Motycka et al. Int Arch Nurs Health Care 2016, 2:029
Volume 2 | Issue 1
ISSN: 2469-5823

International Archives of
Nursing and Health Care

Review Article: Open Access

Side Effects and Drug Interactions of Marijuana

Carol Motycka*, Marissa Glinton and Courtney Brennan

University of Florida Jacksonville Campus, Jacksonville, USA

***Corresponding author:** *Carol Motycka, Pharm.D. BCACP, Clinical Associate Professor, Assistant Dean and Campus Director, University of Florida Jacksonville Campus, 580 W. 8th Street, Jacksonville, FL 32209, USA, Tel: 904-244-9590, E-mail: motycka@cop.ufl.edu*

Abstract

The use of marijuana as a medication continues to be debated around the United States with legalization being discussed in several states. Understanding the adverse effects and drug interactions of marijuana are important as more people look to using this substance as a form of treatment. Marijuana has been associated with several adverse effects when used both short term and long term. It is also a substance which may interact with commonly used medications. This article will discuss some of the commonly known adverse effects and interactions.

Keywords

Medical Marijuana, Adverse effects, Drug interactions

Introduction

The use of marijuana as a medication continues to be debated around the United States with legalization being discussed in several states. Health care providers should familiarize themselves regarding potential complications of use, as would be done with any other product used for medicinal purposes. Perhaps the most important information that needs to be studied and reviewed is the adverse effects and drug interactions of marijuana.

Side Effects

First and foremost, we will discuss the associated short term and long term effects of marijuana use. An article recently published in the New England Journal of Medicine shed some light on the adverse effects of marijuana use. Marijuana, when used short-term, has been found to impair short-term memory and motor coordination, alter judgment, increase or cause paranoia, and precipitate psychosis [1]. A study by Hartman et al. revealed the potential increased risk of motor-vehicle accidents caused by significant driving impairment linked to immediate short-term marijuana use. Notably, drivers were observed to drive more slowly after smoking marijuana, with a decreased control as task complexity increased [2]. Although data is often misconstrued, epidemiological data shows a 2 fold increase involvement in motor-vehicle accidents after smoking marijuana [3].

Marijuana has also been shown to have significant long term effects on individuals as well. Brain development in particular is affected with long-term marijuana use or exposure to tetrahydrocannabinol, which is the hallucinogenic active ingredient. Adolescents and young adults are the mostly likely individuals to have an increased risk of impaired neuronal connectivity affecting certain brain regions due to long-term marijuana use. Impaired neuronal connectivity can affect alertness, self-awareness, and inhibitory control. Although further studies are needed to show definite causality, long-term use has also been associated with increased risk of anxiety and depression. Finally, poor educational outcomes, diminished life satisfaction, and overall cognitive impairments have been observed from long-term marijuana use. These issues appear to be more prominently observed in individuals who begin marijuana use earlier in life [1].

The issue of addiction with chronic marijuana use has also been studied. It has been found that long-term use of marijuana can lead to addiction in approximately 9% of individuals who experiment with the drug [4] and the risk of addiction is greater increased when marijuana use is started early in adolescence [5]. Marijuana has also been called a "gateway drug" and has been linked to enhancing the response to other drugs such as nicotine [6].

Drug Interactions

In addition to side effects, it is important for us to consider the drug interactions. There are few studies looking at drug interaction with marijuana in the smokeable form. This means we should take into consideration the enzymes responsible for metabolizing exogenous cannabinoids, including those found in the herb (marijuana) or resin forms of cannabis as well as those found in the synthetic cannabis products (dronabinol and nabilone). Stout et al. summarized the data, drawing conclusions about the potential for cannabinoids to act as substrates, inhibitors, and inducers of various enzymes, and attempted to assign significance to these findings. The authors concluded that, *in vivo*, the primary metabolism of THC occurred via cytochrome P450 pathways, mainly 2C9 and 3A4, and that the secondary metabolism of THC metabolites may also occur through the CYP450 pathways (also primarily 3A4 and 2C9), UGT pathways, and by epoxide hydrolase. In addition to glucuronidation by several UGT isoforms, cannabinol and cannabidiol (other cannabinoid compounds) also undergo metabolism via CYP2C9 and 3A4, and by CYP2C19 and 3A4, respectively [7].

