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MEDICINE AND PHISIOLOGY

ANALYSIS OF CHANGES IN THE LEVEL OF SERUM BILIRUBIN IN PATIENTS WITH PANCREATIC HEAD TUMOR

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Annotation. *Surgical treatment of patients with the pancreatic head tumors complicated by the severe degree of obstructive jaundice is associated with an increased risk of postoperative complications. One way to reduce the level of bilirubin in blood before the radical surgery is drainage of biliary tract. However, this procedure also associated with certain risks of complications. Therefore, it is so important to perform the radical surgery before the severe obstructive jaundice develop. In this work the rates of bilirubin levels growth were calculated depending on the age and the level of incoming bilirubin in patients with the pancreatic head tumors. The obtained data allow to predict the dynamics of bilirubin level growth in each particular case of the disease.*

Key words: *tumor of the pancreatic head, obstructive jaundice, rate of bilirubin level growth.*

Introduction. The problem of oncological diseases of the pancreatoduodenal zone does not lose its relevance. Thus, according to studies in Europe, malignant tumors of the pancreatic head occupy the 4th place among diseases of the gastrointestinal tract (morbidity - 7-10%) [1]. One of the main symptoms of pancreatic head cancer is mechanical jaundice, which develops as the result of the tumor pressure on the biliary tract.

It is known, that in patients survived the operation for obstructive jaundice, the number of post-surgery complications and lethality are directly correlated with the level of bilirubinemia [2, 3, 4, 5, 6]. The standard treatment of the severe obstructive jaundice caused by a pancreatic head tumor involves a two-stage approach. The first stage is decompression of the biliary tract, the second stage is the radical surgery, if it is possible. Percutaneous drainage of the biliary tract is associated with the level of complications about 7-10% and mortality of up to 2% [7,9,]. It also has an additional risk of tumor seeding along the drainage tube, which leads to a faster growth of a potentially curable tumors [8]. All this points at the expediency of radical surgery to development of the severe jaundice. It is known that such factors as an initial bilirubin level, the age of patients, the secondary illness presence (diabetes mellitus, hepatitis, urinary tract disease, etc.) can affect on the rate of bilirubinemia increase [5].

Thereby, the rate of bilirubin level increasing is interesting in patients with a distal block of choledochus on the background of the pancreatic head tumors as a criterion for the rate of the severe jaundice development, depending on a number of factors.

Determination of the rate of bilirubin level growth depending on the age and the level incoming bilirubinemia in patients with pancreatic head tumors.

Materials and research methods. We carried out a retrospective analysis of the diseases history of the patients with obstructive jaundice caused by the pancreatic head tumors, who were examined and treated at the Department of Surgery and Transplantology of I. Mechnikov Regional Hospital in the period from 2008 to 2018. A correlation analysis was performed to determine the relationship between the incoming values of bilirubin level in blood serum, the age of patients and subsequent increase in the rate of its growing. The patients with secondary illnesses could affect the rate of bilirubin growth (diabetes mellitus, hepatitis, urinary tract disease, etc.) were excluded from the study. Measures of bilirubin level were carried out daily before drainage of biliary tract or operations. The rate of bilirubin increase was calculated for each patient and compared with resectable and non-resectable cases using the Student's t-test.

The study included 159 patients with the malignant tumors of the pancreatic head, 84 women and 75 men, with an average age of ± 57.3 years. 3 groups were formed by the incoming bilirubin level: I - incoming bilirubin level is up to 100 μmol/l - 44 patients (50.3%); II - 100-200 μmol/l - 59 patients (18.2%); III - more than 200 μmol/l - 56 patients (24.5%). Each group is divided into the subgroups by age. The WHO classification-2014 was used in the work: "a" subgroup – 44-60 years old (middle age); "b" – 60-75 years old (late maturity age). The majority were the patients with late maturity age – 87 patients (54.7%). The rate of bilirubin growing in each subgroup was calculated using the method of the dynamic rows analysis.

The rate of increase in serum bilirubin calculated in the study can be used to predict the number of days required for bilirubin to rise from the initial value to any selected threshold. Thus, we hoped to determine the average length of time during which patients with a certain bilirubin level would be able to pass radical surgery without drainage of the bile ducts. All calculations were made using STATISTICA 6.1 software. StatSoftlnc.

Results and discussion. The average level of bilirubin in blood serum at the first measurement was 163.5 μmol/l, and the interquartile range (IQR) was 56-282 μmol/l. In this case, the distribution of patients depending on the level of bilirubinemia at the first measurement had the following form (Table 1).

