal and/or paternal recreational drug use (cocaine, opiates, or marijuana) during the periods of conception and pregnancy and postnatally (ingested through breastfeeding and/or passively inhaled in the home) increased the risk of SIDS within a racially diverse group. This is a secondary analysis of a previously published article on passive tobacco smoking and SIDS; a detailed description of the methodology of that study appears elsewhere.23

STUDY SAMPLE

A total of 400 eligible cases were initially identified from death certificates located in the health departments of southern California. One hundred of these case parents were untraceable despite tremendous effort to locate this transient population by implementing 14 strategies that have been described previously.24 Hence, matching control parents for the 100 case parents were not chosen from the corresponding birth hospitals. During the study period, 300 cases and 260 controls were interviewed; this was before the height of the publicity on SIDS and its correlation with sleep position. Overall, there was a 70% response rate (560 of 800). After couples with missing recreational drug data were dropped and matching was implemented, a total of 239 cases and 239 matched controls were retained for this analysis.

This study sample consisted of 239 white, African American, Hispanic, and Asian American infants who had died of SIDS and 239 control infants born between January 1989 and December 1992 in 5 counties in southern California (San Diego, San Bernardino, Riverside, Orange, and Los Angeles Counties). All SIDS diagnoses were based on an autopsy data sheet and final autopsy report. A SIDS death was defined as a death occurring between 1 week and 1 year of age, with a diagnosis of SIDS confirmed by autopsy. Contact was made with parents of infants who had died of SIDS approximately 6 to 12 months after the infant’s death, to comply with the requirements of the Committee on Human Subjects regarding observance of the grief period.

Control infants were randomly selected from all eligible live births from the same 110 birth hospitals of the case infants, and were additionally matched to the case by date of birth, sex, and race. The medical records department at each hospital contacted the control parents by mail to maintain confidentiality. On average, control parents were contacted 3 to 6 months after the case interview. All study infants were required to be free of pulmonary, cardiac, or neurologic complications and metabolic disturbances. Unautopsied deaths were excluded.

INTERVIEW

A telephone interview examined sociodemographic characteristics and the timing and frequency of use of cigarettes, alcohol, and recreational substances for both case and control parents. Detailed maternal and paternal recreational drug histories were obtained from the mother and father (if possible), including the time frame and frequency of substance use. The period of conception was defined as the interval between the last menstrual period and the confirmation of a positive pregnancy test by the physician. “Postnatally” included recreational drug exposure from 2 sources: during breastfeeding, or smoking marijuana in the presence or vicinity of the infant, which may passively expose the infant to this drug. Other substances (tobacco, alcohol, and over-the-counter and prescription medications) used during the specified periods were also recorded. Complete paternal and maternal medical histories, labor and delivery complications, and neonatal characteristics were primarily obtained from the interview and medical records and verified with obstetric and pediatric records. The time span of responses for the control parents was limited to the life span of the case infants (eg, if a case infant lived for 6 months, the matched control’s history would coincide to 6 months).

This study was approved by the Institutional Review Boards of all hospitals involved and the University of California, San Diego, Committee on Human Subjects.

STATISTICAL ANALYSES

Conditional logistic regression was used to examine the relationship between SIDS and marijuana or other drug use by the mother and father during conception, pregnancy, and infancy. Potential confounders (maternal or paternal tobacco smoking, alcohol use, age, level of education, infant medical conditions at birth, low birth weight, sleep position, and bed sharing) were identified from previous literature and stratified analyses. Confounders were included in the final models if they changed the magnitude of association between SIDS and drug exposure by at least 15%. Multiplicative interactions (eg, between maternal and paternal drug use or between drug and tobacco or alcohol use) were assessed through significance testing. Stata 3.0 statistical software (Stata Corp, College Station, Tex) was used for all analyses.

