

Fluoroscopic-guided Intradiscal Oxygen-Ozone Injection Therapy for Thoracolumbar Intervertebral Disc Herniations in Dogs

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Abstract. *Background:* To investigate the effect of oxygen-ozone (O_2-O_3) injection on thoracolumbar intervertebral disc herniation (IVDH) in dogs. *Materials and Methods:* Ten herniated discs of five dogs were treated with percutaneous injection of an O_2-O_3 gas mixture with O_3 concentration of 32 $\mu\text{g}/\mu\text{l}$ intradiscally (1.5-2 μl) under fluoroscopy guidance. *Results:* Five weeks after treatment, the mean size of herniated discs was measured by computed tomography and showed significant reduction of disc volumes in all animals ($8.8\% \pm 3.82\%$). The degree of shrinkage was negatively linearly correlated with disc mineralization (correlation coefficient = -0.636) and statistically significant at $p < 0.05$. All five dogs regained their gait function and none recurred. *Conclusion:* We conclude that intradiscal O_2-O_3 injection can decompress affected discs by disc shrinkage.

Oxygen-ozone (O_2-O_3) injection therapy was first used in human medicine to treat disc herniation. This is currently available in the management of disc herniation as one of the various minimally invasive treatments. O_2-O_3 therapy was reported to give a satisfactory clinical result via a well-tolerated, low-cost procedure. It is based on the action of O_2-O_3 in bringing about shrinkage of the herniated disc and an anti-inflammatory and analgesic effect on the compressed spinal cord. The effect of O_2-O_3 therapy has been reported in many studies in human medicine, however, to our knowledge, it has not been introduced to veterinary medicine yet.

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Therefore, in the present study, we investigated the effect of O_2-O_3 therapy in dogs diagnosed with thoracolumbar intervertebral disc herniation (IVDH). Clinical outcomes, size of the herniated disc and the relationships between the disc size and disc calcification, and size of herniated disc were observed.

Materials and Methods

Animals. Five dogs presented with paraparesis or paraplegia and were referred to the Veterinary Medical Teaching Hospital, College of Veterinary Medicine at Konkuk University. They each had a history of chronic recurrent ambulatory difficulties. The patients were diagnosed with thoracolumbar intervertebral disc herniation (IVDH) on physical, neurological, diagnostic imaging views, complete blood count profile and serum biochemical analysis. The disc herniation was observed in ten intervertebral spaces. The dogs had deep pain perception (DPP) but no other systemic abnormalities.

Premedication and anesthesia. The dogs were premedicated with 0.04 mg/kg atropine sulfate (Atropine sulfate, Jeil Pharm, South Korea) subcutaneously and 0.4 mg/kg butorphanol (Butorphan, MyungMoon Pharm, South Korea) intravenously. General anesthesia was induced with 6 mg/kg thiopental sodium (Pententol sodium, ChoongWae Pharm, South Korea) intravenously. Anesthesia was maintained with 0.5% ~ 2.5% isoflurane (Rhodia Organique Fine Ltd., South Korea) in 100% oxygen.

Computed tomography imaging and measurement of size of disc herniation. CT (GF CT/eR[®], General Electric Medical System, Yokogawa, Japan) was used at 120 V and 100 mAs with 1 mm thickness at 1.5 mm intervals under general anesthesia. The area of vertebral canal was measured on vertebral window and the images were viewed with a window width of 2000 Hounsfield units (HU) and a window level of 350 HU. And then, the size of herniation disc was measured on spine window with a window width of 400 HU and a window level of 40 HU. All measurements were made directly from the CT video image using a standard internal measurement device (CT scanner) by the same radiologist without having any previous knowledge of clinical findings or

Table I. Characteristics, lesions, clinical signs and outcomes of five dogs with thoracolumbar intervertebral disc herniation which were treated with O₂-O₃ injection.

