

# PALLIATIVE TREATMENT WITH THE USE OF PHOTODYNAMIC THERAPY OF PATIENTS WITH MALIGNANT TUMORS OF PANCREATOBILIARY ZONE COMPLICATED BY OBSTRUCTIVE JAUNDICE

Tseimakh A.E.<sup>1</sup>, Lazarev A.F.<sup>1,2</sup>, Sekerzhinskaya E.L.<sup>2</sup>, Kurtukov V.A.<sup>3</sup>, Mitschenko A.N.<sup>3</sup>, Teplukhin V.N.<sup>3</sup>, Shoykhet Ya.N.<sup>1</sup>

<sup>1</sup>Altai State Medical University, Barnaul, Russia

<sup>2</sup>Altai branch of FSBSI «N.N. Blokhin RCRC» Ministry of Health Russia, Barnaul, Russia

<sup>3</sup>KSBIH «State hospital № 5», Barnaul, Russia

## Abstract

The paper presents the results of a complex palliative treatment using photodynamic therapy of patients with pancreatobiliary malignancies complicated by obstructive jaundice. In the main group, which included 22 patients, palliative comprehensive treatment was performed using local and systemic photodynamic therapy of pancreatobiliary neoplasms complicated by obstructive jaundice. In the comparison group, consisting of 165 patients, palliative complex treatment of complications was performed without the use of photodynamic therapy. The used photosensitizers were chlorin-based fotoditazin (21 patients) and radachlorin (1 patient). The first step was a systemic PDT. In the course of infusion through a peripheral access into the cubital vein, blood was irradiated externally by laser with monochromatic light with a wavelength of 662–665 nm and a light dose of 1200–1400 J/cm<sup>2</sup>. As the second stage of the treatment, 3–5 hours after the end of the infusion, an intraductal PDT was carried out by irradiation with monochromatic light with a wavelength of 662 nm and a light dose of 220 J/cm<sup>2</sup>. After the use of local and systemic photodynamic therapy, a statistically significant decrease in the size of the tumor focus in patients with pancreatic malignant neoplasms was established within a week after treatment in the main group according to the ultrasound examination of the abdominal cavity. Restoration of bile excretion into the intestine was noted in 100% of patients with malignant neoplasms of the bile duct and head of the pancreas. We also note an increase in median survival of patients in the main group to 5.9 months compared with 4.7 months in the comparison group.

**Keywords:** malignant tumors of the pancreatobiliary zone, obstructive jaundice, photodynamic therapy.

**For citations:** Tseimakh A.E., Lazarev A.F., Sekerzhinskaya E.L., Kurtukov V.A., Mitschenko V.N., Teplukhin V.N., Shoykhet Ya.N. Palliative treatment with the use of photodynamic therapy of patients with malignant tumors of pancreatobiliary zone complicated by obstructive jaundice, *Biomedical Photonics*, 2020, vol. 9, no. 1, pp. 4–12. (in Russian) doi: 10.24931/2413–9432–2020–9–1–4–12

**Contacts:** Tseimakh A. E., e-mail: alevtsei@rambler.ru

## ПАЛЛИАТИВНОЕ ЛЕЧЕНИЕ С ПРИМЕНЕНИЕМ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ ПАЦИЕНТОВ СО ЗЛОКАЧЕСТВЕННЫМИ НОВООБРАЗОВАНИЯМИ ПАНКРЕАТОБИЛИАРНОЙ ЗОНЫ, ОСЛОЖНЕННЫМИ МЕХАНИЧЕСКОЙ ЖЕЛТУХОЙ

А.Е. Цеймах<sup>1</sup>, А.Ф. Лазарев<sup>1,2</sup>, Е.Л. Секержинская<sup>2</sup>, В.А. Куртуков<sup>3</sup>, А.Н. Мищенко<sup>3</sup>, В.Н. Теплухин<sup>3</sup>, Я.Н. Шойхет<sup>1</sup>

<sup>1</sup>Алтайский государственный медицинский университет, Барнаул, Россия

<sup>2</sup>Алтайский филиал ФГБУ «НМИЦ РОНЦ Н.Н. Блохина» Минздрава РФ, Барнаул, Россия

<sup>3</sup>КГБУЗ «Городская больница № 5», Барнаул, Россия

## Резюме

В работе представлены результаты комплексного паллиативного лечения с применением фотодинамической терапии (ФДТ) больных со злокачественными новообразованиями (ЗНО) панкреатобилиарной зоны, осложненными механической желтухой. В основной группе, включавшей 22 больных, было проведено паллиативное комплексное лечение с применением локальной и системной ФДТ новообразований панкреатобилиарной зоны, осложненных механической желтухой. В группе сравнения, состоявшей из 165 больных,

