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,
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 are required to better understand the best practices for managing chronic pain in patients with CP.

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 are required to better understand the best practices for managing chronic pain in patients with CP.
are needed to address opioid use in CP.

REFERENCES

1 Machicado JD, Dudekula A, Tang G, Xu H, Wu BU, Forsmark CE, Yadav D. Period prevalence of chronic pancreatitis diagnosis from 2001-2013 in the commercially insured population of the United States. *Pancreatology* 2019; 19: 813-818 [PMID: 31350077 DOI: 10.1016/j.pan.2019.07.003]

2 Drewes AM, Bouwense SAW, Campbell CM, Ceyhan GO, Delhaye M, Demir IE, Garg PK, van Goor H, Halloran C, Isaij S, Neoptolemos JP, Olesen SS, Palermo T, Pasricha PJ, Sheel A, Shimosegawa T, Szigethy E, Whitcomb DC, Yadav D; Working group for the International (IAP – APA – JPS – EPC) Consensus Guidelines for Chronic Pancreatitis. Guidelines for the understanding and management of pain in chronic pancreatitis. *Pancreatology* 2017; 17: 720-731 [PMID: 28734722 DOI: 10.1016/j.pan.2017.07.006]

3 Whitcomb DC, Shimosegawa T, Charit SI, Forsmark CE, Frulloni L, Garg P, Hegyi P, Hirooka Y, Irisawa A, Ishikawa T, Isaij S, Lerch MM, Levy P, Masamune A, Wilcox CM, Windsor J, Yadav D, Sheel A, Neoptolemos JP; Working Group for the International (IAP – APA – JPS – EPC) Consensus Guidelines for Chronic Pancreatitis. International consensus statements on early chronic Pancreatitis. Recommendations from the working group for the international consensus guidelines for chronic pancreatitis in collaboration with The International Association of Pancreatology, American Pancreatic Association, Japan Pancreas Society, PancreasFest Working Group and European Pancreatic Club. *Pancreatology* 2018; 18: 516-527 [PMID: 29793839 DOI: 10.1016/j.pan.2018.05.008]

4 Drewes AM, Olesen AE, Farmer AD, Szigethy E, Rebours V, Olesen SS. Gastrointestinal pain. *Nat Rev Dis Primers* 2020; 6: 1 [PMID: 31907359 DOI: 10.1038/s41572-019-0135-7]

5 Beyer G, Habtezion A, Werner J, Lerch MM, Mayerle J. Chronic pancreatitis. *Lancet* 2020; 396: 499-512 [PMID: 32798493 DOI: 10.1016/S0140-6736(20)31318-0]

6 Lühr JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch MM, Haas S, Aksik F, Kartalis N, Iglesias-Garcia J, Keller J, Boermeester M, Werner J, Dumonceau J-M, Fockens P, Drewes A, Ceyhan G, Lindkvist B, Drent H, Ewald N, Harden P, de Madaria E, Witt H, Schneider A, Manfreddi R, Brondum F, Rudolf S, Bollen T, Bruno M; HaPanEU/UEG Working Group. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis.
Shah I et al. Opioid use in chronic pancreatitis

(HaPanEU). United European Gastroenterol J 2017; 5: 153-199 [PMID: 28344786 DOI: 10.1177/2050640616684649]

Singhvi A, Yadav D. Myths and realities about alcohol and smoking in chronic pancreatitis. Curr Opin Gastroenterol 2018; 34: 355-361 [PMID: 29965868 DOI: 10.1097/MOG.0000000000001466]

Edderkop NI, Thrower E. Smoking and Pancreatic Disease. J Cancer Ther 2013; 4: 34-40 [PMID: 23660091 DOI: 10.4236/jct.2013.410A005]

Warshaw AL, Banks PA, Fernández-Del Castillo C. AGA technical review: treatment of pain in chronic pancreatitis. Gastroenterology 1998; 115: 765-776 [PMID: 9721175 DOI: 10.1016/S0016-5085(98)70157-x]

Zhou D, Wang W, Cheng X, Wei J, Zheng S. Antioxidant therapy for patients with chronic pancreatitis: A systematic review and meta-analysis. Clin Nutr 2015; 34: 627-634 [PMID: 25035087 DOI: 10.1016/j.clnu.2014.07.003]

Takuldar R, Lakhtakia S, Nageshwar Reddy D, Rao GV, Pradeep R, Banerjee R, Gupta R, Ramchandani M, Tandan M, Murthy HV. Ameliorating effect of antioxidants and pregabalin combination in pain recurrence after ductal clearance in chronic pancreatitis: Results of a randomized, double blind, placebo-controlled trial. J Gastroenterol Hepatol 2016; 31: 1654-1662 [PMID: 26945817 DOI: 10.1111/jgh.13332]

Jadad AR, Browman GP. The WHO analgesic ladder for cancer pain management. Stepping up the quality of its evaluation. JAMA 1995; 274: 1870-1873 [PMID: 7500338]