COCAINE USE AND SIDS

In the 1980s, cocaine use in its freebase form (“crack”) overtook heroin as the main drug problem in the United States11; however, the causal relationship between cocaine use during pregnancy and SIDS remains unclear. Two studies suggest an increased risk of dying of SIDS when exposed to cocaine in utero.14,15 Chasnoff et al14 reported a 15% incidence rate of SIDS among 66 infants of mothers who had used cocaine during pregnancy compared with 4% among infants whose mothers used opiates. The finding of 8.8 SIDS deaths per 1000 infants born to cocaine-using mothers in this group was similar to Davidson-Ward et al’s15 reported incidence of 8.4 SIDS deaths per 1000 live births to cocaine-using mothers in Los Angeles County, California. Durand et al13 studied the SIDS rate for cocaine-exposed hospital-born infants; they noted that unrecognized maternal drug abuse may have occurred in the control group.

In contrast, the prospective study by Bauchner et al17 found no increased risk of SIDS among infants exposed...
MARIJUANA AND SIDS

One study addressed the effects of maternal marijuana use and SIDS. Ostrea et al determined that there was an increase in the OR for SIDS among drug-positive infants exposed to all drugs, including marijuana (OR=1.5; 95% CI, 0.46-5.01). For those infants exposed to cocaine (OR=1.9; 95% CI, 0.58-6.20) and opiates (OR=2.3; 95% CI, 0.66-7.76), there was an association with SIDS; however, the CIs were wide and included the OR of 1. Ostrea et al concluded that “prenatal drug exposure in infants was not associated with an increase in the incidence of SIDS during the first 2 years of life.”

Conflicting results among these studies may be due to small sample sizes, inability to document maternal and paternal drug use (including variations, type, dose, duration, and timing during conception and pregnancy), failure to differentiate between prenatal and postnatal drug exposure, and absence and/or inadequate adjustment of potential confounders (eg, socioeconomic status, prematurity, low birth weight, and prenatal care).4-10,14-21

To our knowledge, no other studies have investigated paternal substance use, including marijuana, during pregnancy and conception, nor have any studies examined maternal recreational drug use during the period of conception.

Table 1. Timing of Maternal Recreational Drug Use (Excluding Marijuana) and Marijuana Use and Risk of Sudden Infant Death Syndrome, Unadjusted and Adjusted Conditional Logistic Regression Results*

<table>
<thead>
<tr>
<th>Timing of Exposure</th>
<th>Cases, No. (%)</th>
<th>Controls, No. (%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>P</th>
<th>Adjusted† OR (95% CI)</th>
<th>P</th>
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<tbody>
<tr>
<td>Recreational drug use (excluding marijuana)</td>
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<td></td>
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<tr>
<td>During conception (n = 478)</td>
<td>13 (5.4)</td>
<td>7 (2.9)</td>
<td>2.0 (0.8-5.3)</td>
<td>.17</td>
<td>1.2 (0.4-3.5)</td>
<td>.68</td>
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<tr>
<td>During pregnancy (n = 478)</td>
<td>19 (8)</td>
<td>9 (3.8)</td>
<td>3.5 (1.2-10.6)</td>
<td>.03</td>
<td>2.0 (0.6-6.5)</td>
<td>.25</td>
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</table>

Marijuana use

<table>
<thead>
<tr>
<th>Timing of Exposure</th>
<th>Cases, No. (%)</th>
<th>Controls, No. (%)</th>
<th>Unadjusted OR (95% CI)</th>
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<th>Adjusted† OR (95% CI)</th>
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<tbody>
<tr>
<td>During conception (n = 478)</td>
<td>30 (12.6)</td>
<td>23 (9.6)</td>
<td>1.4 (0.8-2.5)</td>
<td>.29</td>
<td>1.1 (0.6-2.0)</td>
<td>.82</td>
</tr>
<tr>
<td>During pregnancy (n = 478)</td>
<td>14 (5.9)</td>
<td>14 (6.9)</td>
<td>1.0 (0.4-2.2)</td>
<td>1.0</td>
<td>0.6 (0.3-1.6)</td>
<td>.33</td>
</tr>
<tr>
<td>Postnatally (n = 456)</td>
<td>10 (4.3)</td>
<td>11 (4.7)</td>
<td>1.1 (0.4-2.9)</td>
<td>.81</td>
<td>0.6 (0.2-1.8)</td>
<td>.42</td>
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*OR indicates odds ratio; CI, confidence interval.
†The following were examined as potential confounders: maternal smoking during pregnancy, maternal alcohol use during pregnancy, maternal age and level of education, low infant birth weight, infant medical conditions at birth, infant sleep position, and bed sharing. All multivariate models were adjusted for maternal smoking during pregnancy.

