

Portalsystemic hemodynamic changes in chronic severe hepatitis B: An ultrasonographic study

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Abstract

AIM: To evaluate portalsystemic hemodynamic changes in chronic severe hepatitis B.

METHODS: Hemodynamic parameters included portal vein diameter (PVD), portal vein peak velocity (PVPV), portal vein volume (PVV), spleen length (SPL), spleen vein diameter (SPVD), spleen vein volume (SPVV) and umbilical vein recanalization. They were measured by Color Doppler ultrasonography in 36 patients with chronic severe hepatitis B, compared with 51 normal controls, 61 patients with chronic hepatitis B, 46 patients with compensable cirrhosis, and 36 patients with decompensable cirrhosis.

RESULTS: In the group of chronic severe hepatitis B, PVD (12.38 ± 1.23 mm) was significantly different from the normal control, compensable cirrhosis and decompensable cirrhosis groups ($P = 0.000-0.026$), but not significantly different from the chronic hepatitis group. PVPV (16.15 ± 3.82 cm/s) dropped more significantly in the chronic severe hepatitis B group than the normal control, chronic hepatitis B and compensable cirrhosis groups ($P = 0.000-0.011$). PVV (667.53 ± 192.83 mL/min) dropped significantly as compared with the four comparison groups ($P = 0.000-0.004$). SPL (120.42 ± 18.36 mm) and SPVD (7.52 ± 1.52 mm) were longer in the normal control and chronic hepatitis B groups ($P = 0.000-0.009$), yet they were significantly shorter than those in the decompensable cirrhosis group ($P = 0.000$). SPVV (242.51 ± 137.70 mL/min) was also lower than the decompensable cirrhosis group ($P = 0.000$). The umbilical vein recanalization rate (75%) was higher

than the chronic hepatitis B and compensable cirrhosis groups. In the course of progression from chronic hepatitis to decompensable cirrhosis, PVD, SPL and SPVD gradually increased and showed significant differences between every two groups ($P = 0.000-0.002$).

CONCLUSION: Patients with chronic severe hepatitis B have a tendency to develop acute portal hypertension, resulting in significantly reduced portal vein perfusion. Observation of the portalsystemic hemodynamic changes may be contributed to the disease progression of chronic liver disease.

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Key words: Color doppler ultrasonography; Portalsystemic hemodynamics; Chronic severe hepatitis B

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INTRODUCTION

Chronic severe hepatitis carries a very high mortality rate (60%-80%), and causes about 22 600 deaths in China annually. It is widely known that progression of liver diseases is accompanied by histological changes of the hepatic parenchyma, such as inflammation, necrosis and fibrosis, as well as hemodynamic changes. Because hepatic circulation closely correlates to chronic liver disease, confirmation of the changes in the hepatic circulation is important for clarifying the disease progression. Liver biopsy is the gold standard for the grading and staging of the viral hepatitis. However, this procedure causes discomfort, and is invasive for the patients, especially those with prolonged prothrombin time^[1-3]. Ultrasonography has the advantages of low cost, easy operation and high acceptability by the patients. It can provide not only valuable information on the morphological changes of the liver but also liver hemodynamics by color Doppler flow imaging^[4-7]. The introduction of color Doppler

ultrasonography has been an important breakthrough in the noninvasive evaluation of splanchnic hemodynamics. Both qualitative and quantitative evaluations of the portalsystemic circulation are being widely used in patients with chronic hepatitis and cirrhosis^[8-10]. However, until the present, there have been only a few reports on portalsystemic hemodynamic changes in chronic severe hepatitis B in the literature. Furthermore, there is no consensus on the role of Doppler parameters in grading the severity of chronic liver disease^[11-16]. The purpose of this study is to evaluate portalsystemic hemodynamic changes in chronic severe hepatitis B non-invasively, and to delineate more definitively the role of Doppler parameters in patients with chronic hepatitis B and cirrhosis, as compared with normal subjects, chronic hepatitis B, compensable cirrhosis and decompensable cirrhosis patients.

