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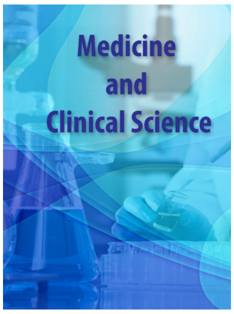

The Evaluation Formula of Acute-on-Chronic Liver Failure Based on PCT and Conventional Indicators

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Keywords

Hepatitis B virus; acute-on-chronic liver failure; PCT

Abstract

Aims: *The aim of this article is to develop and demonstrate an efficient evaluation formula to assess the liver function, prognosis, and in the usage of antibiotics as well.*

Method: *The case study of 118 patients with our clinical observations and treatments was carried out together with statistical analysis method for the collected data by using the Statistical software SPSS 24.0 and Sigmaplot 14.0. The evaluation formula of PCT was developed from the regression of binary logistic equation.*

Results*: It has been confirmed that PCT is significantly increased in patients with acute-on-chronic liver failure, with high sensitivity and specificity, and that that the new evaluation formula of acute-on-chronic liver failure as 6.941 PCT + 1.387 PT can be used to evaluate liver functions.*

Conclusions: *This is a significant contribution to the control and treatment of Hepatitis B virus (HBV) infections and other liver failure diseases. This new method will not only provide an efficient and simple tool to evaluate the liver failures, but also to reduce the unreasonable application of antibiotics in patients with acute-on-chronic liver failure in clinical practice.*

Introduction

Hepatitis B virus (HBV) infections challenge the global public health continuously [1], there are more than 257 million existing infected people all over the world, and about 1 million people die each year from the final-stage liver disease associated with HBV [2]. A variety of factors could cause liver failure resulting serious liver damage, such as synthesis, detoxification, metabolic and biological transformation function serious dysfunction or decompensation. The main manifestation of a clinical syndrome includes jaundice, coagulation dysfunction, liver and renal syndrome, hepatic encephalopathy, and ascites, acting as the main cause of death of final-stage liver disease [3]. The mortality within 28 days is significantly higher than acute decompensated cirrhosis [4]. Herein, we sought to demonstrate the relationship between PCT and other clinical indicators together with the different liver function status of liver cirrhosis caused by HBV by case study and data analysis, affording slow and acute liver failures with the treatment within our hospital.

Data and Methods

General data

Using a retrospective study, information of 118 patients with non-infected final-stage liver disease and compensated cirrhosis, age (53.11 ± 10.55), including 90 men, age (49.54 ± 11.46), admitted from January 2016 to June 2019 were collected. All patients were tested for PCT and routine indicators.This study and the data usage have been approved by the Ethics Committee of Dingxi People's Hospital with the approval number of DXLL2019-034. It was Complied with the ethical criteria.

Inclusion criteria

(1) slow plus acute liver failures: For previous hepatitis B cirrhosis, a slow progressive liver function decline and decompensated, fitting with the diagnostic criteria for the diagnosis and Treatment of Liver Failure (2018 edition);[ ] (2) For after hepatitis B cirrhosis: the history of chronic viral hepatitis B for more than half a year, with clinical characteristics of cirrhosis or typical imaging manifestations of cirrhosis. (3) There was no fever, and the white blood cell count and neutrophil ratio were basically normal together with normal pulmonary imaging and no infectious ascites, neither the application of antibiotics.

Exclusion criteria

(1) other hepatophilvirus infected persons; non-viral liver disease; liver cancer; (2) patients with other diseases causing abnormal PCT elevation, such as various infections, severe trauma, burns, autoimmune diseases, thyroid disease, paraquat poisoning, pregnant women.

