ASSESSMENT OF HEPATIC ENCEPHALOPATHY IN CHILDREN WITH LIVER CIRRHOSIS

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Abstract. Evolution of liver cirrhosis in children is accompanied by occurrence of complications of portal hypertension. Hepatic encephalopathy (HE) is not yet fully characterized and evaluation methods are still being perfected. Aim: To evaluate incidence and classify HE in a cohort of cirrhotic children. Materials and methods: The retrospective study was done upon 42 children diagnosed with liver cirrhosis. Assessment of HE was made by clinical elements and using a battery of psychometric tests. Results: HE was found in 67% of children with cirrhosis, 48% exhibiting minimal HE detected only by rigorous psychometric testing. No difference in HE score was observed in patients undergoing surgery, before and after the procedure. Conclusion: HE should be rigorously evaluated in children with liver cirrhosis, due to its important incidence and implications in the future of those children.

Keywords: hepatic encephalopathy (HE), psychometric testing

Introduction

During the course of cirrhotogenic evolution of chronic hepatopathies, the onset of complications of portal hypertension is a crucial moment. Digestive, neurological, renal, pulmonary manifestations of portal hypertension can overcome the practitioner by their gravity, optimal management of those conditions being a necessity for patients.

Hepatic encephalopathy (HE) is a syndrome with a series of neuropsychiatric abnormalities in patients with hepatocellular dysfunction, with or without porto-systemic shunting, after exclusion of any other known brain disease [1]. HE is the late consequence of portal hypertension with a high grade of porto-systemic shunts, spontaneous or surgically created. The pathogenesis of HE is based on diffuse impairment of cerebral metabolism as a consequence of diversion of portal blood into the systemic circulation through portosystemic collateral vessels [2].

The insufficient metabolization or liver shunting by toxic ammonium products of intestinal origin leads to accumulation of the latter in the brain, leading to a broad spectrum of clinical manifestations of HE [3, 4].

Clinical signs of hepatic encephalopathy are observed in 28% of patients with liver cirrhosis [5] and if we were to include the subclinical forms – up to 70% of patients with cirrhosis exhibit a degree of HE [6]. In the case of patients with portocaval or distal splenorenal shunts HE appears in 24-53% [7, 8].

In children with liver cirrhosis HE prevalence is not that well established. Yadav et al. [9] reports a prevalence of 32% of HE in children with extrahepatic portal vein obstruction. There are difficulties in appreciating the real extent of HE in children because of several reasons: (i) lack of standardized methods, (ii) particular pathogenic aspects of HE at pediatric age and (iii) possible confusing issues (mental development, cultural and social conditions).

Classification and nomenclature of HE has been recently revised by a Working Party Consensus (table I) [10].

Diagnosis of HE is mainly clinical. At present, the most widely used HE grading method is the West Haven Criteria (WHC) [11], based on the clinical
evaluation of the mental state. There are 5 grades of HE: 0 = absent or minimal HE, 1 = mild, 2 = moderate, 3 = severe manifestations, 4 = coma. As such, this method has been criticized for its poor sensitivity in differentiating milder forms of HE due to difficulties in detecting subtle neurocognitive impairments (table II) [12].

<table>
<thead>
<tr>
<th>HE type</th>
<th>Nomenclature</th>
<th>Subcategory</th>
<th>Subdivision</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Encephalopathy associated with acute liver failure</td>
<td>Episodic HE</td>
<td>Precipitated</td>
</tr>
<tr>
<td></td>
<td>Encephalopathy associated with portal-systemic bypass and no intrinsic hepatocellular disease</td>
<td>Persistent HE</td>
<td>Spontaneous</td>
</tr>
<tr>
<td>C</td>
<td>Encephalopathy associated with cirrhosis and portal hypertension / or portosystemic shunts</td>
<td>Minimal HE</td>
<td>Recurrent</td>
</tr>
</tbody>
</table>

Tabel I. Classification and nomenclature of HE [10]

<table>
<thead>
<tr>
<th>Grade</th>
<th>Level of consciousness</th>
<th>Personality and intellect</th>
<th>Neurologic signs</th>
<th>Electroencephalographic abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Subclinical</td>
<td>Normal</td>
<td>Abnormalities only</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inverted sleep pattern</td>
<td>Abnormalities on psychometric analysis</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Restlessness</td>
<td>Tremor</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Normal</td>
<td>Forgetfulness</td>
<td>Apraxia</td>
<td>Slow Alfa activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mild confusion</td>
<td>Incoordination and impaired handwriting</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Agitation and irritability</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimal disorientation for time or place</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtle personality change</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impaired behavior</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Lethargy</td>
<td>Inappropriate behavior</td>
<td>Asterixsis</td>
<td>Triphasic waves (5 cycles/s)</td>
</tr>
<tr>
<td></td>
<td>Slow responses</td>
<td>Impaired performance of subtraction</td>
<td>Ataxia and hypoactive reflexes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gross disorientation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>regarding place</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amnesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Somnolence but rousable</td>
<td>Confusion</td>
<td>Hyperactive reflexes</td>
<td>Triphasic waves (5 cycles/s)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Confusion</td>
<td>Babinski’s sign and muscle rigidity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disinhibited</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Coma</td>
<td></td>
<td>Decerebration</td>
<td>Delta activity</td>
</tr>
</tbody>
</table>

Tabel II. West Haven classification for grading mental status in HE [10, 11]

Mouzaki et al., in the context of acute liver failure, present a correspondent West Haven scale for children under 3 years of age (table III) [13]. Grade 0 HE includes both absence of HE and minimal HE. Minimal hepatic encephalopathy is a prevalent asymptomatic condition, especially in patients with advanced liver disease [14], with important consequences on everyday living. For the evaluation of minimal HE, there have been proposed a series of easy-to-use screening tests which assess the most important features: attention deficit and slow information processing [15, 16].

