



Perinatal Effects of Maternal Cannabinoid Use

Relevant Background of Cannabinoids

- ♣ *Cannabis sativa* has many chemical properties: cannabinoids, terpenoids, phenols, all with individual and synergistic effects.
- ♣ THC (delta-9-tetrahydrocannabinol, the psychoactive compound) is just 1 of 60 cannabinoids in the marijuana plant
- ♣ 1980s: Discovery of the endocannabinoid system with its 2 receptors (CB1 and CB2) and endogenous ligands.
- ♣ Marijuana (MJ) is the most used illicit drug in the US and UK. Its use is rising, especially among junior high and high schoolers.
- ♣ Adult prevalence is stable around 4%, but adult abuse and dependence are rising.
- ♣ Neurobiological activity of THC includes modulating dopaminergic, GABAergic, and glutamatergic neurons.
- ♣ THC concentrations are rising: more indoor cultivation, specific seed strains.
- ♣ Acute intoxication: euphoria, time distortion, anxiety, depression, impaired short-term memory, paranoia, mystical thinking.
- ♣ The slow release of THC stored in fatty tissue and enterohepatic recirculation can impair concentration and motor performance for 12 to 24 hours.
- ♣ Fatal traffic accidents occur more often among people who test positive for THC. 10% to 57% of impaired drivers test positive.
- ♣ It is possible to differentiate smoked marijuana from ingested dronabinol on urine testing. Urine tests can help suggest that a patient is taking prescribed THC rather than selling it. It can be detected for 1-7 days with light use and for up to a month with heavy use as it is fat soluble.
- ♣ Withdrawal does occur with MJ. Heavy use for more than 21 days results in a withdrawal syndrome: irritability, agitation, depression, insomnia, nausea, anorexia, and tremor. Symptoms peak in 48 hours and last for 5-7 days. Tolerance can build as well.
- ♣ 4 times as much tar in MJ than cigarettes
- ♣ 50% more carcinogens in MJ than tobacco. However, MJ users are 5-10 times more likely to smoke tobacco.
- ♣ A systematic review (n=19) did not find a significant association between lung cancer and MJ use after adjusting for tobacco use.
- ♣ Regular smokers of 3-4 MJ joints per day lead to cough, wheezing, and sputum production and histologic changes equivalent to smoking 20 cigarettes per day. This is believed to be from MJ joints delivering 2x the smoke, 33% greater depth of inspiration, and 4x breath holding time.

Relevance to the Perinatal Period:

- MJ is the most widely used legal drug amongst women of reproductive age. Self reported use amongst pregnant women is 2.9% (NIDA 1996) and 10.4% amongst women aged 19-32, these are likely underestimates. Its use amongst teenagers has been steadily rising in the past decade. THC content in MJ is increasing.
- Pregnant women who smoke cigarettes are 10 times more likely to smoke MJ than non cigarette smokers (Perinatal Substance Exposure Study Group).
- There is a paucity of data on the perinatal effects of maternal cannabinoid use. Most human data on cannabinoids comes from Canada and Europe and much of the science is still young as the endogenous cannabinoid receptors were only discovered in the 1980's compared to the opioid receptors for example.

Short Term Effects

- *What does/may it cause?*
- Growth restrictions: intrauterine hypoxia is thought to be the mechanism. One study attempted to examine the difference in growth dynamics between early and late gestation use of MJ. A Swedish cohort of aborted fetuses (44 exposed, 95 unexposed) showed MJ use before 22 weeks lead to decreased wt. and length with consumption averaged at 3-6 joints per week. Height and head circumference weren't changed by 22 weeks and are believed to be affected later (Hurd et al 2004).
- SIDS: One study adjusted for tobacco use showed MJ as an independent risk factor (Scragg et al 2001)

- Faster onset of labor
- Shortened gestation length of approximately 1 week was observed (although a 1-week shortened gestation length has little clinical significance, the finding that the effect was dose-related may be of significance given the increased THC content in MJ today).
- In the neonatal period, exposed infants were more likely to be hyperexcitable, irritable and jittery, and have an increased arousal response compared with non-exposed healthy infants according to one observational study of adolescent mothers (exposure to marijuana was ascertained by analysis of maternal hair, neonatal meconium, and maternal review).

▪*What does it not cause?*

Our best data comes from two longitudinal cohort studies described below and neither showed an increase in miscarriage rates, types of presentation at birth, Apgar status, nor the frequency of complications or major physical abnormalities at birth.

Long Term Effects

▪Longitudinal Data:

1. Ottawa Prenatal Prospective Study (OPPS), the objective has been to examine the association between marijuana (and other socially used drugs) consumed during pregnancy and effects upon offspring in the areas of growth, cognitive development, and behavior. This longitudinal work has been underway since 1978.
2. The Maternal Health Practices and Child Development Study (MHPCD) was initiated in 1982 at Pittsburg and has focused upon the consequences of prenatal use of marijuana, alcohol, and cocaine. The subjects in this high-risk cohort are of low socioeconomic status and just over half are African American. Growth, cognitive development, temperament, and behavioral characteristics have been reported in offspring up to the age of 10.

▪ADHD: symptoms of decreased memory, attention deficit, hyperactivity, and impulsivity were observed in a cohort of children exposed to MJ in utero who were studied at age 6 and age 10 (Leech et al 1999). An additional study showed increased delinquency amongst boys exposed in utero (Goldschmidt et al 1999).

▪Cognitive Function/Executive Function: One study showed as little as 1 joint per day led to a decreased scholastic aptitude of the child when adjusted for sociodemographic variables and tobacco use. Several cohort studies have reported an inverse association between maternal smoking during pregnancy and offspring cognitive ability. However, in many of these studies, confounding variables (particularly maternal characteristics such as socioeconomic status, use of other drugs of abuse, and maternal cognitive ability) were not well controlled.

▪Further Studies: tobacco smoking has been associated with an increased risk for DM2. A study based upon data from the British National Child Development Study reported that patients exposed to prenatal episodes of heavy maternal smoking (>10 cigarettes per day) had a four-fold increased risk of diabetes mellitus as young adults (16 to 33 years of age) compared to those without prenatal tobacco exposure. Such studies should be examined for MJ use alone.

Take Home Points to Apply in the Clinic

- If a pregnant woman does or has smoked cigarettes, keep MJ higher on your radar.
- Always ask about marijuana use in addition to tobacco use, especially in younger moms.
- Counsel patients about the potential short and long term risks of MJ use while pregnant (LBW, pre-term labor, SIDS, ADHD, cognitive impairments).

Sources:

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