

Pain management in chronic pancreatitis incorporating safe opioid practices: Challenge accepted

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Abstract

Patients with chronic pancreatitis often experience severe, unrelenting abdominal pain, which can significantly impact their quality of life. Pain control, therefore, remains central to the overall management of chronic pancreatitis. Most of the strategies aimed at treating the pain of chronic pancreatitis are based on expert opinion and vary from one institution to another, as there are no uniform guidelines to direct a stepwise approach towards achieving this goal. In this editorial, we comment on best practice strategies targeted towards pain control in chronic pancreatitis, specifically highlighting the use of opioid medications in this patient population. We discuss various safe and efficacious prescription monitoring practices in this article.

Key Words: Chronic pancreatitis; Chronic pain; Pain management; Opioid use disorder; Prescription opioid misuse; Prescription opioid abuse

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Core Tip: Pain management in chronic pancreatitis is complex; collaboration with local pain specialists maybe necessary to provide optimal care.

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INTRODUCTION

Chronic pancreatitis (CP) is a fibro-inflammatory disorder characterized by irreversible parenchymal and ductal injury of the pancreas caused by a variety of genetic, metabolic and environmental factors. Globally, the prevalence of CP ranges between 36 and 125 per 100000 persons[1]. Patients with CP almost universally present with abdominal pain. Although the pathophysiology of the pain is poorly understood, it seems to be related to various factors such as pancreatic inflammation, duct obstruction and nerve damage[2-6].

With abdominal pain being the predominant symptom, pain management is central to the treatment of CP. Lifestyle modifications such as alcohol and tobacco cessation along with frequent consumption of small meals remain the first-line treatment for CP [7,8]. Efficacy of pancreatic enzymes has been debated based on results from multiple randomized controlled clinical trials, and the current consensus is that uncoated preparations containing large amounts of pancreatic enzymes can be used for pain control in selected patients, in addition to treating symptoms of pancreatic insufficiency[2,9]. Similarly, some studies have shown that antioxidants with or without other analgesics could be beneficial in treating pain *via* suppression of oxidative stress which would reduce pancreatic inflammation[10,11].

PAIN MANAGEMENT STRATEGIES

Several experts have recommended following the World Health Organization (WHO) pain relief ladder while choosing the appropriate analgesic in CP[2,3,5,12]. Acetaminophen continues to remain the analgesic of choice. This is followed by neuromodulators such as gabapentin, pregabalin and tricyclic antidepressants. Antispasmodics and muscle relaxants such as baclofen and hyoscyamine have also been used as adjunctive therapies. Oftentimes, endoscopic intervention with sphincterotomy and stent placement is employed in patients with distal pancreatic duct obstruction. Surgical techniques aimed at ductal decompression or parenchymal resection or both, albeit limited by their invasive nature, are often employed in patients who have pain that is refractory to other treatment measures. In the United States, total pancreatectomy with islet auto transplantation has shown promising results, although there have been mixed results on long term diabetes control and insulin dependence[13-16]. Denervation techniques such as celiac plexus blocks are also used when other treatments fail[17]. Use of neurostimulation techniques such as spinal cord stimulation and transcranial magnetic stimulation have shown promising results, although rarely employed in standard practice owing to paucity of literature [18,19]. When these strategies fail, providers are often left with opioids for pain management although there is limited published literature outlining their use in patients with CP. Knowing about the devastating nature of the current opioid epidemic that has been prevalent for more than 25 years, it is important to have a mindful and cautious approach while effectively using opioids to treat pain in such patients[20,21].

Opioid use disorder (OUD) has evolved into a major health emergency over the last few years, contributing to more than 600000 deaths just in the United States, mandating judicious opioid use and close prescription monitoring in an attempt to prevent opioid misuse[22]. Although potentially effective in pain management, opioid use has serious consequences including narcotic bowel syndrome and opioid-induced hyperalgesia[23]. It has been shown that about 13%-50% patients with inflammatory bowel disease and irritable bowel syndrome use chronic opioids, and similarly, up to 66% patients of CP are known to use opioids[24-27]. Over the last two decades, opioid use among several gastrointestinal conditions with chronic pain has steadily continued to increase with an 88% increase in inflammatory bowel disease and a 57.6% increase in CP[27].

With the increased use of opioids, there remains a high level of concern among gastroenterologists and other providers for the risk of opioid dependence and abuse along with increased healthcare utilization. In CP, opioid use has limited data and uniform guidelines are lacking to direct prescription practices, which can lead to further apprehension and confusion among providers when deciding upon an ideal approach. Although the WHO pain relief ladder has been recommended by some experts while choosing an appropriate analgesic in patients with CP, it should be noted that this stepwise approach was originally designed for achieving pain control primarily in cancer patients, and the feasibility of its use has not been studied in CP[2,

12]. Absence of a uniform stepwise approach towards analgesic use in CP, may further result in irregular and scattered methods of opioid prescription among various providers, further adding to opioid overuse and associated adverse outcomes.

Curbing the overuse of opioids and regulating a streamlined opioid-prescription system, is a critical task for providers caring for patients with chronic pancreatitis. There is a need for treatment approaches that are successful in minimizing pain while minimizing the risk of developing OUD. Several pain societies have developed prescription guidelines for patients with non-cancer pain and thus it is important to partner with experienced pain clinics who can provide appropriate attention to patients requiring narcotic therapy[28-31].