MATERIALS AND METHODS

Subjects and diagnostic criteria

Between April 2005 and August 2007, 230 subjects were recruited in this study. Among them, 191 were males and 39 were females, with an average age of 34.7 ± 13.5 years (ranging from 10 to 77 years). According to the program of prevention and cure for viral hepatitis amended by the Chinese Society of Infectious Disease and Parasitology and the Chinese Society of Hepatology of Chinese Medical Association in the Xian meeting held in September 2000^[17], the subjects were divided into five groups: 36 patients with chronic severe hepatitis; 51 normal controls; 61 patients with chronic hepatitis B; 46 patients with compensable cirrhosis; and 36 patients with decompensable cirrhosis. There were no significant differences in the gender and age among these five groups. Diagnoses of patients in the control groups except the normal group were made on the basis of pathological examination of liver biopsy specimens and laboratory findings. Ethical approvals of the liver biopsy were obtained before the operations. Subjects in the normal control group had normal hepatic functions, and no histories of chronic liver disease. Compensable cirrhosis belonged to Child-Pugh A, the diagnostic criteria included $A \geq 35$ g/L, $Bil < 35$ μ mol/L, $PTA > 60\%$, and portal hypertension but no ascites, hepatic encephalopathy and upper gastrointestinal bleeding. Decompensable cirrhosis belonged to Child-Pugh B, C, the diagnostic criteria included serious hepatic function abnormalities, such as $A < 35$ g/L, $A/G < 1.0$, $Bil > 35$ μ mol/L, $PTA < 60\%$, and ascites, hepatic encephalopathy, upper gastrointestinal varices or bleeding. Diagnostic criteria of chronic severe hepatitis B^[18] included the basic conditions, i.e. the course of hepatitis B surface antigen-positive exceeded six months and the level of serum bilirubin in liver failure index exceeded ten times compared by normal level (17.1 μ mol/L), which was above 171 μ mol/L. Two additional conditions included (at least one liver failure index or more than one indexes below): (1) Prothrombin activity $< 40\%$; (2) Hepatic encephalopathy; (3) Ascites; (4) Progressive reduction in liver size; (5) Hepatorenal syndrome. Exclusion criteria for patients in

this study were autoimmunity hepatitis, alcoholic hepatitis, and the abnormality of cardiac and renal function accompanied by systemic hemodynamic changes.

Doppler measurements

All subjects were tested in the morning after an overnight fast and informed consents were obtained. All Doppler studies were performed with a color and pulsed Doppler unit (BIOSOUND AU4) armed with a 3.5-5.0 MHz convex probe. According to our previous study with the aim to select valuable ultrasonographic predictors for the evaluation of hepatic inflammation and fibrosis degree in chronic hepatitis^[10], we selected the following Doppler parameters for this study: portal vein diameter (PVD), portal vein peak velocity (PVPV), portal vein volume (PVV), spleen length (SPL), spleen vein diameter (SPVD), spleen vein volume (SPVV), and umbilical vein recanalization.

The conditions of Doppler measurement: the sampling size was nearly equal to the vessel diameter, the angle between the Doppler beam and the longitudinal axis of the vessel was kept at less than 60° . Portalsystemic Doppler parameters were automatically determined for all samples of the Doppler signal that lasted for more than two cardiac cycles. Doppler ultrasound parameters were measured in triplicate, and the results were averaged.

In order to reduce inter-observer variability to a non-significant level, all examinations were performed by one of the author's that was blind to the patients' clinical details. Feasibility of a satisfactory Doppler US examination was required for each patient recruited in this study. All patients were not affected by cardiopulmonary, circulatory, renal, or abdominal diseases and were not taking medications. The formula of blood volume was $(V) = 1/4\pi \times a \times b \times 0.57 V_{\text{peak}} \times 60$ (mL/min) a: antero-posterior diameter of vessel, b: transverse diameter of vessel, Unit: cm, V_{peak} : peak velocity.

Statistical analysis

Results were described as mean \pm SD and analyzed on the computer with SPSS 11.0 software (SPSS Inc, Chicago, IL, USA). Differences in means among the groups were evaluated by one-way ANOVA and LSD. Proportions were evaluated by χ^2 -test. P values < 0.05 were considered statistically significant.

RESULTS

Means of the portalsystemic hemodynamic parameters in different groups are shown in Table 1.

