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Myelography in calves: a comparative study between the contrast agents iopamidol and iohexol

[*Mielografia em bezerros: estudo comparativo entre os meios de contrastes iopamidol e ioexol*]

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ABSTRACT

Due to the scarcity of myelogenous studies in cattle, the present study aimed to evaluate the efficacy and distribution of iopamidol and iohexol contrast agents in calves, in order to determine guidelines for obtaining diagnostic radiographs of spinal cord disorders in these animals. Ten healthy Holstein calves, seven days to two months of age, were divided into two groups, according to the contrast medium applied. Myelographic studies of the spine were performed with the calves in lateral recumbency, with radiographs repeated 20 times during a two-hour period. On the radiographs, the contrast medium was analyzed for opacity, detail of the image, distension of the medullary canal, and progression of the contrast line. After seven days, the myelographic studies were repeated, with the contrast media exchanged between the groups. There were no significant differences in the quality of the images and speed of the spinal column filling between the two contrast media. Furthermore, the best quality radiographic images were obtained six to eight minutes after injection of the contrast in the cervical spinal segment, 80 minutes in the thoracic, and 20 minutes in the lumbar, sacral, and cauda equina segments.

Keywords: cattle, diagnostic imaging, digital radiography, spinal cord, spine

RESUMO

Devido à escassez de estudos mielográficos em bovinos e relatos de complicações no procedimento, o presente estudo teve por objetivo avaliar a eficácia e a distribuição dos meios de contraste iopamidol e ioexol em bezerros, a fim de nortear a melhor conduta para o diagnóstico de afecções vertebrais e medulares nesses animais. Foram utilizados 10 bezerros Holandeses, hígidos, com idade entre sete dias e dois meses, distribuídos em dois grupos, conforme o meio de contraste aplicado. O estudo mielográfico da coluna vertebral foi realizado na posição laterolateral, repetido em 20 momentos, durante o período de duas horas. Nas radiografias, analisou-se o meio de contraste quanto à opacidade, detalhes da imagem, distensão do canal medular e progressão da linha de contraste. Após sete dias, foi realizado o segundo período experimental, que compreendeu a troca do meio de contraste dentro de cada grupo. Não houve diferenças significativas em relação à qualidade da imagem e à velocidade do preenchimento da coluna medular entre os dois meios de contraste. A partir da administração dos meios de contraste, a obtenção de imagens radiográficas de melhor qualidade deu-se após seis a oito minutos no segmento medular cervical, 80 minutos no torácico e 20 minutos nos segmentos lombar, sacral e cauda equina.

Palavras-chave: bovinos, diagnóstico por imagem, radiografia digital, coluna vertebral, medula espinhal

INTRODUCTION

Myelography is the radiological examination of the spinal cord by subarachnoid administration of a contrast medium (Wheeler and Davies, 1985; Thrall, 2010). It is used in veterinary practice to define the location and extent of spinal cord injuries (Kirberger *et al*., 1992).

Radiological contrast media provide high definition images that allow for a precise diagnosis (Bontrager, 1999). Radiographic image

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quality depends on the miscibility of the contrast media with cerebrospinal fluid (CSF), agent viscosity, sufficient iodine concentration for adequate radiopacity, and lack of neurotoxicity (Widmer, 1989; Widmer *et al.*, 1992). Iohexol and iopamidol are 2,4,6-triiodobenzoic acid derivatives that have similar pharmacological characteristics (non-ionic, low osmolality, CSF miscibility, inert, water soluble, radiopaque even in isotonic concentration, rapid and complete elimination in the subarachnoid space, and opacity for the time required to obtain the necessary radiographs) (Widmer, 1989; Widmer and Belvins, 1991; Roberts and Selcer, 1993; Fatone *et al.*, 1997).

Myelographic techniques are widely described for dogs (Wheeler and Davies, 1985; Widmer, 1989; Widmer *et al.*, 1992; Costa *et al.*, 2011) and horses (Scrivani *et al.*, 1997; Widmer *et al.*, 1998; Biervliet *et al.*, 2004; Hudson and Mayhew, 2005). However, few studies have involved cattle (Bargai, 1993; Marques *et al.*, 2004; Zani *et al.*, 2008). The standardization of specific radiographic techniques and the adequate choice of contrast media may help to obtain better quality images, with minimal adverse effects. Therefore, this study aimed to compare the quality of myelography images between iopamidol and iohexol contrast agents and to determine the times at which their radiopacity provides excellent image quality. The study also aimed to assess the rate of filling of the contrast media in each segment of the spine.