Case	Breed	Age (years)	Body weight (kg)	Lesions	Clinical signs	Outcome (Gait)	Recovery period ¹ (days)
1	Pekingese	6	6.6	T12-13, L2-3	Paraplegia	Stumbling	2
2	Shih-Tzu	2	4.14	L1-2	Paraparesis	Normal	3
3	Cocker spaniel	4	7.6	L2-3	Paraplegia	Normal	12
4	Maltese	2	4.9	T12-13, L2-3, L3-4	Paraparesis	Normal	3
5	Dachshund	2	5.3	T9-10, T10-11, T11-12	Paraparesis	Normal	5

¹Cases 2 to 5 showed no recurrence up to 20 months of monitoring after O₂-O₃ injection; ²case 1 was able to walk progressively but revealed a mild decreased proprioceptive reflex 20 months after O₂-O₃ injection.

chronology. The degree of calcification was determined using the mean HU value of the herniated disc in the spine window before injection. The size of the disc herniation in relation to the size of the spinal canal was calculated according to Thelander (4). The A-index describes the relation between the true areas of the herniation and the spinal canal.

$$\text{A-index (\%)} = \frac{\text{Area of disc herniation} \times 100}{\text{Area of spinal canal}}$$

Intradiscal O₂-O₃ injection. A volume of 1.5 ~ 2 ml O₂-O₃ mixture with an O₃ concentration of 32 µg/µl was injected into the intradiscal area of a total of ten discs of five dogs under general anesthesia. The oxygen-ozone gas mixture was obtained using O₃ generator (OKC-6000®, Ozoneskorea Inc., South Korea). The dorsal thoracolumbar area was clipped and sterilized before the procedure. Using a rotating C-arm fluoroscope, a 2.5 inch 22 G spinal needle was inserted through the skin and epaxial muscles and positioned from the lateral side of the articular facet to the center of the herniated disc. Special attention was needed to prevent iatrogenic damage of nerve branches, spinal artery and vein located throughout the intervertebral foramen. With the needle in position, the fluoroscope was rotated in the ventrodorsal direction of the dog. The position of the needle was ensured to be in the midline, approximately in one third the width of the disc. When the dog presented multiple lesions, spinal needles were pre-placed sequentially into each disc followed by O₂-O₃ injection. The average time of injection was around 10 sec. After all procedures, needles were removed and the puncture site was compressed for 30 sec. Neither pre- nor post-operative medications were given. All dogs were observed for 24 h and discharged the following day. Owners were instructed to restrict the dog activity for the first 2 weeks and then gradually increase activity for the following 4 weeks, beginning with leash walking. Follow-up was performed for up to 20 months; during this period, general condition, gait status and any complications were assessed.

Statistical analysis. Spearman's test was used to identify the existence of relationships between the size of the herniated disc, disc calcification and the degree of disc shrinkage. A level of significance of *p* < 0.05 was used.

Results

The overall characteristics and outcomes of the five dogs treated with oxygen-ozone injection are shown in Table I. Their body weights ranged from 4.2 to 7.6 kg. Three dogs showed paraparesis and the rest paraplegia. Neither urinary nor fecal dysfunction was observed. The total number of lesions was ten sites in five dogs. Three dogs presented multiple lesions from T9 to L4 while the remainder had only one IVDH respectively.

The total procedure time was about 20 minutes, estimated from the induction of anesthesia to the removal of spinal needle. All dogs recovered from the procedure without any complications.

All five dogs showed improvement after O₂-O₃ injection. Of the five dogs, four dogs ambulated normally within 12 days after the procedure, within a mean period of 5.75 (SD: ±4.27) days. Case 1 also regained ambulatory function slowly, yet the dog presented mild residual neurologic deficit and stumbling gait to the end of monitoring. Three dogs seemed to be a little depressed on the day of the procedure however they soon recovered, so that all dogs become bright and active at the time of discharge. No other side-effects were detected during observation.

After the long follow-up period, none showed any sequela or signs of recurrence. Owners were satisfied with the clinical outcomes up to 20 months.

