

Does the Risk of Exposure to Marijuana Outweigh the Benefits of Breastfeeding? A Systematic Review

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ABSTRACT

Little is known about the risks associated with marijuana use by mothers during the breastfeeding period. A search of CINAHL, Cochrane, Embase, ProQuest Nursing, and PubMed was conducted using a variety of text words and database MeSH terms, including cannabis, medical marijuana, lactation, breastfeeding, marijuana abuse, and marijuana smoking. Articles included both human and animal studies, and there were no language or date restrictions. Hand search and reference lists were also used to access grey literature or any other important articles. Six articles met the inclusion criteria ($n = 3$ human studies and $n = 3$ animal studies). In four of the six studies meeting our inclusion criteria, maternal marijuana exposure was associated with detrimental effects, most notably decreased motor development of children at one year of age and lasting neurodevelopmental changes in rats. Breastfeeding mothers should be advised to reduce or cease their marijuana use completely.

KEYWORDS

marijuana, cannabis, breastfeeding, infant, lactation

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Les risques de l'exposition à la marijuana l'emportent-ils sur les avantages de l'allaitement? Une revue systématique

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RÉSUMÉ

Nous ne disposons que de peu de données au sujet des risques associés à l'utilisation de marijuana par les mères pendant la période de l'allaitement. Des recherches ont été menées dans les bases de données CINAHL, Cochrane, Embase, ProQuest Nursing et PubMed au moyen de divers mots clés et termes MeSH, dont cannabis, medical marijuana, lactation, breastfeeding, marijuana abuse et marijuana smoking. Les articles retenus traitaient d'études menées tant chez l'homme que chez l'animal; de plus, aucune restriction en matière de langue ou de date n'a été imposée. Des recherches manuelles et des listes de références ont également été utilisées pour obtenir accès à la littérature grise ou à tout autre article important. Six articles ont satisfait aux critères d'inclusion ($n = 3$ études menées chez l'homme et $n = 3$ études menées chez l'animal). Dans quatre de ces six articles, l'exposition maternelle à la marijuana a été associée à des effets néfastes, plus particulièrement un retard du développement moteur de l'enfant à 1 an et des modifications durables du développement neurologique chez le rat. Les mères qui allaitent devraient être avisées de diminuer leur utilisation de marijuana ou de l'abandonner complètement.

MOTS CLÉS

Marijuana, cannabis, allaitement, nouveau-né, lactation

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INTRODUCTION

It is well documented that breastfeeding is the ideal method of nutrition during a child's first year of life.^{1,2} In addition to contributing to the bond between mother and child, breastfeeding provides the appropriate amount of carbohydrates, fats, proteins, minerals, and vitamins to the baby, as well as maternal antibodies that provide the infant with adequate defence against infection and its growth.¹ Breastfeeding rates have been increasing throughout North America. In 2011, 79% of mothers in the United States initiated breastfeeding, and 49% were breastfeeding infants six months of age; in Canada, 89% of mothers were breastfeeding in 2011 to 2012, and 30% were breastfeeding infants six months of age.³ Compared to breastfed infants, formula-fed infants gain more weight and body fat from 3 to 6 months of age; have higher insulin, serum amino acid, and blood urea nitrogen levels; and are at higher risk for type 1 and type 2 diabetes, obesity, and cardiovascular disease in adulthood.⁴

Little is known about the risks associated with marijuana use during the breastfeeding period.

Marijuana (*Cannabis sativa*) is the most commonly used drug both in developed and developing countries; 2.5% to 4.9% of the world's population between 15 and 64 years of age use it.⁵ As of October 2016 in the United States, medical marijuana has been approved for use in 25 states and the District of Columbia; similar legislation is pending in Arkansas, Florida, and North Dakota. This has resulted in a change in societal attitudes towards marijuana use, and the perceived risk presented by regular marijuana use has been lower in recent years.⁶