MATERIAL AND METHODS

This study was approved by Ethics Commission in Animal Use of the School of Agrarian and Veterinary Sciences, São Paulo State University, Protocol N° 008705/14. Ten healthy Holstein calves, seven days to two months of age, were randomly assigned to two groups of five animals (G1 and G2). For the first myelography, G1 received iohexol, and G2 received iopamidol. Seven days later, for the second myelography, the contrast media were exchanged between the groups. Therefore, both contrast media were evaluated in all ten animals.

Myelography was performed under general anesthesia. First, the animals received 2% xylazine hydrochloride (Rompun®, Bayer, Brazil) as a pre-anesthetic medication, at a dose of 0.05mg/kg intramuscularly. After 10 minutes, anesthesia was induced using Propofol (Propovan®, Cristália Produtos Químicos e Farmacêuticos Ltda., Brazil) at a dose of 4 to 6mg/kg intravenously, and endotracheal intubation was performed. Anesthesia was maintained with isoflurane (Isoforine®, Instituto Biochimico Ind. Farm, LTDA., Brazil) by inhalation. The calves were kept in right lateral recumbency on a wooden ramp with a 45° inclination, with the head facing upward (Bargai, 1993; Zani, 2008; Thrall, 2010).

Direct digital radiography equipment was used (Portable DR system PDX-1417, Poskom Co. LCD, Goyang, South Korea). In the center of the wooden ramp an acrylic case (MR PodoblockTM, Bayer MaterialSicence, Holand) was fitted with overlap surfaces, with a flat panel X-ray detector (Xmaru 1417P, Samsung Eletronics Co. Ltd Hwaseong-si, South Korea). The X-ray generator (PXM-40BT, Poskom Co. LCD, Goyang, South Korea) was positioned 70cm away from the X-ray detector, using 70kV and 2.5mAs. Radiographs were processed and analyzed by acquisition software for X-ray images in veterinary medicine (DicomPACS® DX-R, OR Technology - Oehm und Rehbein GmbH, Rostock, Germany). Prior to the injection of the contrast media, plain lateral radiographs of the cervical (neutral and flexed position), thoracic, and lumbar segments of the spine were obtained.

Subsequently, the atlanto-occipital area, previously shaved, was antisepsis with chlorhexidine degerming and alcohol. With the cervical region in ventroflexion, a 16 gauge intravenous catheter (BD AngiocathTM 16GA x 1.88IN - Becton Dickinson Indústrias Cirúrgicas Ltda., Brazil), parallel with the ramus of the mandible, was introduced slowly through the midpoint between the two wings of the atlas and the lower edge of the occipital bone in the direction of the foramen magnum, until it reached the dura mater (De Lahunta *et al.*, 2015). Upon perforating the dura mater, CSF was expressed, verifying that the cerebellomedulary cistern in the subarachnoid space was accessed. CSF volume corresponding to the animal's size and contrast volume to be injected was withdrawn (Bargai, 1993).

The contrast medium, iohexol (Omnipaque® 300mgI/mL, GE Healthcare Laboratory, China)

or iopamidol (Iopamiron® 300mgI/ml, Schering, Germany), was then injected slowly, over 2 to 3 minutes, at the dose of 0.45ml/kg body weight (Thrall, 2010). The radiographic views taken initially were repeated every 2 minutes until the medium reached the cauda equina, and every 10 minutes thereafter, totaling 20 radiographic times (T2, T4, T6, T8, T10, T12, T14, T16, T20, T20, T20, T30, T40, T50, T60, T70, T80, T90, T100, T110, and T120). Seven days later the same procedures were performed for the second myelogram, and the contrast media were exchanged as described above. All myelogram images were meticulously analyzed according to anatomical segments of the spinal cord (cervical, thoracic, lumbar, and sacral, along with the cauda equina). Scores were assigned as described in Table 1.

Statistical analysis was performed using split-plot, evaluating the group factor (2 levels) in the plots and the time factor (20 levels) in the subplots, with 10 animal blocks, since the animals were the same in the two groups. The mean square of the animal interaction × treatment was used as residue to the test group. Before analysis, the variables were transformed into square roots (measured response + 1), since these involve discrete responses corresponding to scores. For the analysis, the General Linear Models (GLM) procedure of SAS software (SAS 9.1, SAS Institute, USA) was used. Significant differences between means were compared by Tukey test at the 5% level.

