FULL PAPER *Surgery*

Comparison of Excretory Urographic Contrast Effects of Dimeric and Monomeric Non-Ionic Iodinated Contrast Media in Dogs

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ABSTRACT. In excretory urography, the osmolarity of contrast media has rarely been treated as important in veterinary medicine. In this study, the contrast effect of two contrast media (monomeric iohexol and dimeric iodixanol) in the renal cortex and aorta were compared using computed tomography (CT). Five beagle dogs were used and the study employed a cross-over method for each contrast media. The results showed that there was no difference between the media in the aorta, but iodixanol showed higher CT value and a longer contrast effect than iohexol in the renal cortex, in spite of having the same iodine dosage. It is believed that iodixanol, with its low osmolarity, is diluted less by osmotic diuresis than monomeric iohexol. It is important to consider the osmolarity of the contrast media when evaluating the contrast effect, and it is essential to use the same contrast media for each examination, or the renal excretory speed will be under/overestimated.

KEY WORDS: canine, contrast media, CT, excretory urography, osmolarity.

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Excretory urography is a contrast study that takes radiographs of iodinated contrast media, which has been injected intravenously, as it is excreted from the kidney to the urinary tract [3]. It is a useful examination for evaluating renal excretory functions and kidney morphologic abnormality [13] because the glomerular filtration rate is reflected in excretory urography [4, 5] differently than serum biochemical examinations such as BUN or CRE. In veterinary contrast studies, the iodine concentration of the contrast media used is usually emphasized, however little attention is paid to the osmolarity of the media. There are no regulated protocols of contrast media application, so the results of excretory urography sometimes vary among institutions.

The osmolarity of a non-ionic iodinated dimeric contrast media is half of a monomeric media at the same iodine concentration, because the former has twice the amount of iodine in one molecule. The difference in the osmolarity of the contrast media has no significant effect on the contrast study in most organs because the changes in iodine concentration in these organs are influenced mainly by tissue blood flow. On the other hand, in the kidney, which consists of blood vessels and renal tubules, the contrast effects are influenced by the osmolarity of the media because changes in iodine concentration are influenced by both renal blood flow and excretion of iodine to tubules [2, 9–11].

In this study, using computed tomography (CT), the renal change of the CT value was observed to objectively compare the differences in contrast effects between monomeric and dimeric iodinated contrast media in the kidney.

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MATERIALS AND METHODS

Contrast media: In this study, a water-soluble nonionic monomeric and a dimeric contrast media were used. Iohexol (Omnipaque 300®, 300 mgI/m*l*, Daiichi Pharmaceutical, Tokyo, Japan) was selected as the monomeric media, and iodixanol (Visipaque 320®, 320 mgI/m*l*, Daiichi Pharmaceutical) was selected as the dimeric contrast media. The administrated iodine dose of each contrast media was 300 mgI/kg.

Animals: Five clinically healthy beagle dogs (8.9–13.9 kg) were used, and the study was carried out in a cross-over method with an iohexol group (n=5) and an iodixanol group (n=5). All experiments were performed under animal experimental guidelines of Obihiro University of Agriculture and Veterinary Medicine.

Anesthesia: Anesthesia was induced with intravenous injection of 4.0 mg/kg propofol (Rapinovet®, Schering-Plough Animal Health, Tokyo, Japan) and maintained with continuous infusion of 20.0 mg/kg/hr propofol and the dogs were placed in ventral recumbency on the CT patient table.

CT procedure: All CT images were obtained by a multidetector-row CT (Asteion Super 4, Toshiba, Tokyo, Japan). The left kidney was selected for the imaging location to minimize artifacts from the costal region and motion artifacts because of breathing. The cross-sectional image in the middle of the left kidney was chosen to observe the renal cortex, medulla, and pelvis. The dynamic CT scan was performed for 40 min at 30 seconds interval (120 kVp, 200 mAs, 5 mm slice, 1 sec/rotation). Contrast media was injected at a rate of 1.0 m*l*/sec using an auto-injector device (Autoenhance A-60, Nemoto Kyorindo, Tokyo, Japan).

Setting of the region of interest (ROI) and image evalua-

tion: ROI was set in the renal cortex to measure CT value because there are vessels, glomerulus and tubules in the renal cortex, and the enhancement by the contrast media interferes with setting accurate ROI in the renal medulla or pelvis. ROI (20.0 mm^2) was drawn over each renal cortex to measure CT value using an image processing workstation (Virtual Place Advance, AZE, Tokyo, Japan), and a time density curve (TDC) was generated.

Measurement of serum iodine concentration: To compare the differences in contrast media clearance, the serum iodine concentration was measured by use of a colorimetric assay on the blood sample taken one hour after administration of contrast media [1]. The statistical evaluation was performed by student *t*-test.

Serum biochemical examination: In each group, serum biochemical examinations (BUN, CRE, ALT, AST, ALP, ALB, Ca, P, TP) were performed with the blood sample taken before and 24 hr after the administration of contrast media. The statistical evaluation was performed by student *t*-test.

RESULTS

The mean peak CT value right after administration of contrast media showed a similar TDC pattern between the iohexol and iodixanol group. After the peak, the iodixanol group showed a higher CT value than the iohexol group throughout the observation period ($p<0.01$, student *t*-test). In the iohexol group, the mean CT value was attenuated after the peak value. In contrast, in the iodixanol group, the CT value re-ascended after the peak value, and there was no significant attenuation of the CT value throughout the 40-min observation period (Fig. 1). However, the mean CT value of the aorta showed a similar TDC pattern between the two groups (Fig. 2).

