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THE EFFECTS OF CANNABIS ON MALE FERTILITY: A LITERATURE REVIEW

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Abstract

Background: Cannabis is a commonly used drug, both recreationally and in medicine, that has a big impact on endocannabinoid system responsible for human reproductive functions.

Aim: The review of current literature on the effects that cannabis has on male reproductive system.

Methodology: A review was conducted using PubMed, Google Scholar, and ResearchGate. Search terms included: cannabis, marijuana, male fertility, cannabis use disorder, endocannabinoid system. Studies published between 2020-2025 were reviewed.

Results: Chronic marijuana use can potentially lead to fertility problems in male population, such as decreased sperm motility, DNA integrity or compromised capacitation, leading to troubles with egg fertilization and conception, however, the research is not conclusive.

Conclusions: Men planning reproduction should consider abstinence from both THC and CBD, because of their potential impact on male fertility, but further studies in this area should be considered.

Keywords: marijuana, cannabis, male fertility, cannabis use disorder, endocannabinoid system

1. Introduction

Cannabis (marijuana) is derived from two plants, *Cannabis sativa* and *Cannabis indica,* and is a psychoactive substance, causing euphoria, relaxation and altered perception. Cannabis contains 500 active compounds, called cannabinoids, including Δ9-tetrahydrocannabinol (THC), which is believed to have an effect on several crucial hormones. It is said to be one of the most used drugs worldwide, with ESAD 2024 data stating that 13.5% of Polish teenagers aged 15-16 and 36.7% aged 17-18 used it at least once in their lives [1]. In this paper we will closely examine the relation between marijuana use and male sexual and reproductive health.

2. Methodology

To conduct a comprehensive review of the cannabis effects on male fertility, articles available in PubMed, Google Scholar and ResearchGate databases were analyzed. The following keywords were used in the search: cannabis, marijuana, male fertility, cannabis use disorder, endocannabinoid system. The search included studies published between 2020-2025. Reference lists of selected studies were also screened to identify additional relevant sources.

3. Male infertility

Infertility is a widespread health issue that affects millions of individuals of reproductive age globally, often bringing emotional and social strain to both families and communities. Current estimates suggest that approximately 186 million individuals and 48

million couples experience infertility worldwide. Notably, male-related factors contribute to nearly 50% of all infertility cases. From 1990 to 2019 a steady rise of male impotence has been observed [2, 3].

Male infertility can arise from a variety of causes that disrupt sperm production (spermatogenesis), impair the function of reproductive organs, or stem from psychological origins. These causes may be inherited (genetic conditions passed down through families), acquired (developed later in life due to infections, injuries, or lifestyle factors), or idiopathic (where no clear cause can be identified). A range of contributing elements can negatively affect male reproductive health, including age, environmental toxins, genetic disorders, systemic illnesses (diabetes, obesity, autoimmune diseases), medications and drugs. The last one, especially marijuana, is notably underestimated and not taken into consideration by couples planning reproduction. Because of the increase of cannabis use worldwide, it should draw more attention to potential fertility issues associated with it [2, 4].

4. Statistics on cannabis use

Cannabis is, at present, said to be the most widely used illicit substance worldwide, outranking cocaine and opiates in the last decade. Approximately 2.5% of the world's population consumes it, which gives the number of 147 million people [2]. Nine countries have legalized recreational cannabis use nationwide, including Canada, Germany, Thailand, Mexico, and several states in the United States of America. Nearly fifty countries in total have at least partially legalized cannabis for medical use [5].

Studies conducted by National Institute on Drug Abuse (NIDA) in 2023 on the U.S. population show that cannabis use remains at historically high levels for adults aged 19 to 30, with about 10% of those surveyed reporting daily use, and 8% in the 35 to 50 age old. These high figures could be contributed to the rise of vaping popularity, which provides a more accessible and discreet method of marijuana use, which, studies show, can deliver higher levels of THC to the user than regular smoking. Among adults aged 19 to 30, 14% reported cannabis vaping in the previous month, which represents an all-time high and increase from a study conducted five years prior. [6]. Statistics also show decline of cannabis use with age,

pointing towards the fact, that it is mostly used amongst teenagers and young adults [7]. In the latter group, research suggests several reasons for marijuana use, such as social conformity (42%), experimenting (29%) and enjoyment (24%). Some (12%) also state that substance use helps them relax or manage stress. Understanding the motivation behind cannabis use among teenage and young adult males is crucial, as this is the period when its impact on fertility and overall reproductive health is most significant [8]. Although marijuana use is increasing in women, historically men have been subjected to it at almost double the rate [9].