Table 1. Scoring method for myelographic quality concerning opacity of contrast column (O), detail (D), subarachnoid distension (Di), and contrast line progression (P), modified by Widmer *et al*. (1998)

Opacity of contrast column (O)	
0	Opacity insufficient for diagnosis.
1	Opacity adequate for evaluation of lesion, but not optimum.
2	Opacity considered excellent for lesion identification.
Detail (D)	
0	WITHOUT CONTRAST MEDIA – no media in the spinal cord. Impossible evaluation of spinal cord injuries.
1	POOR – detail is sub-optimal, insufficient for evaluation of subtle extradural lesions. The lesion is suspected, but it is not observed in the radiographic image.
2	GOOD – subtle lesions can be evaluated, detail is sufficient to make a diagnosis.
3	EXCELLENT – detail is clear and well defined for the identification of the lesion.
Subarachnoid distension (Di)	
0	Inadequate
1	Adequate
Contrast line progression (P)	
0	WITHOUT – there is no filling of the spinal canal with the contrast medium, in the cranial-caudal direction, in the segment of the spinal cord analyzed.
1	PARTIALLY - partial filling of the spinal canal with the contrast medium, in the cranial-caudal direction, in the segment of the spinal cord analyzed.
2	COMPLETELY - complete filling of the spinal canal with the contrast medium, cranial-caudal direction, in the segment of the spinal cord analyzed.

RESULTS

The mean scores of the detail presented significant values at 40 minutes for the cervical segment (DC) and 20 minutes for the thoracic (DT), lumbar (DL), and sacral/cauda equina (DE) segments after administration of contrast medium. The best time to obtain a high quality and rich detail image was at six to eight minutes in the cervical region, 80 to 120 minutes in the thoracic region, and 20 minutes in the lumbar, sacral, and cauda equina regions (Figure 1).

The medullary column opacity presented averages with significant differences and better opacities at 40 minutes for the cervical segment (OC), 80 minutes for the thoracic (OT), and 20 minutes for the lumbar segment (OL) and sacral/cauda equina (OE) after injection of the contrast medium (Figure 2).

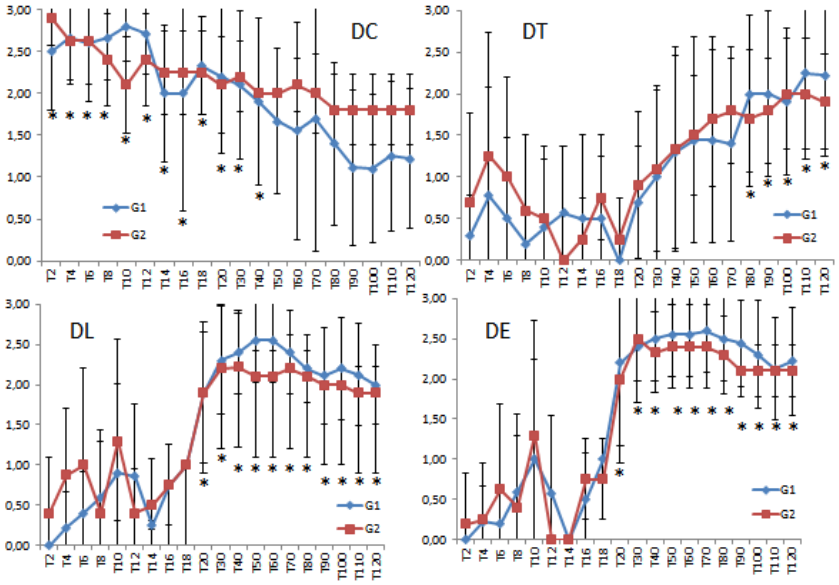

Figure 1. Graphical representation of the mean, standard deviation, and time analyzed for the score of the detail variable in the cervical, thoracic, lumbar, and sacral/cauda equina segments of calf vertebral column (DC, DT, DL, DE) in relation to time. * significant at the 5% level (P< 0.05). (UNESP - Jaboticabal, 2016).

