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ORIGINAL ARTICLE

Chronic viral hepatitis C in pediatric age group; assessment of viral activity and hepatic fibrosis by ^{1}H magnetic resonance spectroscopy and diffusion weighted imaging in asymptomatic patient

Shereen Mansour Galal [a], Fardous Hanem Abdel Aal [a], Alam El-den Mohammed [a], Mohamed Zidan Mohamed [b,*], Yasser Gamal Abd El-Rahman [c]

[a] *Pediatrics Departments, Faculty of Medicine, Assiut University, Egypt*
[b] *Radiology Departments, Faculty of Medicine, Assiut University, Egypt*
[c] *Pathology Departments, Faculty of Medicine, Assiut University, Egypt*

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KEYWORDS

Hepatitis C;
Children;
MRS;
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Abstract *Background:* Chronic hepatitis C is the most common cause of chronic liver disease and cirrhosis. Egypt is the highest affected country with a prevalence of 22%. In children, seroprevalence of HCV is 0.2% in children less than 11 years of age and 0.4% in children equal and more than 11 years of age.

Aim of the work: The purpose of this study was to assess the value of ^{1}H MRS and DW-MRI as noninvasive tool in evaluation of activity and fibrosis of hepatic parenchyma in asymptomatic children with chronic hepatitis C.

Subjects and methods: Across-section study was conducted over a period of two years, included thirty children of asymptomatic chronic hepatitis C virus infection (mean age ± SD 14.1 ± 2.8 years) and twenty healthy children as controls were included. Abdominal ultrasonography, percutaneous liver biopsy, MRS and DW-MRI were done to all cases.

Results: The results showed that HCV infection was more common in our males (83.3%). The results of METAVIR grades showed 29 cases (99.9%) had activity while 17 cases (56.4%) had fibrosis. The results of MRS and DW-MRI showed significant differences between cases and controls and positive correlations between of the results of ^{1}H MRS with the results of liver biopsy (METAVIR grades and METAVIR stages).

Conclusion: Early diagnosis of asymptomatic chronic hepatitis C is essential to prevent or delay end stage chronic parenchymal liver disease. ^{1}H MRS may be a potential noninvasive helpful

Abbreviations: 1H-MRS, 1hydrogen magnetic resonance spectroscopy; DW-MRI, diffusion weighted magnetic resonance imaging; HCV, hepatitis C virus; Glx, glutamine–glutamate complex; PME, phosphomonoesters; Glyu, glycogen–glucose complex; ADC, apparent diffusion coefficient; METAVIR, meta-analysis of histological data in viral hepatitis; ALT, alanine transaminase; CVH, chronic viral hepatitis; HIV, human immunodeficiency virus; HCV RNA PCR, hepatitis C virus-ribonucleid acid-polymerase chain reaction.

* Corresponding author.

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diagnostic tool in the assessment of staging and fibrosis of asymptomatic chronic hepatitis C. The increase in metabolites were correlated with histopathological changes. DW-MRI can be considered as an effective predictor in the assessment of activity in chronic hepatitis C.

1. Introduction

Chronic hepatitis C is the most common cause of chronic liver disease and cirrhosis (1). Children represent only a small proportion of the hepatitis C virus (HCV) infected population. Nevertheless, a substantial number of children have chronic HCV infection and are at risk for complications. In children, seroprevalence of HCV is 0.2% in children less than 11 years of age and 0.4% in children equal and more than 11 years of age (2).

Chronic hepatitis C is marked by the persistence of anti-HCV antibodies (more than 0.8) with HCV RNA PCR (15–100.000.000 IU/ml) in the blood for at least 6 months after onset of acute infection. HCV is self-limiting in only 15–25% of patients in whom HCV RNA PCR in the serum becomes undetectable and ALT levels return to normal (2).

Liver biopsy will continue to be the reference standard in the assessment of the severity of diffuse liver disease until non-invasively measured markers are validated and clinically accepted. Several clinical limitations are associated with the use of liver biopsy. It is an invasive and costly procedure prone to complications, some minor, such as pain, others severe, the recorded risk of death being 0.01% (3–5).

