The Difference of Contrast Effects of Myelography in Normal Dogs: Comparison of Iohexol (180 mgI/ml), Iohexol (240 mgI/ml) and Iotrolan (240 mgI/ml)

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Myelography is the radiographic examination of the spinal cord following injection of contrast medium into the subarachnoid space. Not only the existence but also the location of spinal lesions can be diagnosed by myelography. [5,12] In veterinary science, it is very important to identify the location of a spinal lesion because determination of the clinical lesion is difficult by neurological examination alone. Myelograms used to be taken after the injection of contrast medium but recently the use of computed tomography (CT) has become widespread when diagnosing spinal diseases. In Japan, iohexol and iotrolan are approved by the Ministry of Health, Labor, and Welfare as contrast media for myelography. Contrast media preparations with high iodine concentrations are often also used for myelography in small animal practice [2, 3, 6, 9, 10], however, high-iodine-concentration contrast media preparations often give insufficient contrast effects because of their limited diffusion. The concentration of iodine and the viscosity of contrast media preparations vary, and therefore, the contrast effects can differ [10]. The contrast resolution of CT is different from that of conventional radiography [4], so selection of contrast media preparations for myelography should be considered carefully. In this study, the contrast effects of three different contrast media preparations were examined by conventional and CT myelography.

MATERIALS AND METHODS

Contrast media preparations: Iohexol 180 mgI/ml (Omnipaque® 180, Daiichi Sankyo Company Limited, Tokyo, Japan), iohexol 240 mgI/ml (Omnipaque® 240) and iotrolan 240 mgI/ml (Isovist® Inj. 240, Bayer Yakuhin, Limited, Osaka, Japan) were used in this study. The molecular weight of iohexol is 821.4 (monomeric), and iotrolan is 1626.24 (dimeric). Viscosity (at 37°C) of iohexol 180 mgI/ml is 3.9 mPa.s, iohexol 240 mgI/ml is 3.3 mPa.s, and iotrolan 240 mgI/ml is 3.9 mPa.s. Contrast media were warmed to 37°C in advance of injection.

Animals: Three clinically normal adult beagle dogs (9.1–14.1 kg, castrated male) were used, and the study was carried out in a cross-over method with an iohexol 180 mgI/ml group (n=3), iohexol 240 mgI/ml group (n=3), and an iotrolan 240 mgI/ml group (n=3).

Myelography procedure: Animals were anesthetized by intravenous injection with propofol (8.0 mg/kg, Rapinovet®, Schering-Plough Animal Health K. K., Osaka, Japan) and maintained under anesthesia using inhalational isoflurane/O2 (Forane®, Abbott Japan, Osaka, Japan). Lumbar puncture was performed percutaneously through the L5–6 interarcuate foramen using a 22-gauge spinal needle. After confirmation of the backflow of cerebrospinal fluid, contrast media preparations were administered at a dose of 0.30 ml/kg to each dog over a 1 min period. Immediately after injection of contrast medium, a lateral myelogram of the thoracic, thoracolumbar, and lumbar portions of spine was taken. The dogs were placed in dorsal recumbency within the gantry of the CT scanner (Asteion Super 4, Toshiba, Tokyo, Japan) and a CT scan was done from T2 to L5 at 5, 15, 30, 45 and 60 min after injection (120 kVp, 150 mA, 1.0 mm slice). Then, a lateral myelogram of the thoracic, thoracolumbar, and lumbar spine was done again at 65 min. After the final myelogram, the dogs were permitted to
recover from anesthesia, and all dogs were monitored closely for changes in clinical signs. Not to affect diffusion of contrast media preparations, the dogs were managed to be minimum movement during experiment.

CT myelogram evaluation: Using an imaging processing workstation (Virtual Place Advance, AZE, Tokyo, Japan), transverse CT images were obtained at each intervertebral disc level from T2 to L5 for each dog. The region of interest was set in the dorsal subarachnoid space of the median spinal cord to measure CT number. The statistical evaluation was performed by a two-factor factorial ANOVA test.

