The Quantitative Evaluation of Liver Function Using Gd-EOB-DTPA : Deconvolution Analysis

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Introduction

Liver function is generally assessed by biochemical tests such as quantitative determination of liver enzymes. Measurements of liver enzymes reflect an escape of enzymes from liver cells and are an indirect measurement of hepatocyte injury. They do not directly reflect hepatocyte function. The direct measurement of hepatocyte function is therefore much desired and scintigraphy technique with deconvolution analysis was recently proposed [1]. In this study, we have developed a direct, noninvasive technique to quantitate hepatocyte function with deconvolution analysis of dynamic MR images obtained after administration of liver-specific MR agent, Gd-EOB-DTPA.

Methods and Materials

Hepatic injury model: Hepatic dysfunction was experimentally induced in adult New Zealand white rabbits (n=7, average body weight=3.5kg) using 20% carbon tetrachloride (CCl4, Sigma Chem. USA). The animals received the mixture of CCl4 (0.4 ml/kg) and olive oil (1.6 ml/kg) using oral intubation 3 times a week to induce hepatic injury.

MR imaging: All MRI studies were performed on a 1.5T MR scanner (Vision Plus, Siemens) with human extremity coil. The animals were anesthetized with intramuscular injection of ketamine (35 mg/kg) and xylazine (5 mg/kg). After bolus injection of Gd-EOB-DTPA through ear vein, the 150 dynamic MR images were obtained using turbo-FLASH sequence (TR/TE = 11/4.2 msec, flip angle = 15) with 1.5 sec time interval. The time-intensity curves were measured at abdominal aorta and liver parenchyma.

Deconvolution Analysis: Deconvolution analysis of the aorta (input function) and hepatic (output function) time-intensity curves was performed with a modified Fourier transform technique. Both aorta and liver curves are extended to many times their original length by appending a low-frequency, smoothly tapering curve to the original data series to compensate for high-frequency artifact caused by the abrupt termination of data input at the conclusion of the imaging procedure. Finally, the inverse Fourier transform was performed and the resultant deconvoluted curve, which represents true liver response, was obtained. An exponential curve of best fit was applied to the deconvoluted liver curve and the y-intercept of this curve was used as representing hepatic extraction fraction (HEF).

Biochemical Test and Histopathologic findings: Blood biochemical test includes the measurement of aspartate aminotransferase (AST) and ALT. For histopathologic examination, the liver specimens of both normal and hepatic injury groups were stained with hematoxylin-eosin and examined microscopically.

Results and Discussion

The MR time-intensity curves, which measured at abdominal aorta and liver parenchyma were shown in Fig. 1. Due to recirculation of Gd-EOB-DTPA, the aorta curve showed small residual signals after first pass of contrast agent. However, calculation of the hepatic response function by means of deconvolution analysis corrects the liver time-intensity curve for the constantly changing blood concentration of contrast agent presented to the liver at each moment in time, thus compensating for the systemic recirculation of the agent. Therefore, the resulting hepatic response function mathematically simulates a single bolus injection of contrast agent directly into the hepatic blood supply. Fig. 2 showed the one of typical deconvoluted liver response curves of normal and hepatic dysfunction group. After normalizing the HEF of normal liver as 100%, the deconvoluted curve of dysfunction group revealed less hepatocyte extraction efficiency (HEF=82%). The blood biochemical studies showed that AST and ALT levels were (39.6 ± 4.8) and (60.9 ± 9.4) for normal group whereas AST and ALT levels were (144.7 ± 20.5) and (192.5 ± 45.4) for dysfunction group. The enormous increase of these levels in dysfunction group suggests the acute hepatic injury. However, the change of these liver enzymes reflect escape of enzymes from liver cells and do not directly reflect hepatocyte function. On the other hand, the liver-specific agent, Gd-EOB-DTPA, is uptaken and excreted by hepatocyte. Thus, the HEF from deconvolution analysis is a direct measurement of intact hepatocytes and it should be helpful in providing a quantification of liver dysfunction. Photomicrograph of the resected specimen of normal and injured liver cells were shown in Fig. 3. The histopathologic finding revealed that the thick fibrous capsule and lymphocyte infiltration were presented in the injured liver cells.

Conclusion

Deconvolution analysis with liver-specific MR agent is a direct, noninvasive technique for quantitative evaluation of liver function and may also be valuable in detection of subtle changes in patho-physiology and in comparison of sequential studies.

References

[1] T Vasundhara et al. Clinical Nuclear Medicine, 24:655-659 (1999)

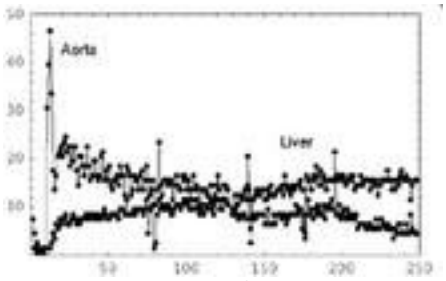

Fig. 1 The time-intensity curves of aorta and liver parenchyma after bolus injection of Gd-EOB-DTPA.

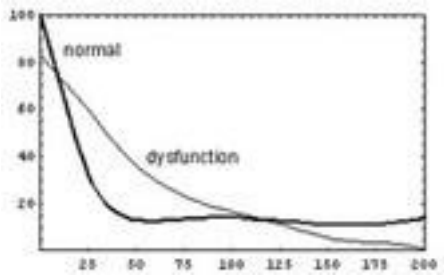

Fig. 2 The deconvoluted liver response curves for normal and dysfunction groups. The hepatic dysfunction group showed less hepatic extraction efficiency.

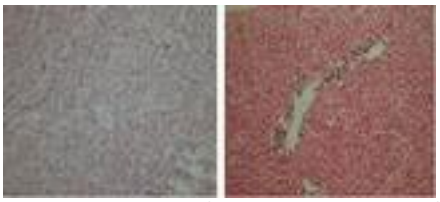

Fig. 3 The photomicrograph of the resected specimen of normal (left) and injured (right) liver cells. The fibrous capsule and lymphocyte infiltration were observed in the injured liver cells