

## Self-medication of achalasia with cannabis, complicated by a cannabis use disorder

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**Ethics approval:** Our research "Self-medication of achalasia with cannabis, complicated by a cannabis use disorder Cannabis in achalasia and manometry" was conducted in accordance with the Helsinki Declaration. We kindly ask for an exemption from providing the Institutional review board (institutional review board) statement, which cannot be available. The case report « Self-medication of achalasia with cannabis, complicated by a cannabis use disorder - Cannabis in achalasia and manometry » was written retrospectively, with the written patient's consent. No review board is required or available in our Institution for this kind of case report, as it has no impact on the care providing process.

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### Abstract

Achalasia is a rare esophagus motility disorder. Medical, endoscopic and surgical treatments are available, but all endorse high relapse rates. No data has been published to date reporting a therapeutic effect of cannabis use neither in achalasia nor on its influence on manometric measurements. We report the case of a patient diagnosed with achalasia. He could benefit from a large panel of therapeutic interventions, but none of them was effective over the time. He first used cannabis at age 20 and identified benefits regarding achalasia symptoms. He maintained regular moderate cannabis use for 9 years, with minimal digestive inconvenience. A manometry performed without cannabis premedication was realized at age 26 and still found a cardiospasm. Cannabis use could explain the gap between functional symptoms assessment and manometry measurement. Further investigations are warranted to explore a therapeutic effect of cannabis in achalasia and possible influence on outcome measurements.

**Key words:** Achalasia; Cannabis; Treatment; Manometry; Addiction

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**Core tip:** Achalasia is a rare esophagus motility disorder. Medical, endoscopic and surgical treatments are available, but all endorse high relapse rates. We report

the case of a patient diagnosed with achalasia who identified benefits from cannabis use on achalasia symptoms. Cannabis non-use before manometry could explain the gap between functional symptoms assessment and manometry measurement. Further investigations are warranted to explore a therapeutic effect of cannabis in achalasia and possible influence on outcome measurements. Particular attention should be given to cannabis addiction risk to vulnerable patients.

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## INTRODUCTION

Achalasia is a rare esophageal motility disorder characterized by the absence of peristalsis and impaired relaxation of the lower esophageal sphincter<sup>[1]</sup>. The main symptoms are dysphagia, regurgitation, heartburn, chest pain and weight loss. The effectiveness of medical treatment is inconsistent, and no trial could support the effectiveness of nitrates or calcium-channel blockers<sup>[2]</sup>. Endoscopic treatment, namely pneumatic dilation and botulinum toxin injection, requires frequent interventions. Surgical options, namely laparoscopic cardiomyotomy and esophagectomy, are proposed for end-stage achalasia<sup>[3]</sup> and have high relapse rates.

To our knowledge, no data have been reported on the therapeutic effect of cannabis in achalasia, nor on the influence of cannabis on manometric measurements.

Medical cannabis extract (Nabiximols) is approved in several countries for the treatment of refractory spasticity in multiple sclerosis<sup>[4]</sup>. Commercialized nabiximols is standardized to contain dronabinol and Cannabidiol (CBD) in a ratio of 1:1 and is sprayed under the tongue using a dose pump. Cannabidiol is the most important non-psychotropic cannabinoid found in the cannabis plant. It is not a cannabinoid (CB) receptor agonist. Dronabinol is the international non-proprietary name for (-)-trans-delta-9-tetrahydrocannabinol (THC). THC is used to refer to the naturally occurring (-)-trans-isomer of delta-9-tetrahydrocannabinol from the cannabis plant (*Cannabis sativa* L.). THC is a CB receptor agonist. THC is responsible for most of the pharmacological actions of cannabis, including the psychoactive effects. Medical cannabis showed positive results for spasticity in patients with multiple sclerosis<sup>[5,6]</sup> or paraplegia<sup>[4]</sup> and in the treatment of anorexia, nausea, and neuropathic pain.

