IJVS 2015; 10(1); Serial No:22

IRANIAN JOURNAL OF VETERINARY SURGERY (IJVS)
WWW.IVSA.IR

Comparison between Iodixanol and Iohexol for Cervical Myelography in Cat

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Abstract

Objective- To evaluate and compare the radiographic efficacy and safety of a non-ionic dimeric and isotonic iodinated contrast medium, iodixanol (320 mgI/ml) and a non-ionic monomer and hypertonic contrast medium, iohexol (300 mgI/ml) in feline cervical myelography.
Design- Experimental study
Animals- Five adult healthy cats.
Procedures- Iodixanol and iohexol were injected into the cerebellomedullary cistern. Radiographs were obtained immediately, 10, 20, 40 and 60 minutes after injection. The myelograms were scored and analyzed for statistical significance.
Results- Diagnostically adequate radiographic examinations were obtained with both agents. Adequate opacity in thoracic and lumbar vertebrae was obtained after 10 and 20 minutes post injection for both contrast agents. After 40 minutes contrast agents were had reached the end of lumbar vertebrae column. No significant differences in scoring for image quality were observed between two contrast mediums ($p>0.05$). Iodixanol and iohexol radiopacified cervical region immediately after injection. Adequate opacity in thoracic and lumbar vertebrae was obtained after 10 and 20 minutes post injection for both contrast agents. Evaluation of each of the radiographs showed good to excellent opacification. No clinical and neurological abnormalities were found related to the myelographic procedure during one week after injection. Vital signs, CBC and some serum biochemical examinations remain in normal ranges.
Conclusion and Clinical Relevance- Iodixanol and iohexol proved to be safe and effective contrast materials for myelographic studies in cats. More mean score of iodixanol suggests that, it is preferable to perform myelography with iodixanol.
Key Words- Cervical myelography, Cat, Iodixanol, Iohexol.

Introduction

Myelography is a special radiographic study of spinal cord after injection of a contrast media into the spinal subarachnoid space.[1,2] Myelography is indicated when: there is absence of a spinal cord lesion on routine radiographs, the lesion seen on routine radiographs does not correlate with the clinical signs, multiple lesions are seen on routine radiographs, more precise localization of a lesion is needed for surgical planning.[3,4] Magnetic resonance imaging (MRI) and computed tomography (CT) are replacing the use of myelography in many practice settings, because they are quicker, noninvasive and in the case of MRI, assessing the integrity of the spinal cord is possible. However, Myelography remains a valuable procedure for assessing spinal cord despite of more expensive use of MRI and CT for neuroimaging. Also myelography is still a commonly used technique in veterinary clinics where MRI and CT are not available.[5-8] A number of contrast agents have been used for myelography in the past, but many have posed considerable problems. The selection of contrast medium has a crucial role in myelographic examination. The intrathecal administration of contrast medium requires radiological products with a high neurological safety. The ideal contrast preparation, should be minimal neurotoxic, should be pharmacologically inert, miscible with CSF and radiopaque at an isotonic concentration. Non-ionic contrast agents are preferred for myelography due to their lower incidence of adverse reactions.[1,3,4,9,10] Cases of serious reactions and of neuropsychological disturbance are however still published, even with the monomeric, non-ionic contrast

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media. Iodixanol is well tolerated in intravascular administrations and myelography, with a lower frequency of adverse events such as injection-associated discomfort than the monomeric non-ionic contrast media.[11-14] Based on our knowledge iodixanol was not used for small animal myelography. The purpose of this study was to evaluate and compare the radiographic efficacy and safety of a non-ionic dimeric and isotonic iodinated X-ray contrast medium, iodixanol (Visipaque®; 320 mgI/ml Nycomed Imaging AS, Oslo, Norway) and a non-ionic monomer and hypertonic contrast medium, iohexol (Omnipaque®; 300 mgI/ml Amersham Health, Cork, Ireland) for cat cervical myelography.