было проведено паллиативное комплексное лечение осложнений без применения ФДТ. В качестве фотосенсибилизатора использовали препараты хлоринового ряда: фотодитазин (у 21 пациента) и радахлорин (1 пациент). Первым этапом проводили системную ФДТ. В процессе инфузии через периферический доступ в кубитальную вену надвенно проводили лазерное облучение крови монохроматическим светом с длиной волны 662–665 нм и световой дозой 1200–1400 Дж/см<sup>2</sup>. По истечении 3–5 ч с момента окончания инфузии вторым этапом осуществлялась локальная внутривенная ФДТ путем облучения монохроматическим светом с длиной волны 662 нм и дозой света 220 Дж/см<sup>2</sup>. На фоне применения локальной и системной ФДТ в основной группе в течение недели после лечения установлено статистически значимое уменьшение размеров опухолевого очага у больных с ЗНО поджелудочной железы по данным ультразвукового исследования брюшной полости, отмечено восстановление выведения желчи в кишечник у 100% больных с ЗНО желчевыводящих протоков и головки поджелудочной железы. Установлено увеличение медианы выживаемости пациентов опытной группы до 5,9 мес по сравнению с 4,7 мес в контрольной группе.

**Ключевые слова:** злокачественные новообразования панкреатобилиарной зоны, механическая желтуха, фотодинамическая терапия.

**Для цитирования:** Цеймах А.Е., Лазарев А.Ф., Секержинская Е.Л., Куртуков В.А., Мищенко А.Н., Теплухин В.Н., Шойхет Я.Н. Паллиативное лечение с применением фотодинамической терапии пациентов со злокачественными новообразованиями панкреатобилиарной зоны, осложненными механической желтухой // Biomedical Photonics. – 2020. – Т. 9, № 1. – С. 4–12. doi: 10.24931/2413-9432-2020-9-1-4-12

**Контакты:** Цеймах А.Е., e-mail: alevtsei@rambler.ru

## Introduction

Malignant neoplasms of the pancreatobiliary zone remain a significant cause of death in the structure of oncological diseases of the Russian population. The standardized prevalence of pancreatic malignancy in 2018 was 13.5 cases per 100,000 population, and the prevalence of gall bladder and extrahepatic bile duct malignancy was 5.9 cases per 100,000 population [1]. The prognostic median survival in non-resectable patients with a high risk of surgical treatment, according to the Harrel concordance index, is 3.7 months [2]. The mortality rate within a year from the diagnosis in patients with malignant disease of the pancreatic head was 66.9% in 2018, in those with gall bladder and extrahepatic bile ducts malignancy, 65.6% [1].

The modern approach to the treatment of patients with pathology of the pancreatobiliary zone is the use of a combined method with the leading role of surgical treatment. At the same time, it is essential to prevent complications of malignant diseases of the pancreatobiliary zone, the most common of which are mechanical jaundice and purulent cholangitis. At the time of detection and diagnosis, fewer than 20% of patients are operable, so the vast majority of patients receive palliative treatment [3–7].

In recent years, photodynamic therapy (PDT) has been used to treat patients with pancreatobiliary cancer [8, 9]. The first clinical study of the effectiveness of PDT in the treatment of locally advanced pancreatic tumors was performed in 2002 by S. G. Bown et al. The authors used the photosensitizer (PS) mesotetrahydroxyphenyl chloride in 16 patients with a tumor diameters from 2.5 to 6 cm. The median survival rate of patients after PDT was 9.5 months, and the 1-year survival rate from the moment of diagnosis was 44%. In 2 patients with tumor invasion into the gastroduodenal artery, gastrointestinal bleeding was observed, which was conservatively stopped, and 3

patients developed duodenal obstruction [10].

Of considerable interest is the research by M. T. Huggett et al., which included 15 patients with locally advanced pancreatic head cancer [11]. The average size of the tumor was 4.0 cm. The authors used Verteporfin as the PS. As a result of the treatment, no signs of tumor progression were observed in 11 patients 1 month after PDT, and in 6 patients 3 months after PDT. The median survival after PDT increased from 3–6 months to 8.8 months, and the survival from the moment of diagnosis reached 15.5 months. The side effects after local PDT included, in 3 patients, mild to moderate abdominal pain, and 1 patient had diarrhea.

More than 80% of patients with pancreatic head cancer and bile duct malignancies have local or remote metastatic lesions [3–7]. PDT in combination with surgical treatment has a great potential in eliminating complications, reducing tumor size, and improving patient survival [8, 9].

The purpose of this study was to evaluate the effectiveness of PDT in complex palliative treatment of patients with pancreatobiliary cancer complicated by mechanical jaundice.

## Materials and methods

The comparative prospective study included 187 patients with mechanical jaundice of tumor origin who received treatment in the period from 2013 to 2019.

The main group consisted of 22 patients with pancreatobiliary malignancy who received complex palliative treatment with PDT. All the patients signed an informed consent for PDT. In 13 patients (59.1%), stage IV of the disease was established, stage III in 3 (13.6%), stage IIa in 5 (22.7%), and stage Ib in 1 (4.6%). In 21 (95.5%) patients, the process was found to be inoperable, and 1 (4.5%) patient underwent nominally radical surgical treatment. In

18 patients with stage III, IIa, Ib of the malignant process, surgical interventions were impossible due to decompensation of concomitant diseases of the cardiovascular or urinary systems, or liver failure. 1 patient was given 5 courses of PDT at intervals of 1 to 6 months, and another patient received 2 courses at the interval of 6 months.

