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Contrast Media of High and Low Molecular Weights in the Detection of Recurrent Herniated Disks

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PURPOSE: **Our goal was to compare contrast enhancement of recurrent herniated disk fragments and scar after intravenous injection of a new high-molecular-weight contrast medium, Gadomer 17 (gadomer), with that after injection of a low-molecular-weight contrast medium, (gadopentetate dimeglumine).**

METHODS: **Recurrent herniated disks were modeled in dogs by placing a fragment of intervertebral disk cartilage in the epidural space at laminectomy. MR imaging was performed with one of the contrast media at 20 and 50 days and with the other medium at 22 and 52 days. The changes in signal intensity from baseline in the disk fragment and in the adjacent scar tissue was measured at 2, 22, and 45 minutes. Differences were tested for significance with a student *t*-test.**

RESULTS: **At 50 days after surgery, signal intensity in the intervertebral disk fragment increased by an average of 0.52 at 2 minutes after injection of gadomer and by an average of 0.90 after injection of gadopentetate. For scar, the increases in signal intensity were 1.41 (gadomer) and 1.62 (gadopentetate). At 22 and 45 minutes after injection, the signal intensity change in the disk fragment continued to be significantly greater after gadopentetate than after gadomer injection. In comparison with the changes at 50 days, both scar and disk fragment tended to show greater signal intensity changes at 20 days. Signal intensity changes in the disk fragments were significantly less after gadomer than after gadopentetate. Signal intensity changes in scar were slightly less with gadomer than with gadopentetate.**

CONCLUSION: **Greater contrast is achieved between scar and recurrent herniated disk with a higher-molecular-weight contrast medium than with one of lower molecular weight. The difference between the high- and low-molecular-weight contrast media increases with maturation of the scar tissue.**

Gadolinium-containing contrast media diffuse into the cartilagenous material of the intervertebral disk (1). The amount that diffuses is a function of time after injection (1), molecular weight (2), and charge (3). Diffusion into the intervertebral disk is decreased by decreasing the time between injection of contrast medium and imaging, by increasing the molecular weight, and by a charge on the molecule.

Contrast medium also diffuses into herniated intervertebral disk fragments in the epidural space (4). Techniques that minimize the diffusion of contrast medium into the disk fragment maximize the contrast between disk fragment and scar so that contrast differences between scar and recurrent herniated disk increase by shortening the interval between injection and imaging and by using an ionic medium. The effect of increasing the molecular weight of the contrast medium on the contrast between scar and disk has to our knowledge not been tested.

A higher molecular weight hypothetically retards the rate of diffusion in herniated disk fragments and slows diffusion into normal intervertebral disk cartilage. The high-molecular-weight medium Gadomer 17 (Schering AG, Berlin) has a charge of −2 in solution and a molecular weight of 40,000 whereas the low-molecular-weight medium, gadopentetate dimeglumine, also has a charge of −2 in solution but has a molecular weight of 546. We compared the low- and high-molecular-weight contrast media in the

