

## **Elimination of pain syndrome in patients with advanced pancreatic head cancer**

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**Key words:** common cancer of the pancreatic head, pain syndrome, medicamentous and endoscopic methods of pain syndrome elimination

Pain is an evolutionarily developed typical process resulting from the action on the body of nociceptive (damaging) factors or weakening of the anti-nociceptive system. This is a physiological phenomenon necessary for normal life and informs us about the harmful effects that pose a potential danger to the body. The most common definition of pain proposed by the International Association for the Study of Pain (IASP, 1994): “Pain is an unpleasant sensation and emotional experience associated with actual or potential tissue damage or described in terms of such damage” [4].

Effective treatment of chronic pain of oncological genesis is considered by WHO experts as one of the main components of palliative care aimed at improving the quality of life of patients: relief of physical, psychological and spiritual condition, as well as social support. According to the WHO, about 70% of cancer patients suffer from pain of varying intensity. If in the early stages of the disease, pain occurs in 30–40% of patients, then in the stage of generalization of the tumor process — in 90%. In Russia, more than 300 thousand people die from malignant neoplasms annually, and at least 200 thousand patients with common forms of cancer suffer from pain of varying intensity. The versatility of the central and peripheral neurohumoral mechanisms of chronic pain requires special knowledge and an integrated approach to its treatment [4].

Pain syndrome in pancreatic cancer has been observed in half of the patients since the onset of the clinical manifestations of the disease and in almost all patients in the later stages [1, 38]. In the course of this disease, almost all patients suffer from abdominal pains of varying intensity [22].

Pain syndrome, along with obstructive jaundice, is one of the most prominent clinical manifestations of pancreatic cancer and is often a sign of unresectable tumors. According to the WHO pain relief committee, in 30–50% of cancer patients, pain is the main symptom, and in patients with incurable tumors, this percentage reaches 70% and only 20–50% of them receive effective pain relief. The fight against chronic pain is one of the priorities in modern oncology. Constant pain syndrome leads to sleep disorders, appetite, psychological problems and absolute social maladjustment, which largely determines the patient's quality of life [3]. Based on the diagnostic data, the localization, cause, type, intensity of chronic pain, associated complications and the patient's mental status are established, which makes it possible to determine a plan for further treatment.

**Drug treatment.** The existing methods of treatment of chronic pain syndrome in cancer patients are diverse and provide for the impact on the different links of pathological pain in various ways: medication, surgical, psychological. Traditionally, the central place among the listed methods belongs to systemic pharmacotherapy, but the selection of drugs to ensure effective pain relief is a difficult task and not always feasible [3].

WHO recommends the use of painkillers in the beginning with analgesics (aspirin and paracetamol), then, as necessary, weak opioids (codeine), then strong opioids, until pain relief is achieved. Morphine, a standard opioid that is widely used to combat chronic pain in cancer, especially in the moderate to severe pain scale [16, 24], is the first line of drug therapy for pancreatic cancer [46]. Fentanyl is an alternative to morphine for relieving pain in pancreatic

cancer and is used through various routes of administration. Transdermal patches are suitable for patients whose opioid requirements are stable [17, 19].

Pain syndrome in unresectable tumors of the pancreas is due to several reasons, and in the first place — tumor compression, infiltration and destruction of the nerve endings of the pancreas and plexuses of the retroperitoneal space. Pain syndrome is often the most severe, debilitating manifestation of the disease. In this case, drug therapy, as a rule, is not sufficiently effective [2].

**Chemical neurolysis.** Pathogenetically justified treatment of pancreatic pain in pancreatic cancer is considered to have an effect on the vegetative structures of the retroperitoneal space (celiac plexus) in order to suppress the activity of generators of pathological arousal [7]. It is also possible to influence the level of the epidural space on the fibers of the sensitive posterior roots, which are involved in carrying out nociceptive information from the pathological focus to the nervous structures of the spinal cord and brain [6].

There are publications on the implementation of intraoperative chemical neurolysis in unresectable pancreatic cancer to relieve pain. For this purpose, during the operation, injection of 6% phenol solution [13] or 50% ethanol solution [43] is used in the celiac trunk region.

The use of this technique for percutaneous administration, i.e. without laparotomy, only under the control of an ultrasound transducer, it seems more logical, with more effective anesthesia arising from the bilateral introduction [49]. With the improvement of percutaneous procedures, the possibility of puncture destruction of the celiac nerve plexus appeared: alcoholization, as well as high or low temperatures to stop or reduce the intensity of pain syndrome [14, 21]. The effectiveness of such interventions, according to individual publications, reaches 80% [14, 28, 36, 40]. The holding of denervation of the celiac plexus with 96% alcohol is indicated for patients with chronic abdominal pain syndrome, refractory to traditional pharmacotherapy, and this is necessary in 63.5% of patients [6].

