INTERIM UPDATE

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

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Committee on Obstetric Practice

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

INTERIM UPDATE: This Committee Opinion is updated as highlighted to reflect a limited, focused change in the language and supporting evidence regarding marijuana use and neonatal outcomes.

Marijuana Use During Pregnancy and Lactation

ABSTRACT: *Cannabis sativa* (marijuana) is the illicit drug most commonly used during pregnancy. The self-reported prevalence of marijuana use during pregnancy ranges from 2% to 5% in most studies. A growing number of states are legalizing marijuana for medicinal or recreational purposes, and its use by pregnant women could increase even further as a result. Because of concerns regarding impaired neurodevelopment, as well as maternal and fetal exposure to the adverse effects of smoking, women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use. Obstetrician–gynecologists should be discouraged from prescribing or suggesting the use of marijuana for medicinal purposes during preconception, pregnancy, and lactation. Pregnant women or women contemplating pregnancy should be encouraged to discontinue use of marijuana for medicinal purposes in favor of an alternative therapy for which there are better pregnancy-specific safety data. There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged.

Recommendations

The American College of Obstetricians and Gynecologists recommends the following:

- Before pregnancy and in early pregnancy, all women should be asked about their use of tobacco, alcohol, and other drugs, including marijuana and other medications used for nonmedical reasons.
- Women reporting marijuana use should be counseled about concerns regarding potential adverse health consequences of continued use during pregnancy.
- Women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use.
- Pregnant women or women contemplating pregnancy should be encouraged to discontinue use of marijuana for medicinal purposes in favor of an alternative therapy for which there are better pregnancy-specific safety data.
- There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged.

Introduction

Cannabis sativa (marijuana) is the illicit drug most commonly used during pregnancy. The self-reported prevalence of marijuana use during pregnancy ranges from 2% to 5% in most studies but increases to 15–28% among young, urban, socioeconomically disadvantaged women (1–5). Higher rates of use are found when querying women at the time of delivery rather than at prenatal visits because some users may not seek prenatal care (5). Notably, 34–60% of marijuana users continue use during pregnancy, with many women believing that it is relatively safe to use during pregnancy and less expensive than tobacco (3, 4, 6, 7). A recent study noted that 18.1% of pregnant women reporting marijuana use in the past year met criteria for marijuana abuse, or dependence, or both. (8). A growing number of states are legalizing marijuana for medicinal or recreational purposes, and its use by pregnant women could increase even further as a result.

The medicinal and psychoactive properties of marijuana are mediated by compounds called cannabinoids, which are absorbed from the lungs when smoked or from the gastrointestinal tract when ingested. Tetrahydrocannabinol (THC) is a small and highly lipophilic molecule that is distributed rapidly to the brain and

fat. Metabolized by the liver, the half-life of THC varies from 20–36 hours in occasional users to 4–5 days in heavy users and may require up to 30 days for complete excretion. In animal models, THC crossed the placenta, producing fetal plasma levels that were approximately 10% of maternal levels after acute exposure. Significantly higher fetal concentrations were observed after repetitive exposures (9). Limited human data suggest that THC also appears in breast milk (10).

It is difficult to be certain about the specific effects of marijuana on pregnancy and the developing fetus, in part because those who use it often use other drugs as well, including tobacco, alcohol, or illicit drugs, and in part because of other potential confounding exposures. Marijuana smoke contains many of the same respiratory disease-causing and carcinogenic toxins as tobacco smoke, often in concentrations several times greater than in tobacco smoke (11). Adverse socioeconomic conditions, such as poverty and malnutrition, may contribute to outcomes otherwise attributed to marijuana. For example, one population-based study reported that pregnant marijuana users were more often underweight and had lower levels of education, had a lower household income, and were less likely to use folic acid supplementation than nonusers (2). Another study found that marijuana-exposed women are more likely to experience intimate partner violence, an additional risk factor for adverse pregnancy outcomes (12). Studies evaluating marijuana use during pregnancy often account for these confounders using data stratification or multivariate analysis. Studies of marijuana exposure during pregnancy are potentially subject to reporting and recall bias, often relying on self-reported habits, including frequency, timing, and amount of marijuana use. Additional confounding issues may arise from marijuana potency that has, in general, increased with time (13).

