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COMPETENCE OF QUANTITATIVE INDICATORS OF THE LEADING CLINICAL SIGNS OF CHOLESTASIS IN DIFFERENTIATION OF ITS GRADES

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Annotation: The syndrome of intrahepatic cholestasis (SIC) is understood as a slowdown or cessation of bile secretion associated with changes either in its consistency (thickening) or in the lumen of the intrahepatic bile ducts (narrowing) [1–3]. Theoretically, any liver pathology can be complicated by the development of SIC, and only cases with a duration of more than 6 months are classified as chronic.

Key words: Between the concepts of cholestasis and hepatic jaundice should not put an equal sign. For, the term cholestasis is a broader concept, and hepatic jaundice is just an integral part of it.

Introduction

The syndrome of intrahepatic cholestasis (SIC) is understood as a slowdown or cessation of bile secretion associated with changes either in its consistency (thickening) or in the lumen of the intrahepatic bile ducts (narrowing) [1–3]. Theoretically, any liver pathology can be complicated by the development of SIC, and only cases with a duration of more than 6 months are classified as chronic. Between the concepts of cholestasis and hepatic jaundice should not put an equal sign. For, the term cholestasis is a broader concept, and hepatic jaundice is just an integral part of it. Moreover, cholestasis can clinically occur with or without jaundice [4,5,6]. It is clear that both forms of cholestasis, even within the same type of liver pathology, can manifest themselves in a different form of its severity [7,8,9].

Clinical practice suggests the need to divide the severity of SIC into separate subunits with their own range of variation. Theoretically, such an approach is able to enhance the information potential of individual gradations, hence their role in assessing the severity of SIC. Consequently, the process of diagnosing SIC in the clinical practice of doctors, who by the nature of their service often encounter them, will be noticeably facilitated. Along with this, favorable conditions will be created for early recognition of SIC and optimization of the daily dose of the drugs used in its therapy.

Despite the obvious need, practitioners to this day do not have a convenient way to distinguish between the severity of SIC. For this reason, they are forced to experience not entirely mandatory difficulties in the management of patients with liver pathology, accompanied by SIC. Hence, any research, the vector of which is aimed at the development of a competent method for delimiting the severity of SIC into separate types, is justified and in demand.

In view of the foregoing, this work has been undertaken, the purpose of which was to assess the competence of the information potential of quantitative indicators of the leading clinical symptoms of SIC in differentiating its gradations.

Materials and methods. To achieve the goals set, a group of patients was examined, consisting of 66 people (of which 18 were men, and the rest were women), with chronic diffuse liver diseases accompanied by clinical and biochemical manifestations of SIC. In 20 patients, intrahepatic cholestasis of pregnancy was verified, in 25 patients, primary biliary cirrhosis (PBC) of the liver, and in the remaining 21 patients, drug-induced cholestasis (DIC). The diagnosis was verified using modern research methods, including X-ray, endoscopic, ultrasonographic, and computed tomography. The contents of biochemical markers of TSV: total bilirubin (TB) and its fractions, cholesterol (X), alkaline phosphatase (AP) and J - glutamyl transpeptidase (GGTP) were studied using conventional methods.

The enrolled patients were prospectively selected from October 2014 to 2014. to May 2016 The presence of pruritus and an increase in at least one of the following laboratory parameters: TB>20.5 mlmol/l, X>5.7 mlmol/l, alkaline phosphatase>130 IU/l, GGTP>61 IU/l. served as the basis for including patients in the study. The reasons for exclusion were: chronic liver diseases without clinical and biochemical signs (CBS) of cholestasis, cases of severe cholelithiasis, skin diseases, allergic reactions. The patients involved in the study circle were orally informed about the research nature of the work. The study was approved by the ethical committee of the Bukhara Medical Institute and was conducted in accordance with the requirements of the Declaration of Helsinki.

