

Medical Marijuana as a Therapeutic Treatment for Pediatric Oncology Patients

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Abstract: In the United States, many children face the life threatening reality of cancer. As the second leading cause of death of children, 1,250 people younger than 15 years old are expected to die from cancer in 2015 alone ¹. Each year, pediatric cancer diagnoses make up less than 1% of all cancers diagnosed; regardless, 10,380 children in the US will be diagnosed in 2015 ¹. Childhood cancers are generally not associated with environmental or lifestyle factors like some adult cancers. Instead, they are most commonly attributed to DNA mutations. Leukemia, central nervous system tumors, neuroblastoma, Wilms tumor, lymphoma, rhabdomyosarcoma, retinoblastoma and bone cancers are the most common childhood cancers ². In adolescence, Hodgkin lymphoma, thyroid carcinoma, brain and central nervous system tumors and testicular germ cell tumors are the most common ². Thankfully, medicine and oncology research continues to expand, improving the survival rate of the youngest victims. Survival forecasts predict that an average 80% of children with cancer will survive at least 5 years ¹. However, with these vulnerable patients, questions and gaps in knowledge still remain. How can doctors treat these unpleasant symptoms effectively and with the fewest rate of negative consequences? With medical marijuana gaining popularity legality in several states, physicians and scientists are faced with the question: should medical marijuana be prescribed as a palliative or therapeutic treatment for pediatric oncology patients?

Introduction

The 21st century is not the first time marijuana has appeared in medicine. Ancient cultures hailed marijuana as a common herbal medicine useful for treating a variety of illnesses. Chinese Emperor Shen Nung in 2700 B.C. explored the healing properties of marijuana to treat rheumatism, malaria, and absentmindedness, while later healers explored the treatment of vomiting, parasitic infections, hemorrhage, diarrhea and dysentery ³. In India, Ayurveda medicine implemented marijuana to increase sleep, appetite and digestion, and relieve pain ³. In ancient Greece and Rome, Galen and Pliny the Elder prescribed it for a variety of conditions including earaches ³. In the 1830s, an Irish physician concluded from his experiments on animals and humans that marijuana was an effective treatment for vomiting, diarrhea and cholera ⁴. Later in 1860, the first conference discussing marijuana as a treatment for chronic coughs, gonorrhea and chronic pain was held at the Ohio State Medical Society ⁵. With this increased medical interest in marijuana, companies such as Grimault and Co. sold marijuana cigarettes for asthma treatment⁵. Today, however, the majority of Americans advocate the plant for its recreation use. In January of 2014, marijuana was defined by

the National Institute on Drug Abuse as the most widely used illicit drug in the US ⁶.

In marijuana, cannabinoids compose the main active chemicals in marijuana responsible for the healing and “high” effects. The cannabinoids, the most common being delta-9-THC, originate in the resin glands of female plant leaves ⁵. Kari Fransom, PharmD. Ph.D., at the University Of Colorado Skaggs School Of Pharmacy concludes that, “Depending on the strain, THC content can vary from 2% or 3% to more than 20%” ⁷. Which part of the plant is processed and how the plant’s contents enter the body affects the overall effect of THC on the physiology of the body. If taken orally, the THC compounds first travel to the liver and then enter the circulatory system causing a slower peak of THC concentration resulting in a slower effects and a higher potential for abuse. However, when the compound is smoked, the contents enter the blood stream almost immediately traveling to the CNS which results in a more “pleasurable” experience and rapid peak THC concentrations ⁸. The metabolized 11-OH-9-THC from the liver is a weaker antiemetic and results in a stronger psychological effect than THC entering the lungs ⁹. Peak plasma concentrations of THC occur 1 to 6 hours after orally taken as

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compared to inhalation which takes 2 to 10 minutes⁸. Once in the circulatory system, cannabinoids bind to receptors on specific cells. Cannabinoids bind to cannabinoid receptors (CB) in the cells of the brain and in the immune system: CB1 located in the brain slows reaction time and CB2 present on white blood cells impedes infection response and reduces inflammation⁵. The binding of THC-9 to the CB1 ligand reduces pain to the benefit of recreational users¹⁰. On the other hand, binding of THC-9 to CB2 works along with CB1 to maximize analgesia¹⁰. The isomer of Δ -THC-9, Δ -THC-8 has been investigated to have no significant side effects and is a possible pediatric antiemetic⁹.

