A rapid weight loss caused by therapeutic cannabinoid use in an elderly individual: a case report

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Abstract

The proportion of older adults using medical cannabis is rising. Most of the cannabinoid research has focused on a healthy, younger population free from frailty and major comorbidity. In this case report, we describe an 82-year-old woman who was autonomous in basic and instrumental activities of daily living and who came to our geriatric department for marked weight loss over the past 2 months (about 10 kg) and anemia. After appropriate clinical and endoscopic checks, it was concluded that the weight loss was induced by the initiation of therapy with oral cannabis for the control of rheumatic pain.

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Introduction

The endocannabinoid system plays an important role in regulating appetite control, acting as both an inhibitor in instances of overconsumption and a stimulator in conditions that involve reduced appetite and weight loss. This is why cannabinoid receptor antagonists, such as cannabidiol (CBD), may manage obesity, while agonists, such as tetrahydrocannabinol (THC), may be a therapy option for anorexia. It is confirmed that endocannabinoids, acting on CB1 cannabinoid receptors in the brain, stimulate appetite and gut behaviors, in part through interactions with more established orexigenic and anorexigenic signals.[1] The nucleus accumbens and hypothalamic nuclei are sensitive sites for the hyperphagic actions of these substances, and endocannabinoid activity in these regions varies with nutritional status and dietary expression.

Medical cannabinoids may also have potential clinical roles in the treatment of older adults. Indeed, the number of cannabis users aged ≥65 years in the U.S. population has grown over the past two decades. A study by Han and Palamar shows that among U.S. seniors aged 65 years and older, there has been an increase in cannabis use from 2.4 percent in 2015 to 4.2 percent in 2018.[2]

Italy has legally recognized the medical use of cannabis since 2006, when the Ministry of Health authorized the import of cannabis from the Netherlands. In 2016, Italian cannabis production was authorized, and Military Pharmaceutical Chemical Works (Florence) began cultivating and processing cannabis in a controlled and standardized environment, according to good manufacturing practice. Medical cannabis can be prescribed as magistral preparations, such as oil extracts, decoction filter bags, and inhalation bags through an authorized device. The medical use of cannabis is authorized in Italy for selected medical conditions (as reported in Official Gazette no. 279 of November 30, 2015): one of these is analgesia in chronic pain (with particular reference to neurogenic pain) in which treatment with nonsteroidal anti-inflammatory drugs or cortisone or opioid drugs has proven ineffective.[3]

Elderly individuals are more likely to experience medical conditions such as chronic pain, which may represent a potential indication for medical cannabinoid therapy. However, this population is also at increased risk for adverse drug reactions.

Despite prescribing restrictions for medical cannabinoids in certain jurisdictions (including Italy) having recently been relaxed, only a few geriatricians have the detailed knowledge and

awareness of the potential risks or benefits of cannabinoid use in older people, and even fewer have direct experience in using these drugs in their own clinical practice.

Risks of cannabinoids in older patients appear to be moderate, and their frequency is comparable to other analgesic drug classes. However, the quality of research is poor, and few older patients have been enrolled in cannabinoid studies.[4]

Case Report

An 82-year-old woman, an independent at-home patient, was admitted to our geriatrics department for anemia normochromic normocytic (hemoglobin: 9.5 g/dL) and marked weight loss (about 10 kg in 2 months, weight 70 kg 2 months earlier). At the geriatric evaluation, the Mini-Mental State Examination and the Geriatric Depression Scale were in the normal range, and she was autonomous in basic and instrumental activities of daily living. Her weight was 60 kg, and her body mass index (BMI) was 23.4k g/m^2. Clinical history showed type II diabetes mellitus and recently diagnosed seronegative arthritis. The rheumatologist of choice, after poor responsiveness to ibuprofen, introduced cannabinoids (to avoid possible cortisone-induced glucometabolic decompensation) in the last 2 months. Home drug therapy consisted of metformin 1000 mg 3 die, insulin glargine 20 international units (IU)/die, bisoprolol 1.25 mg die, cardioaspirin 100 mg 1 die (for primary prevention), gastric protection, and Cannabis Bediol (6% THC e 8% CBD) 6 drops in the morning and 12 drops in the evening (about 150 mg/die). The cannabis was discontinued about 5 days before admission due to the onset of asthenia and inappetence.

Metformin was also discontinued during hospitalization, and rapid insulin was inserted at meals, 4 IU subcutaneously. The patient reported using metformin for more than 10 years, but given the hepatic metabolization of metformin, there could have been a synergistic effect with cannabinoids. Unfortunately, it is not possible to dose blood levels of metformin at our institution.

During hospitalization, whole-body computed tomography scan, colonoscopy, and gastroscopy were all negative for neoplastic pathology, and blood tests revealed no elevation of inflammatory markers, no evidence of active infection, and stable hemoglobin (9.8 g/dL). Glycosylated hemoglobin was 6%, reticulocytes, vitamin B12 and folate, ferritin, and haptoglobin were normal, as were low iron and transferrin. The normochromic normocytic anemia was interpreted as an anemia from chronic inflammatory pathology as frequent during arthritis.

