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• *BRIEF REPORTS* •

Analyses of prognostic indices of chronic liver failure caused by hepatitis virus

Xiao-Mao Li, Lin Ma, Yue-Bo Yang, Zhong-Jie Shi, Shui-Sheng Zhou

Xiao-Mao Li, Lin Ma, Yue-Bo Yang, Zhong-Jie Shi, Shui-Sheng Zhou, Department of Obstetrics and Gynecology, Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510630, Guangdong Province, China

Correspondence to: Professor Xiao-Mao Li, Department of Obstetrics and Gynecology, Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510630, Guangdong Province, China. tigerlee777@163.net

Telephone: +86-20-85515609 Fax: +86-20-87565575
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Abstract

AIM: To analyze the related indices about the prognoses of chronic liver failure caused by hepatitis virus.

METHODS: Retrospectively reviewed 320 cases of chronic liver failure caused by hepatitis viruses. An improved group and an ineffective group (IG) were made to compare and analyze their clinical manifestations, laboratory examination indices and complications. Logistic regression was also carried out.

RESULTS: There were significant differences (P<0.05) between the improved group and the IG upon such indices as age, bilirubin, prothrombin time, albumin, alpha fetoprotein, the size of liver and complications (P<0.05). The regression formula was as follows: $P = 1/(1+e^{-y})$ ($y = 1.7262-0.0948X_1+2.9846X_2+0.6992X_3+1.6019X_4+2.0398X_5$). (Note: X_1-Prothrombin activity; X_2-digestive tract hemorrhage; X_3-hepatic encephalopathy; X_4-hepatorenal syndrome; X_5-pulmonary infection.).

CONCLUSION: Laboratory examination such as bilirubin, prothrombin time and alpha fetoprotein can be regarded as indices of the prognoses of chronic liver failure caused by hepatitis. Moreover, the regression equation can evaluate prognoses more comprehensively and direct our treatments.

Key words: Chronic liver failure; Hepatitis; Prognostic indices; Laboratory indices; Complications; Regression equation

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INTRODUCTION

Hepatitis B virus (HBV) infection is very common in China[1-3]. Fulminant hepatitis (FH) refers to liver diseases that have severe states and poor prognoses, with a mortality rate of more than 50%[4]. In China, the majority of FH is chronic liver failure caused by hepatitis virus (CLFHV) (accounting for 85% of all FH), with the most common cause of HBV infection[5]. Because of the chronic underlying pathological changes (most commonly chronic hepatitis or liver cirrhosis), when liver failure led by necrosis of mass liver cell develops, treatments become more difficult. In order to improve our knowledge about the judgment of the prognoses of CLFHV, we conducted a retrospective study on the potential prognostic influencial factors on 320 cases of CLFHV patients to investigate into the ways of predicting the prognoses of CLFHV.

MATERIALS AND METHODS

The 320 CLFHV patients who met the clinical diagnostic grouping criteria made jointly by infectious diseases branch, parasitic diseases branch and liver diseases branch of Chinese Medical Association (2000, Xi' an)[6] were admitted to our hospital from January 2000 to June 2003. Two hundred and eighty-eight cases were male (90%) and 32 were female (10%), with an average age of 43.00±12.24 years (ranged from 15 to 77 years). Three hundred and one cases were single HBV infected, two were hepatitis E virus (HEV) infected and one with undetermined cause. There were 16 cases who were multi-infected: three were HBV+hepatitis C virus (HCV) infected, two were HBV+hepatitis D virus (HDV) infected, 10 were HBV+HEV infected and one was HBV+hepatitis A virus (HAV)+HDV infected.

We divided those 320 patients into two groups: 123 cases were in the effective group (EG) (improved in symptoms and signs on the whole or significantly, with liver function rebuilt or significantly improved) and 197 cases were in the ineffective group (IG) (discharged by themselves without improving or died in hospital). We compared their laboratory indices, B-ultrasonography, complications and such potential prognoses-influencing factors. Among them, the value of bilirubin was taken at the highest time in our hospital. The results were analyzed by SPSS 10.0 software. It would be significant if P<0.05.

RESULTS

Age

The average age in EG was 39.67±11.13 years and the counterpart in IG was 45.02±12.50 years, with significant difference (P<0.05).

Table 1 Comparison of laboratory indices of the two groups (mean±SD)

Items	Ineffective group	Effective group	Value of *P*
Glutamate-pyruvate transaminase (ALT)	196.70±291.74 U/L	215.54±349.53 U/L	>0.05
Glutamic-oxalacetic transaminase (AST)	214.05±234.75 U/L	207.93±233.69 U/L	>0.05
Alkaline phosphatase (ALP)	137.42±74.60 U/L	150.61±44.94 U/L	>0.05
Total bilirubin (Tbil)	612.332±195.943 μmol/L	506.624±184.454 μmol/L	<0.05
Direct bilirubin (Dbil)	356.837±119.196 μmol/L	306.827±112.52 μmol/L	<0.05
Serum albumin (ALB)	32.80±6.04 g/L	35.17±5.46 g/L	<0.05
Cholesterol (CHOL)	1.601±3.146 mmol/L	1.721±0.884 mmol/L	>0.05
Cholinesterase (CHE)	3 453.69±1 820.24 U/L	3 198.16±1 794.42 U/L	>0.05
Blood glucose (GLU)	4.609±3.932 mmol/L	4.650±2.303 mmol/L	>0.05
Blood urea nitrogen (BUN)	10.33±13.72 mmol/L	4.87±3.60 mmol/L	<0.05
Creatinine (Cr)	159.26±170.88 mmol/L	85.37±37.71 mmol/L	<0.05
Alpha fetoprotein (AFP)	111.46±177.53 ng/mL	170.45±230.25 ng/L	<0.05
Blood ammonia (NH_3)	101.80±54.03 μmol/L	75.23±38.71 μmol/L	<0.05
Prothrombin time (PT)	35.63±14.37 s	27.14±11.04 s	<0.01
Prothrombin activity (PTA)	23.44±9.36%	32.56±9.51%	<0.01

Laboratory indices

There were significant differences between those two groups on such indices as bilirubin, serum albumin (ALB), blood clotting functions, alpha fetoprotein (AFP), creatinine (Cr) and blood ammonia (NH_3), while there were no significant differences on aminotransferase, cholesterol (CHOL) or blood glucose (GLU) (Table 1).

