Fellow Column: Marijuana in Pregnancy

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In a nationwide atmosphere of federally illegal but varying state legalization of marijuana compounded by the effort to reduce opioid prescriptions, interest has risen in finding safer and often more 'natural' alternatives. CBD oil, one component of marijuana, has been proposed as potentially beneficial with a low level of the psychoactive component, tetrahydrocannabinol or THC. Currently, pharmaceutical-grade CBD oil is being used effectively for severe forms of epilepsy but is also being trialed for use with pain, addictions, nausea, spasticity, increasing weight gain, sleep disorders, Tourette Syndrome, and mental health disorders. However, while research is continuing and answers are developing, a markedly high population of use resides among pregnant women begging the question: what is currently known about the effects of marijuana on a fetus and their long-term outcomes?

Due to a long history of recreational non-pharmaceutical marijuana use, the effect of the psychoactive THC is better understood than the proposed medicinal CBD. THC binds cannabinoid receptors such as CB1&2, which are located in the amygdala, hippocampus, and ventral striatum, and reduces dopamine receptor expression in both the ventral striatum and the nucleus accumbens. Furthermore, THC binds the endogenous fetal CB1 receptors and acts to reduce endocannabinoid synthesis (such as 2-arachidonoylglycerol) and thereby the expression of CB1. The long-term implications must include the knowledge that fetal CB1 receptors are distributed among the mesocorticolimbic system compared to the adult, areas of emotional control, cognition, and memory.(1) Alternatively, the non-euphoric CBD has not been found to bind the CB1 receptor, and the full mechanism of action remains unknown.

Currently, marijuana in any form is the most widely used substance during pregnancy, with a wide range of use among an estimated 4.9-28% of 'urban, young, and socioeconomically disadvantaged pregnant women and is associated with higher rates of concomitant substance use.(1,2) It has also been reported that 3.7% of women with significant nausea report marijuana use, as compared to 2.3% without severe nausea. Finally, marijuana use decreased from 9% to 4.5% between the first and second trimesters, correlating with reduction. Importantly, marijuana use during pregnancy compared to tobacco or no substance use was found to increase placental artery resistance, affect pulsatility resulting in lower uterine blood flow and alter axonal cell elongation and neuronal growth.(1)

While many reports contradict one another and most are unable to isolate marijuana use without confounders, most studies agree that intrauterine marijuana exposure results in lower birth weight, smaller head circumferences, earlier deliveries, and increased NICU admissions – some children also exhibit signs of withdrawls like tremors, increased movement, and high pitched cries. However, studies neither report an increased risk of neonatal death with exposure nor the increased incidence of grade 3-4 interventricular hemorrhages, necrotizing enterocolitis, bronchopulmonary dysplasia, or cerebral palsy.(1)As the child's age increases, research has found conflicting results pertaining to school performance, behaviors, and visual-spatial ability. One study completed between 1983 and 1990 in Jamaica controlled for isolated marijuana use and matched to non-uses of similar variables whose children ages birth to 5 years old were assessed behavioral-developmental outcomes. This study found that there was no association between marijuana exposure and IQ, memory, verbal ability, or perception. (2,3)

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At a time when the totality of exposure and outcomes is forthcoming, we as physicians should continue to screen for marijuana use among teenagers, pregnant women, and others at risk for abuse. Two screening tools have been successful in alcohol and substance screening, where two or more positive answers are highly sensitive and quite specific. Then can also be applied to marijuana abuse:

CAGE: Have you ever felt you could cut down use? Have others been annoyed at your use? Have you felt guilty about using? Have you ever needed to use marijuana as an eye-opener to wake up or steady your nerves?(4)

CRAFT: Have you ridden in a vehicle with someone who was "high" or under an influence? Do you ever use to relax or fit in? Do you ever use marijuana when you are alone? Have you ever forgotten things you did while using? Do your family or friends tell you to cut down your use? Have you ever gotten in trouble while using?(5)

To date, we know that non-pharmaceutical marijuana exposure with THC adversely affects uterine blood flow and placental artery resistance. It has also been noted that fetal exposure likely has different effects than adults given different locations of THC receptors, and further concern arises given the locations predominantly in areas of impulse modulation and emotion. Ultimately, the concern remains that the neurologic effects of exposure to marijuana are not fully known, and thereby the effect of exposure on brain development requires continued and ongoing research. As physicians, we must be keenly aware that there have been no rigorous studies performed to assess the safety profile of cannabinoid oils other than Epidiolex, which has been specifically FDA approved for three neurologic disorders: Lennox-Gastaut Syndrome, Dravet Syndrome, and Tuberous Sclerosis Complex; but otherwise, it is not FDA approved for prescription and continues to require screening for intrauterine exposure.

References:

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