RESULTS

MATERNAL RECREATIONAL DRUG USE DURING CONCEPTION AND PREGNANCY AND POSTNATALLY

Marijuana predominated as the drug of choice among the mothers. As indicated in Table 1, SIDS outcome was not significantly associated with maternal marijuana use during conception (defined as the interval between the last menstrual period and medical confirmation of pregnancy) or postnatally.

Other recreational drugs used by the mother included cocaine, crack, crystal, amphetamine, methamphetamine, and speed; cocaine was the most commonly used drug. Of the 28 women who used recreational drugs other than marijuana during pregnancy, 42% used cocaine (n=6 cases, 6 controls), 7% used crack (n=2 cases, 0 controls), 11% used crystal (n=2 cases, 1 control), 21% used methamphetamine (n=5 cases, 1 control), 11% used speed (n=3 cases, 0 controls), and 7% used another drug (n=1 case, 1 control).

Maternal drug use during pregnancy was significantly associated with SIDS in univariate analysis; the unadjusted OR was 3.5 (95% CI, 1.2-10.6; P=.03). However, after adjusting for potential risk factors associated with socioeconomic status (poverty) including maternal alcohol use during pregnancy, maternal age and level of education, low infant birth weight, medical conditions at birth (eg, jaundice, apnea, fever, or meconium aspiration), sleep position, and bed sharing, the OR was no longer statistically significant (OR=1.94; 95% CI, 0.6-6.5). To maintain power, fewer variables were entered into the model. Maternal tobacco smoking during pregnancy was the only potential confounder. Although adjusting for this factor reduced the OR to 2.0 (95% CI, 0.6-6.5; P=.25), it was not statistically significant. The effect of recreational drug use while breastfeeding could not be assessed because few women reported using recreational drugs during this period (n=3). There was no association between SIDS and maternal recreational drug use during the period of conception using multivariate analyses. Dose-response effects could not be calculated because of the small sample of drug users.
as well as missing information for frequency, duration of use, and quantity.

**PATERNAL RECREATIONAL DRUG USE DURING CONCEPTION AND PREGNANCY AND POSTNATALLY**

Marijuana also predominated as the drug of choice among the fathers. As indicated in Table 2, paternal marijuana use during all periods (conception, pregnancy, and infancy) was significantly associated with SIDS outcome in both univariate and multivariate models. The ORs for marijuana use were 2.2 (95% CI, 1.2-4.2; \( P = .01 \)) during conception, 2.0 (95% CI, 1.0-4.1; \( P = .05 \)) during pregnancy, and 2.8 (95% CI, 1.1-7.3; \( P = .04 \)) postnatally (eg, smoking in the presence or vicinity of the infant), while simultaneously adjusting for paternal postnatal tobacco smoking and/or alcohol use during conception. Although the unadjusted and adjusted ORs were very similar, smoking and alcohol were important confounders that had to be adjusted for in the analyses. For example, the OR for paternal marijuana use during conception decreased to 1.8 while adjusting for only smoking, but increased to 2.7 while adjusting for only alcohol use. The OR while adjusting for both smoking and alcohol use was 2.2, which was identical to the unadjusted result. Adjustment for other potential risk factors, including paternal age or education level, low infant birth weight, medical conditions at birth, sleep position, and bed sharing did not alter the ORs.