As with most drugs, however, marijuana consumption is not random in the general population. Higher rates of use are more common among people of lower socioeconomic status, such as single-parent families.⁷⁻¹⁰ Compared to two-parent

families, single-parent families are more likely to live in poverty, and single mothers have higher levels of psychological distress and higher prevalence rates of major depressive illness than married mothers have, largely due to single mothers' greater exposure to stress.^{11,12} Poverty has been shown to be a consistent risk factor for substance abuse, and it is plausible that stress may mediate the relationship between poverty and marijuana use such that financial strain increases stress, which in turn increases the likelihood of substance use disorders.¹³

Marijuana is one of the most frequently used illicit drugs during pregnancy and lactation; the prevalence of use, mostly for recreational purposes, ranges from 3% to 30% during pregnancy for different populations.^{9,14-16} Similar prevalence rates have been reported for lactating women.^{17,18} In fact, the greatest increase in the recreational use of marijuana in the United States has been among women of childbearing age.^{12, 19} It has been suggested that the rate of marijuana use in breastfeeding women is also likely underreported because many women worry about the legal consequences of reporting their marijuana use, fearing that this information will leak out to child protective services.¹² With the growing social acceptance of marijuana as both a recreational and medicinal drug, it is plausible that the incidence of marijuana use during lactation will increase in coming years.⁹

Delta-9-tetrahydrocannabinol (THC) is the primary psychoactive compound of marijuana. In heavy marijuana users (defined as persons who smoke five or more marijuana cigarettes per day) who are mothers, THC has been shown to transfer into breast milk at a level eight times higher than that of maternal blood.²⁰ Yet, despite what is known about the reported use of marijuana during pregnancy and lactation, little is known about the risks associated with marijuana use during the breastfeeding period. This is partly because so many confounding factors are associated with breastfeeding and marijuana use. If these factors are not statistically adjusted for, findings on marijuana exposure and breastfeeding will be unclear. Inaccurate recall, reporting bias, and differing baseline characteristics between users and nonusers may also confound studies of marijuana use during lactation.⁹

To our knowledge, only one systematic review

has assessed the safety of marijuana use during lactation. In Ordean's review of English-language human studies listed in PubMed and Ovid MEDLINE between 1946 and March 2013, the author found that most harm to a child occurs via prenatal marijuana exposure when the child is still a fetus and that no clear risk is associated with exposure to marijuana during lactation.²¹

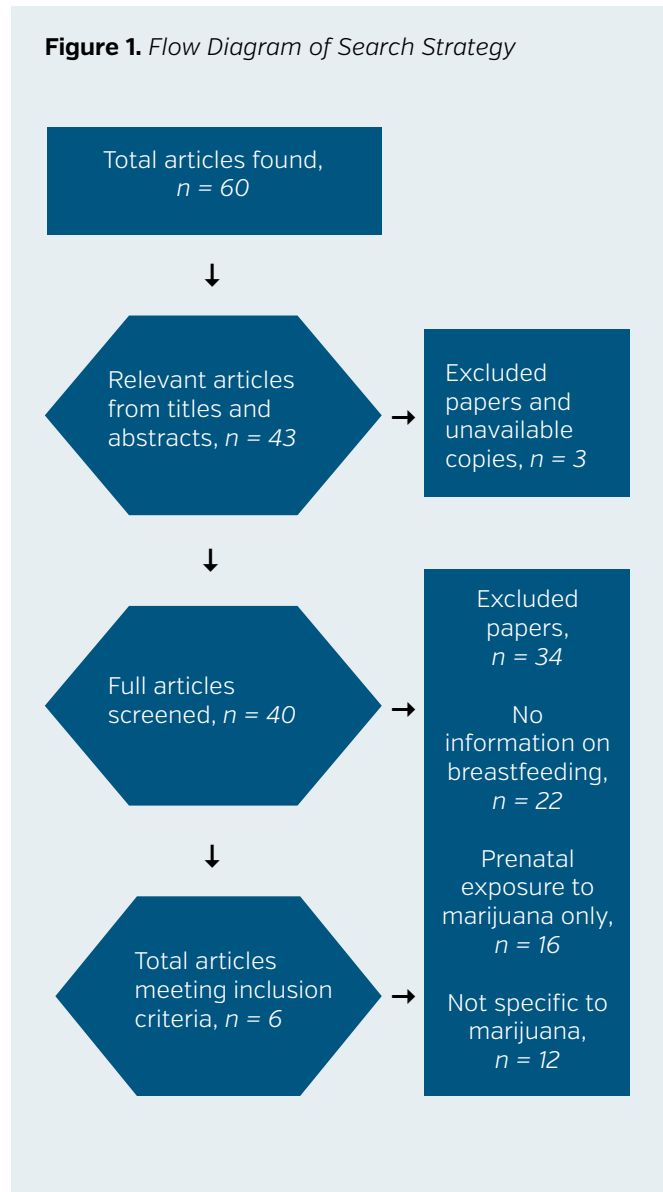
The objective of our study was to provide an updated systematic review of human and animal studies of mothers exposed to marijuana while breastfeeding, using an exhaustive search strategy without any language or date restrictions. Our goal was to determine whether the risks associated with marijuana use outweigh the benefits of breastfeeding.