During hospitalization, she practiced a rheumatology evaluation, which prescribed the initiation of therapy with prednisone 25 mg 1 cp/day. To optimize antidiabetic therapy, we discharged the patient with empagliflozin 25 mg 1 cp/day, metformin 1000 mg 1 cp with meals, and 20 i.u. .s.c of insulin glargine, with indications for frequent glycemic checks and 30-day outpatient follow-up. The patient was discharged without the use of cannabinoids.

At the follow-up visit, the patient no longer manifested inappetence; weight was increased: BMI was 24.8 kg/m^2 (weight: 63.5 kg), glycated hemoglobin was 6.9%, glycemic diary was in order, and good control of pain was reported. Hemoglobin was 10.5 g/dL.

At the follow-up, three months after discharge, the patient showed weight and appetite gain (weight: 65 kg, BMI: 25.3 kg/m^2).

Discussion

Plants of the cannabis family contain two major cannabinoids: THC and CBD. THC is the primary psychoactive compound and appears to have neuroprotective, anti-inflammatory, anti-emetic, and analgesic effects. CBD has no psychoactive properties and appears to attenuate the psychoactive properties of THC when used in combination. CBD, in isolation, reduces proinflammatory cytokine release and displays antioxidant properties.[5]

Medical cannabis, often without a comprehensive understanding of its safety and effectiveness, is now being used for various conditions, including but not limited to chronic pain, multiple sclerosis, chemotherapy-induced nausea and vomiting, Parkinson's disease, epilepsy, and others.[6]

However, the effectiveness of cannabis in treating chronic pain is still an issue of debate. Recent meta-analyses of randomized controlled trials and observational studies continue to conclude there is only weak evidence for the efficacy of cannabis for the treatment of chronic pain.[7]

Nevertheless, the efficacy of cannabis treatment for improving appetite-related symptoms has not been consistently demonstrated in randomized controlled trials.[8] A lot of studies show no net effect of cannabis on appetite: most patients reported no change, and a similar number of patients reported an increase or decrease in appetite.

However, this study was limited by a small number of patients at its follow-up, and at present, the European Society for Clinical Nutrition and Metabolism has concluded that there is currently no evidence to support the use of cannabinoids in the cachexia of dementia.[9]

As already highlighted in the literature, in the geriatric population, they can also induce weight loss. Indeed, a recent systematic review suggests that CBD has an anorectic effect, which is correlated with a decrease in body weight. However, most of the studies included in this review raised some concerns in terms of the risk of bias.[10]

Despite numerous small studies describing a modest side effect profile of cannabinoids, we are aware of only one systematic review evaluating the safety profile of cannabis and cannabis products in the elderly.[11] This systematic review found that cannabinoids were associated with a higher rate of adverse events than the control. Moreover, considering that for pain therapy, there is only weak evidence, and that the geriatric population is at higher risk of adverse drug reactions and paradoxical adverse effects, one should be cautious before using this kind of drug in this population.

Cannabis can give cumulative and potentiating effects when taken concurrently with alcohol, benzodiazepines, or opioids. If taken orally as an herbal tea, there is a first-pass effect that may interfere with drugs metabolized by the CYP2C9 and CYP3A4 isoenzymes of the cytochrome P450 system, such as macrolides, antifungals, calcium channel blockers, HIV protease inhibitors, amiodarone, and isoniazid. Cannabis may also interfere with drugs that bind to plasma proteins. Although it is not contraindicated, caution should be exercised when taking concomitant oral anticoagulants, antiplatelet agents, or heparins.[12] Considering the large number of medications taken by the elderly, this could increase blood levels and thus the adverse effects of some drugs. Therefore, physicians before prescribing cannabinoids should carefully assess the risk of interaction with the therapy performed by the patient to avoid the increase of adverse drug reactions.

Currently, there are no specific clinical studies examining interactions between CBD and metformin. However, it is known that both can affect liver metabolism. CBD can inhibit an enzyme called cytochrome P450, which is responsible for the metabolization of many drugs, including metformin. This could potentially alter the effectiveness of metformin or increase the risk of side effects.

Conclusions

It is important to appreciate that no studies have specifically aimed to evaluate the effect of these drugs on pain in older people. Extrapolation of adult data to older adults is therefore largely speculative, and dedicated research in this group is indicated, also to be able to perform a careful risk-benefit analysis in this class of patients.

Further research is needed to clarify the potential mechanisms involved in the effect of CBD on feeding/appetite; some studies and systematic reviews point out that CBD may have anorectic effects, so discontinuation of these drugs during marked weight loss should be considered.

The existing evidence base appears to indicate that the risks of cannabinoids in older persons are modest but not insignificant. High-quality research is urgently needed to further determine the efficacy and side effect profile of cannabinoids in older persons and compare them to current alternatives.

In addition, clinicians should take into account before prescribing cannabinoids in the elderly the possible interactions with the patient's therapy, considering the effect cannabinoids have on cytochromes and that polypharmacotherapy is known to be unfortunately common in geriatric patients.

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