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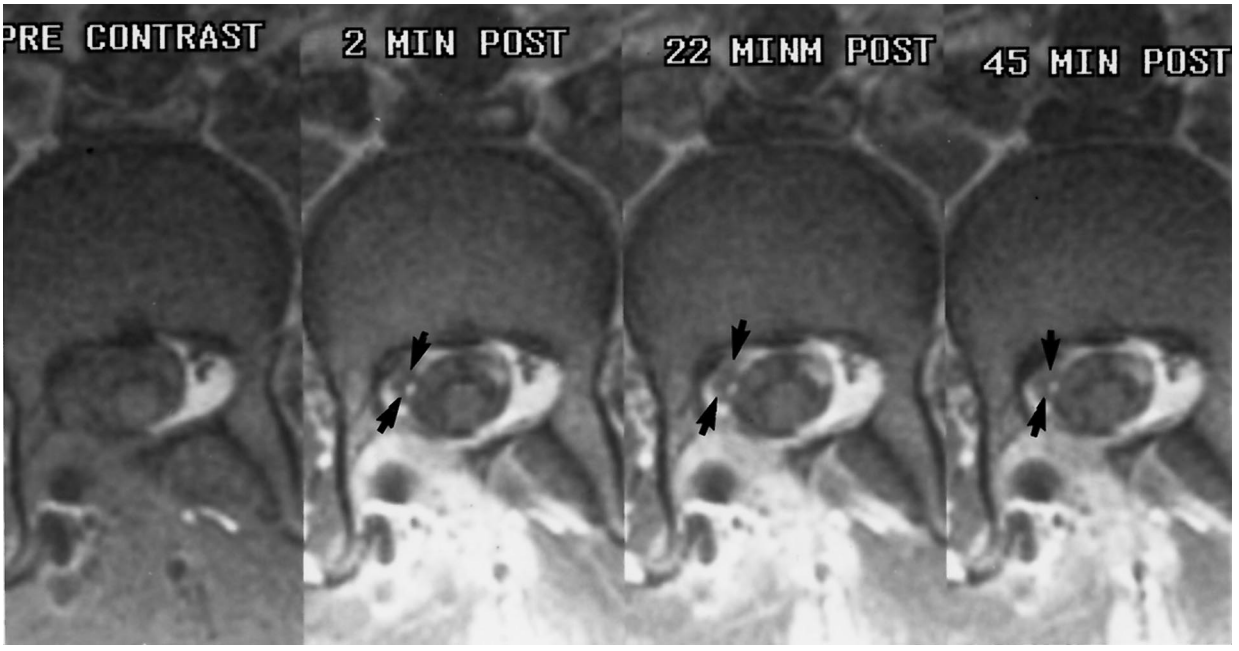

FIG 1. Appearance of the lower laminectomy site in one animal. A baseline (*precontrast*) image and images at 2, 22, and 45 minutes after injection of gadomer are shown. The disk fragment (arrows) is seen better after injection of contrast medium.

detection of recurrent herniated disk in an animal model.

Methods

A canine model of recurrent herniated disks was used (4). The study was approved by our institution's animal care committee. A lumbar hemilaminectomy was performed at the L4-5 and L6-7 levels and a fragment of intervertebral disk was placed in the spinal canal. After surgery, the animals underwent MR imaging with both low and high-molecular-weight contrast media.

Eight mongrel dogs weighing 17 to 24 kg were acquired for this study from a commercial vendor. They were quaranteed for 30 days and tested for mycobacterial and intestinal infections. For surgery, the animals were fasted overnight and sedated with telazol (5 mg/kg intramuscularly) and atropine (0.05 mg/kg intramuscularly). They were intubated and anesthetized with halothane (1% to 1.5%) and oxygen (4 L/min). The skin over the lumbar spine and over a portion of the tail was shaved and surgically disinfected. A vertical midline incision was made from L-4 to L-6. The paraspinal muscles on one side were dissected free of the spinous processes with periosteal elevators. Hemostasis was achieved with electrocautery. With a microburr drill, rongeurs, and curette, the hemilamina and ligamentum flavum were removed to create a laminectomy defect 1.5 cm long and 1 cm wide. Bleeding was controlled with light compression and cold sterile water irrigation and suction. The tail was resected at the prepared site and the stump wound was repaired. From the distal tail, two whole intervertebral disks were removed. A piece of disk 7 mm in diameter and 1.5 mm in height was cut from the disk and inserted into each of the laminectomy sites. The fragments were positioned anterolateral to the dural sac near the origin of the root sheath. After hemostasis was obtained, the wound was closed in layers. The dogs recovered from the anesthetic in a humidified, warmed intensive care unit (Kirchner) for 24 hours and then returned to their cages. Cefazolin (1 g intramuscularly) and buprenorphine hydrochloride (0.3 mg intramuscularly) were given prophylactically for 3 days after surgery. In half the dogs the upper laminectomy was on the left and the lower laminectomy on the right and in the other half the sides were reversed.

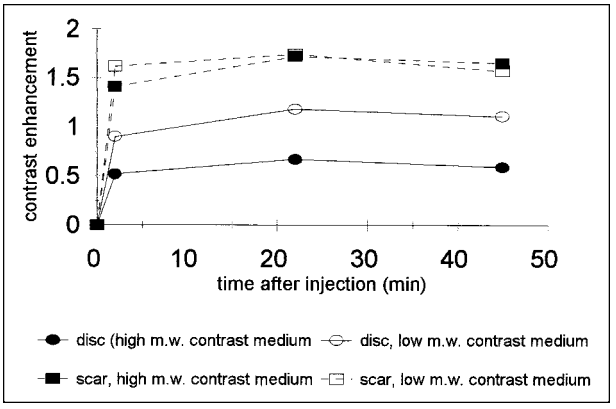

FIG 2. A plot of average contrast enhancement in scar and disk after intravenous injection of gadomer or gadopentetate at 50 days after laminectomy (M.W. = molecular weight).

