PESQUISA VETERINÁRIA BRASILEIRA
Brazilian Journal of Veterinary Research
ISSN 0100-736X (Print)
ISSN 1678-5150 (Online)

Pesq. Vet. Bras. 43:e07132, 2023
DOI: 10.1590/1678-5150-PVB-7132

Original Article
Small Animal Diseases

Non-invasive monitoring of intracranial pressure waveforms using Braincare® BCMM 2000 monitor in dogs with myelopathies undergoing myelography[1]

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ABSTRACT.- Bahr Arias M.V., Rocha N.L.F.C., Cardoso G.S. & Nogueira J.F. 2023. **Non-invasive monitoring of intracranial pressure waveforms using Braincare® BCMM 2000 monitor in dogs with myelopathies undergoing myelography**. *Pesquisa Veterinária Brasileira 43:e07132, 2023*. Departamento de Clínicas Veterinárias, Universidade Estadual de Londrina, Rodovia Celso Garcia Cid, PR-445 Km 380, Campus Universitário, Cx. Postal 10.011, Londrina, PR 86057-970, Brazil. E-mail: vicky@uel.br

Intracranial pressure (ICP) monitoring is considered the gold standard for optimizing the treatment of humans in intensive care units. However, this procedure is not commonly performed in veterinary medicine because of the limitations and complications of the method. There are some new promising non-invasive techniques for monitoring ICP, but they have not been validated in veterinary medicine. This study aimed to correlate the non-invasive intracranial pressure (NI-ICP) waveforms obtained with the BCMM-2000 Brain4care monitor during myelography in dogs with myelopathies undergoing this exam for diagnostic purposes with the waveforms obtained through invasive monitoring of the subarachnoid pressure (SP). The NI-ICP waveform was monitored in six dogs with myelopathies before (M1), during (M2), and after (M3) contrast medium injection into the subarachnoid space. Cerebrospinal fluid (CSF) was collected before contrast injection. The SP waveform was simultaneously monitored in three of the six dogs. Correlations between the two methods were performed using Pearson's coefficient. The analysis of the morphology and amplitude of the waves at each moment was performed, and at M2, an increase in the P2:P1 ratio ($p<0.05$) was observed in both monitoring methods. In M3, the values were similar to those of M1, demonstrating the return of cerebral compliance. The comparison of the NI-ICP and SP had a positive correlation in those moments (Pearson's coefficient r=0.76; $p=0.027$). The speed of contrast administration, degree of spinal cord compression, and volume of CSF previously collected may affect P2:P1 and ICP dynamics. The BCMM-2000 Brain4care monitor was effective in detecting changes in ICP dynamics and abnormal pulse waveforms in dogs with meningoencephalitis of unknown origin, vertebral neoplasm and intervertebral disc disease with and without hemorrhagic myelomalacia, suggesting increased ICP induced by myelography.

INDEX TERMS: Intracranial pressure monitoring, myelography, subarachnoid pressure, dogs.

[1] Received on April 1, 2022.
Accepted for publication on November 28, 2022.
Part of the Master's Thesis of the second author.

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RESUMO.- [Monitoramento não invasivo do formato das ondas de pressão intracraniana usando o monitor Braincare® BCMM 2000 em cães com mielopatias submetidos à mielografia.] A monitorização da pressão intracraniana (PIC) é considerada o padrão ouro para otimizar o tratamento de humanos em unidades de terapia intensiva, entretanto, esse procedimento não é comumente realizado na medicina veterinária devido às limitações e complicações do método. Existem algumas técnicas não invasivas promissoras de monitoramento da PIC, mas elas não foram validadas na medicina

veterinária. Este estudo teve como objetivo correlacionar os formatos das ondas não invasivas da PIC (NI-PIC), obtidas com o monitor BCMM-2000 Brain4care, antes e após a injeção de meio de contraste no espaço subaracnóideo de cães com mielopatias submetidos à mielografia para fins diagnósticos, com as formas de onda obtidas por meio de monitoração invasiva da pressão subaracnóidea (PS). O formato das ondas NI-PIC foram monitoradas em seis cães com mielopatias antes (M1), durante (M2) e após (M3) injeção de meio de contraste no espaço subaracnóideo. O líquido cefalorraquidiano (LCR) foi coletado antes da injeção de contraste. A forma da onda da PS foi monitorada simultaneamente em três dos seis cães. As correlações entre os dois métodos foram feitas usando o coeficiente de Pearson. Foi realizada a análise da morfologia e amplitude das ondas em cada momento, e em M2 observou-se aumento da relação P2:P1 (p<0,05) em ambos os métodos de monitoramento. Em M3, os valores foram semelhantes aos de M1, demonstrando o retorno da complacência cerebral. A comparação do NI-PIC e PS apresentou correlação positiva nesses momentos (coeficiente de Pearson r=0,76; p=0,027). A velocidade de administração do contraste, o grau de compressão da medula espinhal e o volume de LCR coletado anteriormente podem afetar a dinâmica P2:P1 e PIC. O monitor BCMM-2000 Brain4care foi eficaz na detecção de alterações na dinâmica da PIC e dos formatos das ondas de pulso anormais em cães com meningoencefalite de origem desconhecida, neoplasia vertebral e doença do disco intervertebral com e sem mielomalácia hemorrágica, sugerindo aumento da PIC induzida pela mielografia.

TERMOS DE INDEXAÇÃO: Monitorização da pressão intracraniana, mielografia, pressão subaracnóidea, cães.