In the comparison group, which included 165 patients with pancreatobiliary tumors, palliative complex treatment without PDT was performed in the period from 2013 to 2016. 44 patients (26.67%) were diagnosed with stage IV of the disease, 27 (16.36%) with stage III, 12 (7.27%) with stage IIb, 48 (29.09%) with stage IIa, 32 (19.39%) with stage Ib, 2 (1.21%) with stage Ia.

Comparative analysis of the topography of the pancreatobiliary zone in both groups of patients revealed no statistically significant differences (Table 1). According to the paired sample t-test, there were no statistically significant differences in gender, age, or duration of the disease between the compared groups.

In the main group, 5 (22.7%) patients had mild, 6 (27.3%) moderate, and 11 (50.0%) had severe mechanical jaundice. In the comparison group, there were 36 (21.8%)

patients with mild, 33 (20.0%) with moderate, and 96 (58.2%) with severe mechanical jaundice. The severity of jaundice was assessed according to the classification of mechanical jaundice suggested by M. I. Bykov et al. [12].

In the main group, 4 (18.2%) patients had blood leukocytosis, 8 (36.4%) had purulent cholangitis. In 9 (40.9%) patients, clinical and laboratory signs of renal dysfunction with creatinine elevation above 106 mmol/l in men and 90 mmol/l in women were detected, accompanied by oliguria in all patients.

The comparison group included 75 (46.0%) patients with purulent cholangitis. In 73 (44.8%) patients, blood leukocytosis was observed, in 27 (16.6%), clinical and laboratory signs of renal dysfunction were detected with a rise in creatinine above 106 mmol/l in men and 90 mmol/l in women, accompanied by oliguria in 25 (15.3%) patients, and anuria in 2 (1.2%).

According to abdominal ultrasound, the largest sizes of pancreatic tumors before treatment in patients of the compared groups did not significantly differ (Table 2).

Complex treatment in both groups involved palliative surgical interventions, including percutaneous

**Таблица 1**

Топография злокачественных новообразований панкреатобилиарной зоны

**Table 1**

The pattern of the disease in patients with acute complications of tumors of the pancreatobiliary zone

Злокачественное новообразование Malignant neoplasm	Группа больных Group of patients				p
	основная (n – 22) main (n – 22)		сравнения comparison (n – 165)		
	абс. число abs. number	%	абс. число abs. number	%	
Желчных протоков, в том числе: Bile ducts, including:	5	22,73	60	36,81	> 0,1
внутрипеченочных intrahepatic	1	4,55	18	11,04	> 0,1
внепеченочных extrahepatic	1	4,55	21	12,88	> 0,1
желчного пузыря gallbladder	0	0,00	8	4,91	> 0,1
ампулы Фатерова сосочка Ampulla of Vater	3	13,64	13	7,98	> 0,1
Поджелудочной железы, в том числе: Pancreas, including:	17	77,27	105	64,42	> 0,1
головки head	17	77,27	104	63,80	> 0,1
тела и хвоста body and tail	0	0,00	1	0,61	> 0,1

**Таблица 2**

Сравнительная характеристика наибольших размеров злокачественных новообразований поджелудочной железы в двух группах до лечения по данным ультразвукового исследования брюшной полости (Me (Q<sub>1</sub>; Q<sub>3</sub>), в мм)

**Table 2**

Comparative characteristics of the largest sizes of pancreatic malignancies before treatment according to ultrasound examination of the abdominal cavity (Me (Q<sub>1</sub>; Q<sub>3</sub>), in mm)

Метод исследования Method of examination	Максимальный размер образования, мм Maximal size of tumor, mm		
	основная группа main group	группа сравнения comparison group	p
	Me (Q <sub>1</sub> ; Q <sub>3</sub> )	Me (Q <sub>1</sub> ; Q <sub>3</sub> )	
УЗИ Ultrasound	40,40 (35,38; 46,50)	42,66 (39,36; 45,95)	>0,1

Примечание: Me – медиана, Q<sub>1</sub>, Q<sub>3</sub> – нижний и верхний квартили  
Note: Me is the median, Q<sub>1</sub>, Q<sub>3</sub> are the lower and upper quartiles

catheterization of the bile ducts (right and left lobular ducts, external-internal drainage, antegrade and retrograde stenting, etc.) under ultrasound and x-ray control in order to stop mechanical jaundice and impose bypass biliodigestive anastomoses, as well as detoxification, antispasmodic, hepatoprotective, infusion, and antibacterial therapy.

In the main group, 5 (22.7%) patients underwent a single drainage of the bile ducts, while 17 (77.37%) had it twice. During primary bile duct drainage, 20 (91.0%) patients had external bile duct drainage (19 on the right, 1 on the right and left), 1 (4.5%) had external gall bladder drainage, and 1 (4.5%) had bilobate external bile duct drainage. For the second time, 17 (77.3%) patients had external drainage replaced by external-internal drainage, 2 (9.1%) had hepaticojejunostomy, and 1 (4.5%) underwent conditionally radical gastropancreatoduodenal resection. Subsequently, antegrade stenting of the bile ducts was performed in 11 (50.0%) patients. In the post-operative period on the 7th to 30th days, all the patients underwent PDT.

