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Abdominal Pain and Chronic Opiate Use in Patients with Gastroparesis

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Abstract: Introduction: Although opiate narcotics may worsen gastroparesis (GP), patients can take these for abdominal pain (AP) or other chronic pain syndromes. This study aims to evaluate medications patients with gastroparesis use for AP and compare patients who use opiate analgesics for AP to those using opiate analgesics for non-abdominal pain. **Methods:** Patients at a tertiary academic center gastroenterology clinic completed the Patient Assessment of Gastrointestinal Disorders–Symptom Severity Index (PAGI-SYM) and Quality of Life Short-Form 8 (QOL SF-8) surveys between 10/2021 and 03/2023. Patients recorded gastroparesis treatments, pain treatments and indication, and any hospitalizations/emergency department (ED) visits within 3 months of a clinic visit. **Results:** A total of 53 patients were enrolled: 72% reported having AP. Patients were using the following medications for AP: 25% heating pad, ice or hot showers, 20.8% acetaminophen, 14.6% hyoscyamine, 13% opiate use, 13% marijuana use, 10.4% dicyclomine, 8.3% Nonsteroidal anti-inflammatory drugs (NSAIDs), 4% benzodiazepine, and 2.1% gabapentin. The reported reasons for using opiates were 58% AP, 16.6% chronic back pain, 16.6% Reflex Sympathetic Dystrophy (RSD) and fibromyalgia, and 8.3% osteoarthritis. All opiate users reported daily scheduled use. AP severity scores (4.1 vs. 2.8; $p = 0.041$), morphine equivalent usage (77 ± 44 vs. 32 ± 2; $p = 0.037$), and the number of ER visits (1.0 vs. 0 over 3 months) were higher in patients using opiates for AP than those using opiates for non-abdominal pain. **Conclusions:** In this series, 72% of patients with gastroparesis had abdominal pain, and 13% of patients were taking opiates. Patients who used opiate analgesics for abdominal pain had a higher average abdominal pain severity score and used a higher amount of opiate analgesia than patients using opiates for musculoskeletal pain. Abdominal pain in patients with gastroparesis can be harder to control with opiate analgesia compared to non-abdominal pain, supporting the concept of avoiding chronic opiate usage for abdominal pain in gastroparesis.

Keywords: abdominal pain; opiates; gastroparesis

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1. Introduction

Abdominal pain (AP) is a challenging symptom to address in patients with gastroparesis. Abdominal pain has been reported in as many as 79% of patients with gastroparesis [1]. AP can be debilitating and often negatively impacts the quality of life for these patients. In addition, gastroparesis AP leads to increased emergency department visits and hospitalizations, which increases healthcare utilization and costs [1,2]. Abdominal pain in gastroparesis (GP) is a multifaceted symptom that extends beyond delayed gastric emptying alone. While gastroparesis is characterized by impaired stomach motility, the severity of abdominal pain often does not correlate with the degree of delayed emptying, suggesting additional pathophysiological mechanisms [3]. Speculatively, these may include visceral hypersensitivity, neuroinflammation, and neuropathy within the gastric wall, which could

alter pain signaling [3]. Central sensitization due to prolonged pain exposure, psychological factors such as depression and anxiety, and disruptions in the gut–brain axis further complicate pain perception in GP [3–15]. Addressing abdominal pain effectively may require therapies that not only improve motility but also target these underlying mechanisms, such as symptom modulators (tricyclic antidepressants, pregabalin) and behavioral therapies like cognitive behavioral therapy and hypnotherapy, which have shown promise in managing GP symptoms by potentially modulating these complex interactions [3].