Materials and methods

Five domestic short haired, clinically healthy cats, weighted average 3.29 (Range 3.15-3.60) Kg, with different sexes, were selected for the study. The cats were anaesthetized with injection of diazepam (Zepadic®, Caspian Tamin Co. Rasht, Iran) at a dose of 0.2 mg/kg and ketamine 10% (alfasan, Woerden, Holland) at a dose of 15 mg/kg. Ketamine was reinjected when necessary. The dorsal cranial cervical region was clipped and prepared aseptically, from external occipital protuberance to third cervical vertebra. Two orthogonal standard survey radiographs were taken before the procedure. The spinal needle used in the procedure was of 22 G with a stylet for minimizing perimedular tissue damage. The head was held in flexion, the needle was carefully inserted on the midline near the center of a triangle formed by the external occipital protuberance and the wing of the atlas and introduced into the atlanto-occipital space.[2.3.15.16] Cerebrospinal fluid flow into the needle and a lateral radiography were used to confirm needle tip placement within the cerebellomedullary cistern. The table was tilted to nearly 30° to facilitate caudal contrast progression during the injection and first myelograms. After that the cat was put on a soft pad surface which was titled to 30° angle during the study. For taking myelograms the cat was held in a horizontal position. Both contrast agents were warmed in a water bath to nearly 37 degree of centigrade to reduce viscosity.[17] Iodixanol with 320 mgI/ml (Visipaque® 320, Amersham Health, Cork, Ireland) at a dose of 0.5 ml/kg was injected. Iohexol with 300 mgI/ml (Omniopaue® 300 mgI/ml Nycomed, Spain) was used for the study, at least two weeks later. Standard left to right lateral (Lat) and ventrodorsal (VD) radiographs of cervical, thoracic and lumbar vertebrae were obtained immediately, 10, 20, 40 and 60 minutes after injection.

The cats that took part in the study were kept under observation, closely for 48 hours and daily for 7 days in order to prevent and possibly treat any side effects. Vital signs of the animals were recorded 0, 2, 8, 24 and 48 hours after injected contrast media. In each animal, to confirm the absence of any clinical influence, complete blood cell count (CBC) and some serum biochemical examinations (BUN, Creatinine, ALT, AST) were performed on blood samples taken before, 2 and 24 hours after the injection of contrast media.

After completion of the study, the radiographs were evaluated and compared independently by a veterinary radiologist who was unaware of types of contrast agents. The quality of the myelogram was graded on a scale based on radiopacity, ability to define the limits of the subarachnoid space and continuation of dorsal, ventral and lateral myelographic columns (Table 1). Cervical, thoracic (divided to T1 - T7 and T7 - T13) and lumbar VD and Lat myelograms were assessed and scored separately.

Non-parametric statistical analysis of the data was performed by means of the SPSS software package (version 16). Data were evaluated using Mann-Whitney test for comparison of both myelographic methods. A p-value less than 0.05 was considered statistically significant.

Table 1- Critaria for Scoring Methods for the Myelograms after Injection of Iodixanol 320 mgI/ml and Iohexol 300 mgI/ml at a Dose of 0.5 ml/kg in 5 Healthy Cats.

Description	Score
No contrast media was seen in selected anatomic area (No myelogram)	0
Discontinued radiopaque column was seen in one region of selected anatomic area. (Poor myelogram)	1
Interrupted/ Discontinued radiopaque columns were seen in regions of selected anatomic area (Incomplete myelogram)	2
Nearly continuous radiopaque columns were seen in selected anatomic area (Good myelogram)	3
Continuous radiopaque columns were seen in selected anatomic area (Excellent myelogram)	4

Results

No clinical and neurological abnormalities were found related to the myelography during one week after injections. Vital signs, CBC and serum biochemical examinations (BUN, Creatinine, ALT, AST) remain in normal ranges.

Tables 2 and 3 show mean and SEM of scoring of cervical, thoracic and lumbar myelograms after injection of iodixanol and iohexol.

No significant differences in scoring for image quality were observed between two contrast media ($p>0.05$). Mean score of cervical myelogram produced by iodixanol was non-significantly better than iohexol