The presented data show that 64.8% of patients in our study with malignant tumors of the pancreaticoduodenal zone were hospitalized with the levels of bilirubin in serum <200 μmol/l. Only in 5.6% of cases the serum bilirubin level was > 300 μmol/l. Thus, most patients have jaundice, which does not necessarily include preoperative drainage of biliary tract. Therefore, there is a limited time for correct diagnosis, so radical surgery performed before the progressive jaundice will inevitably lead to the need of the biliary tract drainage.

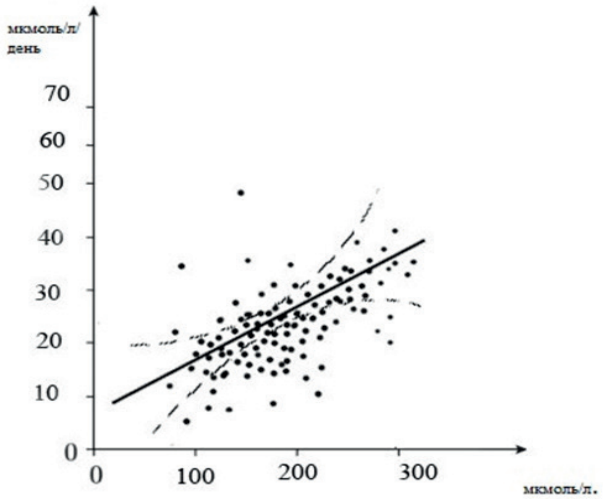
The average rate of bilirubin level increase during 3 days in hospital was 14.3 μmol/l /day (IQR 9.5-30.3). Relationship between the incoming bilirubin level and the rate of its further growing was established by the help of correlation analysis (Chart 1).

Table 1

Number of patients with different indicants of bilirubin in blood serum at the first measurement

Bilirubin in blood serum (μmol/l)	Number of patients	
	Abs.	%
≤50	23	14,5
51-100	21	13,2
101-150	38	23,9
151-200	21	13,2
201-250	25	15,7
251-300	22	13,8
> 300	9	5,6
Total	159	100,0

Chart 1. Relationship between the rate of bilirubin growing and the level of the incoming blood serum bilirubin.



The correlation coefficient is + 0.83, t-2.3 at p≤0.05, it speaks of a direct and strong relationship.

Thus, the higher level of bilirubinemia caused an increase in the rate of its increasing during three days, that patients were in clinic.

Dependence of the serum bilirubin rates growing from the age of patients was established by the dynamic rows analysis (Table 2).

Table 2

The rate of serum bilirubin growing (μmol/l/day) depending on the age of patients with different indicants of bilirubinemia in blood serum at the first measurement

Subgroups of patients	Groups of patients		
	I	II	III
a (n = 72)	9.8±2.0	14.2±3.8	24.5±16.0
b (n = 87)	11.4±2.9	18.9±7.4	30.3±18.0

Increasing of the bilirubin level correlates with the age of patients and the incoming level of bilirubin (coefficient of correlation + 0.7 - +0.6, t-1.9 – 1.7 for $p \leq 0.05$) – direct strong interrelation.

Choosing a threshold for hyperbilirubinemia below which most surgeons would be able to avoid drainage of the bile ducts is difficult, as other factors, including comorbidities, must be considered for individual patients. Many studies mark the adverse effects of jaundice, but none have suggested a threshold below which surgery without billiary drainage for a non-septic patient could be accepted. For example, if a threshold of 300 μmol/l is used, the average patient has about 1.5 weeks to reach this level. Even if you abandon the idea of having a fixed threshold for surgery without preoperative bile duct drainage, knowing that bilirubin increases by an average of about 100 μmol/l/ week and depends on the age of patients and the entry level of bilirubin, it can accelerate preoperative preparation for radical surgery.

We have demonstrated that there is considerable variability in the increase in serum bilirubin levels and that it doesn't depend on the potential operability of the tumor.

The estimated number of days for bilirubin to reach the threshold level has wide confidence intervals and therefore can only be used as a guide. However, it shows that rapid diagnosis and radical surgery are important, as this can avoid drainage of the bile ducts in as many cases as possible. The rapid examination and preparation of patients from admission to the hospital till final surgery is a serious problem that has major implications for resources in modern health care. However, it has the potential to reduce complications of bile duct drainage, shorten number of days in the hospital and improve patients' quality of life.

Conclusions. Thus, the obtained data demonstrate a high degree of dependence of the rate of bilirubinemia increase in the distal block of choledochus in connection with pancreatic tumors with the age of patients and the level of serum bilirubin at the primary study. However, the obtained results have wide confidence intervals and therefore do not allow to reliably guarantee the possibility of calculating the time for reaching the threshold value of bilirubinemia in each case of the disease. In this direction success is connected with additional researches, they will define the degree of dependence of speed of patient reaching the condition of severe obstructive jaundice from other factors.

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