Characteristics of pregnant illicit drug users and associations between cannabis use and perinatal outcome in a population-based study

Marleen M.H.J. van Gelder, Jennita Reefhuis, Alissa R. Caton, Martha M. Werler, Charlotte M. Druschel, Nel Roeleveld

Abstract

Background: According to the 2004 National Survey on Drug Use and Health, 4.6% of American women reported use of an illicit drug during pregnancy. Previous studies on illicit drug use during pregnancy and perinatal outcomes showed inconsistent results.

Methods: This population-based study included mothers who delivered live-born infants without birth defects between 1997 and 2004 and completed interviews for the National Birth Defects Prevention Study (response rate 69%; n = 5871). Prevalence of self-reported illicit drug use (specifically cannabis, cocaine, and stimulants) during pregnancy and its associations with demographic and social factors were assessed. We used multivariable linear and logistic regression analyses to study the associations of cannabis use with birth weight and gestational age.

Results: The prevalence of reported illicit drug use during pregnancy was 3.6% (standard error 0.24). Pregnant users of cannabis, cocaine, and stimulants were younger, had a lower level of education and lower household income, and were less likely to have used folic acid in the periconceptional period than nonusers. Illicit drug users were also more likely to have used alcohol and tobacco. After adjustment for confounding, cannabis use was not associated with mean birth weight or gestational age or with low birth weight or preterm delivery.

Conclusion: Women who report use of illicit drugs during pregnancy differ in demographic and socioeconomic background from nonusers. Reported cannabis use does not seem to be associated with low birth weight or preterm birth.
2. Methods

2.1. The National Birth Defects Prevention Study (NBDDS)

The NBDDS is an ongoing population-based case–control study that includes case infants with major structural congenital malformations identified via 10 birth defects surveillance systems in Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, North Carolina, Texas, and Utah. Control infants are live-born infants without major birth defects from the same geographical areas, randomly selected from birth hospital records or birth certificates. Mothers are interviewed by trained interviewers via telephone in either English or Spanish between 6 weeks and 24 months after the estimated date of delivery. Questions are asked about demographic characteristics, maternal health, lifestyle factors, and occupation. The methods and enrollment of the infants have been described in detail elsewhere (Yoon et al., 2001; Cogswell et al., 2009). For this study, we selected all control infants born between October 1, 1997, and December 31, 2004 whose mothers completed the interview (n = 5871). The response rate was 69%.

2.2. Exposure and outcome assessment

Detailed information on the type, timing, and frequency of maternal illicit drug use during the period from 3 months before pregnancy until birth of the index child was available from the interview. We grouped the illicit substances reported by the mothers into five drug categories (cannabis, cocaine, stimulants, hallucinogens, and opioids) as described elsewhere (van Gelder et al., 2009). Nonusers were defined as women who did not report use of any illicit drug from 3 months before pregnancy through birth of the index child.

Data on birth weight and gestational age were obtained through abstraction of birth hospital records or birth certificates depending on how the infants were selected. During the examination of these data, some reporting inconsistencies were identified (e.g., infants of 3104 g at 21 weeks of gestation). To address these implausible birth weight–gestational age combinations, we used the cut-points of birth weight values within the range for their specific gestational age as proposed by Alexander et al. (1996). For the perinatal outcome analyses, infants with implausible birth weight–gestational age combinations (n = 16), infants with missing birth weight or gestational age data (n = 20), and mothers with multiple gestations (n = 174) were excluded.

2.3. Statistical analyses

We used basic descriptive statistics to describe the characteristics of women who used or did not use illicit drugs during pregnancy. The characteristics of interest were maternal age at delivery, race or ethnicity, level of education, household income, employment status, prepregnancy body mass index (BMI), gestational weight gain (women with a weight gain of >40 kg or a weight loss of >20 kg were excluded), parity, previous induced abortions, use of contraception before or during pregnancy, any periconceptional folic acid use (from 1 month before through the first month of pregnancy), and any use of alcohol and cigarette smoking during pregnancy as well as paternal drug use, since most of these factors are known to affect pregnancy outcome.