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Methods

Group organizing

According to the Child-Pugh grade and liver function status at admission, the study subjects were divided into two groups as Group A (liver cirrhosis group) and Group B (chronic plus acute liver failure group). Group A contained 53 patients, including 37 male and 16 female patients, and were of age (51.49 ± 10.21) years old. Group B contained 65 patients, including 53 males and 12 females, and were of age (49.49 ± 12.14) years old. PCT was detected by fluorescence immune-quantitative analyzer, AU5800 biochemical analyzer, KX-21; CS5100; and fetal protein by Biolumi 8000.

Data collection

Alalanine fasting blood test on the second day of admission (alanine aminotransferase, ALT), aspartate aminotransferase (aspartate transaminase, AST), total bilirubin (total bilirubin, TBIL), direct bilirubin (direct bilirubin, DBIL), albumin (albumin, ALB), prothrombin time (prothrombin time, PT), prothrombin percentage (prothrombin activity, PT%), international standardized ratio (international normalized ratio, INR), white blood cell count (white blood cell count, WBC), neutrophil ratio (proportion of neutrophils, N%), platelet count (platelet count, PLT), procalcitonin (procalcitonin, PCT), C-reactive protein (C-reaction protein,CRP), Clinical data (gender, age, ascites, and presence of hepatic encephalopathy) collected consequently, the Child-Pugh score was performed for all the patients.

Statistical Processing

Statistical analysis was conducted by the Statistical software SPSS 24.0 and Sigmaplot 14.0.`Measurement data are expressed as $\chi \pm s$, compared using independent sample T test; count data are expressed as percentage, and compared between two groups2 checkout. Multivariate analysis used binary logistic regression analysis, and the evaluation formula was constructed. The ROC curve was used to show the positive results of the PCT and the conventional indicators between the liver cirrhosis group and the chronic plus acute liver failure group. A $P < 0.05$ suggested statistically significant differences.

Results

Comparison between the two groups

Statistical analysis showed no significant difference in age, gender, ALB, WBC, RBC, and N% as the P values are all greater than 0.05 (Table 1); whilst ALT, AST, TBIL, DBIL, PCT, CRP, PLT, PT, PT, INR, PTA, and AFP indeed have significant differences as their P values are less than 0.05 ($P < 0.05$, Table 1).

The results in Table 1 demonstrated that significant differences between PCT and PT ($P < 0.05$), with OR values of 1033.327 and 4.001, respectively were obtained, excluding confounding factors by the selection of statistically significant indicators between the two groups for binary logistic regression analysis. The construct evaluation formula equals as 6.941 PCT + 1.387 PT.

Table 1. *Comparison of the clinical data between the two patient groups.*

Metric	Group A (Liver cirrhosis)	Group B (Slow plus acute liver failure)	χ2/t	P
No. of Male (Percent / %)	53(81.53%)	37(69.81)	2.218	0.136
Age (year)	51.49 ± 10.21	49.49 ± 12.14	2.841	0.950
ALT (U/L)	49.49 ± 42.44	291.08 ± 424.95	71.597	0.000
AST (U/L)	50.03 ± 30.66	245.30 ± 319.12	37.636	0.000
TBIL (umol/L)	36.66 ± 29.78	188.86 ± 146.55	48.757	0.000
DBIL (umol/L)	15.52 ± 19.53	114.26 ± 107.85	54.964	0.000
ALB (g/L)	29.66 ± 5.04	35.74 ± 6.01	3.021	0.085
WBC ($\times 10^9$/L)	4.44 ± 2.28	5.08 ± 2.67	2.228	0.138
PCT (ng/ml)	0.14 ± 0.13	0.84 ± 1.14	21.914	0.000
CRP (mg/L)	9.89 ± 10.78	21.85 ± 33.28	7.750	0.006
N%	58.41 ± 13.73	66.67 ± 14.49	0.507	0.478
RBC ($\times 10^{12}$/L)	4.21 ± 0.78	3.72 ± 0.93	1.767	0.186
PLT ($\times 10^9$/L)	109.96 ± 95.40	81.05 ± 53.15	6.105	0.015
PT (s)	14.58 ± 1.67	21.21 ± 6.10	20.056	0.000
PT A (%)	66.60 ± 17.06	41.85 ± 15.75	2.809	0.000
INR	1.24 ± 0.23	1.75 ± 0.50	12.184	0.001
AFP (ng/ml)	9.60 ± 15.41	151.07 ± 294.38	41.056	0.001

