Pain management of pancreatic cancer

Åke Andrén-Sandberg, Asgaut Viste, Arild Horn, Dag Hoem & Hjortur Gislason
Department of Surgery, Haukeland University Hospital, Bergen, Norway

Summary

Quality of life is receiving increasing attention as a criterion for the assessment of treatment, not least for surgery, in pancreatic cancer. In exocrine pancreatic cancer there are three main symptoms that must be dealt with: pain, loss of weight and jaundice. All of them seriously impair quality of life, but most often pain is the most feared by the patients. Despite this, the intensity and the quality of the pain is all too often only scantily described.

In 85 consecutive patients with newly diagnosed pancreatic cancer we have prospectively registered the quality and quantity of their pain and correlated it to tumor and patient characteristics. It was found that about one fourth of the patients were totally pain free and half of all suffered a pain described by two or less on a Visual Analogue Scale. Only one in ten had severe pain. Although more and more patients were treated with morphine, it was still about one third of all patients that had no or only little pain in the last part of their life. Pain had a strong correlation to survival. This may be due to secondary effects like depressing the mood of the patient and reducing the food intake, but is probably more often a reflection of that generalized cancer induces more pain. Analgesic drugs are the cornerstone of the pharmacologic management of pain due to pancreatic cancer. A significant part of the patients do well with only paracetamol and nonsteroidal antiinflammatory agents. Combining these agents with narcotic analgesics can enhance pain control while lessening the dose of narcotics. A wide range of narcotics are available as well as different modes for delivery: regular pills, slow release forms, injections, subcutaneous injections, epidurals etc. Each patient's pain management should be individualized, based on the intensity of pain, the type of pain and the side effects. It is essential not only to describe the medication, but also to follow-up the development of the pain and the patient's total experience of the situation.

As an alternative to narcotics, plexus celiac blocks have been used with somewhat different result; in the hands of the experts the percutaneous approach is usually sufficient, but in the hands of other also poor results are reported. During the last years thoracoscopic splanchnicectomy has been tried as a complement giving long-standing pain relief with little or no side effects in the majority of patients. With this approach the sympathetic fibers lead by the sympathetic chain and further by the nervus splanchnicus major, minor and minoris are divided. The denervation is easily done and can be performed bilaterly in one seance. This method will probably be used more often as the technique is now well described.

Key words: analgesics, pain management, quality of life, splanchnicectomy

Introduction

The majority of patients with exocrine pancreatic cancer have pain as an initial symptom and most will suffer significant pain at some stage before they succumb to the disease [1]. For some patients the pain is so severe that all waking hours are devoted to its control and the quality of life is very poor due to the pain. While the disease is rarely cured, the patients can, at best, be rendered symptom free. The management of symptoms should, therefore, be of prime concern in most individuals with pancreatic cancer. Initially, the cornerstone of pain management is a stepwise escalation of analgesics, but it is also wise to provide patients with full information on their condition and its treatment in order that they themselves may be involved in the management process. Resectional surgery in those with severe pain due to cancer seems to be the most logical treatment and should be considered the first option as it today can be performed with low morbidity and a mortality rate of almost zero [2]. However, the indications for palliative resections as opposed to palliative bypass are still not clear. As only about 15 percent of the patients in unselected series in our part of the world can be resected [3, 4], and as most of the resected patients suffer a recurrence of their disease [5], palliative care must be given a high priority.

Although pain is the most feared part of the terminal life of many patients with cancer, the intensity and the quality of the pain is often scantily described. In reviews [6, 7] pain was said to be a presenting symptom in 70-90 % of the patients with pancreatic cancer, and in one series 83 % of 303 consecutive patients presenting with pancreatic or periampullary cancer had pain at the time of the diagnosis [8]. However, the characteristics of the pain were not given [6-8] even though it was stated that the incidence of pain was not related to the site of the primary lesion, but to the stage of the disease [8].

Prospective studies

Studies on the natural course of pancreatic cancer and the
effect of different treatment modalities have most often focused on survival. Lately, there has been more interest in the quality of life of these patients [10, 11], but the discussion has been hampered by the multidimensionality of quality of life as well as a lack of knowledge of the importance of different components of sensitive and functional aspects of day-to-day living. Patients adjust their expectations of the quality of life according to their perception of their health and function. However, for patients with cancer-related pain, controlling pain is the most critical factor which will improve their life [12]. Therefore it is important to gather as much information as possible on the epidemiology, the pathophysiology and the effects of different options of management of pain.