immediately to 10 minutes after injection ($p>0.05$). Good to excellent cervical and thoracic (T1-7) myelograms produced by iodixanol and iohexol immediately and 10 minutes after injection. Good thoracic (T7-13) and lumbar myelograms produced by iodixanol 20 minutes after injection, while thoracic (T7-13) and lumbar myelograms produced by iohexol were incomplete to good at same time. Golden time for cervical and thoracic (T1-7) myelography with both contrast agents were during 10 minutes after injection. A tendency for better images was obtained by iodixanol, although results were not statistically significant (Figs 1 and 2). Iodixanol and iohexol radiopacified subarachnoid space of cervical region immediately after injection. Adequate opacity in thoracic (T1-7) vertebrae was obtained after 10 minutes and for thoracic (T7-13) and lumbar vertebrae were produced 20 minutes post injection for both contrast agents (Tables 2 and 3). After 20 minutes, contrast agents had reached to the end of lumbar vertebral column. Lateral myelograms shows that they produced comparatively better quality than VD views for different regions of spinal cord in both agents. Although degradation in time of radiographic quality of all myelograms took place and the average radiographic score decreased more rapidly with iohexol. Myelographic artifacts include air bubbles, central canalogram, gravity filling defects, subdural injection and epidural leakage were not seen in both agents.

Table 2- Mean ±SEM of Scoring of Cervical (C), Thoracic (T) and Lumbar Lateral Myelograms after Injection of Iodixanol (Iodix.) and Iohexol (Iohex.) at a Dose of 0.5 ml/kg in 5 Healthy Cats.

		Immediately		**10 min.**		**20 min.**		**40 min.**		**60 min.**	
		Iodix.	Iohex.	Iodix.	Iohex.	Iodix.	Iohex.	Iodix.	Iohex.	Iodix.	Iohex.
C1-7	Mean	3.6	3.2	3.6	3.2	2.6	1.4	2.2	1.2	1.4	0.8
	±SEM	0.24	0.24	0.24	0.37	0.4	0.24	0.58	0.2	0.37	0.24
T1-7	Mean	2.6	3.2	3.6	3.6	3.6	2.2	3.2	2	2.4	1.6
	±SEM	0.4	0.49	0.4	0.24	0.24	0.51	0.2	0.63	0.4	0.73
T7-13	Mean	0.4	0.6	2.8	2.2	3	2.8	2.6	1.8	1.6	1.4
	±SEM	0.4	0.4	0.58	0.58	0.31	0.49	0.4	0.58	0.51	0.67
L1-7	Mean	0	0	1.6	1.2	3	2.8	3	2.2	2.6	2.2
	±SEM	0	0	0.68	0.58	0.55	0.37	0.55	0.58	0.4	0.58

Table 3- Mean and SEM of Scoring of Cervical (C), Thoracic (T) and Lumbar Ventrodorsal Myelograms after Injection of Iodixanol (Iodix.) and Iohexol (Iohex.) at a Dose of 0.5 ml/kg in 5 Healthy Cats.

		Immediately		**10 min.**		**20 min.**		**40 min.**		**60 min.**	
		Iodix.	Iohex.	Iodix.	Iohex.	Iodix.	Iohex.	Iodix.	Iohex.	Iodix.	Iohex.
C1-7	Mean	3	3	3.2	2.4	2.2	1.6	1.4	1	0.6	0.6
	SEM	0.37	0.45	0.2	0.51	0.37	0.37	0.24	0.55	0.24	0.24
T1-7	Mean	2.2	2.6	3.6	2.6	3.2	2	2.4	1.6	2	1.6
	SEM	0.37	0.51	0.4	0.51	0.2	0.58	0.4	0.81	0.45	0.81
T7-13	Mean	0.8	1	3.2	2.4	3	2.4	2.6	1.8	2.2	1.4
	SEM	0.49	0.45	0.58	0.6	0.31	0.49	0.4	0.73	0.58	0.75
L1-7	Mean	0	0	1.6	0.6	2.4	2.6	2.4	1.8	2.6	1.8
	SEM	0	0	0.51	0.4	0.51	0.37	0.4	0.58	0.4	0.73

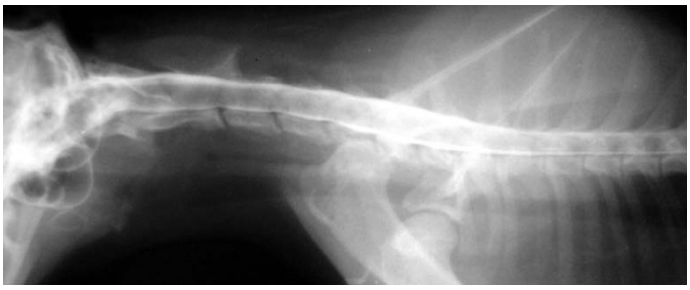

Figure 1- Cervical myelography with iodixanol 320 mgI/ml, 10 minutes after injection.