METHODS

Searches of the Cumulative Index of Nursing and Allied Health Literature [CINAHL], Cochrane Library, Embase, ProQuest Nursing, and PubMed were conducted with a variety of text words and database MeSH (Medical Subject Headings) terms, including cannabis, medical marijuana, lactation, breastfeeding, marijuana abuse, and marijuana smoking. A literature search including articles on both human and animal studies was completed in November 2016. Although animal studies are not directly related to human studies, they contribute to our understanding of the pathways through which marijuana exposure can affect the developing brain. Hand searches and reference lists were used to access grey literature or any other important articles. All articles evaluating the effects of marijuana exposure on mothers who are breastfeeding were used. Excluded items included case reports, letters, and review articles. Figure 1 illustrates the search strategy.

Two of the authors independently searched the literature and coded the studies. Studies that examined only the effects of prenatal exposure to marijuana were excluded. All full-text articles were tracked, as were decisions about which studies met the inclusion criteria for the systematic review. In the case of discordance between the two reviewers, a biostatistician adjudicated the matter. To ensure that no relevant material was missed, a library information scientist from Brescia University College

Figure 1. Flow Diagram of Search Strategy



assisted each reviewer in searching the literature. This is particularly important for a systematic review, because each electronic database requires its own specific search strategy, often with exclusive search strings.²²

Data pertaining to study design, sample size, amount of marijuana exposure, and child health or animal outcomes were extracted and described for each study.

RESULTS

The literature search identified 60 articles, of which 43 were found to be potentially relevant on the basis of the title and abstract only. From this list of 43 articles, two reports were unobtainable

Table 1. Summary of Included Human Studies

Authors, Year	Location	Study Design	Sample Size
Astley and Little, 1990	Seattle, Washington	Prospective case-control study	68 lactation exposed vs. 68 non-exposed [<i>n</i> = 136]
Klonoff-Cohen and Lam-Kruglick, 2001	San Diego, California	Retrospective case-control study	239 infant cases and 239 infant controls [<i>n</i> = 478]
Tennes et al., 1985	Denver, Colorado	Prospective cohort study	756 postpartum women who had received prenatal care

and one was available only as an abstract. Once the remaining 40 articles were reviewed, six met the study's inclusion criteria. Three articles were from human studies and three were from animal research.^{17,18,23-26} The main reasons for excluding 34 reviewed articles were that these articles contained no information on breastfeeding (*n* = 22), assessed only prenatal exposure to marijuana (*n* = 16), and were not specific to marijuana use (*n* = 12).

Table 1 summarizes the three human studies, all of which were conducted in the United States. Two were prospective studies and one was a retrospective case-control study.^{17,18,23} Demographic information about the parents was not available in one study. The other two studies found that marijuana use was more common among single mothers than among married mothers. In one study, users of marijuana were much more likely to use alcohol than those who did not use marijuana.^{17,18,23}

Table 2 describes children's outcomes associated with maternal exposure to marijuana during breastfeeding. Astley and Little found that—controlling for maternal alcohol use, smoking, and cocaine use during both pregnancy and lactation—daily infant exposure to marijuana during the first month post partum was associated with a 14-point decrease in the Bayley index of motor development at one year of age.¹⁷ However, only 14 women in the study reported that they used marijuana during lactation but had not used it during pregnancy. Conversely, in a cohort of 756 postpartum women, Tennes et al. found no differences in IQ at one year of age between children who were exposed to

marijuana and children who were not exposed to marijuana, although only 27 women in the study used marijuana regularly while breastfeeding.²³

