Mapping of liver function in thioacetamide-induced rat acute liver injury using an empirical mathematical model and dynamic contrast-enhanced MRI with Gd-EOB-DTPA

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INTRODUCTION

Various liver-specific contrast agents for magnetic resonance imaging (MRI) have been introduced to increase the accuracy of liver imaging [1]. Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA), a hepatocyte-targeted contrast agent, has been used recently for diagnosis of liver diseases [2] [3].

Our purpose of this study was to evaluate thioacetamide (TAA)-induced acute liver injury in rats using an empirical mathematical model (EMM) and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) with gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA).

MATRIALS AND METHODS

Eighteen rats were divided into 3 groups [normal control (n = 6), TAA (140) (n = 6), and TAA (280) groups (n = 6)]. The rats of the TAA (140) and TAA (280) groups were intravenously injected with 140 and 280 mg/kg body weight (BW) of TAA, respectively, while those of the normal control group were intravenously injected with the same volume of saline. DCE-MRI studies were performed using Gd-EOB-DTPA (0.025 mmol Gd/kg; 0.1 mL/kg BW) as the contrast agent, 48 hours after TAA or saline injection. After the DCE-MRI study, blood was sampled and serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were measured. We calculated the rate of contrast uptake (α), the rate of contrast washout (β), the elimination half-life of relative enhancement (RE) ($T_{1/2}$), the maximum RE (RE_{max}), and the time to (RE_{max}) (T_{max}) from time-signal intensity curves using EMM.