A priori power analyses (α = 0.05, study power 80%) showed that the prevalence of use of cocaine, stimulants, hallucinogens, and opioids was insufficient to study their effects on perinatal outcome with satisfactory statistical power. We used multivariable linear regression techniques to study the associations between cannabis use and birth weight and gestational age, in which we included the potential confounders maternal race/ethnicity (non-Hispanic white or other), level of education (0–12 years or >12 years), cigarette smoking, binge drinking (>4 drinks per sitting), and maternal age, prepregnancy BMI, and gestational weight gain as linear covariates. For the birth weight analyses, we also included gestational age as a linear term. These potential confounders were selected based on a priori knowledge and exploratory data analyses, including the findings of the descriptive analyses. Potential confounders were dropped from the model when their removal did not change the effect estimate for cannabis use by more than 10%. Similarly, we used multivariable logistic regression to study the associations between prenatally exposed and LBW (birth weight < 2500 g) and preterm birth (gestational age < 37 weeks), in which maternal age (<25 years or ≥25 years) and prepregnancy BMI (>18.5 kg/m² or ≥18.5 kg/m²) were categorized, because they did not show linear relationships with the outcomes. In subanalyses, we conducted stratified analyses by trimesters of use, which were not mutually exclusive since the numbers of women who only used cannabis in the second or third trimester were very small. Statistical analyses were performed using SPSS Version 16.0 for Windows (SPSS Inc., Chicago, IL).

3. Results

Of the 5871 women, 277 (4.7%, standard error (S.E.) 0.27) reported use of an illicit drug in the 3 months before pregnancy. Illicit drug use during pregnancy was reported by 210 women (3.6%, S.E. 0.24). Cannabis was the most commonly used illicit drug (n = 189), followed by cocaine and stimulants (n = 27). Of the cocaine users, 22 women used powder cocaine, 1 woman used crack, and 4 women used a combination of both. Opioids and hallucinogens were reported by only 4 and 2 women, respectively. Most illicit drug users (84.3%) took one illicit substance, while 15.7% used two or more illicit drugs.

Women who reported use of cannabis, cocaine, or stimulants during pregnancy were on average younger than nonusers (Table 1). Cannabis users were more often non-Hispanic black and less often Hispanic than nonusers, whereas pregnant cocaine users were more often of Hispanic origin. Women who reported illicit drug use were more likely to have a low level of education, to have a household income below $20,000, or to be unemployed. They were also more often overweight (BMI < 18.5 kg/m²) than women who did not report use of illicit drugs during pregnancy. Cannabis users were more likely than nonusers to have excessive weight gain during pregnancy. Women who reported use of any illicit drug were less likely to have used folic acid in the periconceptional period. In addition, cannabis users were less likely to have had children before, but more likely to have had an induced abortion in the past. A similar pattern was seen for women who reported use of stimulants, but not for women who reported use of cocaine. Illicit drug users more often reported any use of alcohol or cigarette smoking during pregnancy and far more often reported that their partners used illicit drugs.

We included 5661 infants in the analyses of the associations between cannabis use and perinatal outcomes. After adjustment for confounding factors, there was no difference in mean birth weight (−17 g, P = 0.65) or gestational age (−0.1 weeks, P = 0.75) between cannabis-exposed and non-exposed infants (Table 2). No associations between cannabis use and LBW [adjusted odds ratio (OR) 0.7, 95% confidence interval (CI): 0.3–1.6] or preterm birth (OR 1.0, 95% CI: 0.6–1.9) were found either. Stratification by trimester of use did not alter these results greatly, although cannabis use during the second trimester, especially among cigarette smokers, seemed to have a detrimental effect on birth weight. In addition, the risks of preterm birth seemed slightly increased among women who used cannabis in the second (OR 1.6, 95% CI: 0.8–3.3) or third trimester (OR 1.8, 95% CI: 0.9–4.0). We did not detect a dose–response effect of prenatal cannabis exposure on perinatal outcome (data not shown).

4. Discussion

In our study, women who reported using cannabis, cocaine, or stimulants during pregnancy were similar to one another, but different from other pregnant women in a number of demographic and lifestyle characteristics. In general, prenatal cannabis use did not seem to be associated with infant birth weight or gestational age. Although we adjusted for a broad range of confounders, residual confounding by factors that we were unable to measure remains possible.

