Combined therapy of patients with pancreatic cancer complicated with jaundice using amitozyn preparation

O.I.Dronov, Ya.M. Susak, E.A. Kryuchina

Bohomolets National Medical University, Kyiv, Ukraine
Kyiv Center for liver, biliary tracts and pancreas surgery, Kyiv, Ukraine.

Introduction

In the developed countries, pancreas cancer ranks fifth of all the tumors and second of digestive system tumors. Common disease incidence is 2 to 3 % of common oncological one, and the mortality rate is 4 to 5 %. Compared to other tumor localizations, the results on pancreatic cancer treatment are among the worst. Thus, half of the patients die in the period of 4 to 6 months after being diagnosed, and a five year survival is never more than 3%.[1].

The absence of early_pathognomonic symptoms of pancreatic cancer explains its late diagnostics even when jaundice has been found in 80,6% patients, which to great extent limits the potentialities of surgical and chemotherapeutical options. [1,3,4].

The goal of the present work was the elaboration and assessment of the application of preparation amitozyn in patients with pancreatic cancer complicated with jaundice after the patients being operated on (hepaticojejunostomy, in some cases, in the combination with pancreatojejunostomy and gastroenterostomy). Experimental investigations showed that in therapeutic dose amitozyn reveals no toxicity and so can be used for hyperbilirubinemia and at the symptoms of liver impairment [2].

Materials and methods

After the morphological verification of the diagnosis, in 45 patients with pancreas cancer (experimental group), complicated with jaundice, the course of treatment with amitozyn was initiated intraoperatively or starting from day 3 in the postoperative period. In the case when the patients refused chemotherapy or when there were no indications for such therapy, the courses were conducted at a two months interval. Amitozyn was prescribed to stage III and IV patients. The preparation was administered by intravenous injection at 25 mg. in 15 ml. physiologic saline every other day until the total dose reached $\sum$=250 mg. Local negative manifestations were not revealed at the administration of the preparation. In 33 (73,3%) patients the 2 stage temperature reaction was observed. The temperature rose 3±1 h after the administration, remained steady for 6±2 h and afterwards dropped without any analgesics. In the course of therapy the patients showed no signs of intoxication. All the patients received the first course of amitozyn therapy in clinic. Afterwards the therapy was conducted on an outpatient basis with a permanent observation of a clinical picture, control of hematologic indexes and oncomarkers (CEA, CA 19-9). The control group consisted of 33 patients with pancreas cancer complicated with jaundice of about the same age, tumor development, severity rate and surgical operations conducted, who for various reasons did not receive chemotherapy.

At amitozyn application no negative biochemical and hematologic disorders were revealed (Table 1).

After the course of amitozyn treatment only the number of leucocytes increased with certainty ($p<0,05$) and mainly due to lymphocytes. Blood biochemical indexes were studied in the patients who received amitozyn in an early post-surgical period and in those of a control group (Table 2). The biochemical examination indexes of the experimental group patients did not differ from those of the patients of the control group, which proves the experimental data concerning the non-toxic action of therapeutic doses of amitozyn.

Of special interest is a pronounced immunomodulatory action of amitozyn in its application at therapeutic doses (Table 2).

Positive changes in the immunogram were registered in 38 (84,4%) patients who received amitozyn. We have determined that when an immunogram index was within the norm or "near"

it, it did not change essentially after the course of treatment. And vise versa – the more the immonogram index deviated from the norm, the more it was observed to get normalized after treatment. Positive changes in immunological indexes were registered after the first and second courses of treatment. After that statistically reliable changes in immunological parameters were not noted.

The dynamics of changes of some oncomarkers was statistically reliable (Table 3).

As can be seen from Table 3, the oncomarkers parameters tended to reduction during the courses of treatment. The studies of CA19-9 level demonstrated its actual reduction after first and second courses of treatment. This was well consistent with the amelioration of the patients' general condition and the absence of ultrasound diagnostics- and computer tomography signs of oncologic disease progression. However, after the third course of treatment CA19-9 indexes were not informative. CEA value had a general tendency to reduction in the course of treatment, prior and after particular courses of therapy the changes of its value were not registered.

At the terminal stage of disease on the background of a pronounced progression of oncological disease the induces in 28 (62,2%) patients had normal or reduced values, which indicates the absolute absence of information about them during this period.

The lifetime of the experimental group patients with non resection pancreas cancer was 10,5 months, which is 3,5 months more than in the control group ($p<0,05$).