The Controlled Substances Act of 1970 established that all drugs with a strong potential for abuse must be classified and regulated according to their medicinal value- drugs such as heroin and LSD are classified as schedule 1¹¹. Schedule 1 substances, including marijuana, have “a high potential for abuse...have no currently accepted medical use in treatment...”⁵. In the early 1990s, surveys regarding drug addictions found that 1 in 10 people who tried marijuana became addicted as compared to 1 in 5 for heroin⁷. Despite its strict classification, marijuana can be legal to treat medical conditions including glaucoma, HIV/AIDS, muscle spasms, seizures, severe pain, severe nausea, cachexia, muscle atrophy and cancer; however, regulations vary from state to state¹².

In assessing the validity of medical marijuana for oncology palliative treatment, gaps in research and knowledge severely limit current knowledge. Most of the research surrounding medical marijuana’s effect on the body comes from case studies; however, these case studies are limited because of the lack of biological or external validation¹³. Very few studies have compared marijuana and the current standards in antiemetic treatment. Also, the variability of THC concentration in each cannabinoid treatment causes analysis to be more nuanced and dose-dependent⁵. Marijuana’s chemical complexity leads to complex responses in each individual that makes the compound difficult to regulate publically. Some researchers describe marijuana as “...a nonmedical, nonspecific, and potentially hazardous method of drug delivery” because marijuana contains so many active chemicals that have not yet been investigated¹⁴. The American Medical Association has stated that “cannabis is a dangerous drug and as such is a public health concern”¹⁵. Despite these gaps in knowledge, some case studies and clinical evidence indicates the positive and negative effects of cannabis on the human body.

Discussion

Evidence in support of medical marijuana largely stems from patient and health care provider

testimony. For example, in *Cannabis in Medical Practice*, Mary Lynn Mathre, R.N. states that “The cannabis plant (marijuana) . . . [has] therapeutic benefits and could ease the suffering of millions of persons with various illnesses such as AIDS, cancer, glaucoma, multiple sclerosis, spinal cord injuries, seizure disorders, chronic pain, and other maladies”³. In case studies, slowing of weight loss and increased appetite occurred in patients who took THC in the form of dronabinol⁵. Researchers have also observed that marijuana is effective for “...quelling nausea, suppressing vomiting, increasing appetite, relieving pain, and soothing anxiety...[and] the apparent advantage of treating several symptoms simultaneously.”⁵. In a patient testimony, the man found that “when I smoked marijuana . . . in a couple of minutes...the symptoms of nausea would go away.”⁵. In the *New England Journal of Medicine*, a physician survey about a 68-year-old diagnosed with metastatic breast cancer found that 76% of surveyed physicians agreed that they would prescribe medical marijuana for this patient’s condition¹⁶. A physician commented that “that physicians who prescribe medicinal marijuana should do so only when conservative options have failed for fully informed patients treated in ongoing therapeutic relationships”¹⁴. In one clinical trial of medical marijuana, the inhalation of medical marijuana resulted in a superior antiemetic effect¹⁷. In a comparative study of orally administered marijuana and prochlorperazine (Compazine), another antiemetic drug, marijuana performed significantly better to decrease nausea and vomiting in patients when the patients recognized marijuana as their antiemetic drug¹⁸. Medical marijuana as compared to other smoking habits has not officially be correlated to cancers of the respiratory system¹⁹. Relatively speaking, the dose needed to relieve symptoms such as nausea amounts to significantly less than the amount needed to make the person feel “high”⁵.

On the other side of the argument, marijuana opponents defend the compound as hazardous and dangerous. Marijuana’s interaction with molecular receptors in the body negatively affects physiological function by compromising complex thought and brain function. The CB1 receptors are present in the structures of the central nervous system responsible for movement, memory, stress and complex thought including the brain stem, spinal cord, cerebellum, hypothalamus and hippocampus⁵. Through positron emission tomography, scientists measured a decreased blood flow to the temporal lobe after smoking just one cigarette, coinciding with decreased auditory abilities with patients⁵. In a study of experienced airplane pilots under the influence of marijuana, even though the pilots stated themselves that their ability to fly would not be impaired, their overall performance on the simulator tests indicated significant impairment²⁰. In clinical cases,

“marijuana psychosis” characterizes a latent psychopathology including marijuana-induced states of schizophrenia, depression and mania²¹. Smoking marijuana can affect the cardiovascular and respiratory systems increasing the risk of heart attack and respiratory cancers. Acute THC effects include decreased ability of the vagus nerve to vary the heart rate in a changing environment causing an impaired “flight or fight” response and increasing risk of heart attacks⁷. Studies indicate that the risk of heart attack will increase by up to 4.8 times in the first hour after smoking marijuana²².

