

Pain in Chronic Pancreatitis: From the Bench to the Bedside

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Pain is the main symptom in chronic pancreatitis and its treatment represents the main therapeutic option because pain severely impairs the quality of life [1]. The mechanisms generating pain are poorly understood, and human and experimental studies have indicated a critical role of neuronal mechanisms which result in peripheral and central sensitization. In a concise review, Pasricha [2] has reviewed these mechanisms describing the pathways of pain characterized by an increased pancreatic nociceptor excitability associated with the downregulation of potassium currents. The author also reviewed the activity of some specific molecules implicated in this process, such as the vanilloid receptor, TRPV1, the nerve growth factor, protease activated receptor 2 and a variety of other substances.

Thus, in order to improve the therapeutic options, we also need experimental data. Many animal models which mimic pancreatic pain are typically short term and invasive in nature, and Westlund and Vera-Portocarrero [3] describe the development and characterization of two non-invasive rat models of pancreatitis, one acute and one chronic. The authors report that the two models described are simple to replicate, giving them an advantage over other animal models of pancreatic inflammation. In this way, we could test new substances in alleviating the pain in pancreatitis.

In passing from experimental studies to human studies, a number of papers have demonstrated that patients with chronic pancreatitis have a compromised antioxidant status [4] which may be a contributing factor to the enhanced oxidative state associated with the disease. Nutrition plays an important role in the treatment of chronic pancreatitis since diet is the main source of several antioxidants and cofactors required

for the production of cellular antioxidant enzymes. It has been demonstrated that patients with chronic pancreatitis have an inadequate intake of macro- and micro-nutrients due to pain and exocrine insufficiency, leading to further complications by preventing adequate digestion and absorption of ingested food. Grigsby *et al.* [5] have reviewed the evidence for the use of antioxidants in the treatment of chronic pancreatitis and concluded that the use of antioxidants in chronic pancreatitis patients receiving an antioxidant supplement resulted in a significantly lower need for hospitalization; they also reduced the use of analgesics, including opiates, and, consequently, improved the quality of life.

Another open question in treating pain in chronic pancreatitis patients is the surgical or endoscopic approach. Ahmed Ali *et al.*, in a review of existing literature [6], assessed and compared the effectiveness and complications of surgical and endoscopic interventions in the management of pain for obstructive chronic pancreatitis. The authors concluded that, in patients with obstructive chronic pancreatitis and dilated pancreatic duct, surgery is superior to endoscopy in terms of pain control; morbidity and mortality were not different between the two intervention modalities, but the small size of the existing trials does not provide sufficient information to detect the differences expected regarding this outcome. In addition, regarding the comparison of surgical intervention *versus* conservative treatment, the review has shown that surgical intervention in an early stage of chronic pancreatitis seems to be a promising approach in terms of pain control and pancreatic function. The current opinion is that endoscopy is a bridge to surgery for patients who are in critical condition and cannot immediately undergo surgery [7].

Key words Endoscopy, Gastrointestinal; Pain; Pain Clinics; Pancreatitis, Chronic; Surgical Procedures, Operative

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References

1. Pezzilli R, Morselli Labate AM, Fantini L, Gullo L, Corinaldesi R. Quality of life and clinical indicators for chronic pancreatitis

patients in a 2-year follow-up study. *Pancreas*. 2007 Mar;34(2):191-6. [PMID 17312457]

2. Pasricha PJ. Unraveling the mystery of pain in chronic pancreatitis. *Nat Rev Gastroenterol Hepatol*. 2012 Jan 24. [PMID 22269952]

3. Westlund KN, Vera-Portocarrero L. Rat models of pancreatitis pain. *Methods Mol Biol*. 2012;851:223-38. [PMID 22351095]

4. Bhardwaj P, Thareja S, Prakash S, Saraya A. Micronutrient antioxidant intake in patients with chronic pancreatitis. *Trop Gastroenterol* 2004;25:69-72. [PMID 15471319]

5. Grigsby B, Rodriguez-Rilo H, Khan K. Antioxidants and Chronic Pancreatitis: Theory of Oxidative Stress and Trials of Antioxidant Therapy. *Dig Dis Sci*. 2012 Feb 3. [PMID 22302241]

6. Ahmed Ali U, Pahlplatz JM, Nealon WH, van Goor H, Gooszen HG, Boermeester MA. Endoscopic or surgical intervention for painful obstructive chronic pancreatitis. *Cochrane Database Syst Rev*. 2012 Jan 18;1:CD007884. [PMID 22258975]

7. Pezzilli R. Treating pain in chronic pancreatitis-is the dilemma over? *Nat Rev Gastroenterol Hepatol*. 28 February 2012. [PMID 22371215]