At 20 to 22 days and at 50 to 52 days after the surgical procedure, the animals underwent MR imaging under heavy sedation with telazol, atropine, and phenobarbital (20 mg/kg intravenously). The dogs were placed supine on a 3-inch surface coil in a 1.5-T imager. Localizer images were obtained, and then axial T1-weighted images (500/25/2 [TR/TE/excitations], 256 × 256 matrix, and 3-mm section thickness) with and without chemical-shift fat saturation. Gadomer was administered in a dose of 0.3 mmol/kg. The T1-weighted images in the axial plane were repeated at 2, 22, and 45 minutes after injection of the contrast medium. At 35 minutes after injection, axial T1-weighted images were acquired with fat saturation. The MR study was repeated 48 hours later with gadopentetate dimeglumine (Berlex) in a dose of 0.3 mmol/kg. In four animals, the study was performed first with gadopentetate and 48 hours later with gadomer.

Images obtained before and after injection of contrast medium were inspected and the location of disk fragments and scar was determined. The relative contrast between scar and disk was assessed visually. Signal intensity in the disk fragment and scar was measured with a region-of-interest cursor adjusted to the size of the disk fragment and resident software.

TABLE 1: Average signal intensity changes in disk and scar after intravenous injection of gadomer or gadopentetate (50 days after surgery)

Time, min	Average Disk Enhancement (Gadomer)	Average Disk Enhancement (Gadopentetate)	Average Scar Enhancement (Gadomer)	Average Scar Enhancement (Gadopentetate)	Difference between Scar and Disk (Gadomer)	Difference between Scar and Disk (Gadopentetate)
0	0	0	0	0	0	0
2	0.52	0.90	1.41	1.62	0.89	0.62
22	0.67	1.18	1.72	1.74	1.05	0.56
45	0.59	1.11	1.65	1.57	1.06	0.46

TABLE 2: Average signal intensity changes in disk and scar after intravenous injection of gadomer or gadopentetate (20 days after surgery)

Time, min	Average Disk Enhancement (Gadomer)	Average Disk Enhancement (Gadopentetate)	Average Scar Enhancement (Gadomer)	Average Scar Enhancement (Gadopentetate)	Difference between Scar and Disk (Gadomer)	Difference between Scar and Disk (Gadopentetate)
0	0	0	0	0	0	0
2	0.76	1.23	1.77	2.12	1.01	0.79
22	0.94	1.38	2.03	2.30	1.09	0.92
45	1.01	1.42	2.00	2.03	0.99	0.61

The investigator made the measurements without reference to the type of contrast medium used. The change in signal intensity relative to baseline signal intensity was calculated. The average signal intensity change for scar tissue and for disk fragment for each contrast medium was then calculated. Differences between the two contrast media were tested with Student's *t*-test (significance set at .05).

The animals were killed after the MR examination at 52 days. The lumbar spine was removed en bloc, fixed in 10% buffered formalin, decalcified and embedded in paraffin, and sectioned and stained with hematoxylin-eosin to verify the location of the scar tissue and disk fragments.

Results

One dog had hindquarter paresis postoperatively and was excluded from the study and killed. Seven dogs recovered from surgery uneventfully.

The contrast between scar and disk fragment was improved with both contrast media (Fig 1). Contrast between scar and disk fragment was considered superior with the high-molecular-weight contrast medium in five of the seven animals and equal in two of the animals.

The average signal intensity change (contrast enhancement) in disk fragment and scar for gadomer and gadopentetate at 50 days is shown in Figure 2 and Table 1. The contrast enhancement in disk was 0.52, 0.67, and 0.59 at 2, 22, and 45 minutes, respectively, after injection of gadomer, and 0.90, 1.18, and 1.11, respectively, after injection of gadopentetate. The difference was significant ($P = .01$ at 2 minutes, $P = .005$ at 22 minutes, and $P = .006$ at 45 minutes). In scar, the contrast enhancement was 1.41, 1.72, and 1.65 at 2, 22, and 45 minutes, respectively, after injection of gadomer, and 1.62, 1.74, and 1.57, respectively, after injection of gadopentetate. The difference was not significant.

