Научная статья

https://doi.org/10.23934/2223-9022-2021-10-1-174-180

A Method for Assessing the Severity of Obstructive Jaundice of Non-Neoplastic Origin

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AIM OF STUDY To develop a method for assessing the severity of obstructive jaundice (OJ) of non-neoplastic orogin on the basis of functional parameters of the liver and the activity of pathogenetic agents of hepatodepression.

MATERIAL AND METHODS Clinical and laboratory studies of 142 patients with breast cancer of non-tumor origin. The indicators of the functional state of the liver, the index of plasma toxicity for albumin, and the content of malondialdehyde (MDA) were evaluated.

RESULTS Based on the assessment of a number of blood parameters - the content of total bilirubin (TB), the plasma toxicity index for albumin, the MDA level — the severity index of obstructive jaundice of non-neoplastic origin (SIOJ) was developed:

SIOJ = IT1/ITn + TB1/TB + 5(MDA1/MDAn)

where IT1 is the plasma albumin toxicity index at the current moment, ITn is the normal albumin plasma toxicity index, TB1 is the current bilirubin content, TBn is the normal bilirubin content, MDA1 is the current malondialdehyde content, MDAn is the normal value. The index less than 13 indicates a mild severity, 14–21 is moderate severity, 22 and higher indicates a severe degree of OJ. The method increases the objectivity of determining the severity of non-neoplastic origin by establishing the severity of liver damage and the processes underlying it.

CONCLUSION The suggested clinical and laboratory index allows the severity of obstructive jaundice to be objectively and quickly determined upon admission of a patient to the hospital and also adequate therapy to be initiated in case of severe degree for anticipation of possible post-operative complications, so the treatment should be focused on managing triggers of hepatodepression. The method is simple and available in medical institutions of various levels. The method is especially valuable when used in the dynamics of the early postoperative period.

Keywords: obstructive jaundice, severity index, hepatodepression

For citation Vlasov AP, Sheiranov NS, Markin OV, Vlasova TI, Muratova TA, Ryazantsev VE et al. A Method for Assessing the Severity of Obstructive Jaundice of Non-Neoplastic Origin. Russian Sklifosovsky Journal of Emergency Medical Care. 2021;10(1):174–180. https://doi.org/10.23934/2223-9022-2021-10-1-174-180 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study had no sponsorship

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TI – toxicity index
SIOJ – index of obstructive jaundice severity
MDA – malonic dialdehyde
OJ – obstructive jaundice
TB – total bilirubin
TCA – total concentration of albumin
ECA – effective concentration of albumin

INTRODUCTION

It is an axiom that the treatment of any pathology of the abdominal organs, including urgent ones, is determined by its severity, which depends on the duration of the disease. Of course, the treatment strategy is largely determined by this symptom. Is it legal? This is certainly true. However, opposition to this postulate is also possible. The basis for this is the individual reactivity of the organism, which depends on many factors, both hereditary and acquired [1, 2]. In order to objectify the severity of various pathologies, various criteria are used, various scales have been developed, which makes it possible to determine the severity of the disease in a timely manner and, on this basis, to form adequate therapy regimens [3, 4]. However, practice shows that the use of existing criteria does not always give a full assessment of the severity of the disease. Especially difficult is the assessment of the severity of obstructive jaundice (OJ), since in this case it is essentially about establishing the severity of liver damage [1, 5, 6]. In this regard, in practical surgery, the criteria for the severity of the OJ, developed under the guidance of Prof. E.I. Halperin. The assessment of this kind of test was based on the indicators of bilirubin, as well as signs that increase the severity of the OJ: cholangitis, renal failure, liver failure, signs of encephalopathy, gastrointestinal bleeding, sepsis [6, 7]. Under the guidance of Prof. Yu.S. Vinnik methods for determining the severity of the OJ, based on the assessment of changes in blood corpuscles are developed and successfully applied in the clinic [8–10]. A similar approach has been used by other researchers [5, 12, 13].