In a retrospective case-control study of 478 infants, Klonoff-Cohen and Lam-Kruglick found that maternal marijuana use during conception, pregnancy, or the postnatal period was not associated with sudden infant death syndrome (SIDS) but that paternal marijuana use was associated with SIDS during all three maternal periods.¹⁸ Controlling for alcohol and smoking, the odds ratios for paternal marijuana use and SIDS were 2.2 during conception [95% CI: 1.2, 4.2], 2.0 during pregnancy [95% CI: 1.0, 4.1], and 2.8 during the postnatal period [95% CI: 1.1, 7.3]. Ten mothers who used marijuana post partum had children who died of SIDS, compared to 11 mothers who had not used marijuana and whose children died of SIDS.

Just as research from human studies of the risk of marijuana exposure during breastfeeding is limited, investigation in animal studies of the effects of marijuana exposure during breastfeeding is scant. Table 3 summarizes the animal studies that met our inclusion criteria. Two studies used rats and one used mice.²⁴⁻²⁶ As well, two studies were specific to the effect of marijuana exposure during breastfeeding, and one study examined the influence of marijuana exposure during the prenatal and postnatal periods.²⁴⁻²⁶ Of the two studies specific to marijuana exposure during breastfeeding only, one article assessed the effects of hashish on the behaviour, appearance, and body weight of mice, while the other study investigated radioactivity in various

Table 2. Children's Outcomes of Maternal Exposure to Marijuana during Breastfeeding

Authors, Year	Marijuana Exposure	Key Findings	Sample Size
Astley and Little, 1990	20%–24% reported marijuana use \geq once weekly during pregnancy or lactation; 5%–10% reported smoking 2–5 marijuana cigarettes per day.	Daily exposure to marijuana during first postpartum month was associated with a 14-point decrease in the Bayley index of motor development at 1 year of age.	68 lactation exposed vs. 68 non-exposed ($n = 136$)
Klonoff-Cohen and Lam-Kruglick, 2001	Maternal marijuana use was 4.3% for cases and 4.7% for controls, postnatally; 5.9% for both cases and controls during pregnancy; and 12.6% for cases and 9.6% for controls during conception.	No association between maternal marijuana use and SIDS. Odds ratio for paternal marijuana use and SIDS was 2.2 during conception [95% CI: 1.2, 4.2], 2.0 during pregnancy [95% CI: 1.0, 4.1], and 2.8 during postnatal period [95% CI: 1.1, 7.3].	239 infant cases and 239 infant controls ($n = 478$)
Tennes et al., 1985	34% used marijuana during pregnancy; 45% of breastfeeding mothers at 1 year used marijuana during breastfeeding; 19% of breastfeeding mothers used marijuana \leq once per month, 15% weekly, 10% every day	Neither prenatal nor postnatal marijuana exposure influenced infant growth or mental and motor development at 1 year of age.	756 postpartum women who had received prenatal care

CI, confidence interval; SIDS, sudden infant death syndrome

organs of suckled rats at 4, 8, 24, and 72 hours after the injection of delta-9-tetrahydrocannabinol (THC).^{24,25} The third study assessed the influence of perinatal exposure to moderate doses of THC on the emotional reactivity of the offspring.²⁶

As seen in Table 4, all three studies reported significant negative outcomes for rodent pups exposed to marijuana.^{24–26} Jakubovič et al. found that suckling rats experience at least temporal structure changes in brain cells when exposed to THC or its metabolites when THC is transferred from a lactating mother to its infant.²⁵ Frischknecht et al. reported a significant decrease in the weight of suckled mice reared by dams fed with 3% hashish during the entire lactation period, compared to control mice on and after day 11. They also found that hashish led to malnourishment in mice, probably due to the passage of the drug into the milk or because the effects of hashish indirectly reduced lactation.²⁴ Last, Trezza et al. found that moderate doses of THC

in the perinatal period can produce lasting changes in the emotional behaviour of the offspring of rats.²⁶

DISCUSSION

Of the six studies that met our inclusion criteria, four [i.e., three animal studies and one human study] found that maternal marijuana exposure was associated with detrimental effects. These effects included decreased motor development in children at one year of age and lasting neurodevelopmental changes in rats in one of the animal studies. Indeed, one of the greatest concerns related to breastfeeding and marijuana use is that THC may obstruct connections in the developing brain of infants, which could lead to permanent changes.