Differences of the portalsystemic hemodynamic parameters in different groups are shown in Table 2.

PVD in the chronic severe hepatitis group was significantly different from the normal control, compensable cirrhosis and decompensable cirrhosis groups, but not significantly different from chronic hepatitis B group. Among the four comparison groups, PVD gradually increased and was significantly different between every two groups with disease progression; PVPV in the chronic severe hepatitis group evidently decreased in comparison to the normal control, chronic hepatitis B

Table 1 Means of portalsystemic hemodynamic parameters in different groups

Group	<i>n</i>	PVD (mm)	PVPV (cm/s)	PVV (mL/min)	SPL (mm)	SPVD (mm)	SPVV (mL/min)
NCG	51	11.13 ± 0.91	26.15 ± 4.45	878.52 ± 177.07	94.88 ± 9.91	5.65 ± 0.96	160.66 ± 65.87
CHG	61	12.09 ± 1.14	22.42 ± 5.17	926.51 ± 188.24	105.64 ± 14.29	6.50 ± 1.44	250.96 ± 182.35
RCG	46	13.05 ± 0.87	18.52 ± 2.64	845.21 ± 173.67	120.28 ± 17.88	7.62 ± 1.84	309.43 ± 195.20
ICG	36	14.25 ± 2.42	16.95 ± 3.52	960.89 ± 472.91	152.89 ± 35.80	10.23 ± 3.06	625.43 ± 474.59
SCHG	36	12.38 ± 1.23	16.15 ± 3.82	667.53 ± 192.83	120.42 ± 18.36	7.52 ± 1.52	242.51 ± 137.70

NCG: Normal control group; CHG: Chronic hepatitis B group; RCG: Compensable cirrhosis group; ICG: Decompensable cirrhosis group; SCHG: Chronic severe hepatitis B group; PVD: Portal vein diameter; PVPV: Portal vein peak velocity; PVV: Portal vein volume; SPL: Spleen length; SPVD: Spleen vein diameter; SPVV: Spleen vein volume.

Table 2 Differences of portalsystemic hemodynamic parameters in different groups

Group and group	PVD (P)	PVPV (P)	PVV (P)	SPL (P)	SPVD (P)	SPVV (P)
NCG and CHG	0.000	0.000	0.424	0.033	0.014	0.086
NCG and RCG	0.000	0.000	0.576	0.000	0.000	0.008
NCG and ICG	0.000	0.000	0.174	0.000	0.000	0.000
NCG and SCHG	0.000	0.000	0.001	0.000	0.000	0.177
CHG and RCG	0.000	0.000	0.184	0.000	0.002	0.252
CHG and ICG	0.000	0.000	0.579	0.000	0.000	0.000
CHG and SCHG	0.320	0.000	0.000	0.001	0.009	0.881
RCG and ICG	0.000	0.090	0.061	0.000	0.000	0.000
RCG and SCHG	0.026	0.011	0.004	0.977	0.803	0.259
ICG and SCHG	0.000	0.413	0.000	0.000	0.000	0.000

NCG: Normal control group; CHG: Chronic hepatitis B group; RCG: Compensable cirrhosis group; ICG: Decompensable cirrhosis group; SCHG: Chronic severe hepatitis B group; PVD: Portal vein diameter; PVPV: Portal vein peak velocity; PVV: Portal vein volume; SPL: Spleen length; SPVD: Spleen vein diameter; SPVV: Spleen vein volume.

and compensable cirrhosis groups, but not significantly different from the decompensable cirrhosis group. Except the compensable and decompensable groups, PVPV gradually decreased and was significantly different between every two groups with disease progression; PVV in the chronic severe hepatitis group significantly decreased, but the decrease did not reach significant difference among the four control groups; SPL in the chronic severe hepatitis group remarkably increased in comparison to the normal control and chronic hepatitis B groups but remarkably decreased in comparison to the decompensable cirrhosis group, and there was no significant difference as compared with the compensable cirrhosis group. SPL gradually increased and was significantly different between every two groups with disease progression; SPVD in the chronic severe hepatitis group evidently increased in comparison to the normal control and chronic hepatitis B group, but evidently decreased in comparison to the decompensable cirrhosis group and there were no significant difference as compared with the compensable cirrhosis group. SPVV gradually increased and was significantly different between every two groups with disease progression; SPVV in the chronic severe hepatitis group significantly decreased in comparison to the decompensable cirrhosis group. There was no significant difference in the normal control, chronic hepatitis B and compensable cirrhosis groups.