The treatment of gastroparesis involves dietary modifications, and medicines such as prokinetic agents to enhance gastric emptying and antiemetic agents to reduce nausea and vomiting [4]. Currently, metoclopramide is the only U.S. Food and Drug Administration (FDA)-approved medication for gastroparesis. Clinicians may prescribe other medications such as erythromycin and domperidone [1,4,5]. Antiemetic agents are often given for nausea and vomiting. In patients with severe symptoms, surgical intervention may be needed—enteral nutrition, pyloromyotomy, gastric electric stimulation [4]. A subset of patients suffer from debilitating pain refractory to the above therapies. Medications such as dicyclomine and hyoscamine or symptom modulators such as nortriptyline may be used for the abdominal pain. Despite evidence that opiate narcotics may worsen gastroparesis symptoms, clinicians may resort to the use of opiate pain medications when other modalities do not succeed [15]. Jehangir et al. found 13% of patients with gastroparesis report the use of opiate medications for abdominal pain in their retrospective review at a large tertiary academic center [5].

Patients with gastroparesis may need to use opiate medications for non-gastroparesis pain, such as chronic back pain, knee pain, or other musculoskeletal (MSK) conditions that have not responded to conventional modalities of pain control. To date, there has not been a study that compares the quality of life, abdominal pain severity, or gastroparesis symptom severity between patients who use opiates for AP related to gastroparesis and patients using opiates for non-AP reasons.

This study aims to compare the severity of abdominal pain in gastroparesis patients using opiate analgesics for abdominal pain versus those using opiate analgesics for non-abdominal pain, hypothesizing higher pain severity scores in the former group. Additionally, it seeks to measure and compare the morphine equivalent usage, with an expectation of higher usage among patients taking opiates for abdominal pain. Lastly, this study aims to investigate healthcare utilization, hypothesizing that patients using opiates for abdominal pain will have more frequent emergency room visits and hospitalizations compared to those using opiates for non-abdominal pain.

2. Results

2.1. Patients

Seventy-one patients were given the survey to complete. Fifty-four patients completed the survey in its entirety, and these data were included in this study. Some patients declined to complete the survey during their visit or only partially filled out the questionnaire.

Of the 54 patients in our study cohort, the mean age was 45 years old; 47 were female, and 7 were male (Table 1). Mean Body Mass Index (BMI) was 28.6 (Table 2). Etiologies of gastroparesis were as follows: 30 idiopathic gastroparesis (IGP), 18 diabetic gastroparesis (DGP), 2 post-surgical gastroparesis, and 2 Ehlers Danlos syndrome. The mean percentage of residual meal retention in the gastric emptying study at 2 h was 58.5%, and the mean percentage retention of meal at 4 h was 23.3%.

Table 1. Demographic data of 54 patients with gastroparesis included in this study.

Category	Sub-Category	Number	Percent
Sex	Female	47	87
	Male	7	13
Race	White non-Hispanic	39	72
	African American/Black	6	11
	Hispanic	3	6
	Asian	1	2
	Other/Unknown	5	9

Table 2. Average age, BMI, and gastric retention values during gastric emptying study for 54 patients included in this study.

Category	Average (±SD)
Age (years)	45 (±14.6)
BMI	28.4 (±9.0)
Gastric Content Retained after 2 h (%)	57.5 (±22.5)
Gastric Content Retained after 4 h (%)	22.3 (±19.3)

A total of 39 patients (72%) of all respondents reported experiencing abdominal pain. In addition, approximately 98% of those who reported abdominal pain reported that the abdominal pain was part of the gastroparesis symptoms. Among the surveyed patients, 13% reported opiate use, 13% reported marijuana use, and 4% reported benzodiazepine use. Eleven percent of patients using one substance reported the use of more than one controlled substance.

Of the 54 patients, 42 were not taking opiates, 6 were taking opiates for abdominal pain, and 6 were taking opiates for non-abdominal pain.

2.2. Healthcare Utilization

Patients taking opiates for gastroparesis AP had, on average, 1.0 ± 1.29 emergency room visits and 0.5 hospitalizations per 3 months compared to no visits for those taking opiates for non-gastroparesis pain. Patients not taking opiates had 0.88 ± 1.62 emergency room visits over 3 months and 0.45 ± 1.34 hospital admissions over 3 months.

2.3. Opiate Use Data/Modalities Used to Treat Pain

For modalities used to treat abdominal pain, 25% of patients reported the use of a heating pad, ice, or hot showers, 20.8% acetaminophen, 14.6% hyoscyamine, 10.4% dicyclomine, 8.3% NSAIDs, 2.1% calcium carbonate, 2.1% domperidone, 2.1% gabapentin, and 11% opiate analgesia (Table 3). Notably, 31.3% of patients reported not using anything to treat their gastroparesis pain.