Kessel SI, Smith KA, Gardner TB. Total pancreatectomy with islet autologous transplantation: the care for chronic pancreatitis? Clin Transl Gastroenterol 2015; 6: 473 [PMID: 25630865 DOI: 10.1038/ctg.2015.2]

Bellin MD, Abu-El-Haija M, Morgan K, Adams D, Beilman GJ, Chinnakotla S, Conwell DL, Dunn TB, Freeman ML, Gardner T, Kirchner VA, Lara LF, Long-Simpson L, Nathan JD, Naziruddin B, Nynan JA, Pruett TL, Schwarzenberg SJ, Singh VK, Smith K, Steel JL, Wijikstrom M, Witkowski P, Hodges JS; POST study consortium. A multicenter study of total pancreatectomy with islet autotransplantation (TPITAT): POST (Prospective Observational Study of TPITAT). Pancreatology 2018; 18: 286-290 [PMID: 29456124 DOI: 10.1016/j.pan.2018.02.001]

Gardner TB, Smith KD. Total Pancreatectomy and Islet Autotransplant in the Treatment of Chronic Pancreatitis: Tread Very, Very Carefully. Am J Gastroenterol 2018; 113: 322-323 [PMID: 29134966 DOI: 10.1038/ajg.2017.419]

Bellin MD, Whitcomb DC, Abberbock J, Sherman S, Sandhu BS, Gardner TB, Anderson MA, Lewis MD, Alkaade S, Singh VK, Baillie J, Banks PA, Conwell D, Cote GA, Guda NM, Muniraj T, Tang G, Brand RE, Gelrud A, Murthy HV. Diagnosis and Management of Chronic Pancreatitis in the United States. Am J Gastroenterol 2017; 112: 1457-1465 [PMID: 28741615 DOI: 10.1038/ajg.2017.181]

Sachdev AH, Gress FG, Celiac Plexus Block and Neurolysis: A Review. Gastrointest Endosc Clin N Am 2018; 28: 579-586 [PMID: 30241645 DOI: 10.1016/j.gie.2018.06.004]

Kapural L, Cywinski JB, Sparks DA. Spinal cord stimulation for visceral pain from chronic pancreatitis. Neuromodulation 2011; 14: 423-426 [PMID: 21854493 DOI: 10.1111/j.1525-1403.2011.00381.x]

Fregni F, Potvin K, Dasilva D, Wang X, Lenkinski RE, Freedman SD, Pascual-Leone A. Clinical effects and brain metabolic correlates in non-invasive cortical neuromodulation for visceral pain. Eur J Pain 2011; 15: 53-60 [PMID: 20822942 DOI: 10.1016/j.ejpain.2010.08.002]

Singh VK, Yadav D, Garg PK. Diagnosis and Management of Chronic Pancreatitis: A Review. JAMA 2019; 322: 2422-2434 [PMID: 31860051 DOI: 10.1001/jama.2019.14911]

Stoeica N, Costa A, Periel L, Uribe A, Weaver T, Bergese SD. Current perspectives on the opioid crisis in the US healthcare system: A comprehensive literature review. Medicine (Baltimore) 2019; 98: e15425 [PMID: 31096439 DOI: 10.1097/MD.00000000000015425]

Gostin LO, Hodge JG Jr, Noe SA. Reframing the Opioid Epidemic as a National Emergency. JAMA 2017; 318: 1539-1540 [PMID: 28832871 DOI: 10.1001/jama.2017.13358]

Széghy E, Kinisely M, Drossman D. Opioid misuse in gastroenterology and non-opioid management of abdominal pain. Nat Rev Gastroenterol Hepatol 2018; 15: 168-180 [PMID: 29139482 DOI: 10.1038/nrgastro.2017.141]

Cross RK, Wilson KT, Binion DG. Narcotic use in patients with Crohn's disease. Am J Gastroenterol 2005; 100: 2225-2229 [PMID: 16181373 DOI: 10.1111/j.1572-0241.2005.00256.x]

Nusrat S, Yadav D, Bielefeldt K. Pain and opioid use in chronic pancreatitis. Pancreas 2012; 41: 264-270 [PMID: 21792080 DOI: 10.1097/MPA.0b013e3182240565]

Ahmed A, Yakah W, Freedman SD, Kothari DJ, Sheth SG. Evaluation of Opioid Use in Acute Pancreatitis in Absence of Chronic Pancreatitis: Absence of Opioid Dependence an Important Feature. Am J Med 2020; 133: 1209-1218 [PMID: 32272099 DOI: 10.1016/j.amjmed.2020.03.010]

Bilal M, Chatila A, Siddiqui MT, Al-Hanayneh M, Shah AR, Desai M, Wadhwa V, Parupudi S, Casey BW, Krishnan K, Hernandez-Barco YG. Rising Prevalence of Opioid Use Disorder and Predictors for Opioid Use Disorder Among Hospitalized Patients With Chronic Pancreatitis. Pancreas 2019; 48: 1386-1392 [PMID: 31688606 DOI: 10.1097/MPA.0000000000001430]