There are several ways to describe pain in cancer patients. The best documented is the Visual Analogue Scale, VAS, which has been shown to be a highly valid and reliable tool for measuring pain intensity [13, 14], also specifically in pancreatic cancer patients [15].

The clinical appearance of the pain pattern in pancreatic cancer is infrequently discussed, and attempts to tailor the treatment systematically to the symptoms and signs are almost totally lacking. The management of pain must be based on knowledge of not only the available treatment possibilities, but also of the natural history of the disease. In Lund, Sweden, and Bergen, Norway, a group of patients were prospectively followed to describe the quality, quantity and development of their pain and to investigate whether the pain at the time of diagnosis could give information on the prognosis. It was then found that pain at the time of diagnosis was not so frequent and severe as is usually stated [8, 16-20], but in accordance with the results of a recent prospective american study [21]. They demonstrated that 40 percent of the patients with pancreatic cancer reported no pain at the time of referral, and another 30 percent had only minimal complaints of pain. Similarly, prospective data collected from the Johns Hopkins Hospital demonstrated that only 20 percent of patients reported clinically relevant pain, as assessed by a visual analogue scale [22]. Moreover, after a 10 week follow-up of the Scandinavian patients about one third of the patients were still completely pain free. This underlines the fact that each patient must be treated in his or her own way and it is important not to give analgesics routinely just because of the diagnosis.

On the same time it is important to state that some patients were inadequately treated with regard to pain. If patients are judged to have pain of a type and intensity that needs morphine, it is illogical to undertreat them so that they still suffer significant pain. If morphine is given it should instead always be given in sufficient doses.

In the literature it is stated that patients with cancer in the head of the pancreas have less pain compared to those with cancer of the body or tail [23], or the opposite [6]. The results of the prospective study favor the view that patients with cancer of the head of the pancreas have less pain than those of the body and tail, but also we are of the opinion that the differences documented are not of major clinical importance.

**Pain and survival**

Pain per se has a strong correlation with survival in days. Lillemoe et al [22] performed a prospective, randomized study of the use of chemical splanchnicectomy in patients with nonresectable pancreatic cancer. Although their study confirmed the benefit in treating established pain and in preventing the development of future back pain, they also found a longer survival in the well treated patients. The same was found in the Lund-Bergen study [24]. This may be explained by a direct correlation between pain and tumor biology, but more probable the effect is at least partly indirect. Pain may influence survival by producing a depressed mood and reducing food intake, and the secondary effects of analgesic drugs have an influence of on mobilization, socialization, life expectations, etc.

We have earlier advocated a more standardized reporting of patients with pancreatic cancer [25]. A plea for uniform reporting of patient outcome in the treatment of pain in patients with pancreatic disease was recently made and proposed: (1) the patient’s description of the pain should be given with a VAS, (2) the use of narcotics should be quantified, i.e. none, minimal (1-3 times per month), moderate (daily or weekly), or major (stronger than moderate), and (3) the quality of life should be assessed using tools that focus both on the patient’s perception of his/her health status and on the nonmedical aspects of his/her life [26]. There are also other ways to describe the quality of life in these patients [27, 28], e.g. with EORTC QLQ, which, however, focus less on pain and more on a global assessment of the situation for the patient.

**Procedures directed against nerves**

Pain relief in patients with pancreatic cancer can also be provided by means of procedures directed against the afferent nerves that carry the painful stimuli from the diseased pancreas to the brain. The sympathetic innervation of the pancreas, including the nerves mediating pain, leaves from cells in tractus intermediolateralis in the spinal cord from Th 5 to Th 11. The sympathetic fibres are led to the sympathetic chain and further by the nervus splanchnicus major (from Th 5 to Th 10) and one or more nervi splanchnici minor (from Th 9 to Th 11) to synapses in prevertebral abdominal plexa, at first hand the coeliac ganglion. The postganglionic fibres pass along the arteries of the liver and spleen and the superior mesenteric artery into pancreatic tissue. Some sympathetic axons run directly to the pancreas without intraabdominal synapses, mainly from the lower portion of the sympathetic chain (which partly may explain the limitation of pain control after surgical celiacectomy). From a theoretical point of view the pain can be inhibited by cutting the nerve fibres anywhere along these paths. The procedure most often tried is chemical blockage of the coeliacus ganglion, and a newer alternative is thoracoscopic splanchnicectomy.