## CASE REPORT

A 31-year-old patient came to our addiction clinic seeking care for a cannabis use disorder. He was diagnosed with achalasia at the age of 17, with high disability linked to severe symptoms: Regurgitation of undigested food, dysphagia for solid food, heartburn. He initially benefited from nitrate medication but suffered from unacceptable headaches, that led to treatment discontinuation. At age 18, the symptoms were increasingly severe, resulting in a weight loss of 27% of body weight associated with food disgust. He then benefited from a laparoscopic cardiomyotomy, which improved symptoms for one year and a half before relapse. At age 20, a manometry confirmed relapse with impaired relaxation of the lower esophageal sphincter, and major diffuse esophageal dyskinesia. He first used cannabis and identified benefits regarding achalasia symptoms, specifically with food intake facilitation and weight intake. He maintained regular cannabis use of one joint a day for 9 years. During this time period, he did not lose weight, suffered from minimal inconvenience. A manometry realized at age 26 still found a cardiospasm that did not allow the passage of the catheter. This manometry was performed without cannabis premedication, whether the food intakes were pre-medicated by cannabis use at this time period. This could explain the gap between functional symptoms assessment and manometry measurement. He stopped cannabis use at age 29 for a short time period, but suffered from immediate relapse of previous digestive symptoms. At age 29 a first pneumatic dilatation at 30 mm did not allow to facilitate food intakes. He decided to handle his digestive symptoms by cannabis consumption, leading to their improvement, enduring no more weight loss and only sporadic dysphagia. At age 30, negative life events were followed by increased cannabis use that escalated to a severe cannabis use disorder.

Our research was conducted in accordance with the Helsinki Declaration, and the patient gave written informed consent for publication.

## DISCUSSION

This spontaneous report of a therapeutic effect of cannabis on achalasia symptoms provides a promising and innovative therapeutic approach. The mechanism of action could involve smooth muscle relaxation of the lower esophageal sphincter, as the endogenous ligand of CB1, anandamide, is an effective antispasticity agent<sup>[7,8]</sup>. CB1 receptors are primarily presynaptic; their activation inhibits calcium influx and glutamate release and reduces neuronal excitability by activating somatic and dendritic potassium channels<sup>[9]</sup>. A relaxing effect on other smooth muscles has been reported<sup>[10]</sup>. CBD is also known for its anti-emetics properties<sup>[4]</sup>. Therapeutic effect of cannabis in achalasia could

then be due to both CBD and THC actions. Further investigations are warranted to explore a therapeutic symptomatic effect of cannabis in achalasia and the physiopathology of this potential effect. Use of cannabis should be taken into account to analyze outcome measurements, in particular manometric findings<sup>[11]</sup>, and their correlates to functional symptoms.

Cannabis abuse potential is well documented<sup>[12]</sup>. Although smoked cannabis contains over 400 other chemicals (about 60 are cannabinoids), its reinforcing effects are known to be due to Delta-9-THC<sup>[13]</sup>. A ratio 1:1 of CBD and THC seems to be protective from addiction-onset risk<sup>[14]</sup>. Medical cannabis seems to have a much less addictive potential than those of smoked cannabis<sup>[15]</sup>. However, particular attention should be given to cannabis addiction risk to vulnerable patients.

## COMMENTS

### Case characteristics

A 31-years-old patient suffers from achalasia since 17 years old. Medical, endoscopic and surgical treatments failed. Symptoms were improved by cannabis consumption, which was complicated by a cannabis use disorder.

### Clinical diagnosis

Main clinical symptoms of achalasia were dysphagia, heartburn and weight loss.

### Differential diagnosis

Endoscopic exploration and two manometries confirmed achalasia.

### Laboratory diagnosis

No laboratory blood test found any consequence of weight loss (no malnutrition or deficiency).

### Imaging diagnosis

Manometry was performed two times after surgical cardiomyotomy, and confirmed esophageal dyskinesia.

### Pathological diagnosis

Pathological examination was not performed.

### Treatment

First line medical treatment (nitrites) and second line surgical treatment and pneumatic dilatation failed in preventing long time symptoms return; cannabis consumption was described by the patient as facilitating food and weight intake.

### Related reports

This is the first case report of the effects of cannabis on achalasia symptoms. It provides a promising therapeutic approach in a field with limited medical, endoscopic and surgical therapeutics, which endorse high relapse rates.

### Term explanation

The human endocannabinoid system comprises two major cannabinoid receptors (CB1 and CB2, expressed primarily in central nervous system tissues and immune cells, respectively) and their endogenous ligands, known as endocannabinoids.

### Experiences and lessons

This is the first description of effects of cannabis on esophagus motility disorder probably involving smooth muscle relaxation of the lower esophageal sphincter, nevertheless other effects of cannabis on smooth muscles were previously reported.

### Peer-review

The present manuscript presents a case study speaking to the efficacy of cannabis for the treatment of achalasia in a 31-year-old patient. Findings

highlight the potential therapeutic effect of cannabis for this rare esophageal disorder.

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