

The effect of Gd-DTPA dose on renal function in a rat cisplatin-induced chronic renal failure model

T. Tsuji¹

¹Scientific Investigation, Medical Scientific Affairs, BU Diagnostic Imaging, Nihon Schering K.K., Osaka, Japan

Synopsis

We investigated about the relationship between dose of gadolinium (Gd) contrast agent and deterioration of renal function in a rat cisplatin-induced chronic renal failure (CRF) model, received intraperitoneal injection of the cisplatin solution weekly for 10 weeks at a dose of 1 mg/kg body weight. The body weight and serum creatinine was no significant difference among 0.1, 0.2 and 0.3 mmol/kg of Gd-DTPA intravenous administration and saline group. In conclusion, from 0.1 to 0.3 mmol/kg of Gd-DTPA injection have no effect on renal function in CRF model rat.

Materials and Methods

<Animal model> Cisplatin was dissolved into saline at a concentration of 1 mg/mL. Twenty-eight male Wistar rats, weighing about 300 g, were split into 4 groups of 7 rats. Each rat was intraperitoneally injected the cisplatin solution weekly for 10 weeks at a dose of 1 mg/kg. During the entire study period, all rats were maintained under specific pathogen-free conditions at 22 ± 2 °C with 12 hr of artificial lighting from 7 am, and were fed chow pellets and water ad libitum.

<Administration of contrast agent> Eighty-five days after the first injection of cisplatin, Gd-DTPA (Magnevist, Schering AG, Germany) was intravenously injected into 3 groups at a dose of 0.1, 0.2 or 0.3 mmol/kg. As a control, 0.2 mL/kg of saline was intravenously injected instead of Gd-DTPA.

<Blood sampling> One day before and 1, 2, 3 and 7 days after intravenous injection of Gd-DTPA, blood was collected via a jugular vein of all rats in each group, under anesthesia with ketamine. Whole blood was separated by centrifugation and the serum was analyzed for creatinine concentrations.

<Statistical analysis> The differences in the body weight and the creatinine concentration among the 4 groups were examined by Tukey-Kramer test. The difference between the baseline (1day before) and the peak of serum creatinine level after intravenous injection of Gd-DTPA in each group was evaluated by Student-t test.

<Definition of contrast-induced nephropathy> Contrast-induced nephropathy (CIN) was defined as an increase in serum creatinine level of more than 0.5 mg/dL or by a 25% of the baseline level based on the previous reports 2-5)

Results

The body weight in each group was almost same from 1 day before to 7 days after intravenous (iv) injection of Gd-DTPA (Fig.1). There was no significant difference in the body weight among the 4 groups. The baseline and the peak of serum creatinine after iv injection of Gd-DTPA had similar values in each group (Fig. 2). There was no significant difference between the baseline and the peak of serum creatinine in each group. The serum creatinine in each group was almost same between 1 day before and 1 day after iv injection of Gd-DTPA, and slightly decreased from 2 days after iv injection of Gd-DTPA (Fig. 3). There was no significant difference in the serum creatinine among the 4 groups. The all rats in each group had no increase in serum creatinine of more than 0.5 mg/dL of the baseline level. On the other hand, 1 of 7 rats in saline group, and 2 of 7 in Gd-DTPA 0.2 and 0.3 mmol/kg group increased in the serum creatinine more than 25% of the baseline level.

Discussion

In our best knowledge, the relationship between dose of Gd contrast agent and deterioration of renal function was not clearly shown so far 1-4,6-8). Because the comprehensive study in patients or animals with multiple doses, such as 0.1, 0.2 and 0.3 mmol/kg, had not been performed. In the present experimental study, it was revealed that from 0.1 to 0.3 mmol/kg of Gd-DTPA caused no change in serum creatinine level in the rat CRF model. However, the experiment about the effect of Gd-DTPA on renal function in the case of severe renal damage has not been performed. It might be necessary to do additional study in rats with severe CRF.

Conclusion

From 0.1 to 0.3 mmol/kg intravenous administration of Gd-DTPA have no effect on renal function in CRF model rat

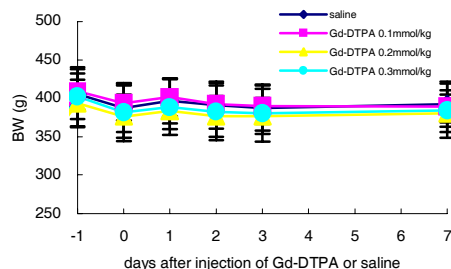


Fig.1 The change of body weight in the 4 groups (n=7, mean±SD). No significant difference among the 4 groups by Tukey-Kramer test.

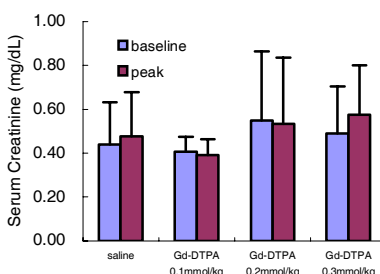


Fig.2 Baseline and peak of serum creatinine after iv injection of Gd-DTPA or saline (n=7, mean±SD). No significant difference between the baseline and the peak of serum creatinine in each group by Student-t test.

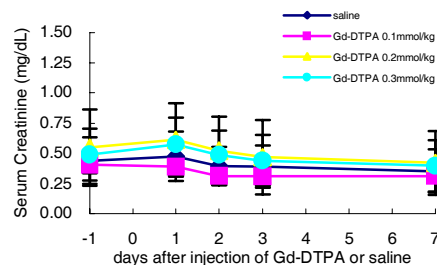


Fig.3 The change of serum creatinine in the 4 groups (n=7, mean±SD). No significant difference among the 4 groups by Tukey-Kramer test.

References

- 1) Thomsen HS et al. Academic Radiology, 1996, 3, Suppl2, S444-S446 /
- 2) Prince MR et al. JMRI, 1996, 6, 1, 162-166 /
- 3) Townsend RR et al. American Journal of Kidney Diseases, 2000, 36, 6, 1207-1212 /
- 4) Zhang HL et al. JMRI, 2006, 23, 3, 383-387 /
- 5) Yenicierioglu Y et al. Scandinavian Journal of Urology and Nephrology, 2006, 40, 1, 63-69 /
- 6) Sam II AD et al. Journal of Vascular Surgery, 2003, 38, 2, 313-318 /
- 7) Haustein et al. Radiology, 1993, 186, 3, 855-860 /
- 8) Kwak HS et al. Journal of Korean Medical Science, 2005, 20, 5, 841-847