Effects of Marijuana Use on Pregnancy

Cannabinoids, whether endogenous or plant derived, exert their central nervous system effects via cannabinoid receptor type 1. Animal models demonstrate that endocannabinoids play key roles in normal fetal brain development, including in neurotransmitter systems, and neuronal proliferation, migration, differentiation, and survival (14). Human fetuses exhibit central nervous system cannabinoid receptor type 1 as early as 14 weeks of gestation, with increasing receptor density with advancing gestational age, which suggests a role for endocannabinoids in normal human brain development (15, 16).

Studies using laboratory animals show that in utero exogenous cannabinoid exposure may disrupt normal brain development and function (14). Manifestations of in utero exposure include impaired cognition and increased sensitivity to drugs of abuse (17). Of further concern, supraphysiologic fetal cannabinoid exposure can potentiate brain susceptibility to the apoptotic effects of ethanol (18), highlighting concerns for polysubstance abuse and suggesting that exposure to exogenous cannabinoids could negatively affect brain development. Studies noted that children who were exposed to marijuana in utero had lower scores on tests of visual problem solving, visual–motor coordination, and visual analysis than children who were not exposed to marijuana in utero (19–22). Additionally, prenatal marijuana exposure is associated with decreased attention span and behavioral problems and is an independent predictor of marijuana use by age 14 years (23–25). Effects of prenatal marijuana exposure on school performance are less clear. Although one longitudinal study found no significant effect on several measures of cognition and school performance among primarily middle socioeconomic class children aged 5–12 years (26, 27), another longitudinal investigation of children of mostly urban, lower socioeconomic means observed poorer reading and spelling scores and lower teacher-perceived school performance (28).

Available evidence does not consistently suggest that marijuana causes structural anatomic defects in humans (29–31). In one large study, the adjusted odds ratio for marijuana users who gave birth to newborns with a major birth defect was not statistically significant. However, the study did not address timing of marijuana exposure during pregnancy (29). A later study identified cases of marijuana use during the month before or the first three months of pregnancy, with nonusers serving as controls. There were no significant differences in the adjusted odds for 20 major anomalies examined among users versus nonusers. However, when the analysis was restricted to marijuana use in the first month of pregnancy, the odds of anencephaly in the offspring of users was significantly increased to 2.5 (95% confidence interval [CI], 1.3–4.9) (30). This finding may be confounded, however, by the separate observation that marijuana users are less likely to take supplemental folic acid than nonusers (2), as well as by the aforementioned multiple-comparisons issue and the possibility of type 1 errors (incorrect rejection of a null hypothesis).

Currently available evidence does not suggest an association between marijuana use in pregnancy and perinatal mortality, although the risk of stillbirth may be modestly increased (31, 32). A meta-analysis of 31 observational and case–control studies assessing neonatal outcomes in marijuana users versus nonusers examined perinatal death and stillbirth as secondary outcomes. Compared with nonusers, marijuana users experienced similar rates of perinatal death (relative risk [RR], 1.09; 95% CI, 0.62–1.91), but had somewhat higher stillbirth rates (RR, 1.74; 95% CI, 1.03–2.93). The latter finding should be interpreted with caution because these results could not be adjusted for tobacco use and there was a tendency in this study for significant associations between marijuana use and other adverse outcomes to become statistically insignificant when adjusted estimates were pooled. Support for this interpretative approach comes from a report included in

the meta-analysis that found that THC was significantly associated with stillbirth at or beyond 20 weeks of gestation, although the finding remained somewhat confounded by the effect of cigarette smoking (33).