The implementation of the denervation of the celiac plexus under the computed tomography control eliminates the development of complications [6]. M.A. Silayev (2007) believes that the relief of pancreatic pain syndrome in pancreatic cancer only improves the somatic status of quality of life, while mental status, a depressive state requiring medical correction is not restored [7].

In the study of 71 patients with pancreatic cancer, it was found that the method of epidural chemical denervation was significantly lower in efficacy (1.54 weeks painless period) than the neurolysis of the celiac plexus (4.61 weeks), but the incidence of side effects with the latter is high (1.6 against 0.3) [6].

According to various researchers, after the puncture percutaneous chemical denervation of the celiac plexus, the duration and severity of the analgesic effect are very variable: from a sufficiently high and long [31] to dubious and short-term [5, 41]. There is no consensus on the importance of this method in relieving pain in pancreatic cancer, and in controlling manipulation. There are no clear data on the management of the postmanipulation period with the development of side effects [34, 39]. In another randomized study conducted by G.Y. Wongetal (2004), patients received either a neurolytic blockade of the celiac plexus or carefully selected analgesic therapy, as recommended by WHO. In this study, it was shown that the neurolytic blockade of the celiac plexus does not improve the quality of life of these patients compared to optimized analgesic therapy. It is also noted that there are no significant differences between the use of analgesics and survival, although the reduction in pain was significantly better with neuropathic blockade [47].

The method of choice for chronic abdominal pain may also be transgastral neurolysis of the celiac plexus under the control of endoscopic ultrasound. According to the mechanism of action, it is similar to the percutaneous chemical blockade [26, 44, 47].

The developed methods of "chemical neurotomy" by intraoperative (under visual control) or percutaneous (under ultrasound and CT control) blockade of the celiac nerves and solar plexus by injection of alcohol or phenol are not widely used due to the technical complexity and short duration of the analgesic effect [3].

**Surgical methods for chronic pain syndrome.** Taking into account the fact that the life expectancy after the diagnosis of an unresectable tumor is 6–8 months, the implementation of a surgical intervention that eliminates pain syndrome significantly improves the quality of life of patients [24, 37].

Treatment of pain by traditional surgical methods for unresectable pancreatic cancer has no evidence. Performing famous laparo- and thoracotomic operations on the nervous apparatus of the pancreas: excision of the splanchnic nerve [11, 18, 35], removal of the celiac and mesenteric ganglia [15], excision of the postganglionic celiac nerves [50] to reduce pain seems unjustified due to the risk of complications and low effectiveness of interventions, which allows to reduce pain in only one third of patients [11, 18, 35]. Currently use intraoperative neurolysis only during the exploratory laparotomy, especially for the elimination of pain surgical procedures do not produce because they significantly worsen the patient's condition.

**Thoracoscopic splanchnicectomy.** In order to eliminate pain in patients with unresectable tumors of the pancreas, the thoracoscopic syndrome has now become widespread. splanchnicectomy [30, 48].

To substantiate the expediency of this intervention, it is necessary to understand the modern ideas about the innervation of the pancreas [1]. It is believed that the nervous apparatus of the pancreas is represented by the sympathetic nervous system (both celiac nerves), which carry pain impulses, and the parasympathetic nervous system (the posterior trunk of the vagus nerve), which controls pancreatic secretion. These nerves are preganglionic nerves, and their nerve fibers form the celiac ("solar") plexus. From the last exit postganglionic nerves which accompany pancreatic vessels directly innervate it.

The first endoscopic splanchnicectomy for the relief of pain in pancreatic cancer was performed by S. Lin in 1994 [29]. The volume of resection of nerve structures is the most important factor providing a full analgesic effect. In the classical description of the technique, isolated splanchnicectomy is performed — resection of the large and small internal nerves [29, 30]. Many authors describe an extended version of the operation — resection of the internal nerves and 4–5 lower thoracic sympathetic ganglia. This is due to the complexity of visualization of the inferior intrinsic nerve (n. splanchnicusimus) and small nerve trunks, which cannot be determined even with a significant increase [2, 48].

Thoracoscopic splanchnicectomy has been performed only in the last decade and has not yet become widespread in our country [8, 23, 25, 42].

A. Pietrabissa et al. (2000) performed 25 thoracoscopic splanchnicectomy in 24 patients with unresectable cancer of the pancreas, who had a pronounced abdominal pain syndrome. A positive effect was obtained in all patients — the pain decreased by about 60%, but after 3 months a third of the patients had increased pain. The authors concluded that the thoracoscopic splanchnicectomy significantly improves the quality of life of patients with unresectable pancreatic cancer [33].

