Echo-Doppler Measurements of Portal Vein and Hepatic Artery in Asymptomatic Patients with Hepatitis B Virus and Healthy Adults*

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Abstract

Background and aim. The aim of this prospective study was to determine the range of various hemodynamic parameters of portal vein and hepatic artery with echo-Doppler imaging in asymptomatic carriers of hepatitis B virus (HBV) and healthy adults. Methods. One hundred and twenty two healthy adults and fifty-three asymptomatic patients with chronic HBV formed two groups. All participants underwent color Doppler imaging of the portal vein and hepatic artery. A single operator performed all echo-Doppler measurements. The examination protocol included measurements of portal vein and hepatic artery diameter (d), blood flow (BF), time averaged velocity (TAV) and calculation of Doppler Perfusion Index (DPI) of liver. Results. Asymptomatic HBV carriers showed a statistically significant decrease in portal vein TAV (12.8±6.1 vs 17.5±8.8), an increase in portal vein BF (411.38±211.31 vs 327.55±188.77) and decrease in DPI (0.18±0.14 vs 0.28±0.15). Conclusions. Echo-Doppler measurements of portal vein and hepatic artery can detect significant hemodynamic changes in asymptomatic HBV carriers.

Key-words
Doppler ultrasound - liver - hepatitis B virus

Introduction

Abdominal ultrasound is a useful imaging modality, which can provide clinically important information when applied to patients with suspected chronic liver disease. Color Doppler imaging may further provide haemodynamic indices that may be correlated with the status of liver disease (1-3). The Doppler perfusion index (DPI) serves as a diagnostic tool that can be derived from the above measurements and there is evidence that it may reflect changes in liver blood flow in cases of underlying chronic liver disease (4). The role of DPI has been investigated in cases of metastatic liver disease (4), chronic hepatitis C (5), fatty liver due to obesity (6) and in alcoholic patients (7) although some reports render its contribution rather ambiguously (8).

Virus-related hepatitis is a global health problem worldwide, with a significant number of carriage-rates. It has been estimated that approximately 2 billion people worldwide have been infected with hepatitis B virus (HBV) and 350 to 400 million have chronic HBV infection with 520,000 dying each year (9). At present, liver biopsy remains the definite test for staging and grading HBV-related liver disease although it is an interventional procedure and carries a small risk of various complications. Therefore, the use of a non-invasive method for monitoring patients with chronic hepatitis B is of major clinical concern.

A number of positive correlation studies along with negative ones have investigated the role of Doppler sonography of liver disease in adults and healthy population (10-14). The aim of the present study is to investigate the hemodynamic changes of chronic liver disease due to HBV in asymptomatic carriers and compare them with healthy adults.

Material and methods

Population of the study

The recruitment of participants formed two separate groups that finally enrolled in the present study. The first group consisted of 122 healthy adults (72 female, 50 male, mean age 49.2 years, range 20 - 90 years) and the second group consisted of 53 asymptomatic patients with hepatitis B (28 female, 25 male, mean age 53.6 years, range 23 – 78 years).

The control group was chosen from healthy volunteers with normal blood profile. Volunteers with complex anatomy related to the hepatic artery were excluded from the study,
in order to technically facilitate the measurements required. None of the adults included in the healthy group consumed in excess of 28U alcohol per week, had a history of cardiac or liver disease, risk factors for viral hepatitis, or were receiving therapy with medications known to alter liver blood flow. Each subject had height and weight measured.

All carriers of HBV included in the study were asymptomatic, hepatitis B surface antigen (HbsAg) positive and with normal serum aminotransferase activities according to recent clinical and biochemical evaluation. The diagnosis of HBV was carried out with preceded biopsy. All patients belonged to the group of mild hepatitis on the basis of the histologic activity index according to Ishak classification (fibrosis f ≤ 2 and necroinflammatory score NI ≤ 3). Patients with biopsy proven liver cirrhosis, coincided with other hepatitis viruses or HIV or having abnormal imaging findings in previous US scan such as ascites, nodules, focal liver lesions, and abnormal liver attenuation were excluded from the study.

Oral informed consent was obtained from each subject in order to perform the sonographic examination.

Ultrasound technique

All asymptomatic patients and healthy adults fasted overnight or for 6 hrs before the sonography examination. All scans were performed with the patients lying supine using the same sonography system (ATL, HDI 3000) by a single experienced observer using a curvilinear 2,5-5MHz transducer. The machine was supported with the proper software for direct and automatic calculation of the hemodynamic parameters based on the spectral Doppler waveform.