In the comparison group, 39 (23.6%) patients had external drainage of the bile ducts, 24 (14.5%) had external drainage of the gallbladder, and 2 (1.2%) had bilobate external drainage of the bile ducts. In 80 (48.5%) patients, hepaticojejunostomy was used, choledochojunoanastomosis in 4 (2.4%), and transhepatic drainage of the bile ducts was performed on 32 (19.4%). During repeated drainage in 4 (2.4%) patients, secondary procedure was performed to transform the external drainage into the external-internal one.

Palliative local and systemic PDT was performed in all patients of the main group, with the use of the following photosensitizers:

1. 21 patients underwent PDT with photoditazine (OOO "VETA-GRAND", Russia), of which 20 had a single

course, and 1 had a double course. The infusion was performed by intravenous drip-feed at the dose of 1 mg/kg of body weight. The calculated dose was dissolved in 200-500 ml of 0.9% normal saline depending on the patient's hemodynamic parameters and administered by intravenous drip-feed for 30-40 minutes;

2. in 1 patient, PDT was performed with Radachlorin (OOO "RADA-PHARMA", Russia); 5 courses were administered. The infusion was performed by intravenous drip-feed at the dose of 1 mg/kg of body weight. The calculated dose was dissolved in 200-500 ml of 0.9% normal saline depending on the patient's hemodynamic parameters and administered by intravenous drip-feed for 30-40 minutes.

At the first stage, a systemic PDT was performed. During the infusion, through peripheral access into the cubital vein supravenuously, blood was irradiated with monochromatic light with a wavelength of 662-665 nm and an exposure dose of 1200-1400 J/cm<sup>2</sup> with "LAMI-Helios", a specialized dual-frequency programmable laser device (OOO "Novyie Khirurgicheskiye Tekhnologii", Russia). In accordance with TU 9444-001-53807582-2010, the radiation power was 0.7 W, and the radiation power density was 0.22 W/cm<sup>2</sup>.

After 3-5 hours since the completion of the infusion, the second stage was implemented, which was local photodynamic therapy by irradiation with monochromatic light with a wavelength of 662 nm at a dose of 220 J/cm<sup>2</sup> with "LAMI-Helios", a specialized dual-frequency programmable laser device with power of 0.7 W and power density of 0.22 W/cm<sup>2</sup> using percutaneous transhepatic antegrade access and/or endoscopically with video esophagoscopy/duodenoscopy via retrograde access depending on the nature of the patient's disease: in patients with malignant tumors of extra- and intra-

**Таблица 3**

Сравнительная характеристика наибольших размеров злокачественных новообразований головки поджелудочной железы у пациентов основной группы по данным ультразвукового исследования и МСКТ с внутривенным болюсным контрастированием брюшной полости в динамике (Me (Q1; Q3), в мм)

**Table 3**

Comparative characteristics of the largest sizes of malignant neoplasms of the head of the pancreas in the main group according to ultrasound and MSCT with intravenous bolus contrasting of the abdominal cavity in dynamics (Me (Q1; Q3), in mm)

Метод исследования Method of examination	Максимальный размер образования, мм Maximal size of tumor, mm		
	до ФДТ before PDT	3–7 дней после ФДТ 3–7 day after PDT	p
	Me (Q <sub>1</sub> ; Q <sub>3</sub> )	Me (Q <sub>1</sub> ; Q <sub>3</sub> )	
УЗИ Ultrasound	39,50 (33,50; 48,50)	35,50 (30,00; 44,00)	< 0,05
МСКТ с внутривенным болюсным контрастированием MSCT with intravenous bolus contrasting	39,00 (32,00; 44,78)	34,00 (27,50; 38,75)	0,438

Примечание: Me – медиана, Q<sub>1</sub>, Q<sub>3</sub> – нижний и верхний квартили  
Note: Me is the median, Q<sub>1</sub>, Q<sub>3</sub> are the lower and upper quartiles

hepatic biliary ducts and gall bladder, only through the antegrade access, patients with malignant tumors of hepatopancreatic ampulla and pancreas, first, through antegrade, and then via retrograde access.

All patients of the main group with pancreatic malignancies had the size of their neoplasm determined before PDT, as well as within 1 week after PDT, with the use of instrumental methods of examination, including ultrasound and multispiral computed tomography (MSCT) with intravenous bolus contrast.

The Shapiro-Wilk test was used to analyze the distribution of the studied indicators. The test results showed an abnormal distribution of all the studied indicators. Statistical evaluation of the results was performed with non-parametric Wilcoxon test for related samples. The survival rate of patients in the study groups was analysed with the Kaplan–Meier estimator, and a log-rank test was used to compare the survival curves. The critical level of the study results significance was assumed to be  $p < 0.05$ . Statistical data was obtained with the use of SigmaPlot 11.0 statistical program (registration number 775050001).

