Cannabis-Based Medicines in Gastroparesis and Related Syndromes

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Introduction

Gastroparesis (GP) is a disorder of delayed gastric emptying characterized by symptoms such as early satiety, nausea, vomiting, and weight loss, with significant contributions from abdominal pain to overall disease burden. Current treatments, ranging from dietary modification and prokinetics to antiemetics and invasive interventions, often provide limited relief and may carry substantial side effects, leaving many patients with persistent symptoms. Given the significant impact of GP on quality of life and healthcare utilization, there is a growing need for more effective therapies. Emerging evidence suggests that cannabis-based medicines may improve symptoms such as nausea, vomiting, and abdominal pain; however, their safety, efficacy, and overall role in management remain unclear. This review evaluates the current evidence on cannabinoid use in GP and related disorders.

Objectives

To systematically evaluate the safety and efficacy of cannabis-based medicines (CBMs) and endocannabinoid system modulation in patients with gastroparesis and related syndromes.

Methods

•Systematic review conducted per **PRISMA 2020** guidelines
•Databases searched: Embase, Medline (Ovid), Cochrane Library, ClinicalTrials.gov, WHO ICTRP
•Dual-reviewer screening (title/abstract → full text) with third reviewer for conflicts
•Evidence graded using **LEGEND criteria**
•Included: Human studies on cannabinoids/ECS in GP, GPRS, or FD with delayed gastric emptying
•Excluded: Reviews, animal studies, non-relevant populations, oncology-related use, CHS, cyclic vomiting

Results

2,834 studies identified → 38 included
Study types: 1 clinical trial, 1 prospective observational study, 14 retrospective studies, 7 cross-sectional surveys, 10 case reports, 5 biological experiments
Studies categorized into: Pathophysiology, Epidemiology, Clinical Use & Associations, Risks & Adverse Effects

Pathophysiology

1. Reduced endocannabinoids in diabetic gastroparesis (Bashashati, 2020): ↓ anandamide (AEA) and 2-AG in female patients with diabetic GP vs controls, suggests endocannabinoid deficiency may contribute to symptom development

2. Genetic variation affecting ECS signaling (Camilleri, 2013): FAAH gene polymorphism associated with FGID symptoms, indicates altered endocannabinoid metabolism may influence GI motility and visceral sensitivity

Epidemiology

1.Increasing prevalence and outcomes of cannabis use in gastroparesis (McCarty, 2022): cannabis use disorder in GP rose significantly over time (~2,000 → >7,000 cases; 2.25% overall)
Users were younger, more often male, and lower socioeconomic status, and had ↓ inpatient mortality (aOR ~0.45) and ↓ length of stay

2. Cannabis use associated with increased 30-day readmission risk in gastroparesis (Shahsavari, 2020): among 5,268 GP patients, 3.7% used cannabis. Cannabis use associated with ↑ 30-day readmission (OR 1.7), though the confidence interval approached 1.0, suggesting a marginal or potentially weak association

3. **Cannabis use associated with reduced healthcare burden in gastroparesis (Dahiya, 2021):** among 99,695 GP patients, 8.9% used cannabis. Cannabis use associated with ↓ length of stay (3.4 vs 4.4 days), ↓ hospital charges (~$30,400 vs $38,100), and ↓ rates of sepsis (aOR 0.22)
Inpatient mortality in cannabis users was low (0.27%), no mortality rate data was reported for the non-cannabis use subgroup for comparsion

Clinical Use & Association

1.Clinical Efficacy in Symptom Management (Zheng 2023, Barbash 2019): High-quality evidence demonstrates that cannabinoids (in both CBD and THC forms) significantly reduce Gastroparesis Cardinal Symptom Index (GCSI) scores, specifically improving nausea, vomiting severity (P=0.006), and abdominal pain (P<0.05).

2. High Patient Preference vs. Low Clinical Adoption (Aivaliotis 2020, Jehangir 2019, Parkmen 2022, Tanner 2023): Patient surveys indicate that marijuana is perceived as one of the most effective treatments for gastroparetic pain and nausea (ranking above synthetic dronabinol) yet retrospective chart reviews show clinical prescription rates remain low, ranging from only 0.4% to 2.7%.

3.**Cannabinoid therapy associated with functional improvement in hypermobility-associated gastroparesis (Dar, 2021):** 18-year-old woman with Ehlers-Danlos syndrome and severe GP requiring parenteral nutrition and high-dose opioids. After transition to cannabinoid-based therapy, patient demonstrated marked improvement with discontinuation of opioids, reduced hospitalizations (54 → 5 days/year), improved functional status (Barthel Index 15 → 100), and decreased care needs.

Risks & Adverse Effects

1. Pharmacodynamic Interactions (Sung 2025): Concurrent use of cannabis and semaglutide may be associated with a significantly higher incidence of gastroparesis, constipation, and acute pancreatitis compared to using either agent alone according to a pre-published abstract.

2. Metabolic and Perioperative Risks (Gallo 2016, Zayouna 2018, Wojtas 2023, Cammarano 2021, Shinha 2011): Chronic cannabinoid use may show an association with recurrent diabetic ketoacidosis (DKA) in patients with diabetes, diabetes being a common cause of gastroparesis.

Discussion

Evidence suggests that the endocannabinoid system plays an important role in gastroparesis pathophysiology, with findings of increased cerebral CB1 receptor availability and depleted plasma endocannabinoids like anandamide.

Clinical studies, including a double-blind RCT, demonstrate that cannabis-based medicines (CBMs) significantly improve total symptom scores and caloric intake, even while paradoxically slowing gastric emptying. Retrospective data show a protective association between cannabis use and inpatient mortality (aOR: 0.45) and healthcare costs, though recent propensity-matched studies suggest conflicting information, there seems to be increase in ED use.

Despite high patient-perceived efficacy (frequently rated second only to IV opioids for pain) clinical adoption remains historically low (0.4–2.7%). However, risks such as recurrent DKA in diabetic populations highlights the critical need for a nuanced, benefit-risk approach to CBM therapy.

Conclusion

While current evidence is limited, CBMs demonstrate significant therapeutic potential for symptom relief and reduced inpatient mortality in patients with gastroparesis. Much work remains to determine safety and efficacy, but preliminary data is encouraging that strategic targeting of the ECS may help treat GP.

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