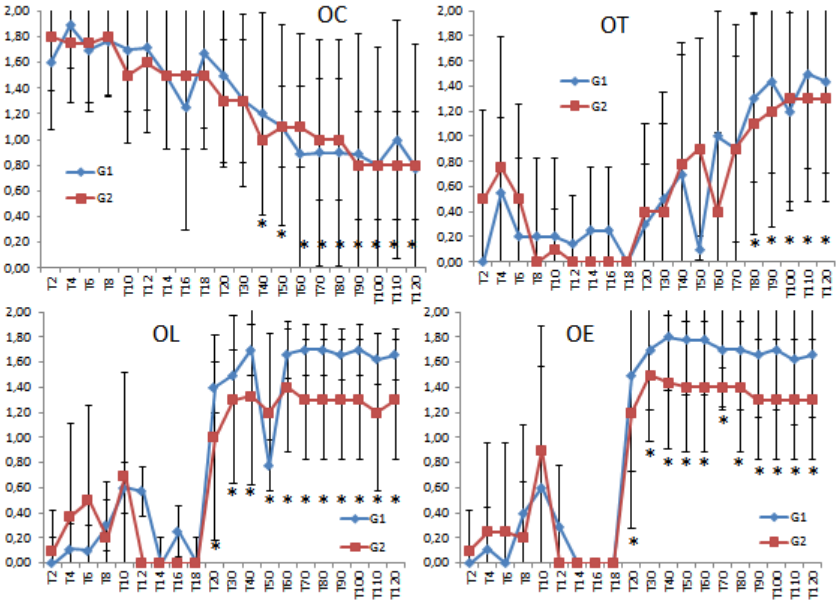

Figure 2. Graphical representation of the mean, standard deviation, and time analyzed for the score of the opacity variable in the cervical, thoracic, lumbar, and sacral/cauda equina segments of calf vertebral column (OC, OT, OL, and OE) in relation to time. * significant at the 5% level (P< 0.05). (UNESP - Jaboticabal, 2016).

The mean distension scores of the subarachnoid space did not show a significant difference for the cervical region (DiC). However, there were significant differences and better distension at 80 minutes for the thoracic segment (DiT) and 20 minutes for the lumbar segment (DiL) and sacral/cauda equina (DiE) after injection (Figure 3).

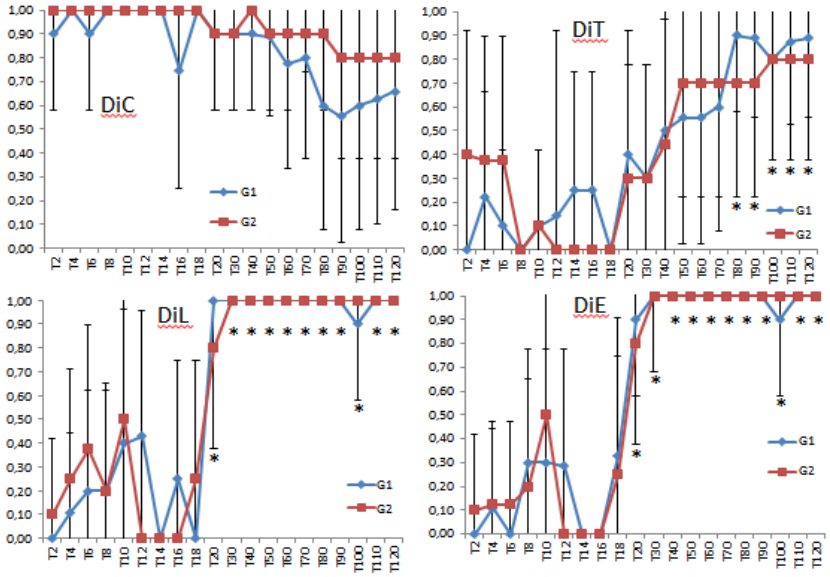

Figure 3. Graphical representation of the mean, standard deviation, and time analyzed for the subarachnoid space distension in the cervical, thoracic, lumbar, and sacral/cauda equina segments of calf vertebral column (DiC, DiT, DiL, and DiE) in relation to time. * significant at the 5% level (P< 0.05). (UNESP - Jaboticabal, 2016).

The mean scores of the contrast line progression presented significant values at 80 minutes for the cervical segment (PC), 50 minutes for the thoracic (PT), and 20 minutes for the lumbar (PL) and sacral/cauda equina segments (PE) after injection. There was progression of the contrast line in each segment up to 20 minutes after the application of the contrast to the cervical region, 80 minutes to the thoracic, and 30 to 120 minutes in the lumbar, sacral, and cauda equina regions (Figure 4).