Psychometric Hepatic Encephalopathy Score (PHES) remains a ‘gold standard’ for the assessment of minimal HE, but its results clearly differ between studied populations. PHES includes Number Connection Tests (NCT) A and B, digit-symbol test.
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(DST), line tracing test (LTT) and serial dotting test (SDT) [17]. This battery is easily applied and has been shown to have a high specificity for the diagnosis of hepatic encephalopathy.

Besides clinical scales in grading HE, new criteria of evaluation include assessment of cognitive performance, EEG, neuroimaging of the brain (CT, MR), functional scales for assessing the impact of chronic low-grade HE [18]. As for quality of life, minimal HE does not have any influence in patients with cirrhosis [19].

Aim of the study

To evaluate prevalence of HE in a cohort of children diagnosed with liver cirrhosis of different etiologies and to classify the children according to HE stage.

Material and methods

The retrospective study was made upon 42 children diagnosed with liver cirrhosis in the 2nd Pediatrics Clinic of Iaşi, Romania over the course of 5 years (2005-2009). Etiology of liver cirrhosis was established using patient history and files. West Haven Criteria were used to assess the clinical stage of HE. Minimal HE was evaluated using standardized PHES battery tests (digit symbol test, number connection test-A, number connection test-B, serial dotting test, line drawing test). Z-score for HE was determined using an online free calculator, available at http://www.redeh.org/TEST_phes.htm; minimal HE was assigned for a Z-score value ≤ -5. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS, version 13.0, SPSS Inc., Chicago, USA).

Results and discussions

The mean age of patients was 12.3 ± 4.05 years (0-18 years), most of them diagnosed with liver cirrhosis beyond the age of 10, after long-term evolution of a chronic liver disease. The sex ratio in the study group was F/M = 1/1.32.

The etiology of cirrhosis was (decreasing frequency): viral (HBV, HBV+HDV, HCV, CMV), cryptogenic, malformative (biliary atresia), metabolic (Wilson disease) (figure 1).

Figure 1. Etiology of cirrhosis

Our results sustain the idea that viral infections are still the main cause of developing liver cirrhosis at an early age and prophylactic measures for stopping the transmission of viral hepatitis are needed.

Cirrhosis stage was assessed by Child classification (figure 2). More than half of the children were in Child A cirrhosis stage. Reversibility in cirrhosis is rare, thus Child A stage at pediatric age implies a reserved later prognosis (higher risk for decompensation and hepatocellular carcinoma at adult age).

Patients with liver cirrhosis diagnosed at small age (3 cases), of malformative or perinatal infection etiology, were placed, according to clinical criteria.
[13], in stage I EH. Other 5 older children were observed and diagnosed with stage I EH upon clinical criteria.

For school age and older children minimal HE was evaluated using PHES battery tests. Each patient had to fill-in all 5 categories of paper-pencil tests, according to precise instructions of completion and standardized monitoring. None of the patients exhibited any signs that would place him in a clinically manifest stage of HE at the moment of testing.

Test results were subsequently copied in the online form, along with age and degree of education for each patient. An overall test result was automatically calculated as the Z-score for PHES battery of tests. Values between -4 and +15 were considered as normal – no minimal HE, while Z-score ≤ -5 confirmed minimal HE. Test results shown in figure 3 state that in 1/3 of all children there was no HE, while in almost half of the cases latent HE was detected through psychometric testing, thus confirming the importance of this procedure (figure 3).

The overall prevalence of HE in the study group was 66.66%, out of which 47.61% (20 children) expressed minimal HE. One third of the children with liver cirrhosis had neither clinical signs nor latent HE, all of them labeled as Child A cirrhosis (figure 4).

Splenectomy emerged as a therapeutic surgical option in 18 patients, being accompanied by portosystemic shunting in 11 cases. The postoperative evolution was favorable in these patients during subsequent long-term monitoring (figure 5).

Psychometric testing was also performed on 12 patients before and after surgery, in order to see the impact of the surgical procedure on HE. There were no significant differences in the quantification of HE in those children before and after splenectomy, measured by Z-score values and confirmed by statistical testing (figure 6).

Splenectomy, with or without shunting procedures, has a relative efficiency in patients with portal hypertension, only improving the hematological parameters; the impact on the systemic complications of cirrhosis being questionable. The long term outcome of these patients is under the sign of acute fatal complications (fulminant hepatic failure, upper gastrointestinal bleeding), so that the only real hope

![Figure 2. Child classification](image)

![Figure 3. Psychometric testing results – Z-score](image)

![Figure 4. Prevalence of HE in the study group](image)

![Figure 5. Clinico-evolutive pattern of HE in the study group](image)
for these patients is liver transplantation.

Conclusions

The systemic impact of portal hypertension in the cirrhogenic evolution of chronic liver disease is a predictor of long-term evolution of the disease, leading to development of complications: esophageal varices, portal hypertensive gastroenteropathy, hepatic encephalopathy, hepato-pulmonary and hepato-renal syndrome.

HE was found in 67% of children with liver cirrhosis, in an overwhelming majority revealed only by accurate psychometric evaluation – minimal HE in 48% of cases.

Hepatic encephalopathy is not influenced by surgical interventions (splenectomy with or without porto-systemic shunting).

Proper and earlier assessment of minimal HE in children with liver cirrhosis can lead to better management of this condition later in adulthood.

References