However, it should be noted that in the existing methods there is no assessment of the most important component of the inhibition of the functional state of the liver - membrane-destabilizing component, on which not only the degree of its damage depends, but also other organs, including the brain.. The disadvantage of this method, and many others, is the assessment of liver damage at a strictly defined moment. Most often, this action is carried out when the patient is admitted to the hospital. Meanwhile, any disease

proceeds in many ways according to an unpredictable scenario, which may not always be associated with the initial manifestations, even against the background of adequate therapy [1].

The aim of this work was to develop a method for assessing the severity of non-neoplastic OJ based on the functional parameters of the liver and the activity of pathogenetic agents of hepatodepression.

MATERIAL AND METHODS

We have developed an original method for assessing the severity of non-neoplastic OJ, which includes determining the content of total bilirubin (TB), the plasma toxicity index for albumin, the intensity of membrane lipid peroxidation based on the content of malondialdehyde - MDA (patent No. 05.08.2019).

The specified spectrum of biochemical parameters was selected for the following reasons.

According to TB in blood serum, we evaluate the pigment-synthesizing and pigment-regulating functions of the liver. By the toxicity index, we determine the albumin-synthesizing and albumin-metabolizing functions of the liver. According to this index, we also determine the detoxification ability of the liver as a whole, which suffers from OJ.

The specified index is calculated as follows. In the blood, the total (TCA) and the effective concentration of albumin (ECA) are determined. Based on the data obtained, the toxicity index is calculated: TI = 1 - TKA / ECA.

By the content of MDA in the blood, the intensity of membrane lipid peroxidation is determined - a process (membrane destabilizing), on which the degree of damage to liver cells depends, and in general, their functional status.

Consequently, the selected list of analyzed indicators, on the one hand, is wide enough to assess the functional state of the liver and the leading mechanisms of its damage, on the other hand, it is quite limited in quantitative terms, which greatly simplifies the calculation.

Let us note the most important advantage of the developed method, which consists in assessing the analyzed indicators in dynamics. This approach makes it possible to fully trace the dynamics of the ongoing pathological processes.

So, based on the data obtained, the severity index of obstructive jaundice (SIOJ) is calculated by the formula:

SIOJ = TI1/TIn + TB1/TBn + 5(MDA1/MDAn),

where SIOJ is the index of the severity of obstructive jaundice, TI1 is the index of plasma toxicity for albumin at the current moment, TIN is the index of plasma toxicity for albumin in the norm, TB1 is the content of bilirubin at the current moment, TBn is the content of bilirubin in the norm, MDA1 is the content of malondialdehyde in current moment, MDAn - the content of malondialdehyde in normal conditions.

The developed method was tested in 142 patients with OJ of non-neoplastic origin. Clinical and laboratory studies were carried out after obtaining the informed consent of the patients. The age of the patients varied from 24 to 87 years (49,3±8,1).

The causes of OJ were as follows: choledocholithiasis - in 89 (62.7%), stricture or stenosis of the large duodenal papilla or stricture of the terminal section of the common bile duct - in 34 (23.9%) and pseudotumorous pancreatitis - in 19 patients (13.4%). In most cases, patients underwent open surgical interventions, including cholecystectomy - in 93 (65.5%), internal drainage of the biliary system: creation of choledochoduodenoanastomosis - in 73 (51.4%) and choledochojejunoanastomosis - in 21 (14.8%), external drainage of bile ducts - 48 (33.8%). The choice of patients with this kind of operations is due to the fact that they have a high probability of disease progression, and therefore, there is a special need for its prognosis. Endoscopic papillosphincterotomy and lithoextraction was made in 12 patients (8.5%) with the OJ developed against the background of choledocholithiasis.

Patients in the early postoperative period underwent complex treatment, which included infusion, antispasmodic, analgesic and other components according to clinical guidelines, depending on the severity of the OJ (2018).

The study excluded patients with masses of the gates of the liver or the head of the pancreas, parasitic liver diseases, the presence of severe concomitant pathology, pregnancy, when patients used hepatoprotectors, etc.