## Results and discussion

In both groups, the clinical manifestations of mechanical jaundice were stopped. The assessment of the biliary tree patency after PDT revealed, in all patients of the main group, that bile excretion in the intestine was restored, the feces had normal color, the urine be-

came light yellow, the skin itching disappeared, the skin jaundice decreased, there were no side effects of allergic origin or postoperative complications from the complex treatment. In the comparison group, 131 postoperative complications were observed among 165 patients.

The analysis of the largest size of the pancreatic head malignant tumor in the main group according to abdominal ultrasound and MSCT with intravenous bolus contrast enhancement performed as follow-up showed a statistically significant reduction in the size of the tumor according to the results of abdominal ultrasound, from 39.50 mm to 35.50 mm (Table 3).

A comparative study revealed a statistically significant decrease in the size of the neoplasm according to abdominal ultrasound 1 week after treatment; no statistically significant decrease or increase in the size of the neoplasm was found according to abdominal MSCT with intravenous contrast enhancement.

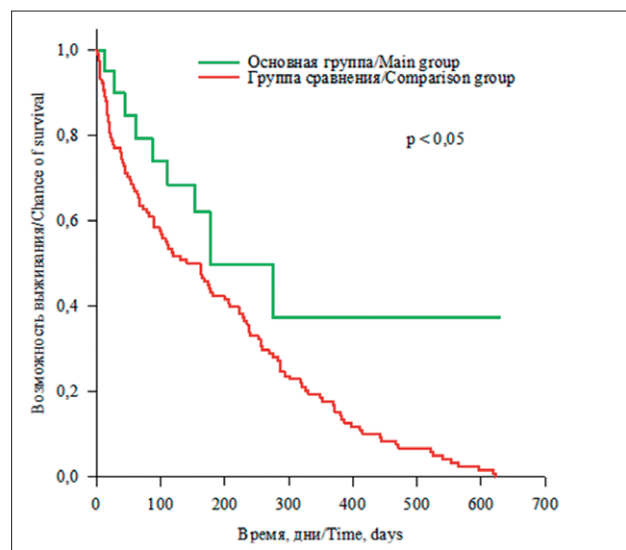
In the compared groups, the Kaplan–Meier estimator was used to perform a comparative assessment of patient survival. The highest average overall long-term survival was found in patients of the main group who were followed for a year or more (Table 4). The survival curves of the studied groups were compared with a log-rank criterion, which revealed that the average overall survival in the main group of patients was higher than in the comparison group ( $p < 0.05$ ) (Fig. 1).



Thus, these results confirm the data obtained from the study by M. T. Huggett et al. [11] concerning an increase in the median survival rate of patients. The proposed new method of local and systemic photodynamic therapy in combination with complex treatment of patients with pancreatobiliary malignancy allowed for the improvement in the quality of life of the patient, with high safety and no surgical complications, increase the overall survival rate and reduce the risk of complications due to the slower growth of the neoplasms. At the moment, PDT is the therapy of choice for patients who are not recommended radical surgical treatment and who are unable to tolerate other types of palliative treatment satisfactorily due to their high toxicity. This is especially important for patients with pancreatobiliary malignancy, since more than 80% of them have local or remote metastatic lesions. PDT has a great potential in combination with the surgical method in eliminating complications, reducing the size of the tumor, increasing survival; unlike chemo- and radiation therapy, PDT does not involve immunosuppression and the risk of systemic complications.

#### Clinical observation

The patient, aged 75, was admitted to the affiliated hospital of the Departmental and Hospital Surgery Sub-department named after Professor I. I. Neymark with a course of Continuing Professional Education in surgery, with complaints of dark urine, discolored stool, jaundice of the skin, itching, aching in the right hypochondrium.



**Рис. 1.** Кривые выживаемости больных после комплексного лечения, включавшего фотодинамическую терапию (основная группа) и без нее (группа сравнения)  
**Fig. 1.** Survival curves of patients after the complex treatment including photodynamic therapy (main group) and without it (comparison group)

He considers himself ill for 5 months, since he noticed the above symptoms. The jaundice was determined to be mechanical, of tumor genesis. The patient underwent external drainage of the bile ducts under ultrasound control

**Таблица 4**

Сравнительная характеристика групп больных со злокачественными новообразованиями панкреатобилиарной зоны по показателям выживаемости (Me (Q<sub>1</sub>; Q<sub>3</sub>), в днях)

**Table 4**

Comparative characteristics of patient groups in terms of survival (Me (Q<sub>1</sub>; Q<sub>3</sub>), in days)

Группа Group	Медиана выживания, дни Median of survival, days	Стандартная ошибка Standard error	95% доверительный интервал 95% confidence interval	p
	Me (Q <sub>1</sub> ; Q <sub>3</sub> )			
Основная Main (n – 22)	177 (275; 87)	59,09	61,17–292,83	0,042
Сравнения Comparison (n – 165)	141 (287; 38)	29,87	82,45–199,55	

Примечание: Me – медиана, Q<sub>1</sub>, Q<sub>3</sub> – нижний и верхний квартили.  
 Note: Me is the median, Q<sub>1</sub>, Q<sub>3</sub> are the lower and upper quartiles.

on the right, with cholangiography. According to cholangiography data, the expansion of intrahepatic ducts and ductus hepaticocholedochus was present, with a break at the level of the middle third of the ductus hepaticocholedochus. The mechanical jaundice was relieved.