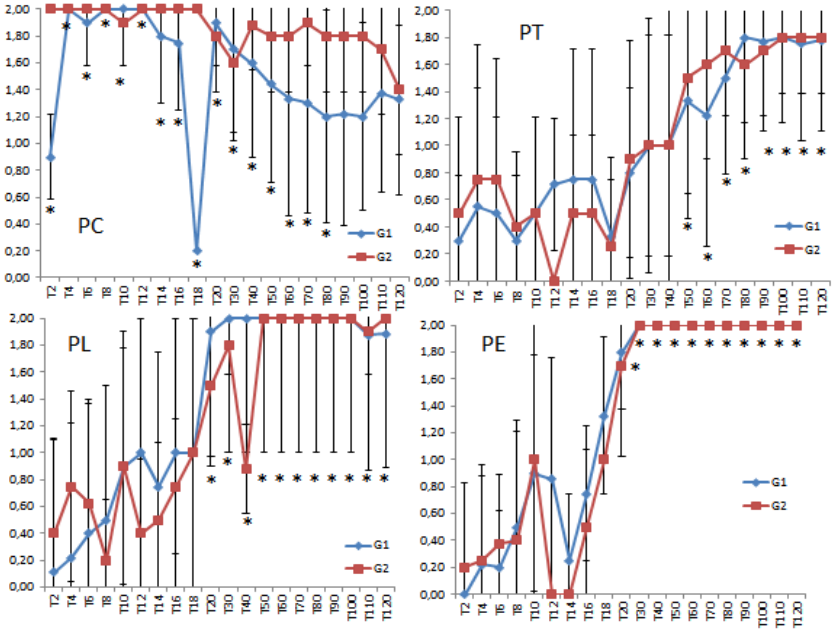

Figure 4. Representation of Tukey's analysis (P< 0.05) in the variable contrast line progression in the cervical, thoracic, lumbar, and sacral/cauda equina segments of calf vertebral column (PC, PT, PL, PE) in relation to time. *significant at the 5% level (P< 0.05). (UNESP - Jaboticabal, 2016).

The time between contrast application and complete filling of the spinal cord segments was, on average, 2.3 minutes for the cervical segment, 33.1 minutes for the thoracic, 15.5 minutes for the lumbar and sacral, and 16.9 minutes for the cauda equina. There were no significant differences between the groups for the variables analyzed.

Images representing the spinal column without contrast (Figure 5), with iohexol (Figure 6), with iopamidol (Figure 7), with eight (Figure 8), 20 (Figure 9), 80 (Figure 10), 120 (Figure 11) minutes after administration of the contrast medium are below.

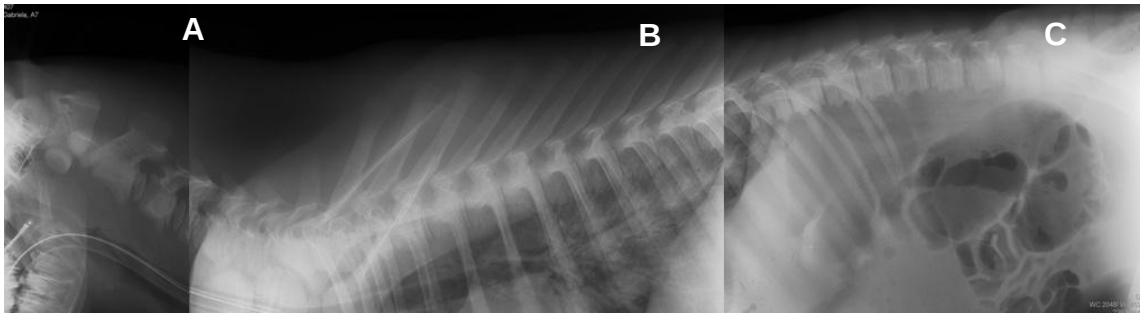

Figure 5. Radiographic image of calf vertebral column prior to contrast injection. A. Cervical segment. B. Thoracic segment. C. Lumbar and sacral/cauda equina segments. (UNESP - Jaboticabal, 2016).

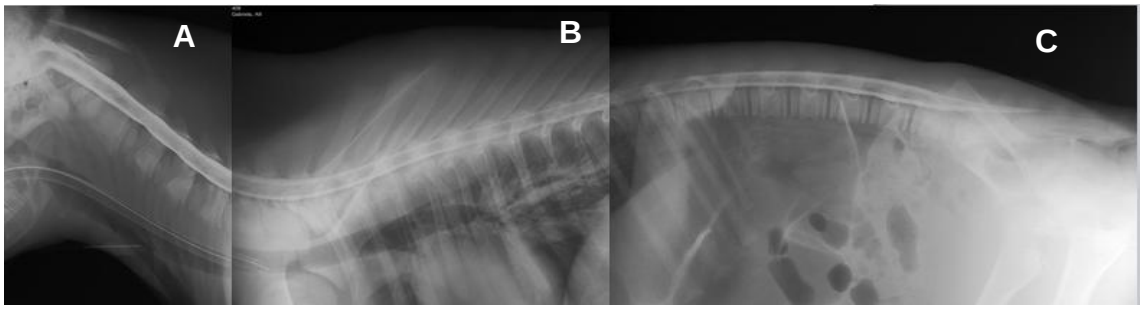

Figure 6. Myelographic image of the spinal column of calf that received subarachnoid iohexol. A. Cervical segment. B. Thoracic segment. C. Lumbar and sacral/cauda equine segments. (UNESP - Jaboticabal, 2016).