The diagnosis was made on the basis of clinical, laboratory and instrumental data (ultrasound scanning, computed tomography, fibrogastroduodenoscopy).

Indicators taken as physiological norm (reference values) were determined in healthy individuals (n = 15) of both sexes at the age of 22–56 years.

Statistical processing of digital data was performed using the statistical package Statistica 6 (USA) using the Student's t test (t), Chi-square ($\chi 2$). To check the samples for normal distribution, the Lilliefors test was used. Differences were considered significant if the magnitude of the possible error was less than 0.05.

RESULTS

When patients were admitted to the clinic and a diagnosis of non-neoplastic OJ was established, which in most cases (115 patients (81.0%)) could be performed already before surgery, after preoperative preparation, which lasted from 4 to 25 hours, depending on the severity of the disease, patients were operated on. The nature and scope of interventions is presented above. At the stage of preoperative preparation, as well as 3 days after surgery, the severity of the OJ was assessed.

Numerous studies have established that with SIOJ equal to 9.4 ± 0.9, there was a rapid recovery of the functional state of the liver, and the course of the early postoperative period proceeded smoothly. We attributed this kind of severity of the disease to a mild degree (Table 1).

Table 1

Severity index values of mechanical jaundice of non-neoplastic origin at different degrees of its severity

Severity	Severity index	Length of hospital stay (bed-day)
Mild	Up to 13 (9,2±0,8)	11,7±0,6
Medium	14–21 (17,2±1,6)	19,1±1,3
Severe	22 and more (25,7±2,0)	25,7±1,7

There were no postoperative complications in patients with mild breast severity. The stay of patients in the hospital was 11.7 ± 0.6 bed-days. In the examined patients, the indicated severity level was found in 40 cases (28.2%) (Table 2).

Table 2

Distribution of patients with obstructive jaundice, depending on the severity, established by the developed index

Severity	Number of patients	
	n	%
Mild	40	28,2
Moderate	81	57,0
Severe	21	14,8

In another group of patients with SIOJ equal to 17.7 ± 1.8, the early postoperative period was characterized by a relatively slow recovery of the main functional parameters of the liver. At the same time, the postoperative period proceeded with a relatively pronounced unfavorable potential for the development of complications. This was found in a significant manifestation and duration of the syndrome of endogenous intoxication, slow restoration of the functional status of the intestine. We attributed this kind of severity of the disease to a moderate degree. In the examined patients, it was diagnosed in most cases - in 81 patients (57%) (Table. 2).

In patients with moderate severity of the OJ, the course of the early postoperative period was lengthened. Restoration of liver function was slow. In the early period after surgery, 7 patients (8.6%) developed tissue infiltration and suppuration of the postoperative wound, 3 patients (3.7%) developed an external biliary fistula, which subsequently closed on its own. There was no postoperative mortality. In patients of this group, hospital stay was 19.1 ± 1.3 bed-days.

In the next group of patients with SIOJ equal to 26.2 ± 2.1, the course of the early postoperative period proceeded against the background of a slow recovery of liver functional parameters, which carried a great negative potential for the development of complications. Undoubtedly, the most important of the predisposing factors in the occurrence of various kinds of complications was a pronounced and difficult to correct syndrome of endogenous intoxication, in the pathogenesis of which enteral distress syndrome was very important. We emphasize that the restoration of the functional status of the intestine occurred only 55.2 ± 4.2 hours after surgery. We attributed this kind of severity of OJ to a severe degree and it was diagnosed in 21 patients (14.8%).

In patients admitted to the hospital with a severe degree of the OJ, in the postoperative period, the restoration of the functional state of the liver proceeded slowly, and in 11 (52.4%) patients, hepatic failure was diagnosed. Wound complications also occurred: in 5 patients (23.8%) - tissue infiltration and wound suppuration, in 2 patients (9.5%) - subcutaneous eventration. In addition, 6 patients (28.6%) had prolonged bile leakage, 7 (33.3%) - pneumonia. The resulting complications significantly worsened the course of the early postoperative period and were the cause of mortality in 3 patients (14.3%). The stay of patients in the hospital was 25.7 ± 1.7 bed-days.