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines *cannabis use disorder* (CUD) in patients who exhibit at least two of the following eleven criteria: (1) taking cannabis in larger amounts or for a longer duration than intended; (2) unsuccessful efforts to cut down or control use (loss of control); (3) spending a great deal of time obtaining, using, or recovering from use of cannabis; (4) intense cravings or a strong urge to use; (5) recurrent use despite failing to fulfill major role obligations at work, school, or home; (6) continued use despite social problems; (7) giving up or reducing important social, occupational, or recreational activities (given-up activities); (8) recurrent use in physically hazardous/dangerous situations; (9) continued use despite a physical or psychological problem that could have been caused or made worse by cannabis; (10) an indication of increased tolerance, i.e., needed more cannabis to obtain the same effect; and (11) the development of withdrawal symptoms (a), which can be relieved by taking more cannabis (b) [7, 10]. Recent studies show that about 30% of cannabis users develop CUD, with the highest risk seen in individuals who begin using before the age of 18. There is also a three- to four-times higher chance of other substance use disorder in marijuana users [11]. It is important to note these statistics as there exists a widespread public opinion that cannabis is not an addictive or harmful substance. However, clinical research suggests otherwise, as dependence syndromes or withdrawal symptoms have been widely documented and should not be underestimated [12].

5. Effects of marijuana

Amongst the 500 active substances found in the plant *Cannabis sativa*, the main psychoactive component in cannabis is THC, giving the user the sought-after intoxication

effect. There are also more than 100 cannabinoids (CBs), which are related to THC in a chemical way [2]. Excluding THC, the most abundant are cannabidiol (CBD), terpenes, and flavonoids. Both CBD and THC bind with cannabinoid receptors (CB1 and CB2), existing in the brain and multiple other organs, causing psychotropic (THC) or non-psychotropic (CBD) effects. The cannabis metabolism depends on the way of consumption. It can be inhaled or ingested. When inhaled, THC is absorbed and travels to the liver, where the process of elimination and metabolization takes place. The metabolites are 11-OH-THC and 11-COOH-THC, of which the first is also psychoactive. The remaining THC, along the metabolic products, enter the circulation. It takes about 6 to 10 minutes for them to achieve peak levels and reach the central nervous system. The fraction of the substance which reaches the bloodstream in inhaled THC is 10% to 35%. In oral THC the percentage is only 4% to 12%. This is due to THC's high lipid solubility. As a result, majority of it is absorbed by fat tissue. The other commonly used substance, CBD, has a bioavailability ranging from 11% to 45% through inhalation and 6% via ingestion. The metabolites hydroxylated from CBD by P450 enzymes in the liver are 7-OH-CBD and 7-COOH-CBD. The plasma half-life of THC is 1 to 3 days in occasional users and 5 to 13 days for chronic users; CBD is 18 to 32 hours [13, 14].

It is generally said that inhalation leads to bigger psychoactive effect than oral use [13, 14]. The primary reason many individuals use THC is for the pleasurable and mind-altering effects it produces, commonly referred to as a "high". This intoxicating experience is often characterized by a sense of euphoria, deep relaxation, and an enhanced perception of sensory input, such as music, colors, or tastes. Many users report feeling more sociable, amused, or content during the high, which contributes to its recreational appeal. Along with these more desirable effects, THC significantly affects normal brain function. It can impair a person's perception of time, often making time seem to pass more slowly. It also disrupts cognitive functions such as attention, memory, and decision-making. This can lead to difficulties in concentrating, forming new memories, or recalling recent events. Additionally, THC affects coordination and motor control, which can compromise physical performance and make activities such as driving or operating machinery dangerous. When consumed in larger amounts, THC can produce a range of adverse psychological effects. These may include heightened anxiety, intense fear, and feelings of paranoia or distrust toward others. In some individuals, especially those who are inexperienced or particularly sensitive to THC, high