The use of illicit substances during pregnancy is likely underestimated because respondents often falsely deny use for fear of judgment or prosecution or because of feelings of shame and guilt. Previous studies have shown that 18–34% of participants who test positive through toxicological screening were missed when a questionnaire was used (Lester et al., 2001; Bauer et al., 2005; Eyler et al., 2005). Therefore, misclassification of the exposure status of study infants has occurred, but this is most likely non-differential, especially since birth weight and gestational age were not the primary outcomes of interest in the NBDDS and evidence for recall bias among case–control studies of pregnancy outcome is scarce. Non-differential misclassification may have resulted in underestimation.
of exposure frequencies and less precise estimates. However, the possibility of differential misclassification of prenatal illicit drug exposure status cannot completely be excluded.

In our study, women who reported cannabis and cocaine use during pregnancy had similar characteristics as those previously reported in the literature. However, there were some discrepancies, such as the lower level of education for cannabis users, the younger maternal age of cocaine users, and the fact that the majority of cocaine users were Hispanic as opposed to African American. Younger maternal age of cocaine users, and the fact that the majority of cocaine users were Hispanic as opposed to African American are additional factors that could contribute to the differences observed in our study compared to previous studies. However, it is important to consider that vital statistics data, in contrast with our study population, include children with birth defects who are often born preterm (Honein et al., 2009), but it could also be due to some selection in our population. A recent study showed that the NBDS control participants, who constitute our study population, are generally representative of their base populations (Cogswell et al., 2009).

Our findings suggest that prenatal cannabis use overall is not associated with birth weight or gestational age, which is consistent with previous studies (Shiono et al., 1995; English et al., 1997; Hutchins and DiPietro, 1997; Finch et al., 2001; Fergusson et al., 2002). However, cannabis use in later stages of pregnancy might have some detrimental effect on perinatal outcomes. Further research is needed to determine the true association between illicit drug use and perinatal outcome, in which other factors such as blood, urine, or meconium analyses, might be used to assess exposure status. Furthermore, it remains uncertain whether prenatal cannabis exposure as well as exposure to other illicit drugs affects the occurrence of birth defects and developmental problems later in life.
Table 2

<table>
<thead>
<tr>
<th>Drug group</th>
<th>Cannabis</th>
<th>Birth weight</th>
<th>Low birth weight</th>
<th>Gestational age</th>
<th>Preterm birth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Users</td>
<td>Nonusers</td>
<td>β (95% CI)*</td>
<td>Number (%) of cases</td>
<td>Odds ratio (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Exposed</td>
<td>Non-exposed</td>
</tr>
<tr>
<td>Any cannabis use during pregnancy</td>
<td>185</td>
<td>5343</td>
<td>−17 (−90 to 56)b</td>
<td>9.49</td>
<td>243 (4.5)</td>
</tr>
<tr>
<td>Non cigarette smokers</td>
<td>51</td>
<td>4557</td>
<td>−31 (−164 to 101)j</td>
<td>1 (2.0)</td>
<td>189 (4.1)</td>
</tr>
<tr>
<td>Cigarette smokers</td>
<td>134</td>
<td>785</td>
<td>−14 (−102 to 75)j</td>
<td>8 (6.0)</td>
<td>54 (6.9)</td>
</tr>
<tr>
<td>First trimester cannabis use</td>
<td>174</td>
<td>5343</td>
<td>−5 (−81 to 72)j</td>
<td>9 (5.2)</td>
<td>243 (4.5)</td>
</tr>
<tr>
<td>Non cigarette smokers</td>
<td>48</td>
<td>4557</td>
<td>−7 (−150 to 131)m</td>
<td>1 (2.1)</td>
<td>189 (4.1)</td>
</tr>
<tr>
<td>Cigarette smokers</td>
<td>126</td>
<td>785</td>
<td>−4 (−95 to 86)m</td>
<td>8 (6.3)</td>
<td>54 (6.9)</td>
</tr>
<tr>
<td>Second trimester cannabis use</td>
<td>76</td>
<td>5343</td>
<td>−100 (−202 to 1)d</td>
<td>6 (7.9)</td>
<td>243 (4.5)</td>
</tr>
<tr>
<td>Non cigarette smokers</td>
<td>19</td>
<td>4557</td>
<td>−41 (−257 to 175)j</td>
<td>1 (5.3)</td>
<td>189 (4.1)</td>
</tr>
<tr>
<td>Cigarette smokers</td>
<td>57</td>
<td>785</td>
<td>−136 (−253 to 18)j</td>
<td>5 (8.8)</td>
<td>54 (6.9)</td>
</tr>
<tr>
<td>Third trimester cannabis use</td>
<td>53</td>
<td>5343</td>
<td>−89 (−209 to 30)m</td>
<td>4 (7.5)</td>
<td>243 (4.5)</td>
</tr>
<tr>
<td>Non cigarette smokers</td>
<td>16</td>
<td>4557</td>
<td>−99 (−316 to 118)j</td>
<td>1 (6.2)</td>
<td>189 (4.1)</td>
</tr>
<tr>
<td>Cigarette smokers</td>
<td>37</td>
<td>785</td>
<td>−87 (−233 to 59)m</td>
<td>3 (8.1)</td>
<td>54 (6.9)</td>
</tr>
</tbody>
</table>