Note that the calculation of the developed index can be performed in the dynamics of the early postoperative period. The severity index was assessed 3 days after surgery. It turned out that in those patients in whom the course of the early postoperative period proceeded without complications and there was a rapid recovery of the functional state of the liver, there was a significant decrease in SIOJ already after 3 days. However, in patients who were diagnosed with the development of complications or they were just forming, the SIOJ, although it decreased, was significantly higher than that in patients who did not develop complications (Table 3).

Table 3

The values of the SIOJ with varying degrees of severity in the dynamics

Severity	Severity index on admission	Severity index 3 days after surgery	
		Favorable postoperative period	Postoperative period with complications
Mild	9,2±0,8	4,1±0,5*	–
Moderate	17,2±1,6	8,1±1,1*	12,7±1,9**
Severe	25,7±2,0	16,3±1,9*	20,1±1,8**

Notes: * — significant differences in the data compared with those upon admission, p<0.05;
** — significant differences in the data compared with those in the group without complications, p<0.05

Thus, a positive result achieved with the use of the developed method is an increase in the objectivity of establishing the severity of a non-neoplastic OJ by determining the severity of liver damage and the processes underlying it. Note that to the last component - the pathogenetic mechanisms of liver damage - was given especial attention. This is determined by the fact that the phenomena of hepatodepression and, accordingly, the rate of restoration of the functional state of the liver in OJ (and other organs and systems) are caused by membrane-destabilizing phenomena in cells, which in turn are largely associated with membrane lipid peroxidation. Therefore, in the formula for calculating the severity assessment index, the indicator of this process - the MDA indicator - is applied with a factor of 5.

We have noticed another important circumstance that made it possible to place special emphasis on this indicator. It turned out that the intensity of the process of peroxidation of membrane lipids in various pathological conditions accompanying the OJ, such as cholangitis, destructive cholecystitis, pancreatitis, etc., significantly increases ($\square^2$=2,132÷4,765, p=0,017÷0,038). This fact was the basis for not taking into account a number of signs and pathological conditions that enhance the manifestations of the OJ, which a number of authors recommend to use when determining its severity [6, 7]. This postulate was confirmed by the data obtained in the analysis of the results of treatment of OJ patients who underwent low-traumatic interventions (laparoscopic cholecystectomy and choledocholitholite extraction). It turned out that when assessing this index in the early postoperative period, it was significantly lower (by 24.3–42.1%) than in patients who underwent open interventions. The course of the early postoperative period was more favorable for them.

Some clinical examples of the use of SIOJ, calculated for a number of the indicated blood parameters and their integral derivatives, are given.

Clinical case 1

Patient N., 47 years old, admitted urgently, examined. Diagnosis: “Cholelithiasis. Choledocholithiasis. OJ". A blood test was performed, on the basis of which the SIOJ was calculated, which turned out to be equal to 7.4. According to SIOJ, the mild severity of the breast was exposed. The patient underwent a retrograde endoscopic papillosphincterotomy followed by stone removal (lithoextraction). After the operation, the patient's condition improved rapidly, the manifestations of hepatodepression and OJ were arrested, and by the 6th day the manifestations of bilirubinemia had significantly decreased. After 8 days, the patient was discharged in satisfactory condition under the supervision of a polyclinic surgeon.

Clinical case 2

Patient N., 53 years old, admitted urgently. From the anamnesis - sick for 4 days. Examined. Diagnosis: “Cholelithiasis. Cholecysto- and choledocholithiasis. Acute cholecystitis. OJ ". The SIOJ was calculated, which turned out to be equal to 15.2 - the average severity of the OJ. The patient underwent surgery: laparotomy, cholecystectomy, hepaticolithoextraction, external drainage of the common hepatic and bile ducts according to Halstead. Six days after the operation, the patient developed a complication from the wound in the form of an infiltrate with symptoms of suppuration. Produced: opening and drainage of the infiltrate; adjustment of therapy (change of antibiotic, increase in the volume of infusions). The patient's condition was stabilized. The phenomena of inflammation un the wound were arrested, the healing of tissues by the type of secondary tension, the indicators of the functional state of the liver came to reference values, in particular, the content of TB in the blood was normalized. The patient was discharged on the 19th day in a satisfactory condition under the supervision of a polyclinic surgeon.

