Magnetic resonance imaging with Mn-DPDP in cirrhotic rat livers

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Purpose

To study the effect of cirrhosis on hepatic transport of Mn-DPDP, a hepatobiliary contrast agent, the MR signal intensity (SI) enhancement was measured over time during perfusion of Mn-DPDP in livers isolated from rats which have previously had a bile duct ligation (BDL) 30 or 60 days before liver perfusion.

Materials and Methods

Biliary cirrhosis was induced by a BDL performed 30 and 60 days before the experiments. To quantify the severity of cirrhosis, hepatic tissues were collected and 3 µm paraffin sections from the right and left lobes were stained with hematoxylin eosin and Masson-Goldner. To evidence the extracellular diffusion space, each liver were first perfused (37°C, 35 mL/min) with KHB solution + 0.5 mM Gd-DTPA during 20 min (extracellular distribution of Gd-DTPA) and KHB solution during 10 min (hepatic elimination of Gd-DTPA). Then, the same livers were perfused with 0.5 mM Mn-DPDP during 30 min (extracellular distribution and hepatocyte entry of Mn-DPDP) and KHB solution during 30 min (hepatic elimination of Mn-DPDP). MR imaging was performed at 1.5 T. Axial image was obtained using a fast-gradient echo T1 weighted MR sequence (FAST) preceded by a 90° saturation pulse with the following parameters: repetition time (6.8 msec); echo time (3 msec); flip angle (90°); matrix 256 x 256; 1 image / 8 sec; FOV 14 cm; slice thickness 0.7 cm. Mean SI was measured in a region of interest (ROI) drawn on the short axis view of the liver excluding all large vessels. For each liver, the SI measured in the ROI was normalized to muscle SI and for comparison between experiments, the SI was normalized to the baseline value.

Results and discussion

Following BDL, cholangiocytes proliferated and formed an organized network of well-defined tubular structures (Fig. 1). Ductular hyperplasia predominated in the portal areas in 15-days BDL livers and extended to the entire hepatic parenchyma in 30- and 60-days BDL livers. Fibrosis also extended with the duration of BDL: fibrous connective tissue septa bridged portal areas and the normal lobular pattern was disorganized. During the perfusion of the extracellular contrast agent Gd-DTPA, the SI increased slightly (Fig. 2). The SI returned to baseline value during the following KHB perfusion. The increase in SI was much higher during the perfusion of Mn-DPDP, a contrast agent that enters in hepatocytes after the extracellular distribution. During the following KHB perfusion the SI slowly decreased. The SI during Mn-DPDP perfusion decreased significantly and progressively (Kruskal-Wallis test: $P = 0.027$) according to the severity score of cirrhosis (Table 1).

Conclusion

Our study clearly shows that experimental bilirary cirrhosis is associated with a concomitant decrease in hepatic SI enhancement during Mn-DPDP perfusion, the higher the severity of biliary cirrhosis, the lower the transport of Mn-DPDP into hepatocytes. Thus, MRI with Mn-DPDP injection can be used to evaluate hepatic injury that increased with the duration of BDL-induced cirrhosis.

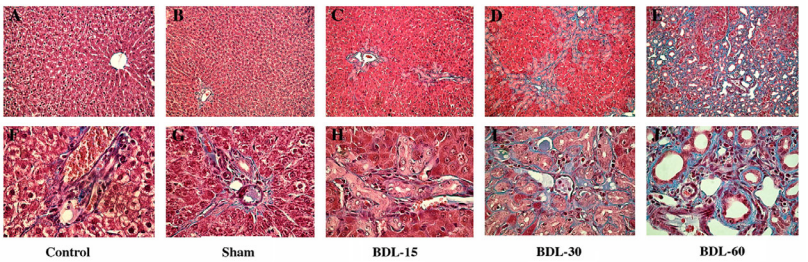

Fig. 1. Hepatic tissues were stained with Masson-Goldner. Control livers (A and F); sham livers (B and G); livers isolated from rat with a 15-days BDL (C and H); livers isolated from rat with a 30-days BDL (D and I); livers isolated from rat with a 60-days BDL (E and J).

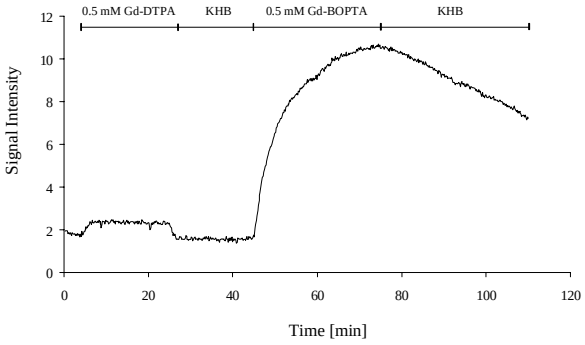

Fig. 2. Hepatic kinetics of the extracellular contrast agent Gd-DTPA and the extra and intracellular contrast agent Mn-DPDP in a control liver. Signal intensities measured in a region of interest drawn on the short axis view of the liver were recorded over time.

Tab. 1. Median [min-max] SI measured at the end of the 0.5 mM Gd-DTPA and 0.5 mM Mn-DPDP perfusion (n = 4 in each group)

	Gd-DTPA	Mn-DPDP
Control	0.29 [0.18-0.46]	8.98 [6.94-9.60]
30-days BDL	0.28 [0.25-0.29]	4.39 [3.60-4.75]
60-days BDL	0.47 [0.44-0.50]	3.23 [1.36-3.24]