Other recreational drugs used by the father included cocaine, speed, methamphetamine, amphetamine, heroin, phencyclidine, lysergic acid diethylamide, crystal, and mushrooms; cocaine was the second most commonly used drug among the fathers. Of the 44 men who used recreational drugs other than marijuana during conception, 59% used cocaine (\( n = 14 \) cases, 12 controls). After adjusting for alcohol use, the OR for paternal recreational drug use (excluding marijuana) during conception was 1.9 (95% CI, 1.0-3.7; \( P = .06 \)).

Because men who used drugs may also have indulged in smoking or alcohol consumption, multiplicative interactions were evaluated between paternal drug use and paternal smoking and drinking. These interactions were not statistically significant (\( P = .95 \)). Furthermore, interactions between maternal and paternal recreational drug use were not statistically significant (\( P = .80 \)); the magnitude of association and significance were dominated by paternal drug use when both maternal and paternal variables were entered into the same model. Hence, ORs were higher and \( P \) values were lower for men than for women.

**COMMENT**

Substance abuse among women and their partners during periods of conception and pregnancy may contribute to SIDS, a national perinatal health problem. Recreational drugs have been implicated as a risk factor for SIDS, although findings have not been consistent. In this study, the number of mothers who reported using drugs during conception or pregnancy was small, and therefore, we had little power to detect statistically significant associations.

Other studies have reported that maternal recreational drug use plays a role in SIDS; however, they generally ascertained substance exposure prospectively prior to the SIDS event, rather than retrospectively. Almost a decade ago, a meta-analysis of 20 articles on the association between maternal recreational drug exposure and SIDS found a nonstatistically significant OR of 3.67 (95% CI, 0.93-14.2) for women using multiple drugs, including cocaine, compared with drug-free controls.

In our study, maternal recreational drug use was not a risk factor for SIDS when potential risk factors associated with poverty and lack of education were included (maternal alcohol use during pregnancy, maternal age and level of education, low birth weight, medical conditions at birth, sleep position, and bed sharing); these factors did not act as confounders in our data. Interestingly, maternal smoking during pregnancy was the overwhelming confounder; adjusting for this factor reduced the OR from 3.5 (95% CI, 1.2-10.6, unadjusted model) to 2.0 (95% CI, 0.6-6.5). Few studies have looked at potential confounders, and only 1 study adjusted for smoking, even though maternal tobacco smoking during pregnancy is a well-documented risk factor. The high association that other studies reported

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<td>During conception (n = 478)</td>
<td>25 (10.5)</td>
<td>19 (8)</td>
<td>1.4 (0.7-2.5)</td>
<td>.35</td>
<td>1.9 (1.0-3.7)</td>
<td>.06</td>
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<tr>
<td>Marijuana use</td>
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</tr>
<tr>
<td>During conception (n = 428)</td>
<td>48 (22.4)</td>
<td>27 (12.6)</td>
<td>2.2 (1.3-4.0)</td>
<td>.01</td>
<td>2.2 (1.2-4.2)</td>
<td>.01</td>
</tr>
<tr>
<td>During pregnancy (n = 428)</td>
<td>37 (17.3)</td>
<td>21 (9.8)</td>
<td>2.1 (1.1-4.0)</td>
<td>.02</td>
<td>2.0 (1.0-4.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Postnatally (n = 416)</td>
<td>22 (10.6)</td>
<td>8 (3.9)</td>
<td>3.3 (1.3-8.3)</td>
<td>.01</td>
<td>2.8 (1.1-7.3)</td>
<td>.04</td>
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*OR indicates odds ratio; CI, confidence interval.
†Adjusted for paternal postnatal smoking and paternal alcohol use during conception.
‡Adjusted for paternal postnatal smoking and paternal alcohol use during conception.
| \( P \) values were lower for men than for women. |
between drug use and SIDS may be due to the possibility that women who used drugs during pregnancy also smoked. This was confirmed by Blair et al.26 who stated, “Maternal use of illegal drugs became nonsignificant in the multivariate model after adjustment for maternal and paternal smoking.”

