SciMedCentral

JSM Gastroenterology and Hepatology

Editorial

Sensory Nerves and Chronic Pancreatitis

Tsukasa Ikeura* and Kazuichi Okazaki

The Third Department of Internal Medicine, Kansai Medical University, Japan

***Corresponding author**

Tsukasa Ikeura, The Third Department of Internal Medicine, Kansai Medical University, 2-3-1, Shinmachi, Hirakata, 573-1191 Osaka – Japan, Tel: 81-72-804-0101; Fax: 81-72-804-2524; E-mail: ikeurat@takii.kmu.ac.jp

Submitted: 10 January 2014

Accepted: 20 January 2014

Published: 22 January 2014

Chronic pancreatitis (CP) is an irreversible and progressive disease characterized by destruction of acinar cells and irregular fibrosis in the pancreas [1,2]. The most frequent and serious clinical symptom is abdominal pain, which occurs in at least 75% of patients. Recurrent or protracted abdominal pain in CP is often difficult to manage and occasionally decreases patient quality of life. Additionally, the mechanism of pain generation in patients with CP is poorly understood. The potential sources of pain in CP include increased pressure within the pancreatic ducts and tissues resulting from pancreatic stones or strictures of the pancreatic duct, pancreatic ischemia, pancreatic fibrosis, and pancreatic pseudocysts [3]. Another possible pain etiology seems to be associated with histological alteration of intrapancreatic neuronal structures. Bockman et al. reported that intrapancreatic nerve fibers in patients become significantly thicker and more numerous during the development of CP [4]. Furthermore, increased immunoreactivity for two sensory neurotransmitters, substance P (SP) and calcitonin gene-related peptide (CGRP), in numerous intrapancreatic nerves has been demonstrated in patients with CP [5]. Previously, in a dye tracing study, we found that axonal branching in primary sensory neurons innervating the pancreas is increased in WBN/Kob rats, a model of human CP; this hyperbranching was found to cause pain in another c-Fos functional tracing and behavioral study [6]. Based on these observations, it has been suggested that alteration of the nervous system, especially primary sensory neurons, in the pancreas likely plays a role in the generation of pain in CP.

The nociceptive information generated in the periphery is transmitted to the central nervous system via the dorsal horn of the spinal cord [7]. Additionally, stimulation of primary sensory neurons causes the release of several neuropeptides, including SP and CGRP, from peripheral nerve endings via axonal reflexes [8,9]. The release of these neuropeptides, especially that of SP, induces local vasodilatation, plasma extravasation, edema formation, and leukocyte infiltration in a phenomenon termed neurogenic inflammation. Furthermore, SP is also known to activate immune cells to produce cytokines, which can exacerbate inflammatory responses [10]. The neurogenic mechanisms of inflammation appear to play a role in determining the severity of acute pancreatitis [11].

Our previous murine study demonstrated that primary sensory denervation by neonatal capsaicin administration histologically attenuated glandular atrophy, pseudotubular complexes, and fibrosis in the pancreas in experimental cases of dibutyltin dichloride-induced CP [12]. This result suggests that the activation of primary sensory neurons induced by pancreatic tissue injury results in the release of pro-inflammatory neuropeptides, leading to deleterious effects in CP. Therefore, modulating the activity of pancreatic sympathetic in CP afferent nerves may not only provide pain relief but may also prevent exacerbation of the inflammatory process in CP.

REFERENCES

1. Steer ML, Waxman I, Freedman S. Chronic pancreatitis. N Engl J Med. 1995; 332: 1482–90.
2. Etemad B, Whitcomb DC. Chronic pancreatitis: diagnosis, classification, and new genetic developments. Gastroenterology. 2001; 120: 682–707.
3. Di Sebastiano P, di Mola FF, Bockman DE, Friess H, Buchler MW. Chronic pancreatitis: the perspective of pain generation by neuroimmune interaction. Gut. 2003; 52: 907–911.
4. Bockman DE, Buchler M, Malfertheiner P, Beger HG. Analysis of nerves in chronic pancreatitis. Gastroenterology. 1988; 94: 1459–1469.
5. Buchler M, Weihe E, Friess H, Malfertheiner P, Bockman E, Müller S, et al. Changes in peptidergic innervation in chronic pancreatitis. Pancreas. 1992; 7: 183–192.
6. Takamido S, Kataoka Y, Tanano A, Cui Y, Ikeura T, Shimatani M, et al. Intrapancreatic axonal hyperbranching of dorsal root ganglia neurons in chronic pancreatitis model rats and its relation to pancreatic pain. Pancreas. 2006; 33: 268–279.
7. Holzer P. Local effector functions of capsaicin-sensitive sensory nerve endings: involvement of tachykinins, calcitonin generelated peptide and other. neuropeptides. Neuroscience. 1988; 24: 739–768.
8. Harrison S, Geppetti P. Substance P. Int J Biochem Cell Biol. 2001; 33: 555–576.
9. Severini C, Improta G, Falconieri-Erspamer G, Salvadori S, Erspamer V. The tachykinin peptide family. Pharmacol Rev. 2002; 54: 285–322.
10. Ho WZ, Kaufman D, Uvaydova M, Douglas SD. Substance P augments interleukin-10 and tumor necrosis factor-alpha release by human cord blood monocytes and macrophages. J Neuroimmunol. 1996; 71: 73–80.
11. Nathan JD, Peng RY, Wang Y, McVey DC, Vigna SR, et al. Primary sensory neurons: a common final pathway for inflammation in experimental pancreatitis in rats. Am J Physiol Gastrointest Liver Physiol. 2002; 283: 938–946.
12. Ikeura T, Kataoka Y, Wakabayashi T, Mori T, Takamori Y, Takamido S, et al. Effects of sensory denervation by neonatal capsaicin administration on experimental pancreatitis induced by dibutyltin dichloride. Med Mol Morphol. 2007; 40: 141-149.