doses can also trigger episodes of panic or even lead to hallucinations. These effects are often more pronounced in unfamiliar or stressful environments and may be influenced by individual factors such as mental health history, genetic predisposition, and the presence of other substances in the system. Another common and well-documented effect of THC use is an increase in appetite. This phenomenon occurs because of THC's interaction with receptors in the hypothalamus, responsible for hunger and satiety. As a result, individuals under the influence of THC often experience strong cravings for food, particularly those that are high in sugar, salt, or fat. This can lead to increased food intake and snacking, sometimes to the point of overeating. The heightened sense of taste and smell caused by THC may further intensify these cravings, making food seem more appealing and enjoyable. While this effect can be seen as a drawback in recreational use, it has therapeutic applications in medical contexts, such as helping patients with conditions like cancer or HIV/AIDS who struggle with appetite and weight loss [15].

CBD, on the other hand, is widely recognized for its therapeutic potential and is frequently referred to as a medicinal compound rather than a recreational one. Unlike THC, CBD does not produce intoxicating or psychoactive effects, making it more appealing for individuals seeking symptom relief without the sensation of being "high". While some people do use CBD for its calming and relaxing properties in a recreational context, its primary use lies in the field of medicine and wellness. CBD has shown promising results in the treatment and management of a wide range of health conditions. One of the most well-established uses of CBD is in the treatment of certain forms of epilepsy, particularly severe childhood-onset syndromes such as Dravet syndrome and Lennox-Gastaut syndrome. Beyond epilepsy, CBD is increasingly studied and used for its potential role in pain management. As such, it is sometimes used by individuals with conditions such as arthritis, fibromyalgia, and multiple sclerosis. CBD is also being explored for its potential in managing various neuropsychiatric disorders, including anxiety, depression, and post-traumatic stress disorder. Its anti-inflammatory and neuroprotective properties suggest it may be beneficial in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, potentially slowing progression or alleviating some of the associated symptoms. In addition, CBD has shown anti-inflammatory effects, making it a candidate for treating autoimmune and

inflammatory diseases such as inflammatory bowel disease (IBD) and rheumatoid arthritis. [14, 16–19].

When investigating the adverse effects of cannabis on the human body, it is essential to concurrently consider its potential therapeutic and beneficial properties. Maintaining a balanced and objective approach is critical for minimizing bias that could otherwise lead to stigmatization, misinformation, and missed opportunities for therapeutic use. By systematically evaluating both the risks and the medical utility of cannabis, researchers can develop a more comprehensive and accurate understanding of its overall impact on human health. This approach facilitates the differentiation between harmful patterns of use and evidence-based clinical applications, outside of the negative impact we focus on in this paper.

6. Endocannabinoid system

The endocannabinoid system (ECS) is an extensive network that modulates the nervous system, playing a key role in the development of the central nervous system and regulating various cognitive and physiological functions. These include fertility, pregnancy, developmental stages before and after birth, immune system activities, appetite, pain perception, mood, and memory. The ECS is crucial for many neural functions, such as movement control, motor coordination, learning, memory, emotional regulation, motivation, behaviors resembling addiction, and pain management, among others [20, 21].

The main components of the ECS are two receptors: CB1 and CB2. The first receptor is present in brain structures such as the frontal cortex, basal ganglia, hippocampus, hypothalamus, cerebellum, spinal cord and peripheral system. It was found in both excitatory glutamatergic neurons and inhibitory GABAergic neurons. The second receptor, CB2 is commonly found in immune system cells, hematopoietic cells and glial cells. Research suggests it is mostly expressed in unhealthy states of the body. Both receptors are abundant in the cardiovascular system [13]. They are classified as G protein-coupled receptors and, after linking with inhibitory G proteins, they inhibit adenylyl cyclase and voltage-sensitive calcium channels to stimulate mitogen-activated protein (MAP) kinases causing inward rectification of potassium channels and recruitment of beta-arrestins [22].

The endocannabinoid system also consists of endogenous ligands (endocannabinoids), of which the most crucial are N-acylethanolamines, constituting mainly of anandamide (AEA), and monoacylglycerols, represented mainly by 2-arachidonoylglycerol (2-AG), in addition to the enzymes that synthesize and degrade them and transport systems that guarantee their reuptake [23].