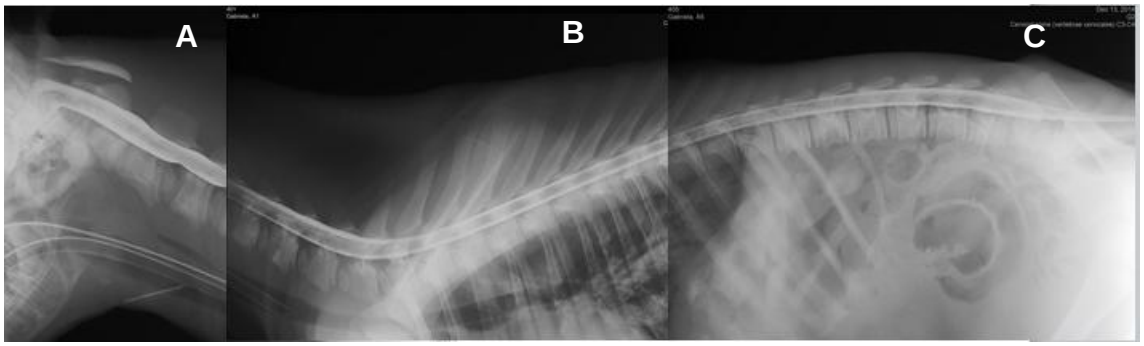

Figure 7. Myelographic image of the spinal column of calf that received subarachnoid iopamidol. A. Cervical segment. B. Thoracic segment. C. Lumbar and sacral/cauda equina segments. (UNESP - Jaboticabal, 2016).

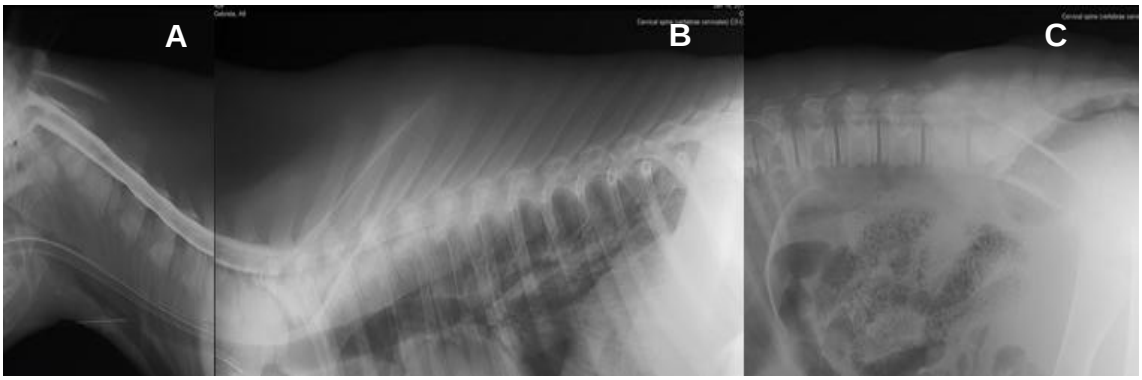

Figure 8. Myelographic image of the calf spinal column eight minutes after contrast administration. A. Cervical segment. B. Thoracic segment. C. Lumbar and sacral/cauda equina segments. The cervical segment has excellent opacity and detail, as well as adequate distension of the subarachnoid space and complete progression of the contrast line. (UNESP - Jaboticabal, 2016).

