EVALUATION OF NEPHROTOXICITY OF ISO- VERSUS LOW-OSMOLAR IODINE CONTRAST MEDIA BY BOLD AND DIFFUSION-WEIGHTED MR IMAGING

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TARGET AUDIENCE

This study is expected to provide information about contrast-induced kidney injury to interventional radiologists as well as nephrologists.

PURPOSE

To dynamically monitor the changes of renal diffusion and oxygenation after CM administration using diffusion-weighted MR imaging (DWI) and blood oxygen level dependent (BOLD) MRI , and to observe the different MRI changes caused by iso- and low-osmolar CM in vivo during a relative long period of time (18 days).

METHODS

Thirty male New Zealand white rabbits (body mass ranged from 2.2 to 2.5kg) were recruited, and randomly divided into 3 groups. After 8 hours fasting, 3 groups were randomly administrated iodixanol or iopromide at a dosage of 2gI/kg or an equivalent amount of 0.9% physiological saline respectively. MR scanning was performed with a clinical 3.0T imager (Magnetom Verio, Siemens, Germany) at pre-CM (baseline) and post-CM (1 hour, day 1, 3, 6, 11, 18) administration. Apparent diffusion coefficient (ADC) and R2* values of different renal compartments (cortex, outer medulla, inner medulla) were acquired using DWI and BOLD. Blood sampling and pathological examination were performed at part of the above time-points. Serum creatinine values were used to evaluate renal function. Pathological changes were assessed by Hematoxylin-Eosin and Periodic Acid-Schiff stain.

RESULTS

All MRI data were normalized and expressed as percentage of baseline (Figure 2). For the iodixanol group, ADC values were significantly lower than the baseline at day 1 (95.1%±4.7%), day 3 (95.4%±5.4%), day 6 (94.9%±4.9%), day18 (92.9%±4.3%) in the outer medulla and at day 6 (92.3%±6.5%) in the inner medulla ($P<$ .05), while R2* values were significantly higher than the baseline at 1 hour (121.7%±9.8%) in the outer medulla and 1 hour (124.5%±19.1%), day 6 (129.0%± 23.0%)in the inner medulla ($P<$ .05). For the iopromide group, no significant difference in ADC or R2* was observed between post-CM administration and the baseline. There were no significant differences of serum creatinine values within different time-points or between the two CM groups. Pathological sections showed renal tubular epithelial cells edema after day 3 without significant differences between the two CMs.

DISCUSSION

Contrast induced nephropathy was assessed by the standard of short-time increase of SCr [1], previous study [2] suggested that iso-osmolar contrast media (IOCM) has better renal tolerability compared with low-osmolar contrast media (LOCM); however it ignored the long-term incidence of renal dialysis and failure [3]. A study performed by Liss et al [4] found that high-viscous IOCM could cause significantly more often renal failure than low-viscous LOCM in the long run, Using functional MRI, we find IOCM can induce more pronounced and persistent renal diffusion restriction and hypoxia than the LOCM, which is in line with Liss's findings. The mechanism of our findings may contain: 1, IOCM can lower down renal blood flow for its high viscosity, this will be followed by renal hypo-perfusion and hypoxia [5], thus the activity of Na+-K+ ATPase will be reduced which may limit the ability of water transport function between extra- and intra-cellular, finally cytotoxic edema will show up and restricted diffusion can be noticed on DWI [6]. 2, IOCM can lead to prolonged iodine retention for its high viscosity, which in turns to longer iodine exposure and thereby more pronounced cytotoxicity to renal parenchyma. Such effect is more remarkable in medulla where is full of tubules, and it is showed in our study evidently. 3, Iopromide results in renal cells dehydration and shrinkage due to high osmotic pressure [7], which in our opinion would partly offset cellular edema caused by cytotoxicity, thereby reducing the impact on ADC values. What is more, because of the osmotic diuresis effect, the CM can be eliminated faster than the IOCM. In this regard, the LOCM can protect kidney potentially [8], which is safer than IOCM.

CONCLUSION

Iodixanol (IOCM) resulted in a more significant decrease of renal diffusion and oxygenation than iopromide (LOCM) did in the setting of mild dehydration. DWI and BOLD could be served as noninvasive biomarkers in monitoring the nephrotoxicity caused by CM of different osmolality.

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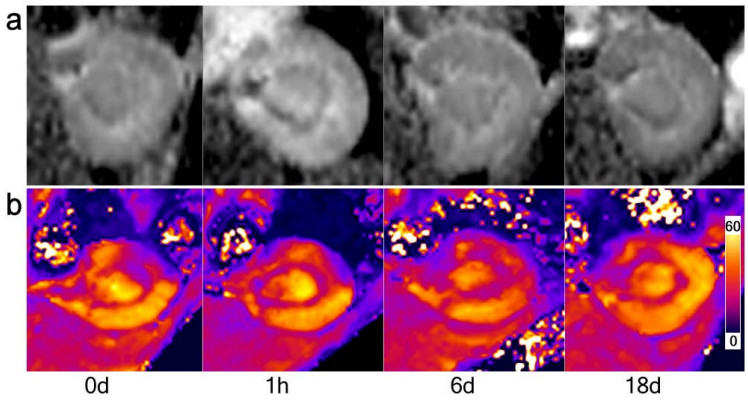

Figure 1. ADC map (a), T2* map (b) at day 0, 1, 6, 18 in two representative rabbits in the iodixanol group. The ADC signal intensity increased at 1 hour followed by decrease at day 6 and 18, while the T2* value decreased at day 6 followed by restoration at day 18.

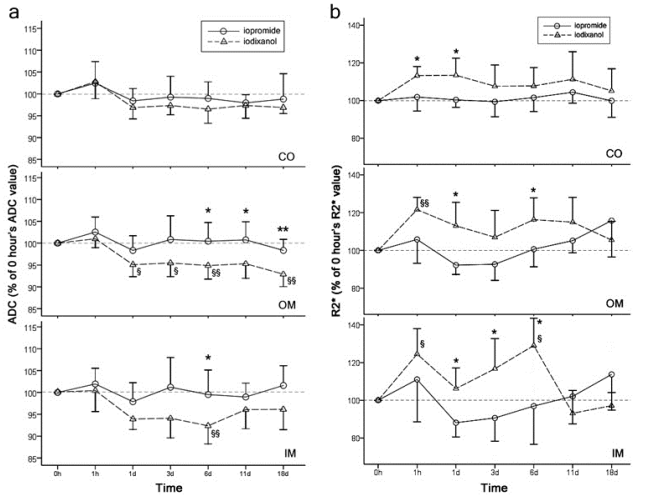

Figure 2. ADC (a) and R2* (b) percentages of baseline in the CO, OM and IM, ADC percentages were much lower (a), while R2* percentages were much higher (b) in the iodixanol group than that in the iopromide group at most time-points. Both (a) and (b) show the iodixanol group changed more significantly after CM injection compared with baseline. * $P < .05$, ** $P <$ .01 compared with the iodixanol group; § $P < .05$, §§ $P < .01$ compared with the baseline.