RESULTS and DISCUSSION

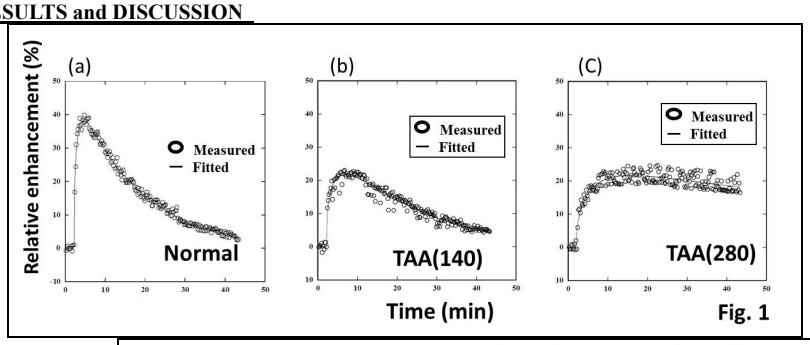

Fig. 1

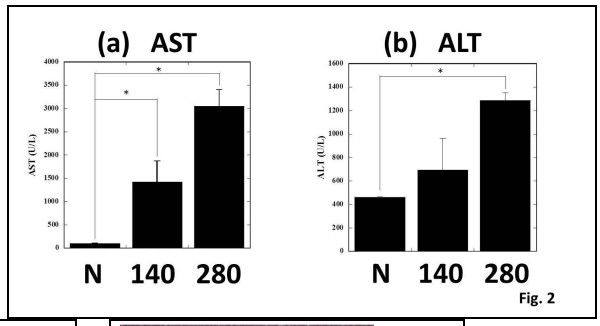

Fig. 2

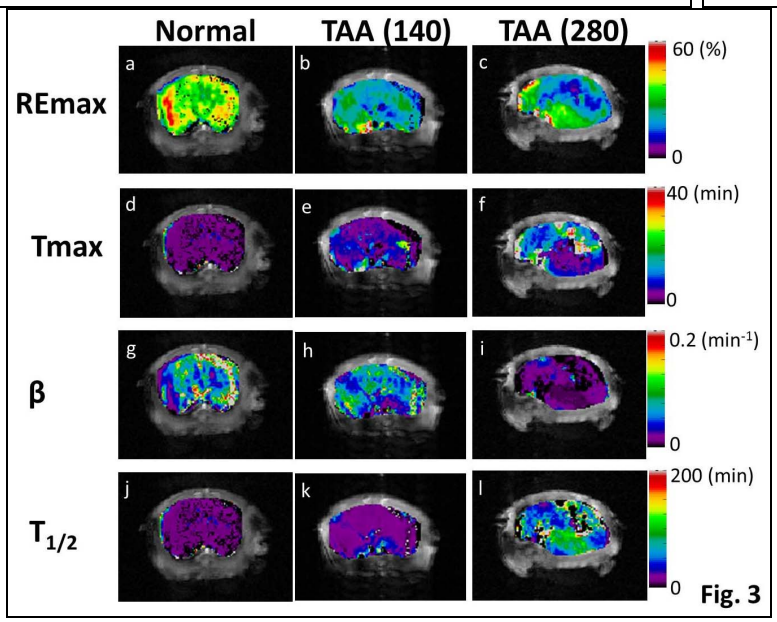

Fig. 3

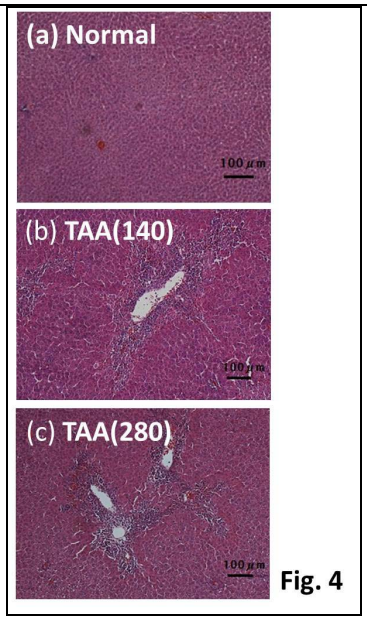

Fig. 4

Fig. 1. Time course of relative enhancement before and after injection of Gd-EOB-DTPA at 0.025mmol/kg in the normal control (a), TAA (140) (b), and TAA (280) groups (c), in which the open circles and solid lines represent the measured and fitted data, respectively. TAA (140) denotes the group in which the rats were intravenously injected with 140 mg/kg body weight (BW) of Thioacetamide (TAA), while TAA (280) denotes the group in which the rats were injected with 280 mg/kg BW of TAA. In the normal control group, the rats were injected with the same volume of saline. **Fig. 2.**(a) Serum aspartate aminotransferase (AST) level in the normal control, TAA (140), and TAA (280) groups. (b) Serum alanine aminotransferase (ALT) level in the normal control, TAA (140), and TAA (280) groups. There were significant differences in AST between the normal control and TAA (140) groups and between the normal control and TAA (280) groups. There was also a significant difference in ALT between the normal control and TAA (280) groups. Error bar represents the standard error (SE). *P<0.05. **Fig. 3.** Images generated by calculating each parameter on a pixel-by-pixel basis in the normal control (left), TAA (140) (middle) and TAA(280) groups (right). (a - c) for the maximum relative enhancement (RE_{max}), (d - f) for the time to the RE_{max} (T_{max}), (g - i) for the rate of contrast washout (β), and (j - l) for the elimination half-life of relative enhancement ($T_{1/2}$) maps. It was clearly demonstrated that the RE_{max}, and β maps were reduced and the T_{max} and $T_{1/2}$ maps were prolonged in the TAA (280) group compared to those in the normal control and TAA (140) groups. **Fig. 4.** Light micrographs of the liver tissue stained by hematoxylin and eosin in the normal control (a), TAA (140) (b), and TAA (280) groups (c). Calibration bar (100 μm) is also shown. Liver necrosis and infiltration were observed in the central areas in TAA (140) and TAA (280) groups.

CONCLUSION

In conclusion, this study demonstrated that the EMM is useful for the assessment of TAA-induced rat acute liver injury using DCE-MRI with Gd-EOB-DTPA.

REFERENCES

[1] Ba-Ssalamah A, et al. Eur Radiol 2009.[2] Weinmann HJ, et al. Magn Reson Med 1991.[3] Reimer P, et al. Eur Radiol 1997.