Clinical case 3

Patient K., 68 years old, was admitted on an emergency basis to the intensive care unit. From the anamnesis, he was ill for 7 days. The condition is severe, the skin and visible mucous membranes are of a bright icteric color, tachycardia (heart rate 112 per minute), hypotension (95/45 mm Hg), febrile temperature (38.3 ° C), intestinal murmurs are rare and weak, in the right hypochondrium there is a sharp soreness. Examined. Diagnosis: “Cholelithiasis. Acute destructive calculous cholecystitis. Choledocholithiasis. Cholangitis. OJ". According to a blood test, the SIOJ was 27.3, which corresponded to a severe OJ. Within 4 hours, the patient underwent preoperative preparation - including infusion, antibacterial and other therapy. After adjusting the activity of the cardiovascular system and stabilizing the general condition, the patient was operated on. Laparotomy, cholecystectomy, hepaticolithoextraction, external drainage of the common hepatic and bile ducts according to Vishnevsky were performed. The early period after surgery was difficult. The patient has developed bilateral pneumonia. He underwent massive therapy, including antibacterial and hepatoprotective preparations. The patient's condition did not improve. On the 14th day, against the background of an increase in respiratory and cardiovascular insufficiency, signs of bacterial-toxic shock, multiple organ failure were registered, which led to the death of the patient.

DISCUSSION

Thus, currently there are many ways to assess the severity of the OJ. However, the severity of the patient's condition is still assessed by the clinical and biochemical severity of icterus and progressive liver failure. Other syndromes are not taken into account sufficiently. It is especially important to determine the systemic inflammatory response syndrome, which reflects the severity of the developing inflammatory process in the biliary system. [1]. A significant disadvantage of most methods is the fact that the indicators on which the calculations are based do not fully reflect the functional status of the liver, do not analyze the specific criteria for the manifestations of OJ. Of course, their main disadvantage is that the evaluation criteria do not include indicators of pathological processes underlying the lesion of hepatocytes - the main object of damage.

The analysis of the obtained materials gives reason to believe that the developed method for determining the severity of non-neoplastic OJ is distinguished by the following advantages: first, ease of execution (analysis of only three indicators); secondly, the ability to assess not only the severity of liver damage, but also the intensity of the main processes involved in damage to hepatocytes; third, the availability of research in medical institutions of various levels; fourthly, the low cost of all studies and the ease of calculating the index; fifth, when assessing the state of one of the main trigger mechanisms of membrane-destabilizing

processes, it is possible to determine the consequences of the systemic inflammatory response syndrome in the form of damage to various organs and systems; sixth, it is possible to use the index in the dynamics of the early postoperative period, which makes it possible to assess the course of the disease against the background of ongoing therapy, which is especially valuable in patients with moderate to severe and severe degrees of the OJ.

CONCLUSION

The proposed clinically-laboratory-grounded index makes it possible to determine objectively and quickly the severity of obstructive jaundice of non-neoplastic origin when a patient is admitted to the hospital and, in cases of its severe degree, timely prescribe adequate therapy, anticipating possible postoperative complications, directing the main vector of treatment to correct the triggering agents of hepatodepression. In this regard, the emphasis should be on the use of drugs with membrane-stabilizing hepatoprotective activity.

The method is simple in execution and is available in medical institutions of various levels. A special informative value was noted when it was used in the dynamics of the early postoperative period. Undoubtedly, the use of the developed index is of particular importance in severe obstructive jaundice.

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Received on 15.05.2020

Review completed on 17.07.2020

Accepted on 29.09.2020