Several studies evaluated newborn birth weights and multiple biometric parameters after in utero marijuana exposure. A primary outcome of the aforementioned meta-analysis (32) was birth weight less than 2,500 g. Marijuana use alone was not associated with an increased risk of birth weight less than 2,500 g. However, when marijuana use alone was stratified by amount of use, women who used marijuana less than weekly were not at increased risk of giving birth to a newborn less than 2,500 g (8.8% versus 6.7%; RR, 1.22; 95% CI, 0.91–1.64). However, women using marijuana at least weekly during pregnancy were significantly more likely to give birth to a newborn less than 2,500 g (11.2% versus 6.7%; 95% CI, 1.44–2.45). A recent retrospective cohort study not considered in the meta-analysis found a modestly increased risk of birth weight less than the 10th percentile among marijuana users after adjusting for confounders among tobacco nonusers (16.3% versus 9.6%; odds ratio, 1.36; 95% CI, 1.09–1.69) and tobacco users (20.2% versus 14.8%; odds ratio, 1.21; 95% CI, 1.00–1.45) (31). Several studies noted statistically significantly smaller birth lengths and head circumferences as well as lower birth weights among exposed offspring (34, 35–38). These findings were more pronounced among women who used more marijuana, particularly during the first and second trimesters (34, 36, 39). The clinical significance of these observations remains uncertain.

Most reports do not show an association between marijuana use and preterm birth (12, 31, 32, 38, 39). The above-cited meta-analysis' other primary outcome was preterm birth before 37 weeks of gestation (32). Compared with women using marijuana less often, women using marijuana at least weekly were at increased risk of preterm delivery (10.4% versus 5.7%; RR, 2.04; 95% CI, 1.32–3.17). When marijuana use was stratified by concomitant tobacco use, marijuana use alone was not associated with an increased risk of preterm birth, but use of both substances did exhibit an association in comparison to women not using either substance (11.4% versus 5.7%; RR, 1.85; 95% CI, 1.21–2.81) (32). Similarly, a retrospective cohort study published simultaneously with the meta-analysis also found that the risk of preterm delivery among marijuana users was observed only among those also using tobacco (38). Thus, concurrent tobacco use may be an important mediator for some adverse pregnancy outcomes among marijuana users. Of note, another report observed no increase in preterm delivery among marijuana users regardless of reported tobacco use (31).

Although there are limitations to the data on marijuana use during pregnancy—animals are frequently poor surrogates, and studies in humans often are heavily confounded by polysubstance use and lifestyle issues—worrisome trends do emerge. Therefore, because of concerns regarding impaired neurodevelopment, as well as maternal and fetal exposure to the adverse effects of smoking, women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use. Because the effects of marijuana use may be as serious as those of cigarette smoking or alcohol consumption, marijuana also should be avoided during pregnancy. Before pregnancy and in early pregnancy, all women should be asked about their use of tobacco, alcohol, and other drugs, including marijuana and other medications used for nonmedical reasons. Women reporting marijuana use should be counseled about concerns regarding potential adverse health consequences of continued use during pregnancy. Patients should be informed that the purpose of screening is to allow treatment of the woman's substance use, not to punish or prosecute her; however, patients should also be informed of the potential ramifications of a positive screen result, including any mandatory reporting requirements. Seeking obstetric–gynecologic care should not expose a woman to criminal or civil penalties for marijuana use, such as incarceration, involuntary commitment, loss of custody of her children, or loss of housing (40). Addiction is a chronic, relapsing biological and behavioral disorder with genetic components, and marijuana use is addictive in some individuals. Drug enforcement policies that deter women from seeking prenatal care are contrary to the welfare of the mother and fetus (41).

Effects of Marijuana Use on Lactation

There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged (42). Breastfeeding women should be informed that the potential risks of exposure to marijuana metabolites are unknown and should be encouraged to discontinue marijuana use. The American College of Obstetricians and Gynecologists' Breastfeeding page, available at www.acog.org/About-ACOG/ACOG-Departments/Breastfeeding, provides more resources about breastfeeding for clinicians and patients.

Medical Marijuana

Because marijuana is neither regulated nor evaluated by the U.S. Food and Drug Administration, there are no approved indications, contraindications, safety precautions, or recommendations regarding its use during pregnancy and lactation. Likewise, there are no standardized formulations, dosages, or delivery systems. Smoking, the most common route of administration of THC, cannot be medically condoned during pregnancy and lactation. Therefore, obstetrician–gynecologists should be discouraged from prescribing or suggesting the use of marijuana for medicinal purposes during the period before pregnancy, and during pregnancy and lactation. Rather, pregnant women or women contemplating pregnancy

should be encouraged to discontinue use of marijuana for medicinal purposes in favor of an alternative therapy for which there are better pregnancy-specific safety data. High-quality studies regarding the effects of marijuana and other cannabis products on pregnancy and lactation are needed.

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