In another study, 44 patients with pancreatic cancer or chronic pancreatitis were treated using bilateral transthoracic splanchnicectomy. It was shown that after this procedure, the pain syndrome decreased by 50% and the effect remained stable after the intervention for up to 4

months [20]. V.A. Kubyshkin et al. (2003) believe that this intervention is indicated for patients with severe pain in the upper abdomen, mainly due to unresectable tumors of the body and tail of the pancreas (distant metastases, vascular invasion, serious condition of the patient, and intensity of pain syndrome at least 4 points on the scale of pain sensitivity) [2]. Some authors believe that thoracoscopic splanchnicectomy complex and accompanied by a certain risk, in 9% of patients with thoracotomy intraoperative bleeding occurs [9].

Despite the fairly good results of Western clinics, there are pessimistic points of view regarding thoracoscopic splanchnicectomy, giving preference to percutaneous neurolysis by injection of alcohol or phenol [32]. At the same time, it is described that the procedure of alcohol neurolysis of the celiac plexus has undesirable complications, such as diarrhea or orthostatic problems in 40% of patients [12].

Of particular interest are the data of the authors, who describe the correlation between pain and poor prognosis of the disease [45]. K.D. Lillemoe et al. (1993) conducted a randomized study comparing the results of treatment of patients who underwent chemical neurolysis during the operation with the introduction of 50% alcohol and saline, with a placebo group. Good pain reduction results were observed after 2, 4 and 6 months and were obtained using this technique, there were no side effects [27]. Interesting are the observations, where in the subgroup of patients with severe pain there was an improvement in survival after successful pain reduction in comparison with patients who underwent simulation therapy. This confirms the observations of several authors that the intensity of pain syndrome is associated with a poor prognosis of pancreatic cancer [45]. There is a view that the effectiveness of pain control is possible without splanchnicectomy in most cases, with the conclusion that the neurolytic blockade of the celiac plexus can be used as a method of choice if there is a risk of intervention in individual patients with unbearable pain. In addition, it is clear that it is not the neuropathic blockade of the celiac plexus, but aggressive pain therapy, not counting technology, that is the main factor in increasing the life expectancy of patients [9].

In contrast, others believe that the thoracoscopic Splanchnicectomy is one of the most effective methods of pain surgery for unresectable pancreatic cancer. Splanchnicectomy is the base — the basis for the subsequent effective lifelong systemic drug therapy [2]. To perform such an operation, it is customary to resort to persistent pain syndrome with unresectable pancreatic cancer and the absence of obstructive jaundice or duodenal obstruction [2, 8].

Left side thoracoscopic in 63.6% of cases, splanchnicectomy makes it possible to refuse to take narcotic painkillers. In 60% of patients who underwent this surgery, there was a significant or moderate decrease in the intensity of the pain syndrome. At the same time, this surgical intervention has a number of disadvantages that complicate the postoperative period [3].

**Conclusion.** Thus, in the complex of palliative measures aimed at improving the quality of life of patients with advanced pancreatic head cancer, the problem of anesthesia remains one of the leading ones. The introduction of new technologies in endoscopic surgery and the improvement of techniques for performing surgical interventions helps to improve various methods of palliative treatment of pain in advanced pancreatic head cancer. Chemical neurolysis allows to reduce the intensity of pain, which in combination with other methods of symptomatic relief patients of this category of increased quality of life, in addition, it can be used several times. Left-sided thoracoscopic splanchnicectomy is a minimally invasive and effective surgical intervention, which allows to reduce the intensity of the pain syndrome or to stop it, and thus improve the quality of life of patients with common pancreatic head cancer.

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Pain syndrome, along with mechanical jaundice, is one of the most evident clinical manifestations of pancreatic cancer and is often a sign of tumor neglecting. Existing treatment options for chronic pain in cancer patients are diverse and include the various ways of impact on the different links of pathological pain: medicinal, endoscopic, surgical. With this pathology, drug therapy using analgesics, weak and strong opioids, is usually not effective enough. In such cases, preference is given to chemical neurolysis — denervation of the autonomic structures of the retroperitoneal space, carried out under the guidance of ultrasound or computed tomography. Conducting percutaneous neurolysis of the celiac plexus with the use of alcohol or phenol is prescribed upon insufficient effectiveness of pharmacotherapy. Surgical methods of anesthesia are used extremely rarely, as they considerably worsen the patient's condition, without significantly affecting the quality of life or the prognosis. Thoracoscopic splanchnicectomy is considered a modern and effective method of endoscopic treatment of pain in unresectable pancreatic cancer, the conduction of which can significantly decrease the intensity of pain, reduce the number of narcotic analgesics and improve the quality of life of cancer patients. This minimally invasive intervention is the basis for the subsequent lifelong systemic drug therapy.