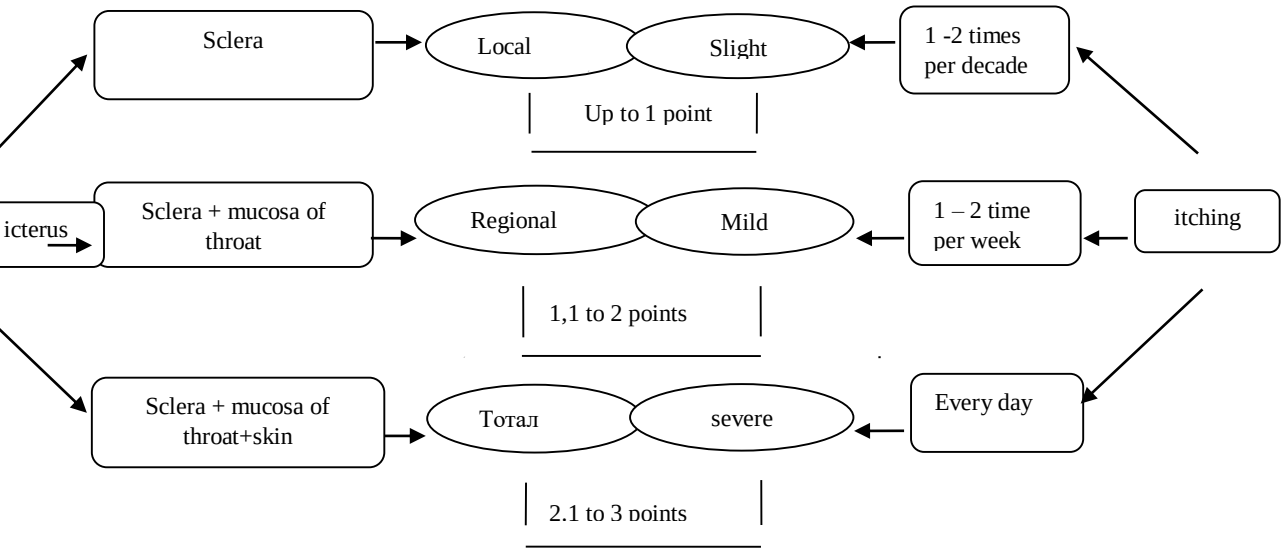
Statistical analysis was carried out using STATISTICA 5.0 software. (Statsoft, USA). The results were expressed as mean ± standard deviation (SD). Normally distributed parametric data were compared using Student's t-test. A value of $p < 0.05$ was considered statistically significant.

Research results. The task set for this study obliged, first of all, to find opportunities for quantitative assessment of the leading clinical signs of cholestasis. For this purpose, a modified scale for quantifying parameters according to Likert was used. Using this scale, it is convenient to calculate the quantitative parameters of various indicators, including medical ones. At the same time, they relied on the real parameters of the assessed clinical signs of cholestasis as much as possible. At the same time, aspects of the involved scoring criteria, such as prostate and convenience, were carefully considered.

As expected, the process of quantifying the main clinical signs of SIC: jaundice and pruritus turned out to be somewhat laborious in terms of finding criteria for their division. For its actual implementation, an indispensable condition was the establishment of the possibilities of objectively distinguishing the severity of clinical signs of cholestasis into independent types. The most acceptable delimiting condition: for jaundice was the extent of its distribution, and for pruritus - the intensity of its manifestations. If the spread of the symptom of jaundice was limited to the sclera, then it was referred to as local. Cases of the spread of the symptom of jaundice not only in the sclera, but also in the mucous membrane of the pharynx were called regional. When the spread of the symptom of jaundice covered the sclera, the mucous membrane of the oral cavity and the skin, then it was recognized as total.

To differentiate the symptom of pruritus into separate types, its intensity served as the basis. Manifestation of skin itching with a frequency of 1-2 times during the last 10 days was called - moderate (+), weeks - severe (++), days with a predominant manifestation in the evening - at night - painful (+++). Separated fragments of clinical signs of cholestasis were assigned the corresponding number of evaluation points. Depending on the

number of points scored, a gradation of the severity of one or another clinical sign of cholestasis was established [Fig. one].



Quantification of the leading clinical symptoms of cholestasis.

The leading clinical signs of cholestasis, taking into account their severity, were quantified in the range from 1 to 3 points. It should be noted that the information potential of indicators of jaundice and pruritus turned out to be quite competent for differentiating SIC into separate gradations. At the same time, the indicators of jaundice were the most informative [tab. one].

Table 1

Quantification of indicators of clinical signs of SIC

№	Clinical signs	Points		
		1	2	3
1.	Pruritis	Mild (+)	Manifest (++)	Painful (+++)
2.	Jaundice	Local (+)	Regional (++)	Total (+++)

Depending on the number of points scored, the severity of SIC was divided into separate independent gradations. If the accumulated amount did not exceed 2 - 3 points, then this gradation was called easy (+). In cases where the sum of the points scored fluctuated within 4 - 6 units, then such a gradation was called medium (++) severity. If the total number varied within 7 - 9 points, then this gradation was recognized as severe (+++).