The results at 20 days are shown in Table 2 and Figure 3. At 20 days, the enhancement of disk was greater with both the low- and the high-molecular-weight contrast media than at 50 days. The gadomer produced significantly less enhancement in the disk than did the gadopentetate ($P < .003$ at 2, 22, and 45 minutes). The enhancement in scar was also greater with both agents at 20 days than at 50 days. The differences for the two agents were marginally significant at 2 minutes ($P = .036$) and not significant at 22 or 45 minutes.

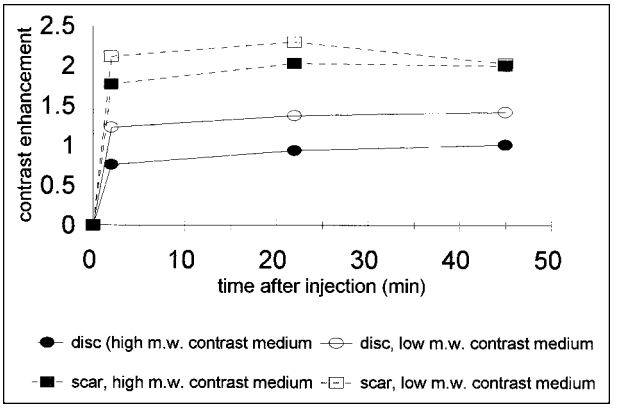

FIG 3. A plot of average contrast enhancement in scar and disk after intravenous injection of gadomer or gadopentate at 20 days after laminectomy.

The difference between the enhancement of disk and the enhancement of scar for both agents was calculated (Tables 1 and 2). For gadomer, the differences were between 0.89 and 1.09; for gadopentetate, they ranged from 0.46 to 0.92. For each time interval in the 20-day or the 50-day study the difference for gadomer was greater than the difference for gadopentetate.

On histologic sections, dense fibrous tissue in the laminectomy defect and epidural space stained intensely. The cartilagenous disk fragment stained very weakly. In each case the disk fragment was identified in the location suggested by the MR findings (Fig 4).