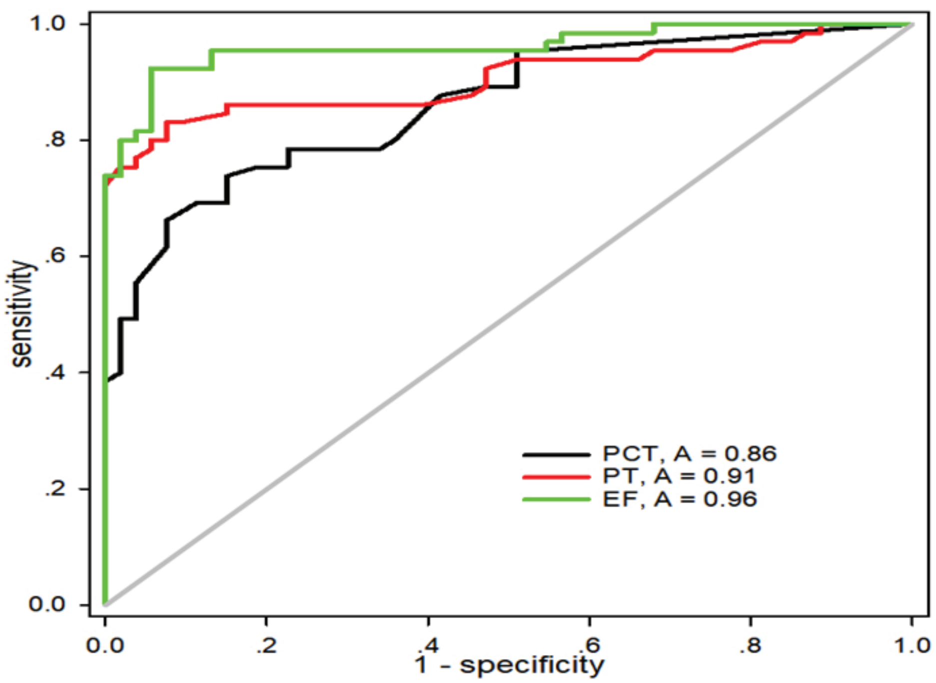
($P < 0.05$ represents a statistically significant difference)

***Table 2**. Efficacy analysis of the evaluation formula, PCT, and PT for evaluating liver function.*

Metric	AUROC	95% CI	Cutoff value	Sensitivity (%)	Specificity (%)	P
Evaluation formula	0.961*	0.923-0.994	25.31	92.31	94.34	<0.0001
PT	0.906▽	0.849-0.963	16.65	83.08	92.45	<0.0001
PCT	0.861	0.796-0.926	0.27	73.85	84.91	<0.0001

**versus PT, P = 0.1058, versus PCT, P = 0.0074.▽Compared with the PCT, P = 0.3040.*

***Figure 1.** ROC curve analysis of PCT, PT and evaluation formula*



Evaluation formula and individual

Evaluation of liver function in slow and acute liver failure (Table 2), and diagram of ROC curve analysis of evaluation formula, PT and PCT (Figure 1).

AS shown in Table 2 and Figure 1, the AUROC of the evaluation formula was 0.961, with a chosen cutoff of 25.31, sensitivity of 92.31%, specificity of 94.34%, and P value of < 0.001 for statistically significant. While with an AUROC of 0.906 and a chosen cutoff of 16.65, P value of < 0.001 for statistically significant still achieved, albeit a slight lower sensitivity of 83.08% and a specificity of 92.45% for PT. The PCT had an AUROC of 0.861, with a chosen cutoff of 0.27, even lower sensitivity of 73.85% and specificity of 84.91%, and P value of < 0.001 for statistically significant. Therefore, the comparison between the evaluation formula and PT showed no significant difference, and the sensitivity and specificity were higher than PT. The comparison between the evaluation formula and PCT afforded statistically significant, but with no statistically significant obtained for the comparison of PT vs PCT.