Selection of patients who would benefit from opioid therapy and predicting their risk of misuse potential should be carefully executed. Several validated screening tools for OUD can be used for this purpose including the Current Opioid Misuse Measure, which has been studied in nonalcoholic CP[32-35]. Clinicians should be vigilant for commonly encountered psychosocial risk factors that may be associated with a higher risk of abuse potential such as active or prior concurrent substance abuse, alcohol use, polypharmacy with sedating medications such as benzodiazepines, mental health disorders, *etc.*[36]. Since CP patients could often have comorbid substance abuse disorder, close attention should be paid to either completely avoiding or at least minimizing opioid prescriptions in patients with these risk factors[35,36].

While there is limited data on the opioid prescription guidelines in patients with CP, most experts recommend a one-to-four-week course of low dose opioids (less than 40 morphine milliequivalents) before committing to a long-term opioid therapy for patients with non-cancer pain. This is because higher doses of more than 60 to 90 morphine milliequivalents have been associated with increased risk of dependence and adverse outcomes[30,31,37]. Furthermore, there is a dearth of evidence to suggest better efficacy and safety profile of any one opioid over another[30]. Priority should be given to weaker opioids such as tramadol and extended-release formulations should be avoided due to their higher risk of overdose[30,37]. Transdermal opioids such as fentanyl should only considered when patients are unable to tolerate oral medications [30].

Prior to initiating long term opioid therapy, it is important to extensively educate the patient about its abuse potential and its associated consequences. Many states have mandated opioid treatment agreements that should be signed by both the prescriber and the patient and renewed on a regular basis[38-40]. Once long-term opioid therapy has been initiated, it is important to closely monitor for opioid misuse *via* various physician-based and state-mandated tools. Frequent office visits should be scheduled, no less than once in every 90 d[41]. During each visit, *via* means of a comprehensive history taking and physical exam, an assessment should carefully made to determine need for continuing opioid therapy. If continuing opioid therapy is deemed necessary, an attempt should be made to assess if the opioid dose can be progressively reduced to the minimum effective dose. Additionally, many experts recommend urine drug testing (UDT) prior to starting opioids and eventually for regular monitoring in an effort to curb opioid misuse[28,30]. The United States has mandated prescription monitoring programs (PMP) to track controlled prescriptions which is an efficient tool that can be regularly used by providers to reduce misuse of opioids and other controlled substances[28,30,31,37]. Close attention can thus be paid to patients with frequent emergency room visits who may be receiving multiple overlapping prescriptions of short course opioids. At any point, if lack of response, adverse events or opioid misuse are encountered, opioids may need to be discontinued[37]. Our approach is summarized in **Figure 1**.

CONCLUSION

Abdominal pain is the central symptom for most patients with CP resulting in high healthcare utilization. While several non-opioid therapies exist, unfortunately patients remain symptomatic and thus opioids may be necessary to treat ongoing abdominal pain. With the ongoing opioid epidemic and elevated risk of OUD, several strategies should be incorporated while using opioids for the treatment of pain in patients with CP. These include robust screening measures to predetermine the risk of OUD, safe prescription practices using tools such as UDT and PMP, close clinical follow up and frequent reassessment to assess the need for continuing opioids. Finally, a multidisciplinary approach and coordination with pain management physicians is recommended to adequately cater to each patient's individual needs. Further studies and guidelines

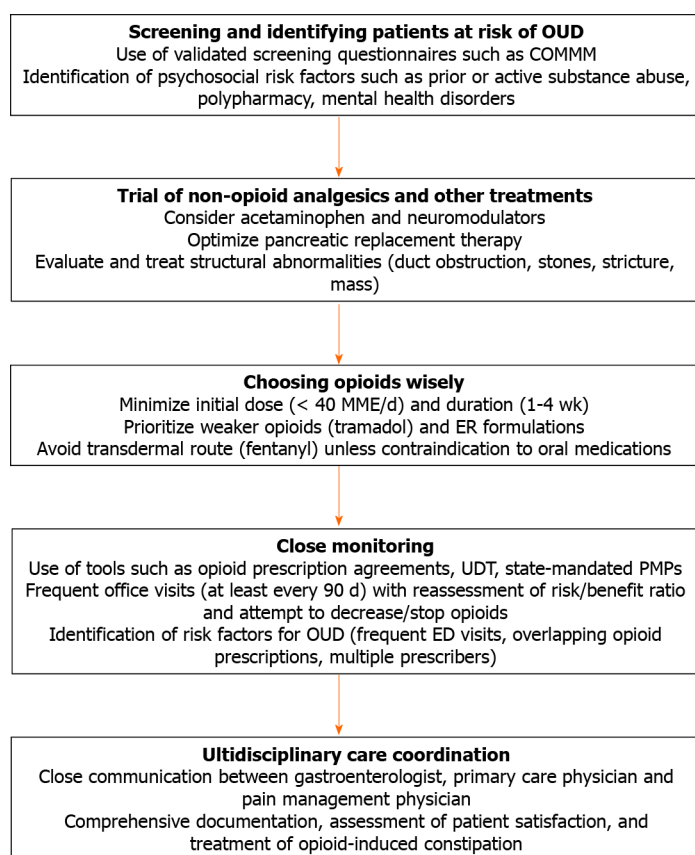


Figure 1 Stepwise approach to management of pain in chronic pancreatitis. OUD: Opioid use disorder; COMMM: Current opioid misuse measure; ER: Extended release; UDT: Urine drug testing; PMP: Prescription monitoring program; ED: Emergency Department.

are needed to address opioid use in CP.

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