In reviewing the literature on cannabinoids and their relation to various metabolic pathways, Stout et al. attempted to identify whether these interactions held any clinical significance [7]. However, specific human data are lacking. One clinical study found an interaction between ketoconazole, a known CYP3A4 inhibitor, and oromucosal cannabis extract (Sativex), in which coadministration increased the maximum concentration and AUC of THC by 1.2 and 1.8-fold,

Citation: Motycka C, Glinton M, Brennan C (2016) Side Effects and Drug Interactions of Marijuana. Int Arch Nurs Health Care 2:029

Received: December 02, 2015: **Accepted:** January 25, 2016: **Published:** January 29, 2016

ClinMed International Library

respectively, and also increased the maximum concentration and AUC of the THC metabolite (11-OH-THC) and cannabidiol. The UK Summary of Product Characteristics (SPC) for Sativex also describes a study in which marijuana was administered with rifampin, a CYP3A4 inducer. Co administration with rifampin decreased the maximum concentration of THC by 40% and the AUC by 20%. The maximum concentration of 11-OH-THC was reduced by 85% and the AUC of 11-OH-THC was reduced by 87%. Additionally, the maximum concentration of cannabidiol was reduced by 50% and the AUC reduced by 60% [8]. This suggests that any other product that acts on CYP3A4 could potentially either increase the concentration of cannabinoids to a supratherapeutic concentration, leading to an increase in adverse effects, or decrease the concentration to a subtherapeutic level.

Stout et al. also looked at two studies which demonstrated a "higher average estimated theophylline clearance in more frequent marijuana smokers," which suggests a possible marijuana-related induction of CYP1A2. However, this may not be due to the cannabinoids themselves, as this effect can also be seen with tobacco smoking. In vitro data suggesting CYP1A2 induction, and evidence of this induction effect from studies using non-smoked forms of cannabinoid, is also lacking [7]. Due to the lack of specific in vivo data on drug interactions, the jury is still out on what types of interactions health care providers need to be aware of.

The issue of medical marijuana is highly politically charged, but we must take a step back and examine not only the potential benefits of its use, but also the risks such as side effects and drug interactions that inevitably accompany any chemical patients choose to put into their body. It is important for health care providers to recognize the potential issues associated with marijuana's use and to educate patients appropriately.

References

1. Volkow ND, Baler RD, Compton WM, Weiss SRB (2014) Adverse health effects of marijuana use. N Engl J Med 370: 2219-2227.
2. Hartman RL, Huestis MA (2013) Cannabis effects on driving skills. Clin Chem 59: 478-492.
3. Li MC, Brady JE, DiMaggio CJ, Lusardi AR, Tzong KY, et al. (2012) Marijuana use and motor vehicle crashes. Epidemiol Rev 34: 65-72.
4. Lopez-Quintero C, Perez de los Cobos, J, Hasin DS, Mayumi Okuda, Shuai Wang, et al. (2011) Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend 115: 120-130.
5. Hall W, Degenhardt L (2009) Adverse health effects of non-medical cannabis use. Lancet 374: 1383-1391.
6. Panlilio LV, Zanettini C, Barnes C, Solinas M, Goldberg SR (2013) Prior exposure to THC increases the addictive effects of nicotine in rats. Neuropsychopharmacology 38: 1198-1208.
7. Stout SM, Cimino NM (2014) Exogenous cannabinoids as substrates, inhibitors, and inducers of human drug metabolizing enzymes: a systematic review. Drug Metab Rev 46: 86-95.
8. http://www.gwpharm.com/Sativex.aspx