Reproduction of mammals, such as humans, is a multifaceted process governed by the hypothalamic-pituitary-gonadal axis (HPG). The management of hormonal and cellular communication is essential for the formation of gametes and the success of pregnancy. Various factors influence the interaction of these processes. Over the past twenty years, important elements of the ECS, particularly endocannabinoids (eCBs), along with the enzymes involved in their production and breakdown, have been identified as significant regulators of both male and female reproductive functions. Furthermore, research has demonstrated that the ECS is crucial in human reproduction, influencing everything from gametogenesis and fertilization to embryo implantation and the progression of pregnancy, including prenatal fetal development and the postnatal life of the newborn. Any substantial imbalance within this network can disrupt the pregnancy process [23].

The regulation of the hypothalamic-pituitary-gonadal (HPG) axis begins with the secretion of gonadotropin-releasing hormone (GnRH), a peptide hormone produced by neurons in the preoptic area of the hypothalamus. GnRH is released in a pulsatile manner, which plays a crucial role in controlling the secretion of two pituitary hormones through its action on receptors in the anterior pituitary (adenohypophysis). Specifically, low-frequency GnRH pulses stimulate the release of follicle-stimulating hormone (FSH), whereas high-frequency pulses promote the secretion of luteinizing hormone (LH). In males, the frequency of GnRH pulses remains relatively constant, while in females, it increases markedly around the time of ovulation, resulting in a surge of LH. FSH and LH are critical for reproductive function: they regulate follicular development, ovulation, and corpus luteum maintenance in females, as well as spermatogenesis in males. Additionally, both hormones are involved in modulating the production and secretion of sex steroid hormones, highlighting their central role in human reproductive physiology [23].

7. Testosterone, LH, FSH

So how exactly does cannabis influences male fertility? Studies suggest it happens through cannabinoid interaction with the ECS, which can create multiple problems in male physiology. Hypothalamic neurons that release GnRH appear sensitive to the effects of endocannabinoid signaling, particularly from AEA and 2-AG, as well as the enzyme fatty acid amidohydrolase (FAAH). AEA, in particular, suppresses GnRH secretion in the hypothalamus, which in turn lowers the production of LH and FSH by the pituitary gland, ultimately leading to decreased testosterone levels. This drop in testosterone then leads to reduced expression of CB1 receptors, dampening endocannabinoid signaling in both the hypothalamus and pituitary. The same result occurs with exogenous cannabinoids, such as THC or CBD, by competing for the CB receptors [2, 23].

Studies conducted on chronic marijuana users visiting urology clinics showed that patients experienced lowered testosterone, LH and FSH levels, alongside reduced testicular size. Some of them experienced gynecomastia. It should be noted, that in individuals who were abstinent, testosterone levels were back to normal [2]. This conclusion was backed up by several more studies, however it is still in discussion, as other studies showed various different results, some even opposite ones, when it comes to testosterone [24]. Research on animals suggests chronic THC exposure can lead to significant testicular atrophy, which is possibly due to oxidative stress caused by marijuana, which damages the seminiferous tubules. Increased levels of LH and FSH and decreased sex steroids levels were also observed [25]. In other human studies, FSH and LH levels were usually decreased in long-time marijuana users [2].

8. Sperm

The existence of cannabinoid receptors on sperm cells suggests that cannabis use may interfere with sperm function, alter reproductive hormone levels, impair semen quality, and

reduce sexual desire and performance. A decline in libido can also negatively influence mental health, contributing to relationship difficulties, heightened stress in intimate situations, and overall poorer physical well-being. These psychological effects may further lead to sexual dysfunction, independent of the direct impact on semen quality [2].

In human semen, endocannabinoids like AEA and 2-AG interact with specific receptors – CB1, CB2, and vanilloid receptor 1 (TRPV1) – which are important for sperm function. The enzymes that produce and break down these endocannabinoids also help regulate sperm activity and, in turn, affect male fertility, for example, N-acyl phosphatidylethanolamine phospholipase D (NAPE-PLD) and FAAH for AEA, or diacylglycerol lipase (DAGL) and monoacylglycerol lipase (MAGL) for 2-AG. Studies have found that infertile men have lower levels of AEA and 2-AG in their semen compared to fertile men. This is often linked with a higher rate of endocannabinoid breakdown relative to production. Interestingly, while TRPV1 receptor binding was seen in sperm from fertile men, it was absent in sperm from infertile men. However, there wasn't a big difference in CB1 and CB2 receptor binding between the two groups. The ECS plays a key role in two important sperm processes – capacitation (when sperm become capable of fertilizing an egg) and the acrosome reaction (when enzymes are released to help sperm penetrate the egg). Seminal fluid contains high levels of AEA, which decrease gradually as sperm travel through the female reproductive tract – from the uterus to the fallopian tubes to the egg, where this high initial concentration may keep sperm in a low-activity state, preserving their energy until they are closer to the egg, where lower levels of AEA allow them to "wake up" and become capable of fertilization [2, 23]