*a Regression coefficient, which represents the difference in birth weight (g) or gestational age (weeks) between exposed and non-exposed infants, with 95% confidence interval.

*b Adjusted for gestational age, maternal age at delivery, race or ethnicity, cigarette smoking, binge drinking (≥4 drinks per sitting), prepregnancy BMI, and gestational weight gain.

*c Adjusted for gestational age and cigarette smoking.

*d Adjusted for maternal age at delivery, race or ethnicity, cigarette smoking, binge drinking, prepregnancy BMI, and gestational weight gain.

*e Adjusted for cigarette smoking, binge drinking, and gestational weight gain.

*f Adjusted for gestational age, maternal age at delivery, race or ethnicity, cigarette smoking, binge drinking, prepregnancy BMI, and gestational weight gain.

*g Adjusted for gestational age.

*h Adjusted for gestational age and cigarette smoking.

*i Adjusted for maternal age at delivery, race or ethnicity, binge drinking, prepregnancy BMI, and gestational weight gain.

*j Adjusted for gestational age, maternal age at delivery, race or ethnicity, cigarette smoking, binge drinking, and gestational weight gain.

*k Adjusted for gestational age, maternal age at delivery, race or ethnicity, prepregnancy BMI, and gestational weight gain.

*l Adjusted for gestational age, maternal age at delivery, and cigarette smoking.

*m Adjusted for gestational age and cigarette smoking.

*n Adjusted for gestational age, maternal age at delivery, race or ethnicity, level of education, binge drinking, prepregnancy BMI, and gestational weight gain.

*o Adjusted for gestational age and binge drinking.

*p Adjusted for binge drinking, prepregnancy BMI, and gestational weight gain.

*q Adjusted for gestational age, maternal age at delivery, and cigarette smoking.

*r Adjusted for gestational age and cigarette smoking.

*s Adjusted for gestational age, maternal age at delivery, race or ethnicity, and prepregnancy BMI.

*t Adjusted for gestational age, maternal age at delivery, and gestational weight gain.

*u Adjusted for gestational age.

*v Adjusted for gestational age and cigarette smoking.

*w Adjusted for gestational age, maternal age at delivery, race or ethnicity, and prepregnancy BMI.

*x Adjusted for gestational age, maternal age at delivery.
Role of the funding source

Author van Gelder was supported by grant 021.001.008 from the Netherlands Organisation for Scientific Research (NWO). The NWO had no further role in study design; in the collection, analysis, and interpretation of data; in the writing of the report, or in the decision to submit the paper for publication.

Contributors

Authors van Gelder, Reehuis, Caton, Werler, Druschel, and Roeleveld designed the study. Van Gelder, Reehuis, and Roeleveld wrote the protocol. Van Gelder and Caton conducted statistical analyses. Van Gelder wrote the first draft of the manuscript, all authors contributed to and approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

Acknowledgements

We would like to thank all parents who participated in the National Birth Defects Prevention Study and all staff at the Centers for Birth Defects Research and Prevention. We would also like to thank Drs. Peggy Honein and Owen Devine for their contributions to this paper.

References