Conventional myelogram evaluation: According to the method reported by Van Bree, the myelograms were evaluated visually and compared independently by 3 observers (JS, KY, MK) [10]. The quality of the contrast was graded on a scale (4=excellent, 3=good, 2=moderate, 1=poor). The films were coded and shuffled before grading. The radiographic quality assessed was radiographic density on the basis of radiopacity and ability to define the limits of the subarachnoid space. The statistical evaluation was performed by a two-factor factorial ANOVA test.

In each dog, to confirm the absence of any clinical influence of each procedure, complete blood cell count and serum biochemical examinations (BUN, Cre, ALT, AST) were performed on blood samples taken before and 125 min after the injection of contrast media preparations.

The institution’s animal use and care administrative advisory committee approved the animal protocols.

RESULTS

Represented conventional and CT myelogram were shown in Fig. 1.

In CT myelography evaluation, the CT number 5 min after the injection of iohexol 180 mgI/ml was the highest from T2 to T8, iohexol 240 mgI/ml was the highest from T9 to T12 and iotrolan 240 mgI/ml was the highest from T13 to L5. The CT numbers of L3–4 were significantly different (p<0.05) among the three contrast media preparations (Fig. 2).

Fifteen min after the injection, the CT number of iohexol 180 mgI/ml was the highest from T2 to T6, iohexol 240 mgI/ml was the highest from T7 to T11, and iotrolan 240 mgI/ml was the highest from T12 to L5. The CT numbers of L3–4 were significantly different (p<0.05) among the three contrast media preparations (data not shown).

After 30 min, the CT number of iohexol 240 mgI/ml was the highest from T2 to T9 and iotrolan 240 mgI/ml was the highest from T10 to L5. The CT numbers of T11–12 were significantly different (p<0.05) among the three contrast media preparations (Fig. 3).

After 45 min, similar to the result after 30 min, the CT number of iohexol 240 mgI/ml was the highest from T2 to T9 and iotrolan 240 mgI/ml was the highest from T10 to L5. The CT numbers of T10–11 were significantly different (p<0.05) among the three contrast media preparations (Fig. 4).

After 60 min, the CT number of iotrolan 240 mgI/ml was the highest at all measurement sites, from T2 to L5. The CT numbers of T9–10, L2–3, and L3–4 were significantly different (p<0.05) among the three contrast media preparations (Fig. 5).

In the conventional myelography evaluation, immediately after injection of all contrast media preparations lumbar myelographic scores were higher than any other sites. Towards the cranium, the scores of all three contrast media preparations became lower. And there is no significantly difference among three contrast media preparations. At 65 min after the injection at the thoracic site, the score of iohexol 240 mgI/ml was the highest of all the contrast media preparations, at the thoracolumbar site that of iotrolan 240 mgI/ml was the highest, and at the lumbar site that of iohexol 240 mgI/ml was the highest of all contrast media preparations (Fig. 5).

The differences in the blood test results were not significant among all contrast media preparations (data not shown). No changes in the clinical signs of the dogs were observed.
Fig. 2. CT numbers 5 min after injection of contrast media. The CT numbers of L3–4 were significantly different among the three contrast media preparations. *: $p<0.05$.

Fig. 3. CT numbers 30 min after injection of contrast media. The CT numbers of T11–12 were significantly different among the three contrast media preparations. *: $p<0.05$.

Fig. 4. CT numbers 60 min after injection of contrast media. The CT numbers of T9–10, L2–3 and L3–4 were significantly different among the three contrast media preparations. *: $p<0.05$.  

![Graph showing CT numbers at different times after contrast media injection.](image-url)
DISCUSSION

Contrast medium injected into the subarachnoid space is absorbed through meninges or arachnoid granulations. Contrast effects decrease as the contrast medium is absorbed. In addition, the degree of absorption is influenced by the molecular structure of the contrast media [10, 11]. In this study, the CT number 5 min after the injection of iohexol 180 mgI/ml was the highest in cranial sites. This means diffusion of iohexol 180 mgI/ml is rapid because of its low viscosity (2.0 mPa⋅s), and absorption of iohexol is smoother than iotrolan because iohexol is monomeric and has a molecular weight of 821.4. As a result, the decrease in CT number for iohexol occurred rapidly.

