Abstract
Cannabis is the most cultivated and abused illicit drug worldwide. Paradoxically to the antiemetic properties attributed to cannabis, a relatively new cannabinoid hyperemesis syndrome (CHS) started to be recognized and is characterized by cyclic vomiting that are interspaced by asymptomatic phases.
We present a case of a 36-year-old woman who repeatedly presented to the emergency room with cyclic vomiting that alleviated with hot showers. She was a long-term cannabis user and the diagnosis was only established several years later after the onset of symptoms. The diagnostic work up was unremarkable, and the only effective treatment was cannabis cessation. Hot bathing behavior is a key characteristic of this syndrome.
CHS is a new clinical condition that should be considered in a setting of recurrent and intractable vomiting in patients with a history of cannabis use.

INTRODUCTION
According to the World Health Organization, Cannabis is the most abused illicit drug, being consumed by over 147 million people worldwide. Its use has been growing especially in North America, western Europe and Australia. In fact, only in European Union (EU) around 91.2 million adults with an age span between 15 and 64 years are estimated to have used cannabinoids at least once during

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Palavras-chave: Abuso de Marijuana/complicações; Banhos; Canabinóides/efeitos adversos; Síndrome; Vômito/induzido quimicamente

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their lives. Regarding the frequency of its consumption, 1% of adults in EU consume cannabis on a daily or near-
daily basis, being the prevalence significantly higher in
young people aged below 35 years. Aligned with this data,
the cases related to cannabinoids use disorder entering to
an analysis for the first time increased 76% between 2006
and 2017.23 Portugal figures follow this trend with canna-
abis ranking first as the most used psychotropic substance.4
Cannabis has been credited with some medical properties
showing efficacy in reducing nausea and vomiting during
chemotherapy treatment, enhancing appetite and weight
gain and improving chronic pain.5,6 Paradoxically to the
antiemetic properties attributed to cannabis, a syndrome
characterized by cyclic vomiting episodes in long term
cannabis users started to be recognized. The first report
describing cannabinoid hyperemesis syndrome was pub-
lished in 2004 by Allen et al, giving account of a series of
patients observed for persistent vomiting alleviated by hot
showering, a core behavior exhibited by the patients in the
acute phase of the illness.7 However, most of the people presenting this syndrome
remain without a diagnosis for several years and it is
therefore extremely important that clinicians are aware of the
existence of this condition. Given the growing use of
 cannabis, the purpose of this report is to provide a better
understanding of CHS and draw readers attention to its
recognition.

CASE REPORT
We report the case of a 36-year-old woman who was sent
to the psychiatry outpatient clinic after recurring multiples
times to the Emergency Room (ER) with gastrointestinal
complaints.
For the last 14 years, the patient kept coming to the hospi-
tal emergency department presenting with persistent vom-
iting associated with abdominal pain and nausea. There
were no complains of chills, fever, diarrhea, palpitations,
thoracic pain, loss of conscience and genitourinary tract
symptoms. She had a history of cannabis consumption
since she was 16 years old and used the substance almost
on a daily basis. She denied using other illicit drugs.
She admitted spending a significant amount of time taking
hot water showers at home, stating that this behavior was
the only way to mitigate the symptoms. In fact, even dur-
ing the observations in the ER, she was frequently found
in the bathroom showering. The patient described to have
experienced numerous similar episodes before in an inter-
mittently fashion. Each episode would start 7 days prior
seeking medical attention.
Regarding her past medical history, she had no other chron-
ic medical conditions and allergies. She had been admitted
twice into the psychiatry ward after two of these episodes
due to psychomotor agitation and anxiety causing familiar
distress. She was diagnosed with dysfunctional personality
traits and medicated with venlafaxine and quetiapine with
poor therapeutic adhesion.
Physical examination was unremarkable with the ex-
ception of the mild epigastric tenderness the patient
complained during abdominal palpation and mild dehy-
dration. Often, the laboratory values revealed electrolyte
imbalances such as hypokalemia and positive urine testing
for cannabinoids.
Reviewing the previous workup records, the patient was
submitted to an extensive diagnosis investigation includ-
ing imagiology and laboratory exams. Abdominal radiol-
ography and ultrasonography were normal. Other analytic
results extending to complete blood count, liver function,
amylase, lipase, thyroid hormones, viral serologies and
urinalysis were unremarkable.
During these episodes the patient remained under observa-
tion in the ER. Supportive treatment with fluid therapy and
antiemetic agents like metoclopramide and ondansetron
were given in the acute phase and abstinence of cannabis
consumption was advised.
Cannabinoid hyperemesis syndrome was only pointed out
as the diagnosis for this patient 6 years after the first time
she went to ER with this clinical picture.