In the current study, the risk of SIDS was approximately 2 times higher for men who used recreational drugs (excluding marijuana) during conception compared with those who did not, although these findings were of borderline significance (OR = 1.9; P = .06). To our knowledge, no other studies have examined paternal drug use during this period. However, Blair et al26 reported that paternal use of all illegal drugs after the infant’s birth remained significant in the multivariate model for SIDS (adjusted OR = 4.68; 95% CI, 1.56-14.03). In addition, we believe that our study is the first to examine marijuana use by the father during the periods of conception and pregnancy and postnatally. When multivariate analyses were conducted and an adjustment was made for the father’s tobacco smoking and alcohol consumption during conception, there was an association between paternal marijuana use and SIDS during conception (OR = 2.2; P = .01), during pregnancy (OR = 2.1; P = .05), and postnatally (OR = 3.3; P = .04). These tentative results may be biased because it is unknown how often and for how long the fathers smoked marijuana in the proximity of the pregnant mothers or infants, although this fact does not negate the potential role of this drug at the time of conception. Hence, whether a father’s drug use plays a significant role in SIDS needs to be extensively explored and replicated in future studies.

We found an association between SIDS and paternal marijuana use during all periods, whereas this was not the case with maternal use. This may be due to the larger number of men who smoked marijuana (compared with very few women) or to the greater amount, frequency, and duration of their use. Finally, men may not be aware that their lifestyle habits affect pregnancy outcomes.

A potential limitation of this study was ascertainment bias for the 100 untraceable cases, with the possibility that they were the heaviest drug users. Furthermore, the drug histories were based primarily on self-report because recreational drug use is rarely noted in medical records. No maternal or infant drug screening was conducted. Although the ideal way of addressing this issue would be direct documentation of drug use collected prospectively, the number of mothers and infants, length of time, and cost required to obtain a large enough sample would be prohibitive. In our study, telephone interviews occurred 6 to 12 months after the infant’s death. Recall bias and reliability of sensitive and confidential information could be questionable. Because of societal pressures and the stigma surrounding substance use during pregnancy and postnatally, underreporting by both men and women could have been a potential problem. Both case and control parents may have resisted the truthful reporting of drug use. If this occurred equally, nondifferential bias classification would have resulted, and estimates would have been biased toward nonsignificance. Parents of infants who died of SIDS reported exposure up until 2 years previously, whereas control parents had no reason to spend so much time reviewing the exposure. If the case parents remembered more accurately, perhaps out of guilt, this could have resulted in an association between drug use and SIDS.27 To reduce recall bias, a drug history was obtained with a structured interview (which had been pilot tested) in a nonthreatening environment, which has reportedly improved the rate of maternal admission to illicit drug use.1 To ensure valid and reproducible reporting for both case and control parents, great attention was devoted to the interview technique, questionnaire design, sensitivity of information, and data collection methods (eg, wording, chronological order of questions, and use of memory probes).

The advantages of this study were that patient inclusion was based on disease and not drug status, the study design was adequate to assess polydrug use (eg, tobacco, alcohol, and drugs), both maternal and paternal drug consumption were factors in intrauterine and postnatal exposure to drugs (through breastfeeding and passively), and multivariate analyses were conducted.

Whether or not a true relationship exists, direct and oblique references linking SIDS to maternal substance use appear in both scientific and lay literature. An increasing number of SIDS deaths list maternal drug use on death certificates.2 In the future, it is necessary to test the relationship between all recreational drugs and SIDS in a much larger study sample; to further separate the different types of drugs by frequency, quantity, and timing for different racial groups of mothers and fathers; to use biochemical measures (eg, hair, nail clippings, or meconium) to validate self-reporting; to clarify physiologic and pathophysiologic mechanisms; and to determine if there are variations in neonatal growth parameters.

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