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To review on the medicinal use of Marijunna

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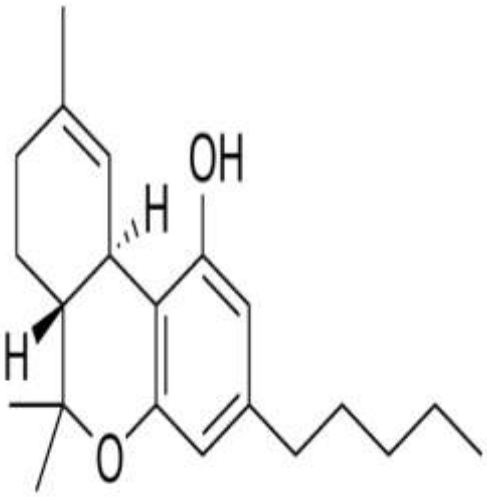
ABSTARCT - The cultivation and use of Marijuana is historically rooted in the Indian subcontinent and this rich heritage of cannabis use dates back to at least two thousand years. Cannabis remains an illicit substance in India despite its changing status globally with many countries legalizing cannabis use in recent years. Scientific research on cannabis use in India has also been sparse.

I. INTRODUCTION

Medicinal marijuana, is a therapy that has garnered much national attention in recent years. Controversies surrounding legal, ethical, and societal implications associated with use; safe administration, packaging, and dispensing; adverse health consequences and deaths attributed to marijuana intoxication; and therapeutic indications based on limited clinical data represent some of the complexities associated with this treatment. Marijuana is currently recognized by the U.S. Drug Enforcement Agency's (DEA's) Comprehensive Drug Abuse Prevention and Control Act (Controlled Substances Act) of 1970 as a Schedule I controlled substance, defined as having a high potential for abuse, no currently accepted medicinal use in treatment in the United States, and a lack of accepted safety data for use of the treatment under medical supervision.

Structure



Theroth

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Uses

Multiple sclerosis

A number of clinical studies have found cannabis orcannabinoids to be moderately effective in the relief of neurogenic pain (pain caused by illness or damage to the nervous system) in multiple sclerosis (Jawahar, Oh, Yang, & Lapane, 2013; Koppel et al., 2014; Langford et al., 2013). The findings have been less consistent with respect to the effects on spasticity. In most of the earlier studies, patients reported subjective relief of the sensation of spasm, but objective measures of spasticity did not reveal any significant improvement (Zajicek & Apostu, 2011). However, in more recent studies, either smoked cannabis or nabiximols oral spray gave objective evidence of decreased spasm as well as of relief of pain (Corey-Bloom et al., 2012 ;Flachenecker, Henze, & Zettl, 2014; Koehler, Feneberg, Meier, & Pollmann, 2014; Lorente-Fernandez et al., 2014; Serpell, Notcutt, & Collin, 2013). In long-term treatment continuation studies, the benefits have continued for up to a year in some patients. However, a substantial percentage of patients did not show clear benefit or dropped out of continued treatment because of adverse effects. The reason for the discrepancy of findings between the earlier and the later studies is not yet clear, but one possible explanation is that the use of combined THC–CBD preparations decreased the side effects of THC and permitted the use of higher doses, with correspondingly better effect (Zajicek et al., 2013).

(b) Epilepsy

Basic laboratory studies of isolated brain tissue have provided evidence that the endocannabinoid system is involved in controlling the activity of brain cells (Hofmann & Frazier, 2013). Exogenous cannabinoids (i.e., those not produced in the body) reduce the excitability and spontaneous activity of brain cells, though different plant cannabinoids act by different mechanisms (Iannotti et al., 2014). THC acts through CB1 receptors, whereas CBD and someother cannabinoids, such as cannabidivarin, act through receptors in the inflammation system. They all decrease the activity of the nerve cells on short exposure, but chronic exposure to THC reduces the number of CB1 receptors and can cause , rather than prevent, seizures (Blair et al., 2009). The availability of CBD-enriched cannabis strains and extracts has enabled some parents to try them in children with severe epilepsy that failed to respond to conventional treatment (Hussain et al., 2015). A number of case reports and interviews of parents indicated that up to 70% of the children treated had a 50% or greater reduction of seizure frequency (Geffrey, Pollack, Bruno, & Thiele, 2015; Porter & Jacobson, 2013; Press, Knupp, & Chapman, 2015; Saade & Joshi, 2015). These encouraging observations have led to the initiation of properly designed clinical trials with a cannabis extract containing 99% pure CBD (Epidiolex®) for the treatment of different types of childhood epilepsy, which are currently in progress in the United States and elsewhere. However, there is not yet sufficient evidence available from well-designed clinical trials to permit recommendation of cannabis or CBD for treatment of epilepsy (Friedman & Devinsky, 2015).

