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Continued overleaf

Management of pain in chronic pancreatitis. New solutions to an old problem

Management of pain in chronic pancreatitis is a challenging clinical problem. Lack of proper understanding of the mechanisms responsible for pain, high morbidity and mortality rates historically associated with pancreatic surgery, and the long held view that pain will eventually subside when the pancreas "burns itself out" as a result of progressive fibrosis have all contributed to a non-surgical therapeutic approach for decades [1]. Many recent studies have challenged this view, and at present there is a shift from the "wait and see" approach to a more pro-active type of therapeutic approach in the management of pancreatic pain [2].

It is accepted that, at least in a majority of cases, the pain results from pressure increase within the pancreatic duct system from obstruction to the main pancreatic duct by stones or from post-inflammatory strictures [3]. Inflammatory pancreatic head mass and visceral hyperalgesia with increased central pain perception because of exposure of pancreatic nerve plexuses have also been implicated as contributory factors [4, 5]. Because obstruction to the pancreatic duct contributes to pain, patients with "large duct chronic pancreatitis" would respond to surgical or endoscopic pancreatic duct drainage.

In the past, many patients with pancreatic pain were on long-term narcotic analgesics. Patients with intractable pain had fluoroscopy guided coeliac plexus block. The overall therapeutic response to coeliac plexus block has been unimpressive [6]. Excisional surgery and surgical drainage of the pancreatic duct have been the mainstay of pain management in those who did not respond. There is some evidence that pancreatic enzyme replacement contributes to the reduction of the severity of pancreatic pain [7].

During last two decades the advancement of pancreatic endotherapy has made a significant contribution to the management of pancreatic pain. Because of its low invasiveness, endoscopic decompression of the pancreatic duct is increasingly recognised as an approach to relieve pancreatic ductal pressure. Many studies on endoscopic decompression of the pancreatic duct, with pain relief as the main outcome, have reported impressive medium and long term benefit [8, 9]. A multicentre trial has shown impressive long term outcome with extracorporeal shock wave lithotripsy (ESWL) to fragment pancreatic stones before main duct clearance, and clarified its role in easing the clearance of obstructing calcium plaques from side branches [10].

Would pancreatic duct decompression together with ESWL be the future direction of pancreatic pain management? Due to the heterogenous nature of the patient population, it is too early to arrive at such expansive conclusions. However, many experts agree that good short term pain relief from endoscopic ductal decompression is a way to recognise patients who will respond to surgical decompression.

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Paucity of properly conducted randomised control trials comparing surgery and pancreatic endotherapy is one of the drawbacks for deciding the best approach to the management of pain in chronic pancreatitis. There are two randomised control trials comparing surgery and endotherapy. The first trial in 2003, which randomised 72 patients, reported similar outcomes in pain relief at one year, and at five years most patients who had undergone surgery were not on analgesics, and also reported better weight gains [11]. This trial was criticised by many endotherapy experts for its bias in patient selection and the types of surgical procedures employed. Of the surgery group, 80% had undergone excisional surgery and the results were compared with the endotherapy group who had undergone endoscopic drainage of the pancreatic duct. The study also used limited endotherapy techniques and no attempt was made to clear the side branches, which may have contributed to suboptimal results seen in the endotherapy group at 5 years. A better planned trial in 2007, which randomised 34 patients, has also reported results favouring surgery [12].

In pancreatic endotherapy therefore, are we merely observing results heavily weighted on the individual expertise? Evidence is that it is possibly not. Appearance of many trials of pancreatic endotherapy with excellent short and medium term outcome of pain relief from many regions of the globe has laid to rest the myth that manipulation of the pancreatic duct and the sphincter is dangerous [9,10,11]. Consensus has emerged that endotherapy is undoubtedly a useful tool for pain relief in chronic pancreatitis in selected patients.

Would surgery become obsolete? Certainly not. There is not a single endotherapy study which has addressed the problem of intractable pain from chronic inflammatory pancreatic head mass. For reasons still not clear, the pancreatic head appears to be the "pivot" to the process of pancreatic fibrogenesis, and excellent response is reported following surgical excision of the diseased head. Furthermore, endoscopic drainage has not shown good results in this subgroup of patients. Although pancreatic head resection is still considered as a formidable procedure, many expert surgical centres have regularly reported impressive results with pancreatic head resection with minimum morbidity and mortality [4].

What does the future hold regarding this difficult clinical problem? Pancreatic fibrogenesis is now considered as a dynamic and potentially reversible condition as a result of the identification and characterisation of pancreatic stellate cells (PSCs) which are morphologically similar to hepatic stellate cells, a principal factor in liver fibrosis [13]. It is recognised that release of pancreatic fibrogenic cytokines causes necro-inflammatory injury in acute and chronic pancreatitis. Ethanol directly activates pancreatic cytokines [14]. Successful therapeutic strategies may require eliminating pancreatic stellate cell activation by inducing apoptosis, an important step in the wound healing, rather than inhibiting or inactivating pancreatic cytokines. Hence potential antifibrotic therapies targeting intracellular pathways responsible for pancreatic stellate cell activation hold promise [15]. Studies with recently developed pancreatic stellate cell lines will accelerate the understanding the role of pancreatic stellate cells in pancreatic disease and direct the future therapeutic applications [16].

So what is the present consensus for pain management in chronic pancreatitis? Many patients have moved away from pain clinics to endotherapy clinics. Many have escaped narcotics. Only a few studies have appeared recently on pain treatment with coeliac plexus block because patients now select their choice based on evidence. Due to its low invasiveness and good safety record, endoscopic pancreatic ductal decompression has become a useful intervention in the management of "large duct chronic pancreatitis".

ESWL is identified as a useful therapeutic adjunct to improve the clearance of side branches [10]. Initial response to ductal drainage will select the patients who will benefit from future surgical interventions. Preservation of pancreatic tissue will obviously help to preserve pancreatic function. Pancreatic head resection is still considered as the best outcome based therapy for painful pancreatic head mass [5]. Total pancreatectomy is not considered now in the management of painful chronic pancreatitis except in exceptional circumstances. Experimental studies leading to better understanding of the character of PSCs may turn out to be the future direction that may lead to the reversal of the cause of pancreatic pain.

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