Notably, the potency of marijuana is also much higher today than when the studies in our systematic review were conducted; one estimate shows that the potency has increased by 300%, from 3% in the 1980s to 12% in 2012.²⁷ Consequently, the negative

Table 3. Summary of Included Animal Studies

Authors, Year	Animals Studied	Study Design	Sample Size
Frischknecht et al., 1980	Mice	Prospective study of mothers fed a diet containing hashish, from birth to weaning	8 drug-fed dams and 8 control-fed dams reared all their 4 pups to weaning
Jakubovič et al., 1973	Rats	Investigation of radioactivity in brain and other tissues of suckled rats after 1 dose of THC 2-4- ¹⁴ C to the lactating rat on day 3 post partum	Not clearly stated
Trezza et al., 2008	Rats	Longitudinal study of effects of perinatal exposure to moderate doses of THC on the emotional reactivity of offspring	Control group, <i>n</i> = 20-26 THC 2.5 mg kg ⁻¹ group, <i>n</i> = 12 THC 5 mg kg ⁻¹ group, <i>n</i> = 5

THC, delta-9-tetrahydrocannabinol

Table 4. Mouse and Rat Pup Outcomes of Maternal Marijuana Exposure during Breastfeeding

Authors, Year	Marijuana Exposure	Key Findings	Sample Size
Frischknecht et al., 1980	Suckled mice reared by dams fed with 3% hashish during the entire lactation period	Body weight of pups was significantly reduced compared to controls on and after day 11.	8 drug-fed dams and 8 control-fed dams reared all their 4 pups to weaning
Jakubovič et al., 1973	Female rats injected with 53 mg/kg THC 2-4- ¹⁴ C on day 3 post partum	Radioactivity was detectable in organs of suckling rats 4 hours after injection of labelled THC in the mother. Highest radioactivity was in the stomach; substantial amounts were in the liver, heart, brain, spleen, and lungs.	Not clearly stated
Trezza et al., 2008	Primiparous Wistar rats given a daily dose of THC from day 15 of gestation to day 9 after parturition; doses equivalent to moderate consumption of marijuana in humans	Moderate doses of THC influence brain maturation and lasting neurodevelopmental changes.	Control group, <i>n</i> = 20-26 THC 2.5 mg kg ⁻¹ group, <i>n</i> = 12 THC 5 mg kg ⁻¹ group, <i>n</i> = 5

THC, delta-9-tetrahydrocannabinol

effects of marijuana exposure on breastfed infants could be much greater today, especially among infants of heavy users.

These results have important implications for health care providers. First, we believe that there is enough evidence to indicate that medicinal marijuana should not be recommended to mothers who breastfeed, because of the risk of poor neurobehavioural outcomes in neonates. Instead, breastfeeding mothers should be advised to reduce their use of marijuana or to cease using it altogether. Given that THC is transferred into breast milk at a level eightfold that of maternal blood for heavy marijuana users, mothers who smoke five or more marijuana cigarettes per day and refuse to reduce their marijuana exposure should be advised to cease breastfeeding and to formula-feed exclusively.²⁰ Our recommendation accords with the advice of Metz and Stickrath in their review of the literature but is contrary to that of Hill and Reed, who contend that “breast is best,” even when the mother uses marijuana.^{9,16}

Second, because THC is absorbed into the developing brain of a newborn, lactating women need to become more aware of the risks of marijuana use so that they can clearly decide whether they want to continue, reduce, or cease their use of marijuana.

Future research should investigate whether there is a specific quantity of marijuana that is not harmful to infants and whether the neurodevelopmental effects on infants exposed to marijuana continue beyond one year of age.

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