

Cannabinoids Improve Gastrointestinal Symptoms in a Parenteral Nutrition–Dependent Patient With Chronic Intestinal Pseudo-Obstruction

Journal of Parenteral and Enteral Nutrition
Volume 00 Number 0
xxxx 2020 1–3
© 2020 American Society for Parenteral and Enteral Nutrition
DOI: 10.1002/jpen.1821
wileyonlinelibrary.com
WILEY

Boutaina Zemrani, MD^{1,2} ; Cécile Lambe, MD¹; and Olivier Goulet, MD, PhD¹

Abstract

Chronic intestinal pseudo-obstruction (CIPO) is a rare and challenging cause of pediatric intestinal failure, requiring long-term parenteral nutrition in most cases. Despite optimal management, some patients experience chronic abdominal pain and recurrent obstructive episodes with a major impact on their quality of life. Cannabinoids have been successfully used in some conditions. However, their use in CIPO has never been reported in the literature. We report a case of successful use of medicinal cannabinoids in a patient with CIPO, resulting in a significant reduction of abdominal pain, vomiting, and subocclusive episodes and increased appetite and weight, without major adverse events. Although further observations are required to consolidate these findings, this case may be helpful for other patients suffering from the same condition. (*JPEN J Parenter Enteral Nutr.* 2020;00:1–3)

Keywords

cannabinoids; children; intestinal failure; parenteral nutrition

Introduction

Chronic intestinal pseudo-obstruction (CIPO) is a rare and challenging cause of intestinal failure (IF).¹ Recurrent abdominal pain, vomiting, and eating difficulties are major features of this dysmotility disorder, requiring long-term parenteral nutrition (PN) in most cases.¹ Cannabinoids have been successfully used in gastrointestinal (GI) disorders, including nausea, vomiting, and pain, and in non-GI conditions.^{2–4} However, their use in CIPO has never been reported in the literature.

We report a case of successful use of synthetic cannabinoid agonists in a patient with CIPO, resulting in improvement of GI symptoms and quality of life (QOL).

Case Report

A 19-year-old female was diagnosed with CIPO in the neonatal period without urological involvement. Because of enteral feeding intolerance, PN was started during the first month of life followed by an ileostomy and gastrostomy, resulting in limited enteral feeding tolerance using a hydrolyzed formula. A brief trial of prokinetics (erythromycin) was inconclusive. An ileostomy reversal at 2 years failed because of intestinal subocclusion, leading to re-formation of the ileostomy. At the age of 6, a subtotal colectomy with ileosigmoid anastomosis and decompression jejunostomy (closed at 14 years) were performed in an attempt to reestablish continuity and reduce PN dependence. The patient remained PN-dependent since birth with PN covering around 75%–85% of energy requirements,

the rest being provided by oral intake. Since the age of 16, she has been receiving PN 3 nights a week, providing: 23 Kcal/kg/day (1150 kcal/day) of nonprotein energy and 0.6 g/kg/day (30 g/day) of protein over the course of a week with small oral intake. Her clinical course was marked by frequent, mild abdominal pain and about 2–3 moderate subocclusive episodes per year, mostly managed at home with gut rest, venting of jejunostomy, and nonopioid analgesics.

At the age of 16, she developed chronic knee pain unresponsive to routine analgesics. In this context, she started smoking cannabis daily at the age of 17 without informing the medical team. Consequently, her knee pain was relieved, and interestingly, her abdominal pain and appetite also improved. However, because of trouble with the law, she stopped smoking cannabis after 1 year, which brought her symptoms back to baseline.

From the ¹Pediatric Gastroenterology-Hepatology-Nutrition Unit, Necker-Enfants-Malades Hospital, Paris, France; and ²Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland.

Financial disclosure: None declared.

Conflicts of interest: None declared.

Received for publication September 23, 2019; accepted for publication February 25, 2020.

This article originally appeared online on xxxx 0, 2020.

Corresponding Author:

Boutaina Zemrani, MD, Lausanne University Hospital, Rue du Bugnon 46, 1005, Lausanne, Switzerland.
Email: boutainazemrani@gmail.com

Table 1. Summary of Gastrointestinal, Nutrition, and General Changes Before and After Use of Cannabinoid Receptor Agonists.