The examination started with the observation of liver size and parenchyma in gray-scale scanning. Subsequently, the examination proceeded with spectral Doppler US. The parameters that were measured by Doppler US at the portal vein and hepatic artery were the following: diameter (d), time averaged mean velocity (TAV mean) and blood flow (BF). Diameter was measured in centimeters (cm), TAV in centimeters per second (cm/s) and BF in milliliters per minute (ml/min).

Doppler US measurements were calculated as an average of two uniform appearing consecutive waveforms on the Doppler tracing in each subject. A mean value was obtained to produce a more reliable and reproducible parameter. The Doppler Perfusion Index (DPI) was calculated by the use of the following formula:

\[ \text{DPI} = \frac{\text{BF}_{\text{HA}}}{(\text{BF}_{\text{HA}} + \text{BF}_{\text{PV}})} \]

The hepatic artery was measured as near its origin as was allowed by the angle of insonation or acoustic interference from adjacent vessels at the porta hepatis. At longitudinal view, the diameter was measured with calipers placed at right angles to the long axis of the vessel.

The portal vein was interrogated at the site of the crossing of the right hepatic artery, since no aberrant anatomy was present in the subjects participating in this study and measurements of diameter and time-averaged velocity were obtained. All measurements were performed with insonation angles between longitudinal axis and sound wave being less than 60° (15,16).

The occasional problem of overlying bowel gas was handled with either extension of the scanning time or by setting a new appointment the following day.

Statistical analysis

Results are expressed as mean values ± standard deviation (SD). Comparisons were performed between the group of HBV carriers and the group of healthy adults by ANOVA test (SPSS version 13.0). A p value of <0.05 was considered statistically significant. The type of distribution was tested using the Kolmogorov-Smirnov test.

Results

The sonographic findings of healthy adults and asymptomatic carriers are summarized in Table I.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy adults</th>
<th>HBV carriers</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(mean ±SD)</td>
<td>(mean ±SD)</td>
<td></td>
</tr>
<tr>
<td>PV diameter</td>
<td>0.78±0.15</td>
<td>0.82±0.13</td>
<td>↑NS</td>
</tr>
<tr>
<td>PV TAV</td>
<td>17.5±8.8</td>
<td>12.8±6.1</td>
<td>↓p&lt;0.05</td>
</tr>
<tr>
<td>PV BF</td>
<td>327.55±188.77</td>
<td>411.38±211.31</td>
<td>↓p&lt;0.05</td>
</tr>
<tr>
<td>HA diameter</td>
<td>0.38±0.08</td>
<td>0.34±0.1</td>
<td>↓p&lt;0.05</td>
</tr>
<tr>
<td>HA TAV</td>
<td>20.5±10</td>
<td>17.5±10.55</td>
<td>NS</td>
</tr>
<tr>
<td>HA BF</td>
<td>133.41±99.31</td>
<td>101.73±99.44</td>
<td>NS</td>
</tr>
<tr>
<td>DPI</td>
<td>0.28±0.15</td>
<td>0.18±0.14</td>
<td>↓p&lt;0.05</td>
</tr>
</tbody>
</table>

PV=portal vein; TAV=time average mean velocity; BF=blood flow; HTA=hepatic artery; NS=not significant

Measurements of portal vein and hepatic artery parameters were performed in all healthy adults and all HBV carriers. There was no statistically significant difference between the mean ages of healthy adults and HBV carriers. Portal vein diameter was greater in HBV carriers than in healthy adults but the difference was of no statistical significance. The hepatic artery diameter was found to be diminished in HBV carriers compared with healthy adults, and the difference was significant (Table I).

Portal vein TAV was lower in HBV carriers than in healthy adults (p<0.05). Hepatic artery TAV was 17.7±10.55 in HBV carriers and 20.5±10 in healthy adults, and no statistically significant difference between the two groups could be detected.

Portal vein BF was increased in HBV carriers compared with healthy adults (p<0.05). No statistically significant difference between the two groups regarding hepatic artery BF could be detected.

With respect to DPI, HBV carriers have significantly lower values compared with healthy adults.
Doppler ultrasound in asymptomatic HBV patients

Discussion

Abdominal ultrasound is the imaging examination of choice for the follow-up of patients infected with HBV due increased risk of developing hepatocellular carcinoma (HCC). Echo-Doppler measurements can reliably provide information related to the patency of portal and hepatic vessels and the direction of blood flow, but they do not possess an established role for the monitoring of patients infected with hepatitis (1,17,18). Furthermore, there are neither standard reference values related to the parameters of echo-Doppler measurements nor definite sonographic indexes for the assessment of the underlying liver disease. This is also reflected in the lack of standardization site of measurement related to the diameter of portal vein and hepatic artery that may vary from study to study (15). Therefore, discrepancies between reported data can be observed and most published data are based upon small control populations. Interestingly, the number of reported data regarding the diameter of hepatic artery is very limited (15).