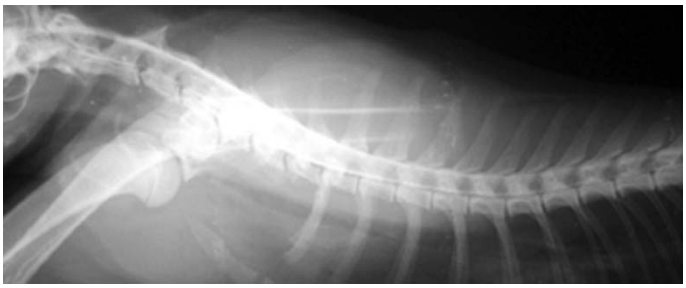

Figure 2- Cervical myelography with iohexol 300 mgI/ml, 10 minutes after injection.

Discussion

Myelography is injection of a positive contrast medium into the subarachnoid space of the spine, after which radiographs of the opacified region of the spine are taken. A myelogram is indicated to highlight a lesion that is undetectable on survey radiographs. Positive contrast in the subarachnoid space can be used to identify extradural lesions, intradural-extramedullary lesions, intramedullary swelling, and intramedullary opacification.[2-4]

The findings reported here show that iodixanol, produce good to excellent cervical myelograms in healthy cats. Also satisfactory results were obtained with iohexol. Iodixanol obtained more mean score than did iohexol, so that there was a tendency for better images produced by iodixanol. This might be partially due to the higher iodine concentration of the iodixanol (320 mgI/ml) compare to the iohexol (300 mgI/ml). Based on our knowledge iodixanol was not used for cat myelography. Nearly the same results as ours was obtained in a study in man that there was no major difference in the image quality between iodixanol and iohexol and very satisfactory results were obtained with both. Statistically, significant better results were obtained with iodixanol (320 mgI/ml) both in cervical and lumbar myelography. However, this difference in image quality did not influence the diagnostic contribution.[13] Also in a comparative myelographic study in 315 patients, iodixanol 270 and 320 mgI/ml provided a similar or better efficacy profile and a similar safety profile in myelography than did iotrolan 300 mgI/ml.[14] Iodixanol has been found to be a safe and radiographically satisfactory myelographic contrast medium in man and some experimental animals.[13, 14, 18, 19] Our study has shown it is also suitable for the cat. Although expensive, non-ionic contrast agents are suitable for both intravascular and myelographic studies.

Timetable: Timetable will be important for expected procedure time and expected time which the contrast agent must opacified special region. A timetable for taking radiographs in myelography has not been mentioned in veterinary radiology textbooks.[2.3.15.16] Based on our findings adequate opacity were obtained during 10 minutes in cervical, and thoracic (T1-7) myelograms and after 10 to 20 minutes in thoracic (T7-13) and lumbar myelograms after injection for both contrast agents in healthy cat. This observation may be partially due to the fact that the table was tilted nearly 30 degrees. In a study in dog 10 to 15 minutes after injection, iohexol and iopamidol reached to thoracic vertebrae.[20] In another research ioversol (Optiray®) injected intracisternally, opacified cervical vertebrae during 5 minutes while the opacification period with diagnostic value were of 60 minutes in 60% of thoracic radiographs and in 80% of lumbar radiographs.[21] The difference of contrast effects of iohexol (180 mgI/ml), iohexol (240 mgI/ml) and iotrolan (240 mgI/ml) for myelography in normal dogs were studied by Shimizu et al. They stated in conventional and CT myelography diffusion of contrast media was influenced by viscosity. So that, low viscosity contrast medium results more rapidly spread to the vertebral column.[17] In another study, at 5 and 10 minutes after cisternal injection of iohexol and iotrolan in 6 dogs, no significant difference was observable between the myelograms, but from 45 minutes onward, myelograms with iotrolan were superior.[22] In a study in the cat, iotrolan was a safe contrast medium for myelography because of the absence of actual postmyelographic adverse effects and the high resolution of the myelograms.[23]