A total of 26% (8) of patients diagnosed with idiopathic gastroparesis (IGP) reported the use of opiates to treat abdominal pain, whereas approximately 22% (4) of patients diagnosed with diabetic gastroparesis (DGP) reported the use of opiates to treat abdominal pain (Table 4).

Six patients were taking opiates. The reported reasons for using opiates were 58% AP, 16.7% fibromyalgia, 16.7% back pain, 16.7% reflex sympathetic dystrophy, 8.3% arthritis. All opiate users reported daily scheduled use. Patients taking opiates for abdominal pain had higher morphine equivalent usage than those for non-abdominal pain (77.5 ± 43.7 vs. 31.8 ± 28.2; *p*-one tailed = 0.037) (Table 5). In addition, patients using opiates for abdominal pain had a greater number of Emergency Room (ER) visits than patients taking opiates for non-abdominal pain (1.0 ± 0.1 vs. 0 ± 0; *p*-one tailed 0.032).

Table 3. Modalities reported for abdominal pain control in 54 patients with gastroparesis.

Reported Pain Treatment Modality	N	Percentage (%)
Nothing	15	31.3
Ice, hot showers, heating pads	12	25
Acetaminophen	10	20.8
Hyoscyamine	7	14.6
Opiates	6	11
Marijuana	6	11
NSAIDs	4	8.3
Benzodiazepines	2	3.7
Gabapentin	1	2.1
Domperidone	1	2.1
Dicyclomine	1	2.1
Calcium Carbonate	1	2.1

Table 4. Opiate use stratified by etiology of gastroparesis regardless of indication for opiate.

Gastroparesis Etiology	Total	Opiate Use (N)	Opiate Use Percentage (%)
Idiopathic	30	8	26
Diabetic	18	4	22
Post-Surgical	2	0	0
Ehlers Danlos	2	0	0
Uncategorized	2	0	0

Table 5. Daily morphine milliequivalent (MME) average comparison based on indication for opiate use.

Indication for Opiate Use	Daily MME	CI (95th Percentile)	*p*-One Tailed
Abdominal Pain (n = 7)	77.5 ± 21.9	33.8–121.2	0.037
Non-Abdominal Pain (n = 5)	31.8 ± 14.1	3.6–60.0	

Benzodiazepine use was highest among those taking opiates for abdominal pain (62.5%) and was lowest for those taking opiates for non-abdominal pain (16.7%). Among those not taking opiates, benzodiazepine use rate was 26.19%. A similar trend was noted for marijuana use. Among patients taking opiates for abdominal pain, 43% were also using marijuana. Among patients taking opiates for non-abdominal pain, none recorded the use of marijuana. Among those not using opiates, 20% reported regular use of marijuana.

2.4. PAGI-SYM Comparison Data

Average total PAGI-SYM scores were not different between patients reporting opiate use for AP vs. opiate use for non-AP (56.2 vs. 44.4; $p = 0.22$) (Table 6). However, PAGI-SYM AP-specific severity scores were significantly higher in patients using opiates for AP than non-abdominal pain (4.14 vs. 2.80, $p = 0.041$). Furthermore, PAGI-SYM AP-specific scores were highest among patients using opiates for AP vs. non-abdominal pain vs. patients reporting the use of nothing to treat abdominal pain (4.14 vs. 2.80 vs. 2.34; $p = 0.015$).

Table 6. Comparison via PAGI-SYM, QOL-SF8 of patients using and those not using opiates for abdominal pain.