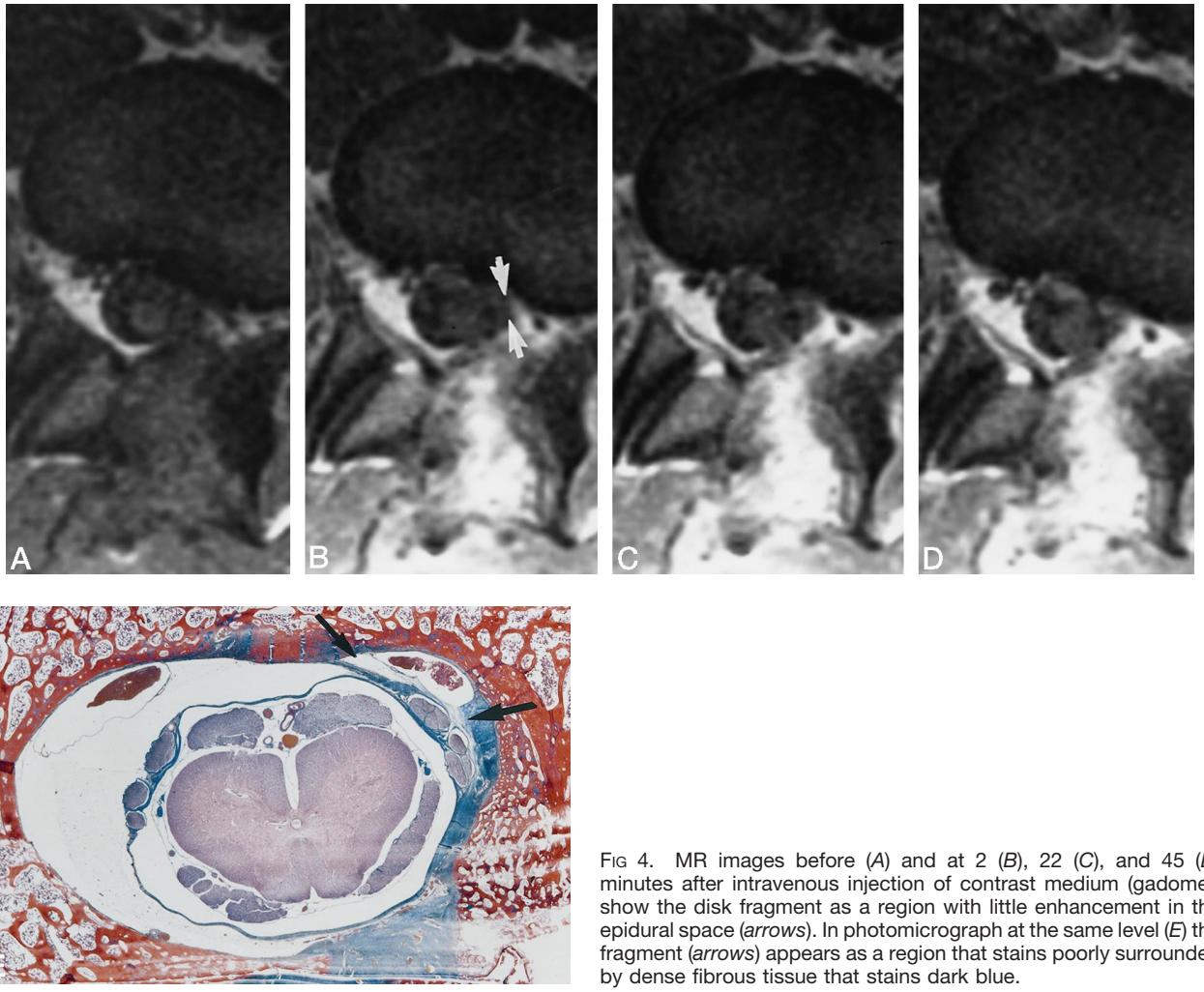

FIG 4. MR images before (*A*) and at 2 (*B*), 22 (*C*), and 45 (*D*) minutes after intravenous injection of contrast medium (gadomer) show the disk fragment as a region with little enhancement in the epidural space (*arrows*). In photomicrograph at the same level (*E*) the fragment (*arrows*) appears as a region that stains poorly surrounded by dense fibrous tissue that stains dark blue.

Discussion

The study shows that the enhancement of disk fragments and the contrast between disk fragments and adjacent scar are affected by the molecular weight of the contrast agent. Recurrent disk fragments modeled in dogs did not enhance as much after gadomer as after the lower-molecular-weight gadopentetate. Detection of recurrent herniated disks may be improved by using higher-molecular-weight contrast media.

The results were similar at 20 and 50 days. The differences may be explained by capillary density and extravascular space in scar tissue, which decrease as scar matures (5). The reduced enhancement in scar seen at 50 days is consistent with maturation of the capillary bed. At either 20 and 50 days, disk fragments in the epidural space enhanced to a lesser degree with gadomer than with gadopentetate.

For this pilot study a small number of animals was used. Because of the small size of the fragment placed in the epidural space, partial volume averaging probably affected the enhancement measurements in the disk fragment. Partial volume averaging tends to diminish the differences detectable between the contrast media. The model may not reproduce the clinical situation perfectly, since in the animals the disk fragment consisted of normal annulus fibrosus and nucleus pulposus whereas in the clinical situation it consists ordinarily of degenerating fibrocartilage. The structure and composition of the disk fragments used experimentally may not elicit the same reaction or diffusion of contrast medium as do herniated human disk fragments. Degeneration and maturation may slow the rate at which contrast medium diffuses into the intervertebral disk (6–8). The high-molecular-weight contrast medium should therefore be studied in patients with recurrent herniated disks. The two contrast media were similar in charge and in relaxivity, although different in molecular weight.

Previously, improved contrast between scar and disk from the use of a higher dose of contrast medium was reported (4). Ionic drugs or contrast media tend to diffuse more slowly into cartilage than do nonionic media (3, 9). Disk composition affects the diffusion of contrast medium in the intervertebral disk (8, 10).

Conclusion

In this experimental model, the higher-molecular-weight contrast medium produced better contrast be-

tween scar tissue and disk fragment. Replacement of conventional contrast medium with high-molecular-weight medium may improve the differentiation of recurrent herniated disk from epidural scar tissue.

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