Medical marijuana laws and pregnancy: implications for public health policy

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An increasing number of states are passing or considering medical marijuana laws. The goal of this paper is to address the public health system's responsibility to educate physicians and the public about the impact of marijuana on pregnancy and to establish guidelines that discourage the use of medical marijuana by pregnant women or women considering pregnancy.

Although there is much to learn yet about the effects of prenatal marijuana use on pregnancy and child outcome, there is enough evidence to suggest that marijuana, contrary to popular perception, is not a harmless drug, especially when used during pregnancy. Consequently, the public health system has a responsibility to educate physicians and the public about the impact of marijuana on pregnancy and to discourage the use of medical marijuana by pregnant women or women considering pregnancy.

Key words: marijuana, medical marijuana, pregnancy

Patterns of marijuana use in pregnancy

The prevalence of marijuana use during pregnancy ranges from 2% to 5% in most studies but is reported as high as 15−28% among young, urban, socioeconomically disadvantaged women.[1] Importantly, the mean potency of marijuana in terms of its content of 9-carboxy-Δ^9-tetrahydrocannabinol, the psychoactive ingredient in marijuana, has increased steadily over the past 30 years.[2]

Although no epidemiological studies of the use of marijuana during pregnancy provide information as to the source of the women's access to marijuana, a recent report from the US Drug Testing Laboratories (Chicago, IL), examined Colorado's 2012 ballot initiative allowing large-scale marijuana production and statewide distribution and studied its impact on patterns of maternal marijuana use.[3] The ballot initiative was passed in November 2012 and went into effect January 2014.

Based on local hospital protocols, meconium specimens from newborns across the nation that were determined to be at high risk of prenatal drug or alcohol exposure were collected and forwarded to the US Drug Testing Laboratories for analysis. Data were analyzed for the presence of marijuana in specimens originating from hospitals within the state of Colorado vs specimens sent from the rest of the United States during the first 9 months of the years 2012 and 2014. Positive samples were confirmed for 9-carboxy-Δ^9-tetrahydrocannabinol using gas chromatography−mass spectrometry.

The rates of positive meconium samples for marijuana were similar at each of the time points in the 2 populations, with an approximately 10% increase in the rate of positive marijuana samples in Colorado and in the rest of the country. More importantly, however, although the concentration of marijuana in exposed neonates' meconium for the US-wide population demonstrated little change across the 2 time periods, the exposed neonates in Colorado experienced substantially more exposure to marijuana in the postlegalization period as indicated by a significant increase (Mann-Whitney, $P = .013$) in the concentrations of 9-carboxy-Δ^9-tetrahydrocannabinol, from a mean concentration of 213 ng/g ± 230.9 ng/g (median, 142 ng/g) in 2012 to 361 ng/g ± 420.3 ng/g (median, 212 ng/g) in 2014.[3]

Consequences of marijuana use in pregnancy

Although increased rates of stillbirths[4] and low-birthweight neonates[5-8] have been documented in pregnancies complicated by prenatal marijuana use, these findings are partially confounded by tobacco use, which is relatively common among women who use marijuana during pregnancy. However, the known action of exogenous cannabanoids could explain the consistent neurological and neurodevelopmental outcomes that have been documented in infants and children prenatally exposed to marijuana.[9]

Marijuana is highly lipid soluble and crosses the placenta and the blood-brain barrier with ease, accumulating in fetal tissues, particularly the brain.[10,11] In the adult central nervous system, 9-carboxy-Δ^9-tetrahydrocannabinol interferes with the endocannabinoid signaling system, responsible for modulating synaptic neurotransmitter release to regulate motor control, memory, and other brain functions.[12]

Components of the endocannabinoid system are present during embryonic central nervous system development as early as 16−22 days' gestation in humans.[13] It is at this time that the neural plate and neural tube, the basic scaffold for the forebrain, midbrain, and hindbrain, are established. A large study conducted by the US National Birth Defects Prevention Center documented a significantly increased risk for anencephaly when the fetus is exposed to

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marijuana during the first month of gestation.[14] This risk was isolated to the period when the neural tube is closing, 1−4 weeks after conception.