The umbilical vein recanalization rates in different

Table 3 Umbilical vein recanalization rates in different groups

Group	Umbilical vein recanalization rate
NCG	0% (0/51)
CHG	0% (0/61)
RCG	22% (10/46)
ICG	56% (20/36)
SCHG	75% (27/36)

NCG: Normal control group; CHG: Chronic hepatitis B group; RCG: Compensable cirrhosis group; ICG: Decompensable cirrhosis group; SCHG: Chronic severe hepatitis B group.

Table 4 Differences of umbilical vein recanalization rates in different groups

Group and group	χ^2 values	P
RCG and ICG	9.954	0.002
RCG and SCHG	23.135	0.000
ICG and SCHG	3.003	0.083

NCG: Normal control group; CHG: Chronic hepatitis B group; RCG: Compensable cirrhosis group; ICG: Decompensable cirrhosis group; SCHG: Chronic severe hepatitis B group.

groups are shown in Table 3.

Differences of the umbilical vein recanalization rates in different groups are shown in Table 4.

The umbilical vein recanalization rate in the chronic severe hepatitis group significantly increased in comparison to the compensable cirrhosis group and there was no significant difference from decompensable cirrhosis group. There were no umbilical vein recanalizations in the normal control and chronic hepatitis B groups.

DISCUSSION

Chronic severe hepatitis B refers to patients with evidence of chronic liver disease that then develops acute decompensation of liver function. Usually, the acute decompensation of liver function is caused by one or more potentially reversible precipitating events, such as superimposed acute hepatic necrosis due to other hepatotropic virus infections drugs, alcohol, or ischemia sepsis, worsening renal function, and gastrointestinal bleeding. Chronic severe hepatitis often includes both acute-on-chronic liver failure and chronic liver failure^[19]. In China,

the majority of fulminant hepatitis is chronic liver failure caused by hepatitis virus B. Because of the underlying pathological changes of chronic hepatitis or liver cirrhosis, when liver failure leads to massive necrosis of the liver, treatments become more difficult^[20]. Obviously, chronic severe hepatitis B threatens the health of hepatitis patients because of its poor prognosis and high mortality.

Our results showed that there were no significant differences in PVV among the four control groups ($P = 0.178-0.580$), but PVV in the chronic severe hepatitis B group obviously decreased and was significantly different from the four comparison groups ($P = 0.000-0.004$). This reason may be, in our opinion, predominantly due to mechanical factors. As the liver disease progresses from chronic hepatitis to decompensable cirrhosis, hepatocellular inflammation, necrosis, development of regenerative nodules and collagen deposition, lobule reconstruction occur. These pathological changes may be resulted in gradual increase of portal vein circumfluence resistance, gradual decrease of portal vein velocity, and gradual dilation of portal vein diameter. In this process, dilation of the portal vein diameter may counteract the decrease in portal velocity, thus PVV was able to retain stability in a certain extent, so that hepatic perfusion could be maintained. However, in chronic severe hepatitis B, because of patchy areas of confluent massive hepatocellular necrosis, condensation of the reticulin framework of the lobule occurs in a short time, hepatic sinus interval becomes narrow, and even obstructed, and blood vessel bed decreases. Rapid increase of portal vein circumfluence resistance may be the result of these pathological changes, and may result in an obvious decrease in PVPV and acute portal hypertension formation. It was reported that patients with acute hepatitis and fulminant hepatitis developed portal hypertension with the aggravation of hepatic inflammation degrees^[21,22]. Additionally, PVD was difficult to dilate to compensate for PVPV decrease in time, so PVV significantly dropped in comparison to the control groups. Because PVV in chronic severe hepatitis significantly decreased (only 76% of the normal group), hepatic perfusion derived from the portal vein was insufficient, and hepatocellular ischemia and hypoxia deteriorated tissue injury. Meanwhile, chronic severe hepatitis B could occur as a result of hepatic ischemia and hypoxia, and finally formed a vicious circle severely affecting the prognosis. This hypothesis may provide a theoretical base for clinical experience of dilating hepatic vessel, relieving portal vein resistance, increasing PVV and perfusion, and improving hepatic microcirculation^[23].