After 1 month in the emergency hospital, the patient had a cholecystectomy due to acute destructive cholecystitis, biliary stone extraction, and a biopsy of the tumor in the ductus hepaticocholedochus. Pathoanatomic conclusion on intraoperative biopsy: cancer of the common bile duct mucosa (adenocarcinoma) T3N1M0 (according to intraoperative data).

Subsequently, the patient, in a state of moderate severity, was admitted to the affiliated hospital of the Departmental and Hospital Surgery Subdepartment named after Professor I. I. Neymark with a course of Continuing Professional Education in surgery. The skin was jaundiced, heart rate: 70 bpm, blood pressure: 110/60 mm Hg, the size of the liver according to Kurlov: 9x8x6 cm, peritoneal signs: negative, feces: acholic, urine: dark yellow.

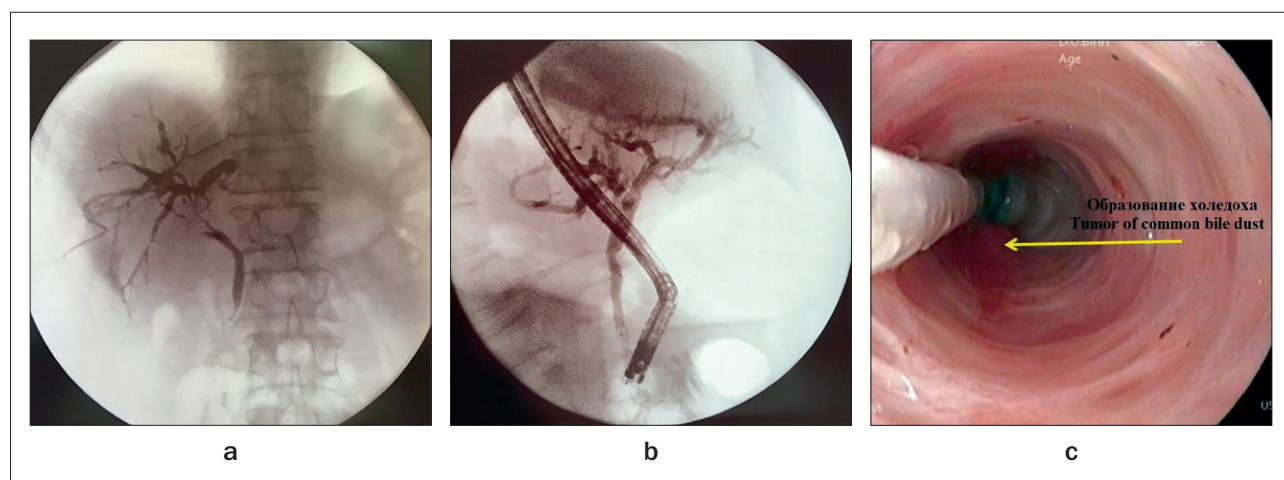
Complete blood count at admission: hemoglobin: 154 g/l, hematocrit: 48.2%, WBC:  $4.8 \times 10^9$ /l, ESR: 10 mm/h. Biochemical blood analysis at admission: total bilirubin: 118 mmol/l, indirect: 5 mmol/l, direct: 113 mmol/l, AST: 67 U/l, ALT: 128 U/l, alkaline phosphatase: 449 U/l, alpha-amylase: 85 mg/l, total protein: 67 g/l, creatinine: 99 mmol/l, fasting glucose: 5.3 mmol/l, sodium: 136 mmol/l, potassium: 4.9 mmol/l.

Abdominal ultrasound findings: liver: Oblique Y-Dimension: 170 mm; thickness of the right lobe: 136 mm;

Craniocaudal dimension: 116 mm; thickness of the left lobe: 80 mm; thickness of the caudate lobe: 23 mm. No space-occupying lesions were found in the liver. The diameter of the portal vein is 12 mm; the IVC diameter is 14 mm. Intrahepatic ducts are expanded: segmental to 5 mm, lobular to 9 mm. The ductus hepaticocholedochus is expanded to 15 mm and is bluntly broken off at the level of the head of the pancreas; its course is non-linear. The maximum size of the head is 30 mm; body: 20 mm, the tail: 25 mm. The Wirsung's duct was not dilated. Conclusion: biliary hypertension syndrome, low block level. The increase in the size of the liver.

The patient underwent antegrade and retrograde cholangiography prior to complex treatment, which provided a visualization of a tumor stricture in the area of the common hepatic duct after the confluence zone of the lobular ducts (Fig. 2a). The procedures performed included endoscopic papillosphincterotomy, stenting of the common bile duct, local and systemic PDT. Retrograde cholangiography and choledochoscopy were performed after complex therapy with PDT based on Rada-chlorin, according to the method outlined above (Fig. 2b, c). Retrograde cholangiography performed in the follow-up after the complex treatment showed a recovered lumen of the common bile duct, with restored borders and patency. Retrograde choledochoscopy performed on the patient after the complex treatment visualized the restored patency of the common bile duct and a reduced size of the neoplasm in the choledochus.