Complication/ Side effects: Nevertheless radiographic quality, no adverse side effects were encountered with both contrast agents in our study. This might be due to both contrast agents were non ionic, low incidence of side effects of iodixanol and iohexol, cats were healthy and number of the myelograms in our study was not too many to show side effects. The same finding was found during an investigation in 6 dogs in cisternal myelography with iohexol and iotrolan, which none of the dogs had seizure activity during a 5-hour postmyelographic observation period.[22] In another study, during the injection of iotrolan for myelography, respiratory arrest that lasted only a few seconds was observed in 2 of the 8 cats and iotrolan was detected intracranially immediately after the subarachnoid injection in 5 of the 8 cats, while no side-effects of any

kind were noticed.[23] Complications from radiologic contrast agents depend on a variety of factors, including the route of administration, chemical composition of the media and the patient's underlying condition. In people, problems associated with myelography have included neurologic signs ranging from muscle fasciculations to generalized seizures, exacerbation of the patient's neurologic condition, headache, nausea, and vomiting. The incidence of seizures depends on lesion location, severity of neurologic deficit, type of myelography (location, contrast medium, volume, concentration, and number of injections of contrast medium), as well as type and duration of anesthesia. Age, sex, and weight can also influence the incidence of seizures. Severe, life-threatening, or even fatal reactions have occurred, but have been more often associated with intravascular administration.[3,4,13,14,24,25]

Conclusion

It is concluded that iodixanol 320 mgI/ml and iohexol 300 mgI/ml at a dose of 0.5 ml/kg are appropriate and safe to be used for myelography in cat. Therefore, both contrast media are suitable for myelography in cat. More mean score of iodixanol also suggest that, it is preferable to perform myelography by administering non ionic contrast media iodixanol.

Acknowledgement

This study was financially supported by Research Council of Shahid Chamran University of Ahvaz

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نشریه جراحی دامپزشکی ایران
سال ۲۰۱۵، جلد ۱۰ (شماره ۱)، شماره پیاپی ۲۲

چکیده

مقایسه بین آیودیکسانول و آیوهکسال برای میلوگرافی گردنی در گربه

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هدف- ارزیابی و مقایسه تاثیر رادیوگرافی و بیخطری ماده حاجب غیر یونی دایمر آیودیکسانول (۳۲۰ میلیگرم ید در هر میلیلیتر) و ماده حاجب غیریونی مونومر آیوهکسال (۳۰۰ میلیگرم ید در هر میلیلیتر) در میلوگرافی گردنی گربه.

طرح مطالعه- مطالعه تجربی

حیوانات- پنج قلاده گربهی بالغ سالم

روش کار- پس از تزریق آیودیکسانول و آیوهکسال در سیسترن مغزیبصلالنخاعی در فضای پس سری اطلسی، رادیوگرافهای شکمی پشتی و جانبی چپ به راست از مهرههای گردنی، سینهای و کمری بلافاصله، ۱۰، ۲۰، ۴۰ و ۶۰ دقیقه بعد از تزریق اخذ شد. بعد از پایان مطالعه، رادیوگرافها توسط رادیولوژیستی که از نوع ماده حاجب بیاطلاع بود مورد ارزیابی و مقایسه مستقل قرار گرفتند. میلوگرامها امتیازبندی و جهت معنیدار بودن از نظر آماری ارزیابی شدند.

نتایج– از نظر رادیوگرافهایی با کیفیت تشخیصی کافی با هر دو ماده حاجب حاصل شد. اپسیته کافی در مهرههای سینهای و کمری ۱۰ تا ۲۰ دقیقه بعد از تزریق برای هر دو ماده حاجب به دست آمد. ۴۰ دقیقه بعد مواد حاجب به انتهای مهرههای کمری رسیده بودند. هیچ تفاوت آماری بین هر دو ماده حاجب وجود نداشت. ارزیابی هر یک از رادیوگرافها بیانگر اپسیفیکاسیون خوب تا عالی بود . هیچ گونه عارضه جانبی حتی یک هفته بعد از پایان مطالعه رخ نداد.

نتیجهگیری و کاربرد بالینی- ثابت شد که در گربه آیودیکسانول و آیوهکسال به عنوان مواد حاجب بی خطر و موثر برای مطالعات میلوگرافیک میباشند. میانگین امتیاز بیشتر آیودیکسانول پیشنهاد میکند که بهتر است میلوگرافی با آن انجام شود.

کلمات کلیدی - میلوگرافی گردنی، گربه، آیودیکسانول، آیوهکسال.