DISCUSSION
Cannabis is a complex plant that contains over 400 che-
metal compounds, including at least 144 unique products
known as cannabinoids.8,9 One of the major substances
produced is ∆9-tetrahydrocannabinol (THC), which is
responsible for the psychoactive effects of feeling high
pursued by its users, but also for other disagreeable effects
like psychosis and impairment of cognitive performance.
THC exerts its effects by activating the endocannabinoid
system that on its turn has two receptors known as CB1
and CB2. CB1 is located in the central and peripheral
nervous system and the stimulation of the latter causes va-
sodilation and decrease gastric emptiness.10 CB2 receptors
can be found in immune cells and are involved in immuno-
modulation by inhibiting inflammation, visceral pain, and
intestinal motility.11
THC demonstrated to have antiemetic properties medi-
ated by activation of CB1 receptors in myenteric plexus
and dorsal-vagal complex in the medulla.12 Nevertheless,
CHB brings evidence for its paradoxical emetic effects,
leading to the elaboration of some explicative hypothesis
over the years. One of them states that as cannabis is a
very lipophilic substance, it accumulates in fat tissue for
long periods. During times of stress or food deprivation,
lipolysis release THC which produces a reintoxification
effect that may contribute to CHB in sensitive subjects.13
Since just a small percentage of long term cannabis users
develop CHS, genetic polymorphisms in the cytochrome
P450 enzymes might be responsible for the higher rate of
emetetic metabolites in these individuals.11
Alongside with THC, other two non-psychotropic can-
nabinoids present in cannabis may contribute for the de-
velopment of CHS. They are cannabidiol (CBD) that in
high doses enhance vomiting and cannabigerol (CBG)
that antagonize CB1 and 5-HT1A receptors contributing to
emesis.11
Cannabinoids also showed to influence gastrointestinal
and colonic dysmotility and THC exerts an inhibitory
action on gastric emptying through inhibition of intrinsic cholinergic mechanisms in peripheral myenteric system. This peripheral action can override the central actions of THC and producing vomiting. The stimulation of CB1 receptors in the hypothalamus and pituitary gland helps to modulate the hypothalamic-pituitary axe. THC produces a hypothermic effect that is amplified by the action of CBD that upregulate CB1 receptors in the hypothalamus. These mechanisms may contribute to understand why patients with CHS show the compulsive bathing behavior.

Concerning the diagnosis, Sorensen et al made a systematic review and identified the major characteristics of CHS as severe cyclic vomiting (100%), abdominal pain (85.1%), weekly use of cannabis (97.4%), consumption of cannabis for over a year (74.8%), resolution of the symptoms after cannabis cessation (96.8%), temporary symptomatic relief with compulsive hot showers (92.3%) and age less than 50 at time of evaluation (100%). 92% of the patients evaluated met at least three of the latter criteria. The diagnosis of CHS is made with a mean delay of 4.1 years after the beginning of the symptoms. The only treatment that showed efficacy is cannabis cessation. In the acute phase, supportive treatment including intravenous fluids should be provided if there is volume depletion and renal failure or electrolytic imbalances. Application of topic capsaicin on the abdomen may relieve the symptoms, and this effect is exerted by activation of TRVP-1 receptors producing a heat sensation. Haloperidol was used successfully in some reports. Opioids are not recommended as they might aggravated the nausea. The acute phase usually resolves in 48 hours, but relapse is likely to occur if the patient resumes cannabis use. The case presented here is paradigmatic of the delay until the recognition CHS in a long-term cannabis user with multiples recurrences to ER with cyclic vomiting. Moreover, the patient went to extensive non conclusive diagnostic workups, showing that CHS is still underdiagnosed.

CONCLUSION

Since the use of cannabis is growing and new medical indications are being considered it is important to pay attention to the paradoxical effects of cannabis and study its underlying pathophysiology.

Responsabilidades Éticas

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