(c) Cancer

Although the anti-cancer effect of cannabinoids has been intensively studied in cell cultures (test-tube studies) and in animals with tumours, no firm conclusions about their clinical use are yet possible. It has been confirmed repeatedly that THC and various other cannabinoids binding to CB1 and CB2 cannabinoid receptors, and CBD acting through different mechanisms, can promote cancer cell death, or retard or prevent the growth of cancer cells of various types, including lung, prostate, pancreas, colon and brain cancer (Dando et al., 2013; De Petrocellis et al., 2013; Haustein, Ramer, Linnebacher, Manda, & Hinz, 2014; Macpherson, Armstrong, Criddle, & Wright, 2014; Zogopoulos, Korkolopoulou, Patsouris, & Theocharis, 2015). The cannabinoids also reduce the ability of cancer cells to invade surrounding normal tissues and to metastasize (i.e., give rise to colonies of cancer cells in many different tissues at a distance from the original cancer site). It has also been suggested that some actions of endocannabinoids might reduce the risk of mutations that give rise to cancer cells (Alexander, Smith, & Rosengren, 2009; Freimuth, Ramer, & Hinz, 2010). Cannabinoids have been shown to inhibit the growth of new blood vessels that are necessary to provide enough oxygen and food to support the rapid growth of cancer cells (Ramer & Hinz, 2015). All of these actions have raised hopes that cannabinoids or derivatives of them might become important anti-cancer drugs.However, these actions have been demonstrated by adding cannabinoids to cultures of growing cancer cells, by injecting cannabinoids directly into cancers growing in living animals, and by administering cannabinoids to animals in which

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cancers have been produced experimentally. Only one small, uncontrolled clinical trial has been carried out in nine patients whose brain cancers had recurred after surgical removal. THC was injected directly into the recurrent brain cancers.

Anti-inflammatory actions

The endocannabinoids, as well as THC and othercannabinoids acting through CB1 receptors, and CBD acting through non-cannabinoid receptors, are all able to decrease the formation and release of chemical factors that give rise to inflammation (Burstein, 2015; Esposito et al., 2013; Koay, Rigby, & Wright, 2014). The endocannabinoid and the inflammatory systems co-exist in most tissues of the body, and the ability of CBD and some other cannabinoids to suppress inflammation reactions has been shown experimentally in such tissues as the endothelial lining of blood vessels (Wilhelmsen et al., 2014), human skin (Olah et al., 2014), human intestinal lining cell cultures (Harvey, Sia, Wattchow, & Smid, 2014) and a mouse model of rheumatoid arthritis (Fukuda et al., 2014). However, the only disease state in which this research has yet progressed to clinical trials is chronic inflammatory bowel disease (Crohn's disease and ulcerative colitis). One double-blin randomized placebo-controlled study found that smoked cannabis improved the symptoms of patients with ulcerative colitis, but did not achieve complete disappearance of the disease process (Irving et al., 2015). In contrast, a different study (Naftali et al., 2013) found complete subsidence of Crohn's disease in 90% of patients treated with THC-rich smoked cannabis, versus 40% of those receiving placebo. Both were fairly small-scale trials, and lasted only eight weeks. The results are encouraging, but much larger and longer-lasting trials are needed to see whether cannabis is a useful therapy in chronic intestinal inflammatory disease.

Adverse Effects

Very little research has been conducted on the risks associated with the medical use of cannabis, making it challenging for physicians to discuss this concern with their patients. A systematic review of 23 randomized controlled trials and eight observational studies of cannabinoids andcannabis extracts for various medical purposes noted that the short-term use of these substances appeared to modestly increase the risk of less serious adverse medical events such as dizziness (Wang,Collet, Shapiro, & Ware, 2008). This review, however, did not provide information on the long-term use of cannabinoids for chronic disorders (e.g., multiple sclerosis) because the available trials wereof relatively short duration (i.e., eight hours to 12 months). Moreover, this review did not assess the adverse effects on the bronchi and lungs associated with the smoking of cannabis A later cross-sectional study examining the effects of inhaled or ingested cannabis on cognitive functioning in patients with multiple sclerosis revealed that individuals who used cannabis performed significantly poorer than those who did not on measures of information-processing speed, working memory, executive functioning, and visual and spatial perception (Honarmand, Tierney, O'Connor, & Feinstein, 2011). Therefore subjective benefits from smoking cannabis reported by patients need to be weighed against the associated adverse effect of cognitive impairment.