Reduction of herniated disc lesions after O₂-O₃ injection was confirmed with CT (Figure 1) at 5 weeks after the procedure. The A-index, the difference between pre- and post- injection values and the mean HU value of each herniated disc before injection are shown in Table II. The A-index, which indicates the degree of disc shrinkage, varies among the discs ranging from 2.69% to 13.89% with an average of 8.8% (SD: ±3.82). The herniation size of disc (A-index before oxygen-ozone injection) did not show any remarkable relation to the degree of disc shrinkage. On the



Figure 1. CT images showing the reduction in the herniated disc volume at L3-4 after O₂-O₃ injection in case 4. The degree of disc herniation was evaluated using the A-index of Thelander's study (4). The A-index was 52.6% before injection (a) and 39% after injection (b). The mean HU value of the discs before injection was 141.02.

Table II. Each A-index % and its difference value between before and after O₂-O₃ injection, and mean HU units of herniated disc on spine window before O₂-O₃ injection in dogs with thoracolumbar intervertebral disc herniation.

Case	Lesions	Herniated disc size (A-index % ¹)			Degree of calcification* (HU units)
		Before O ₂ -O ₃ injection ³	After O ₂ -O ₃ injection	Decrease in disc size at 5 weeks after injection ^{2,3,*}	
1	T12-13	56.15	50.44	5.71	295.16
	L2-3	60.17	54.73	5.44	282.90
2	L1-2	51.53	37.64	13.89	189.18
3	L2-3	50.63	39.38	11.25	190.16
4	T12-13	49.53	46.84	2.69	233.57
	L2-3	53.97	43.36	10.61	114.81
	L3-4	52.6	39	13.6	141.02
5	T9-10	48.22	40.02	8.2	256.17
	T10-11	46.38	35.47	10.91	125.78
	T11-12	50.19	44.52	5.67	279.76

¹A-index described the relation between the true areas of the herniation and the spinal canal in Thelander's study; A-index % = Area of disc herniation / Area of spinal canal X 100; ²decrease in disc size is the difference between the A-index before and after O₂-O₃ injection; ³there was no remarkable correlation (r=-0.042) or significance between herniated disc size before O₂-O₃ injection and the reduction in disc size. *There was significant negative linear correlation (r=-0.636; p<0.05 Spearman) between the reduction in disc size and the degree of disc calcification.

other hand, the degree of disc calcification (HU value of herniated disc) was inversely related to disc shrinkage according to the correlation analysis. There was a significant negative linear relationship (correlation coefficient -0.636; p=0.048).

Discussion

The mechanism of action of the intradiscal O₂-O₃ injection consists of its direct action on mucopolysaccharides that are major components of the nucleus pulposus of intervertebral

discs and the disruption of water molecules. This action leads to disc shrinkage; this is the main therapeutic motif which may reduce nerve root compression and venous stasis, thereby improving local microcirculation and increasing the oxygen supply (1-3).

For determination of the disc shrinkage, we compared the area of herniated disc before and after O₂-O₃ injection. To estimate the size of disc herniation, repeated CT scans were performed prior to and 5 weeks after injection. CT scans clearly revealed the area of the vertebral canal and disc herniation, and the electronic cursor measurement facilities of CT made it possible to perform the measurement of the affected area directly on the monitor, therefore aiding the calculation of the degree of disc herniation (4). Moreover, since CT is more economical and less time-consuming than other radiological techniques such as magnetic resonance imaging, it lifts some of the financial burden from owners.

The areas measured were used in the A-index in Thelander's study to evaluate the degree of herniation, formed by the ratio of the area of the hernia in relation to the area of the spinal canal (4). It is useful as a base reference which is the most reliable method among index calculations (4).

As a result of treatment, a definite decrease of the herniation was observed in all lesions. In particular, it was observed that the degree of disc shrinkage was not constant ranging from 2.69% to 13.89%. Previous studies have demonstrated that the disc shrinkage after O₂-O₃ therapy is influenced by several factors and it is limited when herniated discs are calcified and present large extruded herniations (5). Therefore, the relationship of these two factors was evaluated in this study. The degree of calcification was estimated using the mean HU value of the herniated disc in the spine window before injection, since higher HU units indicates higher calcification. The volume of disc herniation was defined using the A-index before injection. As a consequence, it was observed that the degree of mineralization affected the rate of disc shrinkage noticeably. There was a negative linear relationship, in other words, a more mineralized disc is less reduced by O₂-O₃ therapy. On the other hand, the volume of the extruded disc did not correlate with disc shrinkage. This result is partially in accordance with previous findings of an inverse relation between disc calcification and the degree of disc shrinkage, while the volume of disc herniation had no relation to disc shrinkage (5).