While the high viscosity of iotrolan 240 mgI/ml (3.9 mPa-s) produced insufficient diffusion in the subarachnoid space, so iotrolan 240 mgI/ml stagnated near the injected area for a longer period than other contrast media preparations. As a result, the CT number at the lumbar site 5 min after injection of iotrolan 240 mgI/ml was the highest. Then, iotrolan 240 mgI/ml was carried in the circulation of the cerebrospinal fluid more slowly than any other contrast media preparations, and the contrast effect moved slowly to the cranial site. In addition, because iotrolan is dimeric in structure and has a higher molecular weight of 1626.24, absorption is relatively slow. It was considered that iotrolan 240 mgI/ml produced contrast effects lasting at all measurement points at 65 min after the injection.

The iodine concentration of iohexol 240 mgI/ml is the same as iotrolan 240 mgI/ml, but the viscosity of iohexol 240 mgI/ml (3.3 mPa-s) is lower than iotrolan 240 mgI/ml. Consequently, iohexol 240 mgI/ml spread more quickly than iotrolan 240 mgI/ml through the subarachnoid space. The diffusion of iohexol 240 mgI/ml is slower than that of iohexol 180 mgI/ml due to differential viscosity. The contrast effect of iohexol was lower than iotrolan at 60 min after the injection because iohexol is more easily absorbed from the subarachnoid space than iotrolan. According to the results, the behavior of iohexol 240 mgI/ml was intermediate between that of iotrolan 240 mgI/ml and iohexol 180 mgI/ml in CT myelography.

In conventional myelography, the differential viscosity of the contrast media affected the contrast effects, too. Although in CT myelography iotrolan 240 mgI/ml showed the highest contrast effect at 60 min after the injection, in conventional myelography the contrast effect of iotrolan 240 mgI/ml was the highest at the thoracic and thoracolumbar sites 65 min after the injection. This difference was brought about by the differences in the evaluation method of the contrast effect. The dorsal point of the subarachnoid space was evaluated for the contrast effect in CT myelograms, while the entire subarachnoid space was visually evaluated for the contrast effect in conventional myelograms. It may conceal slight difference of contrast effect in conventional myelography rather than CT myelography in each preparation.

According to a previous report the contrast effect depends on the iodine concentration of the contrast medium preparation [7]. However, it was thought that the difference in the viscosity rather than the iodine concentration of the contrast media preparations influenced the difference in the contrast effect more strongly from our experimental results. Therefore, we consider that iohexol 180 mgI/ml with its low viscosity is appropriate for small animal practice because of the importance of identification of the location of the spinal lesion. In addition, warming the contrast medium to minimize its viscosity helps contrast media diffusion and rolling the dogs promoted contrast medium distribution. It is considered that iohexol 180 mgI/ml with low viscosity might
spread wide contrast effect even if spinal cord swelling because iohexol 180 mgI/ml diffuse to the cranial sites easily.

In our clinical experience, high iodine concentration contrast medium preparations often caused artifacts on images from CT myelography. In addition, the previous report recommends that dilute contrast medium (approximately 100 mgI/ml) is used for CT myelography because of the high-contrast resolution of CT [13]. Consequently, iohexol 180 mgI/ml, which has low viscosity and superior in a wide contrast effect is appropriate for CT myelography.

Although it has been reported that iotrolan (dimeric) is safer than iohexol (monomeric) [1, 8, 10], no influences of the contrast media preparations on clinical signs or in hematological examinations were observed in this study. According to this result, iohexol 180 mgI/ml does not have problems in its use from the point of safety.

In Japan, the costs of contrast media preparations are variable. For example, the cost of iohexol 180 mgI/ml is about 1,000 yen per 10 ml vial, iohexol 240 mgI/ml is about 1,300 yen, and iotrolan 240 mgI/ml is about 7,000 yen. In the choice of contrast media, cost is also an important point to consider.

In summary, contrast media preparations that are in low viscosity and superior in producing a wide contrast effect are suitable for conventional and CT myelography in small animal practice. The characteristics of contrast media preparations should be considered for myelography in each veterinary facility.

REFERENCES