Parameter	Baseline state before cannabinoids use	After cannabinoid receptor agonists use
Abdominal pain	Frequent, mild abdominal pain and distension	Reduction of abdominal pain and abdominal distension
Subocclusive episodes	2–3 moderate subocclusive episodes per year	No subocclusive episodes reported since commencement of treatment
Vomiting	Intermittent vomiting	Reduced vomiting
Stools	Around 5–6 loose stools per day	Stools frequency and consistency unchanged
Weight	Weight -1.2 SD	Weight fluctuated but improved overall to -0.8 SD without a change in PN
PN requirements	Home PN 3 nights a week, cycled over 12 hours Over a week: 23 kcal/kg/day (1150 kcal/day) of nonprotein energy and 0.6 g/kg/day (30 g/day) of protein	Unchanged (because of weight fluctuation)
Appetite and oral intake	Minimal appetite Small oral intake Sensation of blockage after oral intake	Better oral intake and appetite: consumes 2 meals per day with improved tolerance and less sensation of fullness/blockage
Quality of life	QOL affected by the abdominal pain and vomiting (no scale used)	QOL subjectively improved
Fatigue	No fatigue reported	Moderate fatigue with 35 mg/week (5 mg/day) of dronabinol Less fatigue with 25 mg/week but less efficiency as well

PN, parenteral nutrition; QOL, quality of life; SD, standard deviation.

Because of the incidental finding of beneficial effects of cannabis on her GI condition, a special authorization for the use of synthetic cannabinoids was requested. In France, medical use of synthetic cannabinoids is allowed under special circumstances, whereas inhaled cannabis is prohibited. Our patient has been receiving 2.5 mg twice a day of synthetic δ -9-tetrahydrocannabinol (THC), dronabinol, since 15 months. Over this period, her abdominal pain, distension, and vomiting improved. She hasn't had subocclusive episodes since the commencement of the treatment. Her appetite and food tolerance improved with disappearance of the feeling of "fullness" and "blockage" after meals. Feces frequency and consistency did not change. Her weight z -score fluctuated, but overall it improved from -1.2 to -0.8 without a change in PN supply. Her final height z -score is -0.15 with a target height z -score of $+0.5$ and body mass index of 19.8 kg/m². Table 1 summarizes the GI and nutrition changes after dronabinol commencement.

Our patient did not report any major adverse events, especially no psychoactive effects. However, she felt moderately tired. To reduce this fatigue, the dronabinol dose was lowered from 35 to 25 mg/week. Interestingly, this resulted in a decrease of efficacy (diminished appetite, recurrence of abdominal pain, and vomiting), prompting a reincrease at previous doses according to the patient's wishes. Currently, she has transitioned to an adult IF center. She is still taking synthetic cannabinoid pills with close follow-up with an addictology specialist.

Discussion

We hereby report, for the first time, beneficial effects of cannabinoids in CIPO.

"Cannabinoids" is a generic term that includes the cannabis plant, endogenous and synthetic cannabinoids.⁵ The main active ingredients in cannabis are THC and cannabidiol.^{5,6} THC activates 2 membrane receptors: CB1 and CB2. CB1 receptors are located throughout the GI tract, predominantly in myenteric and submucosal neurons, whereas CB2 receptors are mainly located on inflammatory and epithelial cells.

Cannabinoids have been used in several conditions, with positive clinical effects, generally as a second-line therapy when conventional medical treatment has failed. Evidence for benefit in children is strong for chemotherapy-induced nausea and vomiting, with increasing evidence of benefit for epilepsy.² In adults, evidence supports cannabinoids' use for the treatment of chronic pain and spasticity.^{3,4} Among GI diseases, beneficial effects were mainly described in Crohn's disease and irritable bowel syndrome.⁶ Despite the reported positive effects, cannabinoids are often controversial, particularly in children. Their use is often requested or self-initiated by patients or their parents when they desperately seek better control of their symptoms.

CIPO is a serious cause of IF, requiring complex and multidisciplinary medical, surgical, and nutrition management.¹ In children, congenital and primary forms

are predominant with some genetic forms identified; most children require long-term PN.¹ In adults, CIPO is often secondary to systemic diseases, and its outcome is related to the underlying disease.¹ Some patients experience chronic abdominal pain and recurrent subocclusive episodes with major impacts on their QOL.¹ Common therapies of these episodes include gut rest, venting of ostomies, PN, and replacement of losses.¹ Opioids are discouraged because of their counterproductive effect on intestinal motility.