Follow-up examination using CT for evaluation of disc shrinkage was performed at 5 weeks after the procedure. Previous studies have shown that herniated discs gradually shrank after O₂-O₃ injection and complete shrinkage took a maximum of five week (2). Accordingly, this procedure cannot provide the rapid decompression offered by

laminectomy or fenestration, but offers progressive decompression with the passage of time which prevents deterioration or recurrence of clinical signs with further extrusion of the affected disc. For this reason, O₂-O₃ therapy can not be applied to patients requiring rapid decompression, however it is useful to chronic patients, especially those with frequently relapses. In this study, dogs without deep pain perception were excluded because they should be immediately operated on for acute decompression. All dogs included this study were chronic cases which did not require emergency surgery.

Regarding clinical outcome, all dogs definitely regained gait function, yet it is not clear that disc shrinkage with O₂-O₃ therapy is definitely related to regain of gait, although it is suggested that the minimal change of the herniated disc volume from disc shrinkage offered considerable decompression of spinal cord pressure and helped in the recovery of the affected spinal cord.

It is clear that the disc shrinkage with O₂-O₃ therapy inhibited further extrusion of the affected disc and reduced recurrences. Since none of the animals used in this study have shown any recurrence over 20 months after O₂-O₃ therapy, although they had history of repeated recurrence and had been treated with only conservative methods before O₂-O₃ therapy. This observation suggests that disc shrinkage with O₂-O₃ therapy may prevent further extrusion of lesions and reduce recurrence rates, though it is generally known that the recurrence rate is high when the herniated disc is not removed completely by surgical intervention (6-8).

There are other percutaneous techniques, such as chemodiscolysis with chymopapain (9, 10) or chondroitinase (11), laser discectomy (12), or nucleoplasty (13) have been used to decompress the spinal cord and simultaneously reduce invasiveness and subsequent surgical complications. These treatment methods achieve minimal change of the herniated disc volume with maximal decompression of spinal cord pressure (1). However, the above methods have significant complications, for example chemonucleolysis has a high risk of enzyme leakage to the spinal cord thereby damaging the surrounding tissues and causing side-effects such as anaphylactic shock and post-operative back spasm (1, 14), while laser discectomy can cause infection at the site of needle insertion which can develop into abscess formation and pneumothorax or diskospondylitis related to skin contamination (15). In contrast to these techniques, O₂-O₃ therapy has more advantages and fewer complications. If O₂-O₃ gas comes into contact with the spinal cord, it is not harmful, rather it may offer an analgesic and anti-inflammatory effect by inhibiting inflammatory inducers and pain-producing mediators such as prostaglandins (1, 16). Moreover, the risk of abscess formation or inflammation from skin contamination is lower due to its strong bactericidal activity (17). In addition, the

O₂-O₃ procedure is simple (total procedure time in this study is mean 20 minutes) and requires only minimal hospitalization (less than 24 h) to observe for post-surgical side-effects. Its cost is economical due to the lower cost of production and maintenance, therefore owners were all satisfied with the medical fee for the procedure, it being much lower than other procedures such as decompressive surgery or other percutaneous techniques. Therefore, the low cost, convenience and safety of O₂-O₃ therapy were demonstrated throughout this study.

Conclusion

Considerable disc shrinkage with O₂-O₃ therapy was confirmed on CT views in this study. The degree of disc shrinkage was related to the extent of disc calcification, so that more calcified discs may be less reduced by O₂-O₃ therapy; there were no specific complications. Consequently, it is considered that intradiscal O₂-O₃ injection can decompress the disc herniation with minimum invasiveness.

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