Discussion

It is believed that the dominant causes of chronic liver disease are HBV, HCV (hepatitis C virus), alcoholic fatty liver disease, and metabolic fatty liver diseases [6]. HBV infection remains one of the global public health threat, with more than 257 million people infected with chronic HBV worldwide. The World Health Organization (WHO) has committed to eliminate HBV infection by 2030 [7], it, therefore, becomes the first priority to both clinicians and researchers to devote to control the HBV infections as well as to diminish the disease till its extinguish [8-10]. It has also been approved that the infection is closely associated with the prognosis of HBV-associated liver disease, especially in patients with liver failure [11].

PCT has been widely used as an inflammatory marker in recent years.[12,13] It has been confirmed that liver tissue is one of the tissues producing PCT. Although PCT is affected by multiple factors, including an association with liver dysfunction, it has been reported that PCT levels were correlated with liver functional status, especially with bilirubin levels [14,15]. Very interestingly, data results from the cases generated by statistical analysis in this study suggested that the levels of ALT, AST, TBIL, DBIL, PCT, CT, CRP, PLT, PT, INR, PTA and AFP in Group B were significantly higher than those in Group A, well aligning with the requirement of statistically significant difference (Table 1). Furthermore, some indicators were consistent with the results of relevant studies in the literature

[16,17]. The statistically significant indicators between the two groups were analyzed by binary logistic regression, affording a high correlation among PCT, PT and slow plus acute liver failure. The evaluation formula was subsequently confirmed as well. Thus, the PT cutoff value was obtained as 16.65 s, with a sensitivity of 83.08% and a specificity of 92.45% (Table 2, Figure 1). The PCT cutoff value was obtained as 0.27, with a sensitivity of 73.85% and a specificity of 84.91% (Table 2, Figure 1). The evaluation formula (EF) cut-off value was 25.31, with a sensitivity of 92.31% and a specificity of 94.34% (Table 2). All the results revealed that the evaluation formula can assess the liver function status more effectively, providing simple and efficient way for the therapy of liver diseases. However, few example has applied PCT as the evaluation and prognostic index of liver function up to date, neither the combination of it with other liver function detection indicators to form an evaluation formula for clinical application. Compared to the current widely used noninvasive evaluation formula of APRI for liver fibrosis assessment in clinical practice [18] especially in those local and small hospitals, we demonstrated herein first time that PCT can also be used as an efficient evaluation formula to assess the liver function, prognosis, and in the usage of antibiotics as well. It also provides a simple and efficient tool for the primary health care workers. Arguably, there is report on PCT related to renal damage [19], but whether it is affected the final-stage liver disease is not clear yet and needs further investigation.

In summary, we demonstrated in this paper an efficient clinical and easily accessible liver failure evaluation formula correlated to PCT by the case study data of our clinical observation and statistical analysis. The protocol has been practically approved suitable for the application in local and primary hospitals, so as to better evaluate the treatment and prognosis of liver failure. It has been confirmed that PCT is significantly increased in patients with slow plus acute liver failure, along with high sensitivity and specificity, and that the evaluation formula of PT composition can be used to evaluate liver functions. Combined with the comprehensive evaluation of other inflammatory indicators, imaging data and clinical manifestations, this new method will not only provide an efficient and simple tool to evaluate the liver failures, but also to reduce the unreasonable application of antibiotics in patients with slow plus acute liver failure in clinical practice, so were the general health and wealth of the patients. The research on metabolic pathways of PCT in liver tissue is ongoing in our group with intensive efforts and will be published elsewhere in due course.

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