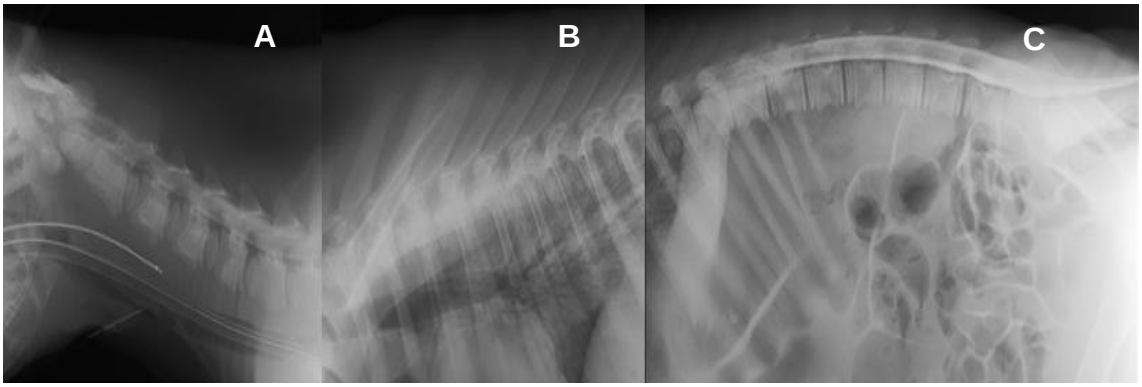

Figure 9. Myelographic image of the calf spinal column 20 minutes after contrast administration. A. Cervical segment. B. Thoracic segment. C. Lumbar and sacral/cauda equina segments. The lumbar spinal segment has excellent opacity and detail, as well as adequate distension of the subarachnoid space and complete progression of the contrast line. UNESP - Jaboticabal, 2016.

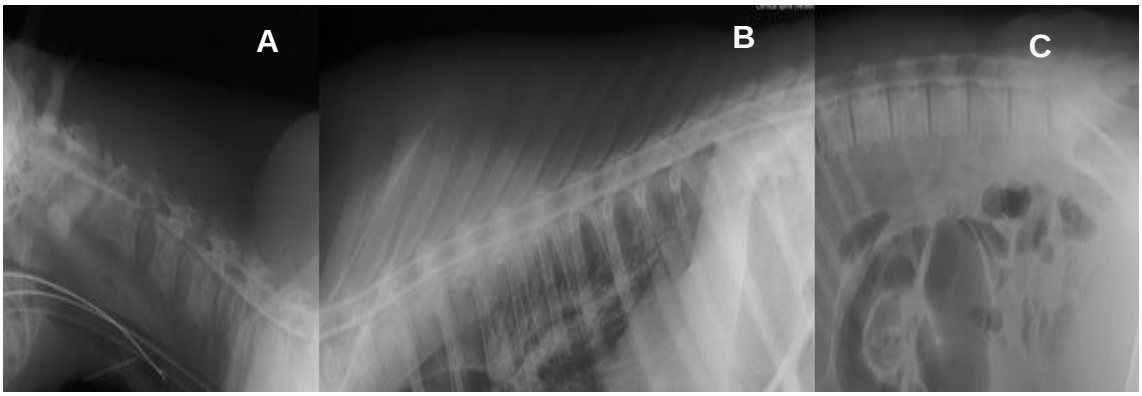

Figure 10. Myelographic image of the calf spinal column 80 minutes after contrast administration. A. Cervical segment. B. Thoracic segment. C. Lumbar and sacral/cauda equina segments. Opacity, detail, adequate distension of the subarachnoid space, and complete progression of the contrast line are noted in the thoracic segment. UNESP - Jaboticabal, 2016.

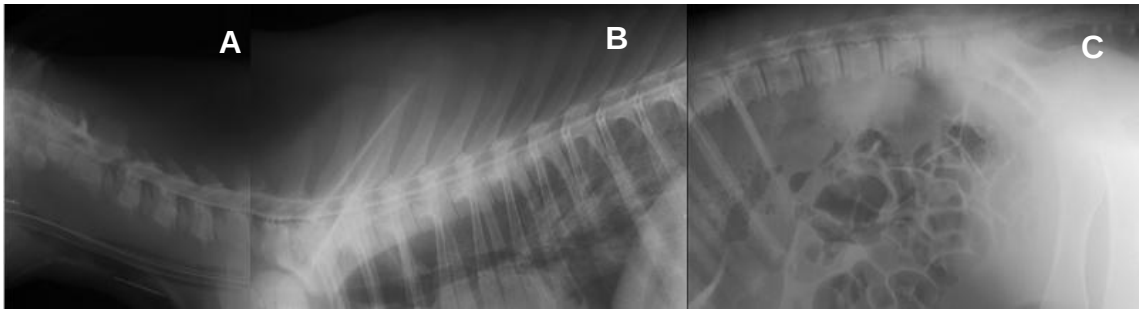

Figure 11. Myelographic image of the calf spinal column 120 minutes after contrast administration. A. Cervical segment. B. Thoracic segment. C. Lumbar and sacral/cauda equina segments. The contrast medium has dissipated in all segments of the spinal cord. UNESP - Jaboticabal, 2016.