Survey	Opiate Use for Abdominal Pain	Total Average Score	*p*	Abdominal Pain Specific Score	*p*
PAGI-SYM	Y (n = 7)	56.2 ± 16.1	0.22	4.14 ± 1.2	0.041
	N (n = 47)	44.4 ± 17.9		2.80 ± 1.5	
QOL-SF8	Y (n = 7)	20.25 ± 4.5	0.031	2.07 ± 0.74	0.0033
	N (n = 47)	25.88 ± 7.5		3.27 ± 1.2	

2.5. SF-8 Comparison Data

Average total scores for QOL-SF-8 were lower for patients reporting the use of opiates vs. patients not reporting opiate use (19.6 ± 4.43 vs. 23.6 ± 7.48 *p*-one tailed = 0.057) (Table 6). QOL scores were not statistically different between patients taking opiates for AP compared to those taking for non-AP (20.3 ± 2.9 vs. 21.9 ± 3.0; *p*-one tailed = 0.19).

3. Methods

Patients at a tertiary academic center gastroenterology clinic were asked to participate in this study. The protocol was approved by Temple University Institutional Review Board (IRB) (Temple IRB protocol number 22347); informed consent was obtained from each patient. All authors had access to the study data and reviewed and approved the final manuscript.

3.1. Patient Selection

The following inclusion criteria and exclusion criteria were used.

Inclusion criteria: We used the ACG 2022 clinical guidelines' definition of gastroparesis which is a motility disorder characterized by upper Gastrointestinal (GI) symptoms without mechanical obstruction and with objective documentation of delayed gastric emptying through tests such as a gastric emptying scan [4]. Patients in our study were diagnosed with gastroparesis via a gastric emptying scintigraphy and upper endoscopy and were being seen in a follow-up visit for their clinical care in the Temple University Hospital GI motility clinic.

Exclusion criteria: The exclusion criteria for this study included patients under 18 years old, pregnant individuals, those unable to understand or speak English, and cognitively impaired adults unable to complete surveys or provide sufficient consent for this study. Children were excluded due to the clinic's focus on adults, while pregnancy poses diagnostic challenges due to conditions specific to pregnancy including the nausea and vomiting of pregnancy and hyperemesis gravidarum [6]. Non-English speakers were excluded because surveys were completed independently, precluding the provision of surveys in multiple languages. Excluding cognitively impaired adults ensures adherence to study protocols, upholding data integrity and ethical standards.

3.2. Data Collection

Data collection occurred from 22 December 2022 to 2 May 2023. Patient histories and medication information were validated through comprehensive reviews of previous medical records and verification by the attending gastroenterologist during patient visits. These measures were implemented to ensure the accuracy and compliance of patient-reported data in this study. Patients completed a questionnaire comprising Patient Assessment of Gastrointestinal Disorders–Symptom Severity Index (PAGI-SYM) and Quality of Life Short-Form 8 (QOL SF-8) surveys [7,8]. Patients were asked to complete these surveys during a clinic visit with their motility specialist. In addition, patients were asked to record gastroparesis treatments, pain treatment, and any hospitalizations/ED visits within 3 months of the clinic visit. Further, patients were asked to record any opiate use, benzodiazepine use, and marijuana use with frequency and the name of provider who wrote the prescription.

Patients recorded the type of opiate used, dose, frequency used, indication for use, and the provider writing the prescription. Patients who recorded the use of opiate pain medications were also asked if the analgesics improved pain symptoms. Patients' demographics and medical history were recorded from the electronic medical record.

3.3. Opiate Use Classification

In order to compare patients' opiate use, we calculated each patient's morphine milligram equivalents (MMEs) using the freely available opioid dosage conversion app developed by Chris Marcellino, MD, at Mayo Clinic and Norris Vivatrat, MD, at UCSD Medical Center [9]. The developers of the app are physicians who used data from Center to Advance Palliative Care (CAPC), a part of the Icahn School of Medicine (https://www.capc.org/). Their app utilizes conversion data sourced from American Society of Health-System Pharmacists (ASHP), the largest association of pharmacy professionals in the United States, which also serves as the accrediting body for pharmacy residency programs. Within the app, they explore how cross-tolerance can vary among diverse populations and across different opioids URL: https://www.ashp.org/about-ashp?loginreturnUrl=SSOCheckOnly (accessed on 1 October 2023) [9].