MR spectroscopy has been found promising. Phosphorus-31 MR spectroscopy has been used to study liver metabolism in vivo (6–8). Lim and colleagues (6) found that in vivo ^{31}P-MR spectroscopy may be promising in evaluation of the severity of chronic hepatitis C. An important limitation of ^{31}P-MR spectroscopy, however, is that it cannot be used to measure hepatic lipid content, which plays an important pathogenetic role in the development of the inflammation and fibrosis associated with liver disease (9–13). Unlike ^{31}P-MR spectroscopy, ^{1}H-MR spectroscopy may be accurate for in vivo quantification of liver fat deposition (14,15).

Diffusion-weighted magnetic resonance imaging (DW-MRI) is a functional MRI technique that takes advantage of the diffusion properties of water molecules in biological tissues. The microscopic movement of water molecules in biological tissues can be measured by apparent diffusion coefficient (ADC) values derived from DW-MRI. The ADC values were reported to be inversely related to the degree of severity of CVH (16,17). In liver fibrosis, extracellular collagen fibers, glycosaminoglycans and proteoglycans may inhibit molecular diffusion of water, which suggest that DWI can be an effective method for the evaluation of fibrosis. However, considerable overlap in ADC values between tissues with cirrhosis and with no to moderate fibrosis was also observed (18).

2. Aim of the work

The purpose of this study was to assess the value of ^{1}H MRS and DW-MRI as noninvasive tools in evaluation of activity and fibrosis of hepatic parenchyma in asymptomatic children with chronic hepatitis C.

3. Patient and method

3.1. Patients

Thirty (25 males and 5 females) asymptomatic patients known to have chronic hepatitis C infection were included in this study that conducted in hepatology unit of Assuit university children hospital and radiology and pathology departments of Assuit university hospital from January, 2013 to December, 2014. They were aged 10–18 years and they were not treated by antiviral therapy. Inclusion criteria were the presence of anti-hepatitis C virus (HCV) antibodies detected by Enzyme Immunoassay (EIA) and a serum HCV-RNA by real-time quantitative HCV RNA PCR (more than 15 IU/ml) for more than six months. Patients with chronic hepatitis B, cirrhosis, autoimmune hepatitis and patients received antiviral therapy or lipid lowering medications as well as patients with co-infection as Epstein Barr virus, Cytomegalovirus, HIV virus or fascioliasis or with schistosomiasis were excluded.

Also twenty apparently healthy children of matchable age, sex, nutritional status and body mass index with nonreactive anti-HCV antibodies and undetected HCV RNA PCR, anti-hepatitis B virus or anti-HIV antibodies were taken as controls.

This study was approved by our internal committee of ethics. All patients and controls gave written informed consent (see Figs. 1 and 2).

Liver biopsy was performed after spectroscopic and diffusion weighted analysis in all subjects from the right lobe using a disposable automatic core biopsy 18-Gauge needle (Auto-Vac biopsy needle, Germany) under conscious sedation by intravenous valium and ultrasound guidance. The length of each liver fragment was about 15 mm length. All liver specimens were analyzed by an experienced pathologist blinded to results of MRS and DW-MRI. Histological features were analyzed for steatosis of increasing fat contents in liver and METAVIR group scoring system, consists of 5 stages according to the architectural features of the portal fibrosis: F0 = no fibrosis; F1 = portal fibrosis without fibrous septa; F2 = portal fibrosis and few fibrous septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis. When there was a disparity between 2 adjacent stages, scores were allocated for the more advanced stage in all children. The active grades including the intensity of necroinflammation were scored as: A0 = no histological activity; A1 = mild; A2 = moderate; A3 = severe (19,20).

3.2. MR spectroscopy and diffusion weighted imaging

All patients and control were subjected to ^{1}H MR spectroscopy and DWI upon Philips 1.5 T (Achieva, Philips