The complete blood count at discharge: hemoglobin: 140 g/l, hematocrit: 45.4%, WBC:  $5.48 \times 10^9$ /l, ESR: 34



**Рис. 2.** Результаты исследований, полученные в ходе терапии пациента:

- a – антеградная и ретроградная холиангиография до проведения комплексного лечения с применением фотодинамической терапии;
- b – ретроградная холангиография после проведения комплексного лечения с применением фотодинамической терапии;
- c – холедохоскопия после проведения комплексного лечения с применением фотодинамической терапии

**Fig. 2.** The results of the study conducted during the patient's therapy

- a – antegrade and retrograde cholangiography before the complex treatment using photodynamic therapy;
- b – retrograde cholangiography after the complex treatment using photodynamic therapy;
- c – retrograde patient choledochoscopy after the complex treatment using photodynamic therapy

mm/h. Biochemical blood analysis at discharge: total bilirubin: 11 mmol/l, indirect: 6 mmol/l, direct: 5 mmol/l, AST: 14 U/l, ALT: 19 U/l, alkaline phosphatase: 158 U/l, alpha-amylase: 98 mg/l, total protein: 67 g/l, urea: 5.2 mmol/l, creatinine: 79 mmol/l, fasting glucose: 7.04 mmol/l, sodium: 145 mmol/l, potassium: 4.5 mmol/l.

The patient was discharged for outpatient observation and treatment, in a satisfactory condition.

## Conclusion

Palliative treatment with PDT of the pancreatobiliary zone malignant tumors complicated by mechanical jaundice allowed to restore the lumen of the bile ducts,

which stopped the clinical presentation of life-threatening complications.

Palliative treatment with PDT of malignant neoplasms of the pancreatic head complicated by mechanical jaundice made it possible to reduce the largest size of the neoplasm within a week (according to abdominal ultrasound) and to increase the survival rate of patients who are not recommended radical surgical treatment.

The findings of our study indicate the good prospects of further research into the possibilities of the use of PDT in the complex treatment of this severe category of patients.

## REFERENCES

1. *Sostoyanie onkologicheskoy pomoshchi naseleniyu Rossii v 2018 godu* [Status of oncological care for the population of Russia in 2018] by Kaprin A.D., Starinskogo V.V., Petrova G.V. as eds. Moscow, MNIОI im. P.A. Gertsena - filial FGBU «NMIRTs» Minzdrava Rossii Publ., 2019. 236 p.
2. Hang J., Wu L., Zhu L., Sun Z., Wang G., Pan J., Zheng S., Xu K., Du J., Jiang H. Prediction of overall survival for metastatic pancreatic cancer: Development and validation of a prognostic nomogram with data from open clinical trial and real-world study, *Cancer Med.*, 2018, vol. 1, no. 7, pp. 2974–2984. doi: 10.1002/cam4.1573.
3. *Klinicheskie rekomendatsii. Rak podzheludochnoy zhelezy* [Clinical guidelines. Biliary cancer]. Available at: [http://oncology-association.ru/files/clinical-guidelines\\_adults%C2%A0-%20projects2018/rak\\_zhelchevyvodyashey\\_sistemy\\_pr2018.pdf](http://oncology-association.ru/files/clinical-guidelines_adults%C2%A0-%20projects2018/rak_zhelchevyvodyashey_sistemy_pr2018.pdf). (accessed 15.11.2019) (in Russian)
4. *Klinicheskie rekomendatsii. Rak podzheludochnoy zhelezy* [Clinical guidelines. Pancreatic cancer] Available at: [http://oncology-association.ru/files/clinical-guidelines\\_adults%C2%A0-%20projects2018/rak\\_podzheludochnoy\\_zhelezy\\_pr2018.pdf](http://oncology-association.ru/files/clinical-guidelines_adults%C2%A0-%20projects2018/rak_podzheludochnoy_zhelezy_pr2018.pdf). (accessed 15.11.2019) (in Russian)
5. Ducreux M., Cuhna A. Sa., Caramella C., Hollebecque A., Burtin P., Goéré D., Seufferlein T., Haustermans K., Van Laethem J.L., Conroy T., Arnold D. Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, *Annals of Oncology*, 2015, vol. 26, pp. 56–68.
6. Valle J.W., Borbath I., Khan S.A., Huguet F., Gruenberger T., Arnold D. Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, *Annals of Oncology*, 2016, vol. 27, pp. 28–37.
7. *Klinicheskie rekomendatsii. Mekhanicheskaya zheltuha* [Clinical guidelines. Obstructive jaundice]. Available at: <http://xn--9sdbbejx7bddua-hou3a5d.xn--p1ai/stranica-pravleniya/klinicheskie-rekomendaci/urgentnaja-abdominalnaja-hirurgija/klinicheskie-rekomendaci-mekhanicheskaja-zheltuha.html>. (accessed 15.11.2019) (in Russian)
8. Wei Li, Qingyong Ma, Erxi Wu Perspectives on the Role of Photodynamic Therapy in the Treatment of Pancreatic Cancer, *International Journal of Photoenergy*, 2012, vol. 637429, p. 9.
9. Lu Y., Liu L., Wu J.C., Bie L.K., Gong B. Efficacy and safety of photodynamic therapy for unresectable cholangiocarcinoma: a meta-analysis, *Clin Res Hepatol Gastroenterol*, 2015, vol. 39, pp. 718–724.
10. Bown S.G., Rogowska A.Z., Whitelaw D.E., Lees W.R., Lovat L.B., Ripley P., Jones L., Wyld P., Gillams A., Hatfield A.W. Photodynamic

