

MOTHERISK UPDATE

Effects of prenatal exposure to marijuana

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ABSTRACT

QUESTION I am treating a 27-year-old woman who is now in her 10th week of pregnancy. She smokes marijuana two to three times a week, but does not use other drugs. She also smokes 20 cigarettes a day. I am concerned about the effects of marijuana exposure on her baby.

ANSWER It is not always possible to isolate the effect of marijuana exposure from other possible confounders on pregnancy outcome. Although marijuana is not an established human teratogen, recent well conducted studies suggest it might have subtle negative effects on neurobehavioural outcomes, including sleep disturbances, impaired visual problem solving, hyperactivity, impulsivity, inattention, and increased delinquency.

RÉSUMÉ

QUESTION Je traite une femme de 27 ans qui en est maintenant à sa dixième semaine de grossesse. Elle fume de la marijuana deux à trois fois par semaine, mais elle ne consomme aucune autre drogue. Elle fume également 20 cigarettes par jour. Je m'inquiète des effets de l'exposition de son bébé à la marijuana.

RÉPONSE Il n'est pas toujours possible d'isoler l'effet de l'exposition à la marijuana des autres influences possibles durant la grossesse. Même si la marijuana n'est pas un tératogène humain établi, des études récentes bien effectuées laissent entendre qu'il pourrait y avoir certains effets néfastes subtils sur les issues neurocomportementales, incluant des troubles du sommeil, une déficience au chapitre de la solution de problèmes visuels, l'impulsivité, l'impassivité, l'inattention et l'augmentation de la délinquance.

Marijuana is a drug prepared from the plant *Cannabis sativa*. It contains more than 400 chemicals including tetrahydrocannabinol (THC), its psychoactive component, which is rapidly absorbed from the lungs into the bloodstream and is metabolized primarily by the liver. Prolonged fetal exposure can occur if the mother is a regular user because THC crosses the placenta and because detectable levels can be found in various tissues up to 30 days after a single use.¹

Trying to assess the outcome of in utero exposure to marijuana is complex. In many of the studies on marijuana exposure and pregnancy outcome, women who consume marijuana also smoked tobacco, drank alcohol, or used other drugs. The effect of marijuana exposure cannot always be isolated from other possible confounders. These limitations should be kept in mind when prenatal exposure to marijuana is considered.

Effects on a fetus

Birth weight. Several studies demonstrated a small reduction in birth weight associated with use of marijuana during pregnancy,^{2,3} while others failed to show such an effect.⁴ A recent meta-analysis combined the results from 10 different studies on maternal cannabis use and birth weight⁵ and showed only weak association between maternal cannabis use and birth weight. The largest reduction in mean birth weight for any cannabis use was 48 g (95% confidence interval [CI] 83 to 14 g). Cannabis use at least four times a day was associated with a larger reduction

of 131 g (95% CI 52 to 209 g) in mean birth weight. The authors concluded that there is inadequate evidence that cannabis, at the amount typically consumed by pregnant women, causes low birth weight.

Teratogenicity. Marijuana has not been implicated as a human teratogen. No homogeneous pattern of malformation has been observed that could be considered characteristic of intrauterine marijuana exposure.⁶ Among 202 infants exposed to marijuana prenatally, the rate of serious malformations was no higher than the rate among infants whose mothers did not use marijuana.³

Postnatal mortality. The mortality rate during the first 2 years of life was determined in 2964 infants. About 44% of the infants tested positive for drugs: 30.5% tested positive for cocaine, 20.2% for opiates, and 11.4% for cannabinoids. Mortality rates among the

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Motherisk questions are prepared by the **Motherisk Team** at the Hospital for Sick Children in Toronto. **Dr Kozer** is a member and **Dr Koren** is Director of the Motherisk Team.

cannabinoid-positive group and the drug-negative group were not significantly different ($P > .3$).⁷

Risk of childhood malignancy. A case-control study assessed in utero and postnatal exposures to drugs in 204 children with acute nonlymphoblastic leukemia.⁸ An 11-fold risk ($P = .003$) was found for maternal use of marijuana just before or during pregnancy. These findings should be interpreted cautiously because the rate of marijuana exposure in the control group was less than 1%. This rate is much lower than the 9% to 27% rate reported by others,^{2,4} and might represent recall or reporting bias in this group. Such bias could increase the odds ratio associated with the exposure. In addition to the limitations of this study, another study could not confirm such an association.⁹

Another case-control study found an increased risk for rhabdomyosarcoma among children exposed to marijuana in utero.¹⁰ In this study, it was impossible to differentiate between the effects of other agents on outcome because many women consumed marijuana with other drugs.

Current data are inconclusive, and further studies are needed to determine whether childhood malignancy is a true risk for fetuses exposed to marijuana.

Neurodevelopmental effects. Short- and long-term neurodevelopmental effects of prenatal exposure to marijuana are not clear. Because many women who use marijuana during pregnancy also use other illicit drugs, there are methodologic difficulties in interpreting the effects. In many studies, it is also difficult to isolate the effect of marijuana from other confounders, such as socioeconomic status, family structure, and mother's personality. Despite these limitations, evidence suggests that marijuana exposure during pregnancy has adverse fetal effects.

Sleep disturbances at 3 years of age were more common among offspring of women who used marijuana during

pregnancy compared with controls.¹¹ The two groups were similar in maternal age, race, income, education, and maternal use of alcohol, nicotine, and other substances during the first trimester.

Child behaviour was assessed at 10 years of age in 635 children from low-income families. Prenatal exposure to marijuana was associated with hyperactivity, inattentiveness, inattention, and increased delinquency.¹² In this cohort, women who used marijuana differed significantly from those who did not in many confounders that could affect child development. Although investigators tried to control for these variables, differences in behaviour might be partially explained by other unrecognized confounders. In another study of 146 9- to 12-year-old children, prenatal exposure to marijuana was not associated with intelligence, memory, or attention deficits.¹³ The study showed prenatal exposure to marijuana is associated with poorer visual problem solving.

An example of the difficulties associated with assessing neurobehavioural outcomes after in utero exposure to marijuana comes from Jamaica. A study was conducted in an area where marijuana use is very common, and women who use large doses of marijuana are better educated and more independent than women who consume small doses of marijuana. At 1 month old, infants of heavy marijuana-using mothers had better scores on autonomic stability, quality of alertness, irritability, and self-regulation and were judged to be more rewarding for caregivers.¹⁴ The authors suggested that these differences related to the characteristics of the mothers using marijuana.

It is possible, though, that neurobehavioural effects associated with in utero exposure to marijuana, which were observed in studies conducted in western countries, are partially related to the socioeconomic, behavioural, and psychological characteristics of women who consume marijuana during pregnancy and not to the exposure itself.

Marijuana is probably the most common illicit drug used during pregnancy.¹⁵ Taking into account the large number of infants with prenatal exposure to marijuana, even a small influence on neurobehavioural parameters could have a noticeable effect on public health.

Marijuana and breastfeeding

Tetrahydrocannabinol is transferred into breast milk and levels can be up to eight times higher than in the mother's bloodstream.¹⁶ Exposure to marijuana through breast milk might delay infants' motor development.¹⁷ The American Academy of Pediatrics considers use of marijuana as a contraindication for breastfeeding.¹⁸ It is advisable to abstain from all use of THC while breastfeeding. ❖

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