3.4. PAGI-SYM

Initially validated for gastroparesis in 2004 as the Gastroparesis Cardinal Symptom Index (GCSI), the PAGI-SYM also includes abdominal pain and symptoms of gastroesophageal reflux. The GCSI and PAGI-SYM are dependable self-report tools developed to measure symptom severity [10]. The PAGI-SYM's construct validity is confirmed through significant correlations with SF-36 and PAGI-QOL [10]. Our modified PAGI-SYM survey comprised 15 questions designed to evaluate the severity of gastrointestinal (GI) symptoms experienced by patients, including nausea, abdominal pain, and constipation [10]. Each symptom is assessed on a scale ranging from 0 (indicating no effect from the symptom) to 5 (indicating high severity of the symptom). For our analysis, we examined both individual symptom scores and total scores across different patient groups.

3.5. SF8 Survey

The SF-8 was developed as a concise alternative to the SF-36, representing each of its eight dimensions with a single item to provide comparable results more efficiently [11]. It has not yet been used for gastroparesis. The SF8 survey consists of 8 subjective questions aimed at assessing patients' health and symptoms [12–14]. Participants were requested to answer these questions based on their symptoms over the past 4 weeks. The questions were presented on a scale ranging from "none" to "very severe". We converted this to a numeric score with "none" being "0" and "very severe" being "6". For our analysis, we examined both individual symptom scores and total scores across different patient groups.

3.6. Data Analysis

Patients were divided into three groups: those not prescribed opiates, those prescribed opiates for gastroparesis pain, and those prescribed opiates for a separate pain disorder outside of gastroparesis such as fibromyalgia. Numeric data were expressed as mean $\pm$ standard deviation (SD), median with interquartile range (IQR), or mean difference with 95% confidence interval. Data were correlated using Pearson correlations, as weak (0.00–0.30), moderate (0.31–0.50), and strong (0.51–1.0) correlations, with significance defined at <0.05. Data analysis was performed in a commercially available software package (Microsoft Excel, version 16.78, Philadelphia, PA, USA). ANOVA was used to analyzed the PAGI-SYM and SF-8 data, whereas Student's t test was used to analyzed the morphine milliequivalent data.

4. Discussion

Abdominal pain (AP) poses significant challenges in the management of patients with gastroparesis, as it is prevalent, difficult to manage, and impacts their quality of life [2,13]. This study aimed to assess the medications utilized by gastroparesis patients for AP relief, and explore differences in AP severity between patients primarily using opiate analgesics for AP versus those for musculoskeletal or non-abdominal pain.

In this study, 72% had abdominal pain (AP), with 13% using opiates. This is a lower prevalence of opiate use compared to some previous studies [5]. Patients using opiate analgesics tended to have lower overall QOL-SF8 scores, indicating a potential negative impact on the quality of life, although the difference was not statistically significant. Notably, individuals utilizing opiates for AP displayed higher average AP severity scores on PAGI-SYM compared to those using opiates for non-AP, along with a higher opiate dosage in morphine equivalents. This suggests challenges in managing AP specific to gastroparesis, especially managing with opiates, advocating against their usage. Prior studies have linked opiate use to heightened AP severity in gastroparesis patients [2,5]. This pathologic mechanism is supported by a study which found that patients who used opiates had a significant increase in delayed emptying [14].

Our study utilized the PAGI-SYM survey for assessing gastroparesis symptoms and the SF8 to evaluate the quality of life in gastroparesis patients. The PAGI-SYM is well established to capture the symptom severity of gastroparesis, dyspepsia, and gastroesophageal reflux disease [10]. While QOL-SF8 has been found to produce similar results to the more longer SF-36, unlike the SF-36, it has never been tested in gastroparesis patients [11]. We found that the QOL-SF8 survey, which is short and simple to administer within an office visit's time constraints, captured nuances even in smaller sample sizes. While the average total scores for QOL-SF-8 were lower for patients reporting opiate use compared to those not using opiates, the QOL scores were not statistically different between patients taking opiates for AP versus those taking them for non-AP.