The coeliacus block can be done during laparotomy (not taken into account here) or percutaneously, usually from the...
back. The placement of the injection can be done simply by using anatomical landmarks or by checking the position by fluoroscopy, scout X-ray films, ultrasonography, CT, or at angiography. A nerve block with 25 ml of 50 percent alcohol on each side should be preceded by a positive diagnostic block with long-acting local anaesthesia, carried out at least one day earlier. The method aims at blockage of the splanchnic nerves before they reach the coeliac plexus rather than blockage of more part of the coeliac plexus itself. There are several different ways to ascertain that the needle tips and the fluid injected, respectively, are in the right place. The site of the needle can be documented with scout films [29]. Theoretically more appealing, is to guide the injections of local anaesthetics (and later neurolytica) with fluoroscopy and contrast media in the injected fluid [30, 31].

In a critical review Sharfman and Walsh in 1990 [32] analysed data from 15 series published 1964-1983, including 480 patients, on coeliac plexus blocking in pancreatic patients. At least a satisfactory response to the procedure was reported in 87 percent of the patients. The authors claimed, however, that there were major deficiencies in the reporting of the results. In our practice the results of coeliac block has been rather unpredictable, and as the pain tended to recur in about three months time [33] we think that the indication for this procedure is at present limited to those who are well experienced with it.

As the pain fibres run in the sympathetic chain, pain stimuli can be overcome from within the thoracic cavity where the chain lies immediately subpleural in a wave-like disposition over the ribs in the posterior mediastinum. These nerves are identified easily at thoracoscopy. Thoracoscopic splanchicectomy may be performed bilaterally under general anaesthesia using double-lumen endotracheal intubation. Usually two ports are used on each side: one optical cannula (10.0 mm) and another 5.5 mm operating cannula. A small hole in the pleura on each side of a splanchnic nerve, 10 mm from the sympathetic chain, is burnt with the hook and the nerves are then cut off completely so that the ends are seen to be well retracted from each other. In uncomplicated cases the patient can be discharged from the hospital the day after the operation. In a series of 30 patients treated at the Department of Surgery in Lund, satisfactory stable pain relief was obtained from the first week after surgery [34]. All patients reported clearly reduced pain, but only about 20 per cent of individuals reported immediate complete pain relief. One may concluded that thoracoscopic splanchicectomy is a good alternative, as a safe and relatively simple treatment for severe pancreatic cancer pain.

### Conservative treatment

Analgesic drugs are still the most commonly adopted method for pain relief, such as paracetamol, dextropropoxiphene, prednisolone, non-steroidal anti-inflammatory drugs, tricyclic antidepressants or narcotic analgesic drugs given orally or rectally, opioids also subcutaneously or intrathecally. A problem is that due to the chronic nature of the pain many patients subsequently have a change of mood and even personality. A major concept in prescription is therefore to divide the analgesic treatment into three stages, the principle in each stage being paracetamol, dextropropoxiphene and morphine, and never to proceed to the next step without minute consideration of the short and long-term effects of the escalation.

Overall, standard therapy with at most oral opiates and adjuvant drugs can be successful in up to 90 percent of patients with pancreatic cancer pain [35]. Most opiates are now available as rectal suppository with an efficacy about equal that of oral administration, which is of importance near the terminal state when the patients have difficulties with peroral medication. Also the potent, lipid-soluble opiate fentanyl can then be used transdermally. Recently, patient-controlled analgesic techniques have been offered to ambulatory patients with cancer. Subcutaneous continuous infusions of opiates with patient-directed boluses, as needed, can be valuable in minimizing the fluctuations in blood levels, toxicity and anagesia seen with intermittent-dosing schedules [35].

For the present, the best long-term results of treatment of the pain of in pancreatic cancer are likely to come from a careful appraisal of the patient’s situation and a treatment that is tailor to the individual as well as to his or her disease. Prognosis also related to the attitude and expectations of the patient and the relatives and it may depend as much on awareness of the situation and confidence in the treatment as on technical aspects of medical and surgical management. We experience that if the patient has confidence in the doctor’s management over all he or she will be able to cope with the pain in a better way. Therefore, we think that the continuity in the patient-doctor relationship is of the utmost importance in these patients.

### References


Correspondence to:
Åke Andrén-Sandberg
Department of Surgery
Haukeland University Hospital
Bergen, Norway