学 位 論 文 の 要 旨

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学 位 論 文 名	Ferucarbotran Expands Area Treated by Radiofrequency Ablation in Rabbit Livers
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論 文 内 容 の 要 旨

INTRODUCTION

Radiofrequency ablation (RFA) is one of the first-line treatments for patients with hepatocellular carcinoma (HCC). Since microscopic satellite nodules are sometimes present around the main tumor, the ablated area must maintain a treated margin of 5-10 mm to prevent local recurrence after RFA. As a result, several approaches to enlarge the RF-ablated area have been investigated.

Ferucarbotran is a contrast agent used for magnetic resonance imaging (MRI) that contains superparamagnetic iron oxide (SPIO), which generates heat in an RF electric field and may have an effect in areas treated by RFA. We investigated whether ferucarbotran administration expands the RF-ablated volume using a rabbit model.

MATERIALS AND METHODS

A total of 15 male Japanese white rabbits (16 weeks old) were used and divided into 3 groups of 5 each. A 1-ml saline solution was administered intravenously into a dorsal ear

vein in the control group, while 1 ml of ferucarbotran solution (0.016 ml/kg body weight) was given to the common dose group and 1 ml of a 2-fold concentrated ferucarbotran solution (0.032 ml/kg body weight) was given to the high dose group. Four hours after the administration, rabbits were anesthetized by an intravenous injection of pentobarbital (30 mg/kg body weight). Under the guidance of real-time ultrasonography, RFA was performed in the livers using a single inside-cooling-type 17 gauge electrode with a 2-cm long exposed tip for 8 minutes. RF parameters were recorded during the procedure. Immediately thereafter, the rabbits were euthanized and a T1-weighted fast-low angle shot sequence scan was performed. To confirm the distribution of ferucarbotran in the liver, the signal intensities from the uninvolved hepatic parenchyma and dorsal muscle were measured, and liver/muscle signal intensity ratios calculated. The total volume of the ablated area in each rabbit was calculated to integrate the volume in each MR image slice, which was calculated to multiply the area of thermal lesion, measured using image processing software, and section thickness (1.88 mm). Following MRI, the livers were resected and the maximum short axis diameter of the ablated area in each was measured.

Data values are expressed as the means ± SD. Statistical analysis was performed with ANOVA. A P value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Under the guidance of real-time ultrasonography, the insertion of the RF electrode into the liver was performed easily without complications in all rabbits. None of the rabbits died during the RFA procedure. Further, there were no significant differences among the 3 groups for all RF parameters.

MR image analysis results demonstrated that the liver/muscle signal intensity ratio was significantly decreased in the rabbits that received ferucarbotran (control group, 1.32 ± 0.06; common dose group, 0.79 ± 0.08; high dose group, 0.54 ± 0.15), while the diminution of

intensity was homogeneous in each image slice. These results confirmed that ferucarbotran had been taken equally into the hepatic parenchyma at 4 hours after administration in each of the groups.

The RF-ablated area was shown by MR imaging as a high intensity area or a high intensity rim. The volume of the ablated area estimated on MR images in the ferucarbotran-administered groups was significantly larger than that in the control group, though there was no statistically significant difference observed between the common dose and high dose groups (control group, 5.9 ± 1.1 cm^3; common dose group, 12.3 ± 1.9 cm^3; high dose group, 12.3 ± 3.4 cm^3). In addition, macroscopic assessment showed that the maximum short axis diameter had a tendency to increase with ferucarbotran administration (control group, 24.5 ± 2.1 mm; common dose group, 24.8 ± 3.6 mm; high dose group, 26.7 ± 3.6 mm). We considered it possible that the specific heat generated with ferucarbotran in the RF electric field made the ablated area larger, as compared with the control group.

Since the number of Kupffer cells in HCC decreases in accordance with the progress of dedifferentiation of the tumor, ferucarbotran is scarcely taken into an HCC tumor. However, normal liver tissue surrounding the tumor contains a number of Kupffer cells and ferucarbotran is equally distributed there. In the present study, the ablation procedure was performed using the impedance control mode, which is utilized clinically for RFA therapy, and the volume of the ablated area was not excessively expanded following the administration of ferucarbotran (about 12 cm^3 with the electrode exposed 2 cm). Further, other portions of the liver and other organs were not injured, and none of the rabbits died during the RFA procedure. Therefore, RFA using ferucarbotran for patients with HCC was found to be safe and is proposed as an effective technique to extend the ablation volume.

CONCLUSION

Ferucarbotran may expand the ablated area by RFA.