Patients with gastroparesis taking opiates for AP had more healthcare utilization including emergency room visits and hospitalizations. Those taking opiates for gastroparesis had, on average, 1 emergency room visit and 0.5 hospitalization per 3 months compared to no visits for those taking opiates for non-gastroparesis pain. Patients not taking opiates had 0.88 emergency room visits over 3 months and 0.45 hospital admissions over 3 months. Previous studies have found that among gastroparesis patients, opiate use and marijuana are associated with higher readmission rates [5,15,16]. In one study, patients with severe delay had increased hospitalization and emergency room visits [14]. Opioid use has been well established to worsen symptoms, often leading to patients seeking hospital treatment for their pain [5]. A study conducted at the University of Pittsburgh found that 59% of 570 patients who presented to the ED or were admitted to the hospital did so due to abdominal pain [17]. Taken together, these findings suggest that opioid use exacerbates patients' symptoms, as reflected in symptom severity scores, and increases their frequency of hospital visits. Further research should explore if those taking opiates for non-gastroparesis abdominal pain have lower readmission and emergency room visit outcomes compared to those taking opiates for gastroparesis abdominal pain.

Given our findings, it is especially important to ensure that patients are abiding by current ACG guidelines [4]. A low-particulate diet is recommended for patients with gastroparesis [4]. Currently, metoclopramide is the only FDA-approved medication for treating this condition, although other medications, such as domperidone, are under investigation [4]. Pyloromyotomy can be considered for refractory cases [4]. For symptom management, patients often use treatments like acetaminophen, ice, and heating pads, though these have not been extensively studied. It is important to conduct further research on these alternative treatments to reduce the use of opioids. Additionally, clinicians from other specialties should consider alternative pain management strategies for their patients with gastroparesis to minimize opioid use.

Benzodiazepine use was highest among those taking opiates for abdominal pain (62.5%) and lowest for those taking opiates for non-abdominal pain (16.7%). Among those not taking opiates, benzodiazepine use rate was 26.19%. A similar trend was noted for marijuana use. Interestingly a double-blind placebo-controlled study found that twice daily CBD improved vomiting episodes and perceived symptoms but did not statistically improve abdominal pain [14].

Our study had several limitations, including a small sample size due to the difficulty of recruiting patients who use opiates when guidelines strongly advise against opiate use for gastroparesis. This study was conducted at Temple University Hospital GI motility clinic, which may not represent the broader gastroparesis patient population due to its single-center nature. Only patients who completed the entire survey were included, potentially excluding those with more severe symptoms or cognitive difficulties. Non-English speakers were also excluded, possibly under-representing certain demographic groups. This study relied on patient self-reporting for medication use, pain levels, and quality of life measures, introducing potential recall and social desirability biases. Additionally, patients recorded their treatments, pain management, and hospitalizations/ED visits within three months of the clinic visit, which might not capture the full spectrum of their experiences. The self-reported use of controlled substances like opiates, marijuana, and benzodiazepines could lead to under-reporting due to stigma or fear of judgment. A longer study period should be explored to obtain more patients. Additionally, the higher severity of abdominal pain among opiate users may reflect underlying symptoms leading to opiate prescriptions rather than opiates worsening symptoms.

Future research should aim to address these limitations by including larger and more diverse sample sizes to ensure the findings are more generalizable to the broader gastroparesis patient population. Longer follow-up periods would help capture the full spectrum of patient experiences and outcomes. Additionally, intervention studies comparing opiate alternatives for pain management in gastroparesis patients should be conducted to identify effective treatments that do not carry the risks associated with opiate use. Specifically, research should focus on evaluating non-opioid pain management strategies, such as nerve blocks, antidepressants, anticonvulsants, and non-pharmacologic interventions like cognitive behavioral therapy. These studies should also investigate the impact of these alternative treatments on the quality of life and hospital utilization to provide comprehensive care guidelines for gastroparesis patients.

In conclusion, our findings highlight that patients using opiates for abdominal pain had higher pain severity and healthcare utilization compared to patients not using opiates as well as patients using opiates for reasons other than abdominal pain. These findings underscore the challenges of managing gastroparesis-related AP with opiates as well as the management of other pain disorders in those with gastroparesis.

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