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Letter to Editor

The Legalization of Marijuana and Fertility Implications

Mary Lee Barron*

Family Health and Community Health Nursing, Southern Illinois University Edwardsville School of Nursing, Edwardsville, Illinois, United States

*Corresponding author: Mary Lee Barron, Associate Professor, Family Health and Community Health Nursing, Southern Illinois University Edwardsville, Edwardsville, Illinois, United States, Tel: +1 6186503995; Office: +1 6186503995; E-mail: mabarro@siue.edu

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Marijuana is the most commonly used/abused "illicit" drug in the world [1]. With the legalization of marijuana in 29 US states, for medicinal or recreational use as well as changed social acceptability, it is likely that more young men and women will use this substance [2]. Between 2001 and 2013, marijuana use among US adults more than doubled, many states legalized marijuana use, and attitudes toward marijuana became more permissive [3]. Marijuana is the most commonly used "illicit" drug during pregnancy ranging from 2-5% but as high as 15-28% [3].

In aggregated 2007-2012 data, 3.9% of pregnant women and 7.6% of nonpregnant reproductive-aged women reported past-month marijuana use [3]. The American College of Obstetricians and Gynecologists recommends that pregnant women and women planning pregnancy be screened for and discouraged from using marijuana and other substances [3]. There is an emerging body of research reporting the adverse effects in pregnancy such as fetal growth restriction, fetal neurodevelopment, stillbirth, and preterm birth and may be linked to hyperactivity, poor cognitive function and changes in dopaminergic receptors [3].

In 2015, when only 4 states had legalized marijuana use, over 40% of American men report having ever used marijuana, with approximately 25% of young men reporting use within the past month [4]. Thus, there are approximately 22.2 million current users of marijuana [3]. Moreover, up to 22% of men who intended to have children (or more children) reported using marijuana within the past 12 months [5-7].

Effects on Fecundity

Beyond marijuana use during pregnancy, there is another aspect on reproduction which is less studied: the effect on fertility and fecundity. Infertility is a significant problem in the US with couples experiencing a significant financial and emotional burden. Marijuana has been linked to decreased fertility in both men and women. Subfecundity affects 7-15% of the population [8,9].

Furthermore

- 1/10 couples have problems with infertility [7].
- 1 in 8 couples (or 12% of married women) have trouble getting pregnant or sustaining a pregnancy [3].
- One-third of infertile couples may have a male factor present [8,9].
- The number of women aged 15-44 with impaired fecundity is approximately 7.5 million (12.3%) [3].
- Number of married women aged 15-44 that are infertile: 1.0 million [7].

Physiologic Effects

The Endo-Cannabinoid System (ECS) is part of the complex regulation of male reproduction through the endogenous release of endocannabinoids and then binding to cannabinoid receptors. Disturbing the delicate balance of the ECS due to marijuana use can negatively impact reproductive potential in both men and women [12,13]. Evidence suggests that marijuana can reduce female fertility by suppressing hypothalamic release of Gonadotropin Releasing Hormone (GnRH) leading to reduced estrogen and progesterone production and anovulatory menstrual cycle [11]. Similarly, in men, there are disruptions in the hypothalamic-pituitary-testicular axis, with marijuana users having decreased levels of luteinizing hormone, and lower testosterone levels. Men who smoke marijuana frequently have sperm that behave abnormally, significantly less seminal fluid and a lower total sperm count, all of which may affect fertility adversely. The acrosome

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reaction, necessary to fertilize the ovum, is inhibited by exposure to cannabinoids [8,12,13]. Because there are men who smoke marijuana who are also fathers it is possible that conception may happen. However, it is the men who already of low fertility that are most at risk of become infertile. Marijuana exposure may be the habit which leads them over the threshold for infertility. When women smoke marijuana, the active ingredient (-carboxy- Δ 9-Tetra Hydro Cannabinol (THC) appears in their uterus, fallopian tubes, and vaginal fluids. Sperm exposed to this THC are likely to act just as sperm exposed to THC in the testes [10].

Research Limitations

It is difficult to be certain about the specific effects of marijuana on fecundity, pregnancy and the developing fetus, in part because those who use it often use other drugs including tobacco, alcohol, or illicit drugs, and in part because of other potential confounding exposures [3]. Because marijuana is/was an illicit drug, research on the effects are limited. Another factor complicating the research is that the current marijuana is not the marijuana of the 1980s and prior when earlier studies were completed. The potency of THC content has also increased which may lead to increase previously known effects [14,15].

Lack of Public Health Messaging or Policy

Across the United States, discussion continues over the implications of marijuana use in the public, the research community, and among federal, state, and local policymakers. Although the media reports on the legalization of marijuana, there is a general lack of messaging on the general health implications, much less on the effect on reproduction. Research on adolescents shows that advertising may be responsible for up to 30% of teen tobacco and alcohol use [16]. We can readily consider the effect of marijuana use in movies, television shows and commercials. Raising awareness is key to confronting the health issues secondary to legal and illegal marijuana use and an ongoing challenge for the nation. At minimum, clinicians should include questions on marijuana usage while counseling patients/couples about planning pregnancy and discussing the association and potential impact of marijuana on male fertility.

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