Respiratory injury, cancer, emphysema, heart disease, pregnancy complications and low birth weight are contributed to smoking, no matter the compound smoked⁵. Marijuana especially increases these risks when inhaled because marijuana smoker is held in longer than cigarettes⁵. Polycyclic aromatic hydrocarbons (PAHs) exists as carcinogens when catalyzed by enzymes in the lungs and these enzymes are often readily available in marijuana smoker’s lungs⁵. In addition to impairing cardiovascular and respiratory function, THC impairs the resting immune system function. When marijuana is bound to CB2 receptors on white blood cells, the white blood cells have a reduced capacity to proliferate and the CB2 receptor also impairs T and B cell activity which is responsible for immune response²¹.

For pediatric oncology patients, marijuana has a greater effect psychologically and behaviorally than it would on the more mature adult brain. In a longitudinal study for marijuana users under the age of 20 years, brain function decreased gradually by up to 6 IQ points⁷. Cognitive decline and poor attention and memory are linked to marijuana use in teen brain¹³. Persistent young users of marijuana have a greater global neuropsychological decline than their adult counterparts¹³. This decline impacted the individual’s ability to function in normal cognitive functions¹³. These negative effects of cannabinoids on the brain are attributed to physiological changes within the brain. Young brains have increased vulnerability to toxic insult because of neuronal maturation, neurotransmitter system maturation and rearrangement processes occurring in pediatric brains²³. Also, adolescents are more vulnerable to drug dependence because they more susceptible to behavior consequences even with lower doses of the drug⁵. As compared to adults, children and adolescents experience more predominant mood change side effects from the minor compounds contained in cannabis⁹.

Some health professionals’ observations of medical marijuana highlight the negative side effects of the treatment. Alen Budney, PhD, of Dartmouth College states that “THC can increase risk of acute and future problems with depression, anxiety and psychosis”²⁴.

As a general rule, physician’s state that symptoms such as panic, depress, depersonalization, delusions, illusions and hallucinations disappear within hours and “respond well to reassurance and a supportive environment”⁵. According to Krista Lisdahl, PhD, “regular cannabis use, which we consider once a week, is not safe and may result in addiction and neurocognitive damage, especially in youth”²⁴. In patients with impaired immune systems, researchers note that “smoking marijuana is likely to do more harm than good”⁵. Not to mention, marijuana has not been sufficiently compared to the current standards in antiemetic treatment. In comparison with Ondansetron (Zofran), a current emesis standard, marijuana afforded minimal antiemetic effects in comparison²⁵. Is this palliative or therapeutic treatment worth these risks?

Conclusions

From testimonial observations, medical marijuana has been observed to ease the suffering of cancer patients by increasing appetite and decreasing nausea. On the other hand, medical marijuana has been proven to compromise physiological processes such as brain function, heart rhythm as well as creating a high potential for cancer-causing toxins. In view of these opposing viewpoints, the implementation of medical marijuana as a therapeutic treatment for pediatric oncology patients should not be encouraged until more scientific evidence reveals the benefits and detriments of medical marijuana on the younger population. Medical marijuana does afford antiemetic effect, which should be explored and investigated to its full potential. However, due to the serious negative effects of the marijuana on the nervous system, immune system and cardiovascular system for young patients, marijuana should not be implemented as a therapeutic particularly if it is in the form of smoking. Until more research can definitively state that marijuana will not significantly decrease brain function in young people, this medicinal treatment is not safe for a pediatric patient. Also, once marijuana is proven to supersede the current standards for emesis treatment, it should be implemented, but since very few studies have compared these options, marijuana is currently not a comparable antiemetic treatment. As observed by Bernard Lown M.D., “Caring without science is well-intentioned kindness, but not medicine.”²⁶. Medical marijuana may be helpful in caring for the patient temporarily, but it will not afford lasting beneficial treatment capable of medicine.

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