Manchikanti L, Abdi S, Ailtir S, Balog CC, Benyamin RM, Boswell MV, Brown KR, Bruel BM, Bryce DA, Burks PA, Burton AW, Caldonrey AK, Caraway DL, Cash KA, Christo PJ, Damron KS, Datta S, Deer TR, Diwan S, Eriator I, Falco FJ, Fellows B, Geffert S, Gharibo CG, Glaser SE, Gridler
Predictors and Strategies to Curb Opioid Abuse: Part 1.
Manchikanti L. Prescription Opioid Abuse in Chronic Pain: An Updated Review of Opioid Abuse
Kaye AD
DOI: 10.2174/1574886309666140922095844

McAuliffe Staehler TM
10.1016/j.otc.2020.05.017

Kraus CN
10.1016/j.jpain.2018.04.013

Butler SF
10.1016/j.pain.2007.01.014

Cheattle MD
10.1016/j.pain.2004.07.026

Black E, Khor KE, Demirkol A. Responsible Prescribing of Opioids for Chronic Non-Cancer Pain: A Scoping Review. Pharmacy (Basel) 2020; 8: 150 [PMID: 32825483 DOI: 10.3390/pharmacy8030150]

Butler SF, Budman SH, Fernandez K, Jamison RN. Validation of a screener and opioid assessment measure for patients with chronic pain. Pain 2004; 112: 65-75 [PMID: 15494186 DOI: 10.1016/j.pain.2004.07.026]

Chow R, Fanciullo GI, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foyle KM, Fudin J, Gilson AM, Kelter A, Mauskop A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C; American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain 2009; 10: 113-130 [PMID: 19187889 DOI: 10.1016/j.jpain.2008.10.008]

Dowell D, Haegerich TM, Chow R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. JAMA 2016; 315: 1624-1645 [PMID: 26977696 DOI: 10.1001/jama.2016.1464]

Black E, Khor KE, Demirkol A. Responsible Prescribing of Opioids for Chronic Non-Cancer Pain: A Scoping Review. Pharmacy (Basel) 2020; 8: 150 [PMID: 32825483 DOI: 10.3390/pharmacy8030150]

Butler SF, Budman SH, Fernandez KC, Houle B, Benot C, Katz N, Jamison RN. Development and validation of the Current Opioid Misuse Measure. Pain 2007; 130: 144-156 [PMID: 17493754 DOI: 10.1016/j.pain.2007.01.014]

Barth KS, Balliet W, Pelic CM, Madan A, Malcolm R, Adams D, Morgan K, Owczarski S, Borckardt JJ. Screening for current opioid misuse and associated risk factors among patients with chronic nonalcoholic pancreatitis pain. Pain Med 2014; 15: 1359-1364 [PMID: 24716629 DOI: 10.1111/pme.12403]

Vowles KE, Witkiewitz K, Pielech M, Edwards KA, McIntee ML, Bailey RW, Bolling L, Sullivan MD. Alcohol and Opioid Use in Chronic Pain: A Cross-Sectional Examination of Differences in Functioning Based on Misuse Status. J Pain 2018; 19: 1181-1188 [PMID: 29758355 DOI: 10.1016/j.jpainsym.2018.04.013]

Manchikanti L, Kaye AM, Knezevic NN, McAnally H, Slavin K, Trescoct AM, Blank S, Pampati V, Abdi S, Grider JS, Kaye AD, Manchikanti KN, Cordner H, Gharibo CG, Hameed ME, Albers SL, Atluri S, Aydin SM, Bakshi S, Barkin RL, Benyamin RM, Boswell MV, Buenaventura RM, Calodney AK, Cedenlo DL, Datta S, Deer TR, Fellows B, Fudin J, Gilson AM, Kaye AM, Knezevic NN, Kloth DS, Koyyalagunta D, Lee M, Malia Y, Manchikanti KN, McManus CD, Pampati V, Parr AT, Pasupuleti R, Patel VB, Sehgal N, Silverman SM, Singh V, Smith HS, Snook LT, Solanki DR, Tracy DH, Vallejo R, Wargo BW; American Society of Interventional Pain Physicians. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2--guidance. Pain Physician 2012; 15: 567-116 [PMID: 22786449 DOI: 10.36076/ppj.2012/15/s67]

Shah I et al. Opioid use in chronic pancreatitis
JS, Hameed H, Hameed M, Hansen H, Hamed ME, Hayek SM, Helm S 2nd, Hirsch JA, Janata JW, Kaye AD, Kaye AM, Cloth DS, Koyyalagunta D, Lee M, Malia Y, Manchikanti KN, McManus CD, Pampati V, Parr AT, Pasupuleti R, Patel VB, Sehgal N, Silverman SM, Singh V, Smith HS, Snook LT, Solanki DR, Tracy DH, Vallejo R, Wargo BW; American Society of Interventional Pain Physicians. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2--guidance. Pain Physician 2012; 15: 567-116 [PMID: 22786449 DOI: 10.36076/ppj.2012/15/s67]