In our studies, out of a total of 66 cases, in 17 (26%) cases, the score varied between 2 and 3 points, which corresponded to a mild (+) gradation of the severity of SIC. In 33 (50%) cases of the study, the total scores scored ranged from 4 to 6 units, which corresponded to the average (++) gradation of the severity of SIC. In the remaining 16 (24%) cases of the study, the score varied within 7 to 9 points, which severe (+++) gradation of severity of SIC. The most frequently identified was the average (++) gradation of cholestasis, which was established in almost 50% of the cases of the study. The rest was divided among themselves by the other two gradations - mild (+) and severe (+++), the frequency of which looked approximately equal and amounted to 26% and 24%, respectively.

The severity of the leading clinical signs of cholestasis: jaundice and pruritus were also delimited into separate gradations based on their specific quantitative indicators. Cases of severe pruritus to moderate intensity and limited jaundice with sclera were classified as mild (+) severity of these indicators. It was also recognized as medium (++) in the presence of severe pruritus and yellow staining not only of the sclera, but also of the mucous membrane of the pharynx. Severe (+++) severity was taken as cases of an increase in TB, X, GGTP and alkaline phosphatase by 200 and ↑ mlmol/l, 10 and ↑ mlmol/l, 100 and ↑ IU/l and ALP 400 and ↑ IU/l, respectively with the presence of excruciating skin itching and yellow coloration of the sclera, visible mucous membranes and skin. From a practical point of view, such a division justified itself, because in complicated cases the differentiation of SIC gradations was noticeably simplified.

As expected, the frequency of identification of gradations of individual clinical signs of cholestasis was different in the examined patients with liver disease [Table. 2]. Even at the level of a cursory analysis of the frequency of occurrence of the main clinical signs of cholestasis, the dominant position of the symptom of jaundice over pruritus is immediately felt. As follows from the results obtained, jaundice was most often recorded in the examined persons. Obviously, in this regard, the information potential of this trait was more competent in differentiating individual gradations of SIC.

An analysis of the frequency of occurrence of individual gradations of the leading clinical signs of cholestasis showed the following. Jaundice was presented mainly (about 47%) due to the average (++) gradation, and the other two - mild (+) and severe (+++) made up the rest of them. In 18 (27.3%) cases of the study, its distribution was local and limited to the sclera.

Table 2

The frequency of distribution of gradations of the leading clinical symptoms of cholestasis

№	Clinical signs	Graduation of clinical signs		
		Light (+)	Mild (++)	Severe (+++)

1.	Jaundice	18 27,3±3,4	31 47,0±7,8	17 25,7±3,1
2.	Pruritis	25 43,2±5,4	19 32,7±3,5	14 24,1±3,2

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Local forms of jaundice, according to the conditions of quantitative assessment, were assigned 1 point, which corresponded to a mild (+) gradation of the rating scale. In 31 (47.0%) cases, the spread of jaundice was limited to the sclera and oral mucosa. This form of distribution was called regional and was evaluated in the amount of up to 2 points and corresponded to the average (++) gradation. In 17 (25.7%) patients, the spread of icterus covered not only the sclera and oral mucosa, but also the skin. This form of spread of jaundice was called total. Quantitatively, it was estimated on average no more than 3 points and corresponded to severe (+++) gradation.

The frequency of distribution of the clinical sign - skin itching was somewhat different and significantly different from those of jaundice. If icteric syndrome occurred exclusively in all patients included in the survey group, then pruritus was observed in 58 persons out of a total of 66 patients, which amounted to 87.9%. In 25 (43.2%) cases of the study, pruritus bothered patients on average 1-2 times during the last 10 days. Itching syndrome of similar intensity was quantified up to 1 point, which corresponded to mild (+) gradation. In 19 (32.7%) patients, itching was more pronounced and made itself felt more than 1-2 times a week. Similar cases of pruritus were quantified more than 1, but not more than 2 points, which corresponded to the average (++) gradation. In 14 (24.1%) cases of the study, the severity of pruritus syndrome was very pronounced, sometimes it was excruciating in nature with a daily manifestation, mainly in the evening - at night. These cases of pruritus were assessed from 2.1 to 3 points and corresponded to a severe (+++) gradation of severity. Thus, on the basis of the conducted studies, it can be concluded that from the standpoint of clinical practice, the division of the cholestasis syndrome into separate independent gradations is highly demanded. The leading clinical signs of cholestasis have sufficient information potential suitable for distinguishing SIC into separate gradations of its severity. Such a division noticeably enhances the information potential of individual gradations, hence their role in assessing the severity of SIC.

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