Studies of recreational cannabis use provide some indication of the health risks that might result from smoking cannabis over the long term, including neurocognitive deficits (Crean, Crane, & Mason, 2011; McInnis &PorathWaller, 2016), psychosis (Large, Sharma, S., Compton, Slade, & Nielssen, 2011; McInnis &Porath-Waller, 2016),various respiratory ailments and possibly cancer (Reid, Macleod, & Robertson, 2010; McInnis & Plecas, 2016). Psychosis has usually been seen in individuals who used cannabis non-medically and who took unusually large doses, or who took edible forms, became impatient at the slow onset of effects, and took additional doses (Hudak Severn, & Nordstrom, 2015). However, psychosis has also been observed in healthy experimental subjects who weregiven a moderate dose by mouth (Favrat et al, 2005). The advent of edible preparations for medical use in American states has led to an increase in emergency room visits, as a number of children have mistaken them for ordinary sweets (Ingold, 2014). A small but growing number of cases have been reported of heart attacks (myocardial infarction) produced in men, even young men, who smoked cannabis for non-medical purposes (Franz & Frishman, 2016). No such cases have been reported so far in persons using it at lower doses for medical reasons, but caution should be shown in those with already impaired coronary blood flow.

Route of administration and pharmacology

The pharmacology of cannabis varies depending on the route of administration. The oral route, vaporising, smoking, and oro-mucosal

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sprays are considered. While smoking and oromucosal sprays are not recommended as part of the programme, the information provided below should be considered (Queensland Health, 2017).

Oral route

Cannabis-based medicines consumed in the oral form, such as oils or liquid capsules, are more slowly absorbed than products administered by vaporising. They take at least 30 to 90 minutes before any effects are felt. Bioavailability of oral cannabinoids is lower (10 to 20 per cent) because of intestinal and first pass liver metabolism. Peak effects can occur two to four hours after consumption. Given the longer time frame for peak effects, it is important to allow at least three hours between administration of single oral doses to avoid possible overdose. Effects can last for up to eight hours and as long as 24 hours.

This may be of particular importance in relation to the timing of SACT in order to get the maximum benefitGiven the slower onset and longer duration, it is expected that taking cannabis-based productsvia the oral route would be more useful for medical conditions or symptoms where control over longer periods of time is sought — similar to the use of slow release medications (Queensland Health, 2017).

Vaporising

Vaporised cannabis results in rapid absorption and high blood levels, similar to smoking it. Cannabis is heated at a lower temperature than smoking, producing fewer toxins and no side stream smoke‘, making passive smoking less of a problem. First effects occur within 90 seconds and reach a maximum after 15 to 30 minutes, before wearing off after two to four hours. Vaporising heats the cannabis without burning it and releases the cannabinoids in the form of a vapour, which is then inhaled. Given the rapid onset of action, vaporising cannabis-based products is best for symptoms or conditions where rapid relief is required. The amounts of THC and other cannabinoids delivered by the vaporiser are dependent on the temperature, the duration of the vaporisation and the volume of the balloon in the vaporiser (Queensland Health, 2017). This may pose difficulties for dose titration. The health effects of vaporising as a route of administration for cannabis products are as yet unknown.

Smoking

Smoking is not recommended as a method of administration of cannabis for medical purposes due to the potential other risks associated with smoking, including cardiorespiratory illnesses and cancer. The access programme does not include any products intended to be smoked. Most carcinogens in smoked tobacco are present in smoked cannabis. Typical cannabis use results in a larger volume of smoke being inhaled than with ordinary tobacco products and a fivefold increase in concentrations of carboxyhaemaglobin

2.1.4. Pharmacokinetics and Pharmacodynamics

Following administration, cannabinoids are distributed throughout the body. They are highly lipid soluble and accumulate in fatty tissue. THC and CBD may be stored for as long as four weeks in the fatty tissues, from which they are slowly released at sub-therapeutic levels back into the blood stream, then metabolised and excreted via the urine and faeces. The release of cannabinoids from fatty tissue is responsible for the prolonged terminal elimination half-life (up to 36 hours).THC and CBD are metabolised in the liver through the cytochrome P-450 enzyme system (CYP450); therefore, they could potentially interact with other medicines metabolised by this pathway (see section 3.9) Cytochrome P-450 2C9 is the main enzyme responsible for the breakdown of THC to its active metabolite. Cytochrome P450-3A is also involved in its metabolism. It may take up to five days for 80 to 90 per cent of the total dose to be excreted; therefore, THC is often found in the urine many days after ceasing cannabis use

II. CONCLUSIONS

There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV, sleep disorders, and Tourette syndrome.

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