## ЛИТЕРАТУРА

1. Состояние онкологической помощи населению России в 2018 году/под ред. А.Д. Каприна, В.В. Старинского, Г.В. Петровой – М.: МНИОИ им. П.А. Герцена – филиал ФГБУ «НМИРЦ» Минздрава России, 2019. – 236 с.
2. Hang J., Wu L., Zhu L., Sun Z., Wang G., Pan J., Zheng S., Xu K., Du J., Jiang H. Prediction of overall survival for metastatic pancreatic cancer: Development and validation of a prognostic nomogram with data from open clinical trial and real-world study//*Cancer Med.* – 2018. – Vol. 1, No. 7. – P. 2974–2984. doi: 10.1002/cam4.1573.
3. Клинические рекомендации. Рак желчевыводящей системы: [Электронный документ]. – URL: [http://oncology-association.ru/files/clinical-guidelines\\_adults%C2%A0-%20projects2018/rak\\_zhelchevyvodyashey\\_sistemy\\_pr2018.pdf](http://oncology-association.ru/files/clinical-guidelines_adults%C2%A0-%20projects2018/rak_zhelchevyvodyashey_sistemy_pr2018.pdf). Проверено 15.11.2019
4. Клинические рекомендации. Рак поджелудочной железы: [Электронный документ]. – URL: [http://oncology-association.ru/files/clinical-guidelines\\_adults%C2%A0-%20projects2018/rak\\_podzheludochnoy\\_zhelezy\\_pr2018.pdf](http://oncology-association.ru/files/clinical-guidelines_adults%C2%A0-%20projects2018/rak_podzheludochnoy_zhelezy_pr2018.pdf). Проверено 15.11.2019
5. Ducreux M., Cuhna A. Sa., Caramella C. et al. Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up//*Annals of Oncology.* – 2015. – Vol. 26. – P. 56–68.
6. Valle J.W., Borbath I., Khan S.A. et al. Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up//*Annals of Oncology.* – 2016. – Vol. 27. – P. 28–37.
7. Клинические рекомендации. Механическая желтуха: [Электронный документ]. – URL: <http://xn--9sdbbejx7bddua-hou3a5d.xn--p1ai/stranica-pravleniya/klinicheskie-rekomendaci/urgentnaja-abdominalnaja-hirurgija/klinicheskie-rekomendaci-mekhanicheskaja-zheltuha.html>. Проверено 20.08.2019
8. Wei Li, Qingyong Ma, and Erxi Wu Perspectives on the Role of Photodynamic Therapy in the Treatment of Pancreatic Cancer//*International Journal of Photoenergy.* – 2012. – Vol. 637429. – P. 9.
9. Lu Y., Liu L., Wu J.C., Bie L.K., Gong B. Efficacy and safety of photodynamic therapy for unresectable cholangiocarcinoma: a meta-analysis//*Clin Res Hepatol Gastroenterol.* – 2015. – Vol. 39. – P. 718–724.
10. Bown S.G., Rogowska A.Z., Whitelaw D.E. et al. Photodynamic therapy for cancer of the pancreas//*Gut.* – 2002. – Vol. 50, No. 4. – P. 549–557.
11. Huggett M.T., Jermyn M., Gillams A. et al. Phase I/II study of verteporfin photodynamic therapy in locally advanced pancreatic cancer//*Br. J. Cancer.* – 2014. – Vol. 110. – P. 1698–1704.



therapy for cancer of the pancreas, *Gut.*, 2002, vol. 50, no. 4, pp. 549–557

11. Huggett M.T., Jermyn M., Gillams A., Illing R., Mosse S., Novelli M., Kent E., Bown S.G., Hasan T., Pogue B.W., Pereira S.P. Phase I/II study of verteporfin photodynamic therapy in locally advanced pancreatic cancer, *Br. J. Cancer*, 2014, vol. 110, pp. 1698–1704.
12. Bykov M.I., Zavrazhnov A.A., Katrich A.N., Petrovskiy A.N., Popov A.Yu. *Sindrom mekhanicheskoy zheltuhi: okazanie meditsinskoy pomoshchi bol'nym v usloviyah Krasnodarskogo kraya (regional'nye metodicheskie rekomendatsii)* [Syndrome of obstructive jaundice: providing medical care to patients in Krasnodar Krai (regional guidelines)]. Krasnodar, 2016. 42 p.
12. Быков М.И., Завражнов А.А., Катрич А.Н., Петровский А.Н., Попов А.Ю. Синдром механической желтухи: оказание медицинской помощи больным в условиях Краснодарского края (региональные методические рекомендации). – Краснодар, 2016. – 42 с.