With respect to the comparison of serum iodine concentration one hour after injection of the contrast media, there were no statistically significant differences between the two groups (Table 1). In addition, no statistically significant differences were observed between the two groups in terms of the changes in pre and post serum biochemical examination in all tests.

DISCUSSION

In this study, the contrast effect of iodixanol in the renal cortex was higher than iohexol. However, it is believed that there is no difference in excretion speed from the blood between the two contrast media because the CT value of the aorta showed a similar TDC pattern in both groups and blood iodine concentration after one hour did not show a significant difference. In addition, according to the past reports that indicate there was no significant difference in the contrast effect except in the kidney between monomeric and dimeric contrast media [2, 9–11], and the reports of increasing urinary volume with the use of monomeric contrast media relative to dimeric contrast media [7, 10], it is considered that the remarkable difference in the contrast effect in the kidney is mainly derived from the osmotic diuresis in the renal tubules. This means that, after passing the glomerulus, the monomeric contrast media, with high osmolarity, is diluted in the renal tubules because it receives greater influence of osmotic diuresis than dimeric contrast media by reason of its high osmolarity [6]. Provided that the iodine concentration is the same, the monomeric contrast media have approximately a half of the molecular weight and twice the molar concentration of dimeric contrast

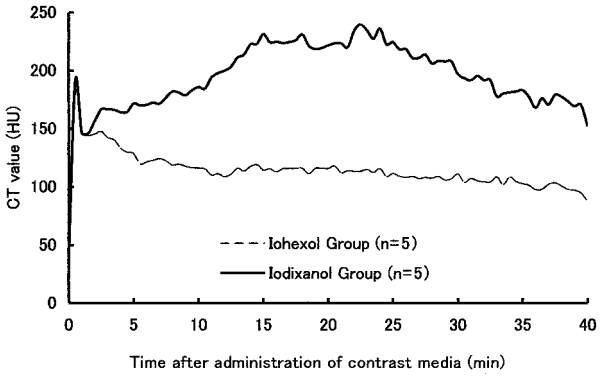

Fig. 1. The time density curve of the iohexol and the iodixanol group in the renal cortex (n=5, mean). The CT value gradually attenuated in the iohexol group after the peak value. On the other hand, the CT value re-ascended after the first peak in the iodixanol group. The second peak of iodixanol represents the urine iodine peak in renal cortex tubules and vessels.

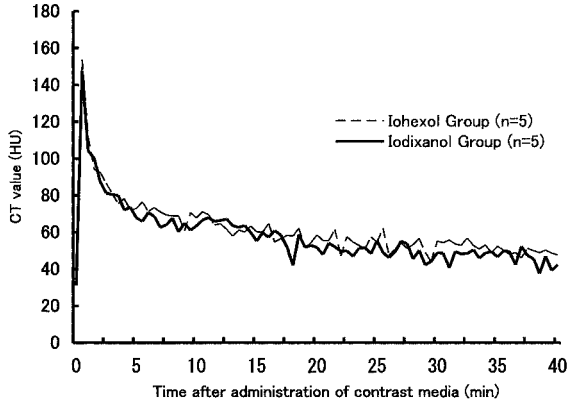

Fig. 2. The time density curve of the iohexol and the iodixanol group in the aorta (n=5, mean). Both of contrast media in the aorta showed similar time density curve.

Table 1. Serum iodine concentration after one hour (μgI/m*l*)

Iohexol group (n=5)	Iodixanol group (n=5)
638 ± 89	779 ± 284

(mean ± SD, p=0.10)

media. In theory, monomeric contrast media have twice the osmolarity of dimeric contrast media in a unit volume of renal tubules because the osmolarity is in proportion to molar concentration (van't Hoff's law of osmotic pressure). This is just as valid for the other organs, except for the kidney, however, it is significant in the kidney because it is the organ that contains tubules to condense urine.

In addition, the re-ascent of the CT value in iodixanol represents the iodine concentration in renal tubules after disappearing from the blood, not the recirculation of blood iodine. In other words, the first peak of iodixanol TDC represents the iodine concentration peak in vessels in the renal cortex, and the second peak represents the peak in renal cortex tubules. In this study the 40-min CT scan allowed for the observation of CT value variation of the dimeric contrast media, and provided the contrast process of the vascular phase and the urine phase in the renal cortex.

In this study, a significant osmotic influence in the kidney was noted. An osmotic influence can exist anywhere in the body, however it is milder than osmotic diuresis. There is a greater probability of osmotic dilution by extravascular fluid with monomeric contrast media than dimeric contrast media in all organs [8]. In veterinary medicine, only iodine dosage is emphasized for the contrast media used in contrast studies, and osmolarity is seldom mentioned. Furthermore there are no regulated protocols of contrast media application. Consequently, various contrast media are used in contrast examinations without considering their osmolarity.

It is important to take into account the osmotic property of the dimeric and monomeric contrast media when evaluating the contrast effect to avoid under/overestimating the renal excretory speed, and it is essential to use the same contrast media in each examination to accumulate the examination experiences, especially in excretory urography.

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