Cannabinoid receptor agonists have been shown to reduce upper and lower GI motility.^{5,6} From our observation, it is likely that they had a positive effect on gastric emptying, as the patient had a better food tolerance with less sensation of gastric fullness and less vomiting. Animal and human studies have shown that cannabinoid agonists relax colonic tone and reduce colonic motility.^{5,6} Our patient had her colon removed, and patients with CIPO usually have their colon excluded via an ileostomy, as per general recommendations.¹ The action of synthetic cannabinoids in CIPO may be due to their analgesic effect by decreasing visceral hypersensitivity in the same way as in irritable bowel syndrome.⁶ The increased appetite noticed in our patient could be due to better control of abdominal pain, reduced vomiting, and/or the central cannabinoids' effects on appetite stimulation.^{4,6} THC also exerts an anti-inflammatory activity in intestinal tissue and reduces gastric and intestinal secretions.⁶

There are few case reports of intestinal intussusception in adults following long-term and massive inhaled-cannabis consumption (10–15 joints per day).⁷ This raises the question whether massive cannabinoids use can lead to a hypermotile and anarchic bowel in patients with a “healthy” gut, which would explain the intussusceptions, whereas their sensible use in “motility disorders” may be beneficial. The dosage seems important, as small doses may be ineffective, and massive doses seem harmful.

Although our patient has a moderate form of CIPO, cannabinoids improved her symptoms, albeit PN requirements were not reduced. The positive GI effects were supported by recurrence of symptoms after reduction and discontinuation of cannabinoids. Furthermore, the ability to maintain an oral diet without abdominal pain is a major aspect of social life, whose importance should not be undermined. However, cannabinoid use raises many questions related to age, short- and long-term side effects, acceptance by parents and professionals, and availability. Our patient started the prescribed treatment at 18 years and was fully supported by her parents. We cannot recommend the routine use of synthetic cannabinoids in CIPO until their efficacy and safety are established. However, they could be carefully considered in cases of chronic abdominal pain refractory to routine treatment and impacting the QOL. They could potentially represent an option before

considering intestinal transplant in patients with poor QOL in the absence of other indications for transplantation. The decision to prescribe cannabinoids might be easier in adult patients than in children. Despite the IF, synthetic cannabinoids seemed to be absorbed in our patient, but the absorption could be erratic in other patients.

Clinicians should be aware of the potential for serious harms. The short-term adverse effects mainly include dizziness, fatigue, somnolence, euphoria, confusion, and hallucination.^{2,4,6} The development of cannabinoid agonists that do not cross the blood-brain barrier could be valuable. Effects related to long-term use are unknown. The use of inhaled cannabis or other nonmedicinal cannabinoids is not recommended. Medicinal products provide a consistent concentration and composition and are adjusted by a specialist according to efficacy and side effects.

This paper reports a fortuitous discovery of positive cannabinoid effects on CIPO symptoms in a patient, leading to significant relief of GI complaints. Although further observations are required to consolidate these findings, this case may be helpful for some patients with the same condition.

Statement of Authorship

B. Zemrani contributed to the design of the case report; B. Zemrani contributed to the acquisition and analysis of the data; B. Zemrani, C. Lambe, and O. Goulet contributed to the interpretation of the data; B. Zemrani drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript

References

1. Thapar N, Saliakellis E, Benninga MA, et al. Paediatric intestinal pseudo-obstruction: evidence and consensus-based recommendations from an ESPGHAN-Led Expert Group. *J Pediatr Gastroenterol Nutr.* 2018;66(6):991-1019. <https://doi.org/10.1097/MPG.0000000000001982>
2. Wong SS, Wilens TE. Medical cannabinoids in children and adolescents: a systematic review. *Pediatrics.* 2017;140(5). <https://doi.org/10.1542/peds.2017-1818>
3. Nugent SM, Morasco BJ, O'Neil ME, et al. The effects of cannabis among adults with chronic pain and an overview of general harms. *Ann Intern Med.* 2017;167(5):319-331. <https://doi.org/10.7326/M17-0155>
4. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use. *JAMA.* 2015;313(24):2456-2473. <https://doi.org/10.1001/jama.2015.6358>
5. Camilleri M. Cannabinoids and gastrointestinal motility: pharmacology, clinical effects, and potential therapeutics in humans. *Neurogastroenterol Motil Off J Eur Gastrointest Motil Soc.* 2018;30(9):e13370. <https://doi.org/10.1111/nmo.13370>
6. Goyal H, Singla U, Gupta U, May E. Role of cannabis in digestive disorders. *Eur J Gastroenterol Hepatol.* 2017;29(2):135-143. <https://doi.org/10.1097/MEG.0000000000000779>
7. Prokopchuk O, Neumann P-A, Hüser N, Friess H, Wilhelm D. Multiple intestinal intussusceptions caused by highly impaired gastrointestinal motility in a patient with chronic cannabis consumption. *J Surg Case Rep.* 2019;2019(5):rjz160. <https://doi.org/10.1093/jscr/rjz160>