Commentary

Medical marijuana patient counseling points for health care professionals based on trends in the medical uses, efficacy, and adverse effects of cannabis-based pharmaceutical drugs

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Summary

The purpose of this report is to present a review of the medical uses, efficacy, and adverse effects of the three approved cannabis-based medications and ingested marijuana. A literature review was conducted utilizing key search terms: dronabinol, nabilone, nabiximols, cannabis, marijuana, smoke, efficacy, toxicity, cancer, multiple sclerosis, nausea, vomiting, appetite, pain, glaucoma, and side effects. Abstracts of the included literature were reviewed, analyzed, and organized to identify the strength of evidence in medical use, efficacy, and adverse effects of the approved cannabis-based medications and medical marijuana. A total of 68 abstracts were included for review. Dronabinol's (Marinol) most common medical uses include weight gain, chemotherapy-induced nausea and vomiting (CINV), and neuropathic pain. Nabiximol's (Sativex) most common medical uses include spasticity in multiple sclerosis (MS) and neuropathic pain. Nabilone's (Cesamet) most common medical uses include CINV and neuropathic pain. Smoked marijuana's most common medical uses include neuropathic pain and glaucoma. Orally ingested marijuana's most common medical uses include improving sleep, reducing neuropathic pain, and seizure control in MS. In general, all of these agents share similar medical uses. The reported adverse effects of the three cannabis-based medications and marijuana show a major trend in central nervous system (CNS)-related adverse effects along with cardiovascular and respiratory related adverse effects. Marijuana shares similar medical uses with the approved cannabis-based medications dronabinol (Marinol), nabiximols (Sativex), and nabilone (Cesamet), but the efficacy of marijuana for these medical uses has not been fully determined due to limited and conflicting literature. Medical marijuana also has similar adverse effects as the FDA-approved cannabis-based medications mainly consisting of CNS related adverse effects but also including cardiovascular and respiratory related adverse effects. Finally, insufficient higher-order evidence to support the widespread use of medical marijuana was found, but a limited amount of moderate-level evidence supports its use in pain and seizure management. Published by Elsevier Inc.

Keywords: Dronabinol; Nabilone; Nabiximols; Cannabis; Marijuana; Smoke; Efficacy; Toxicity; Cancer; Multiple sclerosis; Nausea; Vomiting; Appetite; Pain; Glaucoma; Side effects

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Introduction

Cannabis has been widely prevalent throughout the history of the world for its various religious, spiritual, and medicinal purposes. The term "marijuana" is frequently used in referring to *Cannabis sativa* leaves or other crude plant material.[1] Cannabis, a more generic term, is used to denote the several psychoactive preparations of the plant *Cannabis sativa*.[1] The major psychoactive, centrally acting constituent of cannabis is Δ-9 tetra-hydrocannabinol (THC)[1] and compounds similar to THC are defined as cannabinoids.

Cannabinoids are active compounds that exhibit drug-like effects throughout the body, especially in the central nervous system (CNS) and immune system.[2] The cannabinoid compounds include phytocannabinoids, which are the constituents of *Cannabis sativa* plant, endocannabinoids, which naturally occur within the human body to act as neuromodulators and neurotransmitters,[3] and any synthetic cannabinoid preparations or pharmaceutical drugs. Like THC, another common phytocannabinoid example is cannabidiol (CBD) which may relieve inflammation and pain without causing psychoactive effects or the intoxicating "high." Although the cannabinoid compounds differ structurally and pharmacologically, like THC and CBD, the cannabinoids, in general, share many of their pharmacological properties.[1]

Because of the similarity in structure and pharmacologic properties many cannabinoids, natural or synthetic, are used interchangeably for the treatment of chemotherapy-related nausea and vomiting, chronic pain, neuropathic pain, cachexia, muscle spasms, anxiety, and sleep disturbances. Other proposed effects of cannabis include anti-inflammatory activity, antiviral activity, and antitumor activity by blocking cell growth and preventing the growth of blood vessels that supply tumors.[2] Acute and chronic adverse effects associated with cannabis use include tachycardia, hypotension, paranoia, dizziness,[2] the impairment of cognitive development and psychomotor performance, attention and memory impairment, exacerbation of certain psychiatric illnesses, airway injury and pulmonary disease, risk of dependence and addiction, and reduction in birth weight when used during pregnancy.[1]

Currently there are three approved and seven developmental pharmaceutical drugs based on cannabis[4] (Tables 1 and 2) and intended for the medical uses. Nabiximols (Sativex) is approved in the United Kingdom and several other European countries, while dronabinol (Marinol) and nabilone (Cesamet) are two drugs approved by the FDA for use in the United States. Smoked or orally administered *Cannabis* plant, marijuana, is not FDA-approved, but several localities in the United States legally allow its use for certain medical conditions[2] (Table 3). Also, since the Colorado (U.S. State) Amendment 64 has been enacted, marijuana is now legal for not only medical use but also recreational use and commercial sale in the state of Colorado.

Although there are several existing clinical trials supporting a beneficial effect of the FDA approved cannabinoid drugs, dronabinol (Marinol) and nabilone (Cesamet), as well as the approved nabiximols (Sativex), there is insufficient evidence to recommend inhaled cannabis or medical marijuana as a treatment for any medical condition.[5] Because of this insufficient evidence, many health care professionals may be unaware of the many medical uses and effects of marijuana. With the developing legal status and increasing use of cannabis by patients, both medically and recreationally, in the United States and throughout the world, it is important for an increase in awareness among health care professionals. This awareness should include common uses, safety, efficacy, toxicity, and adverse effects of both cannabis-based medications and marijuana, despite the limited evidence to recommend for or against its therapeutic use. By doing so, health care professionals will have an increased competence in educating, counseling, and providing appropriate recommendations to promote positive patient outcomes. The purpose of article it to review and summarize the medical use, efficacy, and adverse effects of both the approved cannabis-based medications and marijuana in order to develop common patient counseling and educational points for the use of medical marijuana.

Methods

A literature search and categorization of evidence was performed to summarize common medical uses of cannabis-based medications and marijuana, smoked or orally administered extract, in various disease states and patient populations. In addition, available literature pertaining to the efficacy, toxicity, or adverse effects of the cannabinoid medications and marijuana was reviewed