Conclusion

Therefore, in the analysis of clinical symptoms of disease and data of laboratory and biochemical analyses no negative local and general reactions at amitozyn application were registered. At the same time the changes of values of main induces of immunogram revealed an immunomodulatory action of amitozyn that is important for liver impairment. The positive dynamics of CA 19-9 has proved a carcinostatic action of amitozyn. Patients life prolongation with non resection pancreas cancer on average 3,5 months ($p<0,05$) is the most important amitozyn cure rate.

The obtained data confirm the possibility of amitozyn application in pancreas complicated with jaundice cancer patients when a routine chemotherapy is contraindicated.

References

1. Nakao A. Surgical treatment and oncological problems of pancreas cancer//Annals of surgical hepatology.- 2001.- V.6, №1.- p.59-68.
2. Patent 51566 A Ukraine МКП A 61K35/78. Method of pancreas cancer treatment/Ya. M. Susak, S.P. Osinsky, A.I. Potopalsky et al. Submitted 01.07.2002. Published 15.11.2002//Bull.№11.
3. Beger H., Rau B., Gansauge F. et al. Treatment of pancreatic cancer: challenge of the fact // World J.Surg. – 2003. – Vol 27. – P.1075 - 1084.
4. Schelling G., Jeekel J. Palliative chemotherapy and radiotherapy for pancreatic cancer: is it worthwhile // World J.Surg. - 1999. - Vol. 23, N 9. - P. 950 - 953.

Table 1

Main average hematologic and biochemical parameters of patients of experimental and control groups

Parameters	Experimental group (45 patients)		Control group (33 patients)	
	Before treatment	After treatment	Before treatment	After treatment
haemoglobin, g/l	115,68	121,68	117,89	106,80
erythrocytes, $x10^{12}$/l	4,11	3,9	4,08	3,56
leucocytes, $x10^{9}$/l	8,66	9,85	7,7	10,06
basophiles, %	0,86	0,70	0,52	0,68
eosinophils, %	1,17	1,26	2,40	1,81
bacilli, %	7,58	7,13	11,0	10,74
segments, %	68,54	61,44	62,95	64,36
lymphocytes, %	14,00	22,17	17,11	13,23
monocytes, %	7,85	7,30	6,02	9,08
sodium, Na, mgr-molecule/l	135,5	139	136	134,9
potassium, K, mgr-molecule/l	4,6	4,4	4,4	4,2
chlorine, mgr-molecule/l	101	99,35	100	98,3
urea, mgr-molecule/l	7,28	8,15	4,72	7,12
aspartate aminotransferase, mgr-molecule /(lh)	1,17	1,18	1,21	0,85
alanine aminotransferase, mgr-molecule /(lh)	1,98	1,71	2,18	1,43
whole bilirubin, millimole/l	207,56	74,87	236,00	68,32
direct reacting bilirubin, millimole/l	166,57	48,34	187,59	44,12
indirect reacting bilirubin, millimole/l	40,99	26,53	48,41	24,2
glucose, millimole/l	7,12	8,48	6,67	9,35
whole protein, g/l	72,55	64,17	81,62	63,3

Table 2

Main immunological parameters of experimental group patients in amitozyn study (45 patients)

Parameters	Amitozyn	
	Before treatment	After treatment
T-lymphocytes, %	36,88±2,86	48,12±3,44*
B-lymphocytes, %	8,11±1,34	10,69±2,54*
T-helpers, %	25,67±2,44	33,17±1,45*
T- suppressors, %	30,74±1,35	30,12±2,6*
helpers / suppressors	0,84	1,1*
large granular lymphocytes	1,49±0,11	3,77±0,27*
Natural killers activity	25,67±3,11	36,99±4,12*
phagocytic activity	86,61±1,44	99,72±2,03
phagocytic index	9,42±1,43	14,06±1,27*
IgA, g/l	1,48±0,21	1,53±0,11
IgM, g/l	0,91±0,1	1,42±0,18*
IgG, g/l	7,7±1,3	9,24±1,81

Note: * - p< 0,05

Table 3

Average parameters of CA19-9 and CEA oncomarkers before and after treatment of experimental group patients

Parameter	First course		Second course		Third course	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
CA19-9	237,2±22	97,6±25,8	44,3±5,8	24,2±5,6	33,2±4,3	37,4±4,1
CEA	8,1±1,4	8±2,6	2,6±0,8	3,2±1,4	4,4±1,9	3,8±1,7

Note: * - p< 0,05