Ultrasound is capable of accurately detecting and monitoring the nature of flow within hepatic artery and portal vein, provided that a number of technical parameters have carefully been optimized. These technical parameters are operator-dependent and include baseline, frame rate, wall filters, velocity range, angle correction, gate size and position. Changes in these parameters affect both the color and the spectral components of the Doppler examination. Failure to appropriately adjust these parameters may lead to misinterpretations and artifacts, which will affect the result of Doppler examination. For instance, if the color gain is set too low, it is possible that no flow will be detected on the monitor and if it is set too high, flow may be obscured by noise leading to a false Doppler signal. Therefore, thorough knowledge of all these parameters is essential in order to achieve the optimum quality of Doppler examination and improve the overall utility of liver Doppler ultrasound (16).

The comparison of various parameters between healthy adults and asymptomatic HBV carriers revealed some differences that may be of clinical value. Previous studies of patients with chronic liver disease and normal controls have shown that there is no difference related to portal vein diameter and this is in agreement with our findings (1,2,17).

Our findings related to portal vein TAV showed a significant decrease among asymptomatic HBV carriers that may be attributed to the underlying progression of fibrosis with distortion of parenchymal architecture. This hypothesis has also been suggested by previous studies (1,5,18,20,21) although it remains controversial due to conflicting results reported by other authors (4,15,19).

The portal vein BF showed a significant increase according to our study in asymptomatic carriers. Hyperemia of the liver parenchyma due to inflammation may explain the elevation of the above parameter (20). Nevertheless, there is documented evidence from other studies that reject the significance of this finding (4,18).

Our study found no significant differences related to TAV and BF of hepatic artery between asymptomatic carriers and healthy adults, although there was a trend to decrease. Therefore, the above parameters do not seem to contribute to the clinical evaluation at this stage. In cirrhotic patients, the flow in hepatic artery is affected by two compensating mechanisms. Whereas the ongoing distortion of the hepatic lobules results in the narrowing of vascular spaces, the overall decreased liver perfusion aims at the reverse effect (7,22). It has been reported that a significant increment in the BF and TAV of hepatic artery is evidence in advanced cirrhosis due to chronic hepatitis (4). It can be suggested according to our findings that hepatic artery tends to diminish BF and TAV in early stages of HBV, implying an initial decline that is significantly reversed in late stages.

There are a limited number of previous reports that refer to DPI changes in asymptomatic carriers of hepatitis. Our results showed a significant decrease of DPI in asymptomatic HBV carriers compared to healthy adults. These results are in disagreement with a number of previous reports that suggested a significant increase of DPI in patients with chronic liver disease (4,18) due to progressively obstructive portal venous flow and reciprocal increase in hepatic arterial flow. A possible explanation for this disagreement could be the different stage of liver disease. The degree of liver fibrosis may cause changes in hepatic artery hemodynamics in a non-linear fashion and therefore more studies need to be performed in order to understand the turning points of these alterations.

All studies agree, along with the present one, that there are detectable changes related to echo-Doppler measurements in portal vein and hepatic artery in patients with chronic liver disease (1-4,21-25) compared with the control group, yet not sufficient enough to provide a reliable index for clinical evaluation. These discrepancies may be attributed to several reasons. First, there are no standard techniques and parameters which can be measured in all studies. Secondly, the group of patients with chronic liver disease is heterogeneous in various studies and there are no reference values that could serve as a baseline for comparison. Thirdly, the reproducibility of the measurements has been questioned due to inter- and intraobserver variabilities that proved to be unacceptable in some studies.

The present study provided a control group of healthy adults in order to delineate the range of normal values related to basic hemodynamic parameters of portal vein and hepatic artery. In addition to that, the heterogeneity of the asymptomatic carriers group was kept to a minimum with respect to the status of their disease. Therefore, the above measurements may reflect a part of hemodynamic changes that take place during chronic HBV liver disease.

The reproducibility of Doppler measurements is related to the operator-dependent nature of ultrasound as an imaging modality. Nevertheless, dedicated investigators have proved that this is a feasible target. Further studies need to be conducted in larger groups of patients with HBV.
for the complete understanding of liver hemodynamics and standardisation of echo-Doppler measurements.

References