The function of the endocannabinoid system during the preneuronal phase in humans has not been well delineated. However, a long line of research has demonstrated its important role in shaping neuronal circuitry in the developing fetus as well as modulating development of various neurotransmitter systems, primarily the catecholaminergic and opioidergenic systems.[15-17] Gestational exposure to exogenous cannabanoids, as found in marijuana, may target the cannabinoid receptor CB_1, disrupting migration, differentiation, and synaptic communication in the developing neurotransmitter system.[18-21]

There also is evidence that intrauterine exposure to marijuana impairs dopamine D2 mRNA expression in the amygdala and in the nucleus accumbens at around 18−22 weeks' gestation.[22] The resulting defective dopamine D2 signaling in these centers, which play a role in cognitive and emotional functioning, is consistent with the neurobehavioral deficiencies that have been observed in newborns exposed to marijuana.

These deficits primarily reflect impaired regulatory control: irritability, tremors, and poor habituation[23]; difficulty with arousal and state regulation[24,25]; and sleep disturbance.[26] Although 2 studies[27,28] found no neurobehavioral differences between marijuana-exposed and nonexposed infants in the early neonatal period, it has been postulated that these 2 studies differed from the others because of sociocultural differences as well as the varying statistical treatments of the different confounding factors.[25]

Numerous studies have documented neurodevelopmental deficits in older children, adolescents, and young adults who were prenatally exposed to marijuana.[29-36] These studies once again are consistent with 9-carboxy-Δ^9-tetrahydrocannabinol's action on the developing fetal central nervous system. Longitudinal follow-up of children in a large prospective study found a consistent pattern of deficits in cognitive functioning. At 6 years of age, prenatal marijuana exposure was linked to lower verbal reasoning scores and deficits in composite, short-term memory, and quantitative intelligence scores.[29]

In this same cohort at 10 years of age, negative effects of prenatal marijuana exposure had a significant impact on design memory and screening index scores of the Wide Range Assessment of Memory and Learning,[30] and the exposed children had lower test scores on school achievement.[31] In addition, by age 10 years, prenatal marijuana exposure was significantly related to increased hyperactivity, impulsivity, and inattention problems as well as significantly increased rates of child depressive symptoms.[32,33]

Child depressive symptoms and attention problems in these children at age 10 significantly predicted delinquency at 14 years.[34] Fried and Smith,[35] in a review of several well-controlled longitudinal studies, showed that prenatal marijuana exposure was related to a significantly increased rate of difficulties with executive functioning, an aspect of regulatory control that is key to learning and to managing behavior.

A study of functional MRIs in a group of 18-22 year old young adults who had been prenatally exposed to marijuana revealed altered neural functioning that impacted short-term memory.[36] Further animal and human studies are needed, especially studies that can overcome the common limitations found in the majority of studies that investigate teratogenic agents in humans, specifically the inability to conduct randomized, controlled, prospective studies and the reliance on retrospective self-report regarding amounts and patterns of marijuana use.

Policy implications

Although there is much to learn yet about the effects of prenatal marijuana use on pregnancy and child outcome, there is enough evidence to suggest that marijuana, contrary to popular perception, is not a harmless drug, especially during pregnancy. Twenty-four states and Washington, DC, have passed medical marijuana legislation[37] (Table).

In general, the legislation in all states removes state-level criminal penalties on the use, possession, and cultivation of marijuana by patients who possess written documentation from their physician advising that they would derive benefit from the medical use of marijuana. Only Oregon has legislation that requires a point-of-sale warning at

TABLE
States with medical marijuana laws[37]

State	Date of passage of original legislation
Alaska	November 1998
Arizona	November 2010
California	November 1996
Colorado	November 2000
Connecticut	May 2012
District of Columbia	May 2010
Delaware	May 2011
Hawaii	June 2000
Illinois	May 2013
Maine	November 1999
Maryland	April 2014
Massachusetts	November 2012
Michigan	November 2008
Minnesota	May 2014
Montana	November 2004
Nevada	November 2000
New Hampshire	May 2013
New Jersey	January 2010
New Mexico	March 2007
New York	June 2014
Oregon	November 1998
Pennsylvania	April 2016
Rhode Island	January 2006
Vermont	May 2004
Washington	November 1998

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