Within sperm cells, ECS components are located in specific areas: CB1 receptors are found in the head, midpiece, and tail; CB2 receptors are mainly in the head; TRPV1 receptors are in the midpiece and tail; the enzymes NAPE-PLD and FAAH are found in the head and midpiece. When CB1 is activated, sperm tend to remain immobile. CB2 activation is linked to slower movement. Capacitation is a complex process that sperm must go through to fertilize an egg, and ECS plays a key role here. CB1 helps keep cyclic adenosine monophosphate (cAMP) levels low early on, which stabilizes the sperm membrane and prevents it from reacting too soon. Later, TRPV1 gets activated and raises calcium levels inside the sperm. This helps break down the barriers between membrane layers, allowing the acrosome reaction to occur – an essential step for fertilization. A healthy sperm cell, with a properly working

ECS, stays in an uncapacitated state until it reaches the egg. However, THC, imitating natural endocannabinoids, can disrupt the CB1 signaling pathway. This interference can cause sperm to undergo capacitation too early, right after ejaculation, which may prevent it from properly reaching or penetrating the egg, potentially leading to infertility. In addition, lower levels of TRPV1 may also partly explain reduced sperm count (oligospermia) in infertile men [2, 23].

Another important factor to take into consideration is sperm motility. In some studies, high-dose exposition to both THC and CBD significantly diminished spermatozoa motility, which can be directedly linked to CB1 and CB2 receptor signaling. This suggests that the ability of sperm to move through the reproductive tract and reach the egg could be compromised, leading to failure in conception. Sperm motility is a key factor in enabling sperm cells to reach the oocyte and achieve successful fertilization [2, 4, 26].

When it comes to sperm morphology, research suggests a significant difference in cannabis smokers compared to the non-smoker group. In addition to morphology, volume, concentration and motility, sperm DNA integrity was also studied. The biggest decrease was observed in the percentage of immotile sperm and DNA integrity. Studies examining sperm exposed to cannabis have shown notable alterations in DNA methylation patterns. Specifically, cannabis users exhibit hypomethylation at cytosine-phosphate-guanine (CpG) sites, indicating reduced methylation at CpG regions of the DNA. This change suggests that THC can significantly alter the epigenetic profile of sperm. Mitochondria, often referred to as the energy centers of the cell, have their own genome, mitochondrial DNA (mDNA), which encodes 13 proteins essential for the proper formation of mature sperm and for driving flagellar movement after ejaculation. Due to the lack of protective histones and efficient DNA repair systems, mtDNA is particularly prone to mutations. These mutations can play a significant role in the development of certain genetic conditions. Research has shown a link between mtDNA mutations and specific types of male infertility, such as those caused by alterations in the POLG gene, which encodes the mitochondrial DNA polymerase. Furthermore, a high frequency of single-nucleotide polymorphisms (SNPs) in mtDNA has been detected in semen samples with low sperm quality.

Although the impact of marijuana on sperm DNA is still up to debate, current evidence warrants consideration of cannabis exposure as a contributing factor in male infertility [4].

9. Conclusions

As marijuana use continues to rise globally, especially among reproductive-age men, growing evidence suggests a concerning link between marijuana consumption and declining male fertility. Studies have increasingly associated marijuana use with reduced sperm count, impaired motility, and hormonal imbalances that can compromise reproductive health. Research suggests this may be due to dysregulation of the ECS, which impacts fertility in both sexes. Exogenous cannabinoids such as THC compete with endocannabinoids for binding to CB receptors, responsible for hormone production, sperm motility and capacitation process.

Although further research is needed to clarify the long-term effects, current findings warrant caution regarding cannabis use and its potential impact on male fertility. Public health initiatives and clinical guidance should prioritize awareness and education, ensuring that men are informed about the potential reproductive consequences of regular cannabis use.

Disclosure:

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