There was no significant difference in PVPV between the chronic severe hepatitis B and decompensable cirrhosis groups ($P = 0.413$). The reason might be that PVPV in the two groups partly overlapped. It was well known that chronic severe hepatitis B included patients who had decompensable cirrhosis with < 40% prothrombin activity and total bilirubin > 171 $\mu\text{mol/L}$.

In the progression from chronic hepatitis to decompensable cirrhosis, PVD, SPL and SPVD gradually increased and showed significant difference between every two groups ($P = 0.000-0.002$). Our results revealed that PVD, SPL and SPVD were useful predictors of the disease progression from chronic hepatitis to decompensable

cirrhosis. This was identical with O'Donohue^[24].

Normally, after interruption of the placental circulation at birth, the umbilical vein collapses and forms the ligamentum teres in the adult. However, when portal hypertension occurs, the umbilical vein may recanalize and serve as a collateral route^[25,26]. It was recognized in 10%-29% of patients with portal hypertension^[27]. In our results, in the progression from chronic hepatitis to decompensable cirrhosis, the rate of umbilical vein recanalization gradually increased, but it was 75% (27/36) in the chronic severe hepatitis B group, which was obviously higher than that in the control groups. We considered that from chronic hepatitis to decompensable cirrhosis, portal pressure slowly rose and chronic portal hypertension formed, extensive collateral channels opening, portal vein dilation and spleen enlargement occurred. These factors could decompress portal system. However, in chronic severe hepatitis B, PVD and SPL could not compensate in time due to acute portal hypertension formation. Decompression of the portal system had to rely on collateral circulation formation such as umbilical vein recanalization. This was likely to be the reason for the higher rate of umbilical vein recanalization in chronic severe hepatitis.

In addition, there were other factors responsible for portalsystemic hemodynamic changes. Liver circulation included portal vein and hepatic artery perfusion^[28,29]. It was the limitation in this study that portal vein perfusion was measured alone. In recent years, some new techniques and methods have been introduced to the hemodynamic study in liver. For example, hepatic vein transit time was measured by spectral Doppler or pulse-inversion imaging^[30,31].

In conclusion, patients with chronic severe hepatitis B have a tendency to develop acute portal hypertension, resulting in an obvious decrease in portal vein perfusion. Observation of portalsystemic hemodynamic changes may contribute to the disease progression of chronic liver disease.

COMMENTS

Background

The introduction of color Doppler ultrasonography has been an important breakthrough in the noninvasive evaluation of splanchnic hemodynamics. The purpose of this study is to evaluate portalsystemic hemodynamic changes in chronic severe hepatitis B non-invasively, as compared with normal subjects, chronic hepatitis B, compensable cirrhosis and decompensable cirrhosis patients.

Research frontiers

Both qualitative and quantitative evaluations of the portalsystemic circulation are being widely used in patients with chronic hepatitis and cirrhosis. However, up to the present, there have been only a few reports on portalsystemic hemodynamic changes in chronic severe hepatitis B in the literature. Furthermore, there is no consensus on the role of Doppler parameters in grading the severity of chronic liver disease.

Innovations and breakthroughs

The article found that portal vein perfusion obviously decreased in chronic severe hepatitis B; portal vein diameter (PVD), spleen length (SPL), spleen vein diameter (SPVD) gradually increased and showed significant difference between every two groups in the progression from chronic hepatitis to decompensable cirrhosis.

Applications

This study was of important clinical values of evaluation portalsystemic hemodynamic changes in chronic severe hepatitis B and proved that Doppler

parameters could play an important role in grading the severity of chronic liver disease.

Terminology

Chronic severe hepatitis B refers to patients with evidence of chronic liver disease that then develops acute decompensation of liver function.

Peer review

This study was of important clinical values, which could comprehensively clarify portalsystemic hemodynamic changes in chronic severe hepatitis B, and grade the severity of chronic liver disease from chronic hepatitis to decompensable cirrhosis.

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