DISCUSSION

In order to obtain the images, timed serial radiographs were taken to evaluate the behavior of the contrast medium along the subarachnoid space. The use of digital radiography allowed several subsequent radiographic images to be obtained and immediate generation of the image on the computer screen. This technique, in addition to presenting better cost benefit, stores images without altering the quality or adjusting the contrast and brightness and emits minimal radiation when compared to conventional radiographic methods.

In dogs, it has been shown that iopamidol, efficiently mixed with CSF, exhibits good opacity and sufficient contrast duration of up to three and a half hours (Cox and Jakovljevic, 1986). In this study, the opacity period in the calves that received iopamidol lasted up to 120 minutes, considered sufficient to obtain good quality radiographic images.

Bargai (1993) stated that contrast filling in the cervical portion occurred immediately after administration and after 30 minutes in the lumbar and cauda equina portions. In this study, the filling of the entire medullary canals of the calves by means of the contrast used was, on average, 2.3 minutes for the cervical segment and 21.8 minutes for the other segments. Therefore, better radiographic images in calves can be obtained respecting the time of diffusion and progression of the contrast in the different segments. This difference is due to the intrathecal clearance of the contrast medium, which carries it through all segments of the spinal column. CSF carries the substances into the bloodstream through a mass flow system. Furthermore, the contrast media are liposoluble, a characteristic that assists in the transport of particles through the blood-brain barrier (Mayer *et al.*, 1960).

No difference was identified between the contrast media used in regard to opacity, detail of the image, subarachnoid space distension, and progression of the contrast line at the spinal column, corroborating previous studies in dogs (Widmer *et al.*, 1992; Vulcano *et al.*, 2002). Regarding detail, it was observed that 20 minutes after administration of the contrast medium, there was adequate visualization of the detail of the spinal column, except for the thoracic segment, in which it occurred after 60 minutes.

Opacity became adequate 20 minutes after contrast injection in the cervical and lumbar segments and, paradoxically, after 80 minutes in the thoracic segment. In dogs, adequate opacification periods for diagnostic purposes using iohexol and iopamidol were 30 and 37.5 minutes in the cervical spine, 22.5 and 37.5 minutes in the thoracic segment, and 105 and 140 minutes in the lumbar segment, respectively (Thilagar *et al.*, 1996). In the thoracic, lumbar, and cauda equina segments of the calves, it was observed that, 20 minutes after injection of the contrast, the opacity was adequate and remained stable for up to 120 minutes. However, in the cervical segment, the excellent opacity occurred at 20 minutes after injection and then remained relatively adequate for up to 120 minutes.

The variables of subarachnoid space distension and contrast line progression were also adequate for diagnosis 20 minutes after injection. In the thoracic segment, as with the other variables,

they were satisfactory later, 50 minutes after injection.

The dynamics of the thoracic region differ from the other medullar segments, with higher time intervals for the studied variables. This is likely due to the contrast media used, which present osmolality slightly higher than the CSF (300mgI/ml) and lateral decubitus, which tends to cause accumulation of the contrast medium in the middle cervical and lumbar regions, resulting in subarachnoid filling below the ideal in the thoracic segment (Widmer *et al.*, 1992). In the present study, the animals were kept in lateral recumbency on an inclined surface with an angle of 45°, which may have influenced the distribution dynamics, contrast line progression, and opacity of the thoracic segment.

Also, anatomical and flow characteristics of CSF should be considered. Therefore, the CSF is in constant motion, progressing from the cerebral ventricles to the spinal cord, from the spinal cord to the brain ventricles, and granulating the arachnoid (De Lahunta *et al.*, 2015). The CSF carries with it the iodine particles of contrast media, causing differences in the opacity and detail variables in the different segments of the spinal column. After administration, the contrast medium flows caudally, passing through the medullary cone and returning cranially. Since the animals in this study were kept in lateral decubitus on an angular ramp of 45º, with the head facing the highest part, the return of the CSF to the fourth ventricle, after dissipation in the caudal parts of the spinal column, occurred more slowly when compared to the descent. Therefore, a higher concentration of iodine molecules and better opacity and detail in the thoracic segment were observed at time points later than those of the lumbar and cauda equina regions.

CONCLUSIONS

The present study of myelography in calves using iohexol and iopamidol shows that there is no difference between the contrast and that in twenty minutes the spine is filled with contrast medium, but not with adequate opacity for radiographic images. Both means of contrasts studied present times to obtain radiographic images with different adequate opacity for the segments of the spine: six to eight minutes for the cervical segment, eighty minutes for the thoracic segment and twenty minutes for the lumbar, sacrum and cauda equine segments.

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