Complications and the result of B-ultrasonography

There were more significant differences on complications and liver size between the two groups (Tables 2 and 3).

Table 2 Comparison of complication distribution of two groups

Items	Ineffective group, *n* (%)	Effective group, *n* (%)	*P*
Alimentary tract hemorrhage	39 (19.8)	4 (3.3)	<0.01
Hepatorenal syndrome	53 (26.9)	3 (2.4)	<0.01
Primary peritonitis	130 (66.0)	47 (38.2)	<0.01
Hepatic encephalopathy	136 (69.0)	17 (13.8)	<0.01
Infection of biliary tract	117 (59.4)	64 (52.0)	>0.05
Pulmonary infection	34 (17.1)	5 (4.1)	<0.01

Table 3 Comparison of B-ultrasonography of two groups

Items	Ineffective group, *n* (%)	Effective group, *n* (%)	*P*
Liver shrinkage	105 (53.3)	39 (31.7)	<0.01
Enlarge of spleen	125 (63.5)	76 (61.8)	>0.05
Ascites	159 (80.7)	89 (72.4)	>0.05

Analyses of influencing factors

We made Logistic Stepwise Regression about those variable factors. We put together glutamate-pyruvate transaminase (ALT)/glutamic-oxalacetic transaminase (AST), total bilirubin (Tbil)/direct bilirubin (Dbil), prothrombin time (PT) and prothrombin activity (PTA); blood urea nitrogen (BUN), creatinine (Cr) and hepatorenal syndrome. Together with age, ALB, CHOL, cholinesterase (CHE), AFP, liver size, hemorrhage and hepatorenal syndrome, *etc.*, we got 19 variables as regression factors. By Forward method, we got the regression model as follows: $P = 1/(1+e^{-y})$; ($y = 1.7262-0.0948X_1+2.9846X_2+0.6992X_3+1.6019X_4+ 2.0398X_5$); Note: X_1-PTA (numeric), X_2-digestive tract hemorrhage (0-none; 1-develops), X_3-hepatic encephalopathy (0-none; 1-degree I; 2-degree II; 3-degree III; 4-degree IV), X_4-hepatorenal syndrome (0-none; 1-develops), X_5-pulmonary infection (0-none; 1-develops). When $P>0.5$, the patient would get worse. Otherwise, the patient would improve. The coincidence of its rightness was 83.55%, which conformed to the reports abroad[7,8].

DISCUSSION

The mortality rate of CLFHV is very high. The pathological underlyings are mass apoptosis[9-11], necrosis or severe degeneration of liver cells, which lead to liver failure. There are abnormalities of many biochemical indices. The prognoses are related to the extent of liver cell necrosis, regeneration and whether complications will develop. Just as the statistical results of 320 cases in our study, PT and ALB, which represent synthetic functions of liver cells, Tbil and Dbil, which represent transportation function of liver cells[12], all have significant correlations with the prognoses of FH. The increased Tbil and Dbil, prolonged PT[13] and decreased ALB will suggest a poorer function of liver cells and a poorer prognosis. The older a patient is, poorer the ability of liver regeneration is, which is hard for recovery of liver function and leads to a poor prognosis. The increase of AFP in hepatitis is due to the acute reaction of liver cells after infected by viruses and this is also the regeneration label of liver cells after necrosis. A lower AFP suggests a poorer regeneration ability of liver cells and a poorer prognosis[14,15]. The prognosis of FH is greatly correlated with the incidence, amount and severity of complications. The increased and more serious complications will lead to poorer prognoses. Especially when hepatic encephalopathy IV, renal failure[16] or alimentary tract hemorrhage[17,18] develops, a high mortality rate will occur.

The purpose of our multi-factors regression model is to evaluate the influence of many factors on the prognoses of FH more objectively and comprehensively. It is easy for calculation receiving information and is good for observation of the effects of treatments. We applied Forward method to delete those not significant variables and got five variable factors such as PTA, alimentary tract hemorrhage, hepatic encephalopathy, hepatorenal syndrome and pulmonary

infection, which had significant influence on the prognoses of CLFHV, and further suggested that blood clotting function and development of complications are the key determinants of survival of CLFHV. It has been generally accepted that PTA<40% is the affirmative threshold of necrosis of liver cells[19]. The decreased PTA suggests a poorer liver synthetic function of blood coagulation factors and furthermore, the more severe necrosis of liver cells. While the other four variable factors were all complications, which further suggested the importance of the influence of complications on the prognoses of CLFHV. We should pay attention to the prevention and treatment of complications in treating CLFHV.

Heretofore, the treatment of FH has not matured, with a poor recovery rate. However, there are new treatments such as liver transplantation[20-24], which has brought new hope to patients with CLFHV[25-28]. During the course of diagnosis and treatment, the combination of dynamic observation of single indices and comprehensive judgment on prognoses can not only direct our treatments according to the change of condition, but also present objective criteria for timely liver transplantation to shorten the course of FH and relieve patients' burden.

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