INTRODUCTION

Invasive intracranial pressure (ICP) monitoring is the gold standard for monitoring humans in intensive care units (ICUs) to confirm or exclude intracranial hypertension (ICH), to perform the appropriate treatment, to check the response to it, and to increase patient safety (Abraham & Singhal 2015); however, this is not commonly performed in veterinary medicine. In most studies, ICH has been experimentally induced in healthy dogs (Leonard & Redding 1973, Simpson & Reed 1987, Keegan et al. 1995, Bagley et al. 1996, Pluhar et al. 1996, Packer et al. 2011, Sturges et al. 2019) and there are few reports addressing invasive monitoring in dogs with central nervous system disorders. There is a study with 23 dogs with hydrocephalus, one in 17 dogs with brain tumors, and another study described invasive ICP monitoring in two cats and one dog with traumatic brain injury (TBI) (Ballocco et al. 2019, Kolecka et al. 2019, Seki et al. 2019).

Invasive methods have limitations because of the cost of the fiberoptic catheter, the degree of invasiveness of the technique, the need for surgical intervention and patient's admission to the intensive care unit, and complications such as hemorrhage, iatrogenic lesion of the nervous tissue, infection, breakage of the sensor due to its frailty, displacement, and inaccurate positioning (Kawoos et al. 2015). Because of these limitations, there are studies with non-invasive methods of ICP monitoring, which also show controversial results, such as the evaluation of the optic nerve diameter (Ilie et al. 2015), magnetic resonance imaging (MRI) compared with Doppler (Bittermann et al. 2014), and evaluation of optic nerve diameter by ophthalmoscopy in comparison with MRI and invasive ICP monitoring (Giannasi et al. 2020).

Recently, in medicine, a non-invasive ICP monitoring device that uses a "strain gauge" strain sensor, which can detect small bony deformations of the skull resulting from intracranial pressure variation, has been made available (Cabella et al. 2016, Bollela et al. 2017). The method showed a strong correlation with intraparenchymal ICP in mice (Cabella et al. 2016). One study compared the use of this device in dogs with and without neurologic diseases, and the method could detect abnormal pulse waveforms that suggested increased ICP (Bahr Arias et al. 2022). This technique does not display ICP numerically but allows the recording and observation of the morphology of the pressure waves produced by the cerebral arterial pulses (Abraham & Singhal 2015). The ICP waves have three distinct peaks (P1, P2, and P3), which correlate with the blood pressure for each cardiac cycle (Abraham & Singhal 2015, Cabella et al. 2016). When brain compliance is normal, the ICP waves have decreasing P1, P2, and P3 peaks, whereas, in patients with increased ICP and altered compliance, the P2 peak is greater than P1 and P3, or the P2/P1 ratio is ≥0.8. This increase in the P2 peak is an early indicator of ICH (Fan et al. 2008).

ICP can be studied by inducing its increase through the introduction of liquid substances or inflatable balloons into the subarachnoid space. Thus, studies in dogs have used the injection of contrast medium to study changes in ICP dynamics (Arany-Tóth et al. 2012, 2013). In this context, as there is only one study in dogs with this new non-invasive ICP monitoring device, the present study aimed to verify the increase in ICP induced by contrast injection into the lumbar spinal subarachnoid space detected by the non-invasive ICP monitor Brain4care® BMC2000 in dogs with myelopathies undergoing myelography, as well as to compare the ICP waves obtained by this method with those obtained by the invasive monitoring of the lumbar spinal subarachnoid pressure.

MATERIALS AND METHODS

Study local and contextualization. This study was carried out after receiving approval from the Institutional Ethics Committee under the identification number 10052.2018.88. Dogs with the acute spinal disease who presented consecutively to the Veterinary Teaching Hospital of the "Universidade Estadual de Londrina" (UEL) from 2019 to 2020 were recruited prospectively. All procedures were performed with the consent of the owners. Inclusion criteria were as follows: absence of clinical signs indicating systemic disease, no changes in clinical evaluation and laboratory examinations that would contraindicate general anesthesia, the inability of the owner to afford the costs of computed tomography, the need to collect cerebrospinal fluid (CSF) and myelography to confirm or exclude the presence of disc herniation. Signalment, history, and physical and neurological examinations were recorded, including the duration of clinical signs before the investigation. The minimum database for each dog consisted of a complete blood count, serum biochemistry profile, and survey radiographs.

Clinical Score. All the affected dogs underwent physical and neurological examinations. The location of the spinal cord injury was determined by neurological examination, including neurological grading (Sharp & Wheeler 2005). The following degrees of spinal cord injury were considered: cervical spinal segments (C1-C5):

grade I = cervical pain, grade II = pain and ataxia, and grade III = pain, tetraparesis, or tetraplegia; thoracolumbar (T3-L3) and lumbar (L4-L6) segments: grade I = pain, grade II = ataxia and decreased proprioception, grade III = paraplegia, grade IV = paraplegia and urinary retention or incontinence, and grade V = same signs as grade IV but associated with loss of deep pain sensation.

Patient preparation, CSF collection, myelography contrast injection, and ICP and SP monitoring. Non-invasive ICP monitoring (NI-ICP) was performed in six dogs, of which three of them (Dogs 1, 2, and 3) underwent subarachnoid pressure (SP) monitoring. The monitoring records were divided into moments before (M1), during (M2), and after (M3) contrast medium administration. M1 lasted 1 min, M2 for 1.5-3 min, and M3 for 1 min. Initially, venoclysis of the cephalic vein was performed, and the crystalloid solution was infused at 10mL/kg/h over the entire procedure. Subsequently, tranquilization was performed intravenously with 0.5mg/kg diazepam (Diazepam, Teuto), and general anesthesia was induced intravenously with 4 to 6mg/kg propofol (Lipuro, B. Braun) followed by orotracheal intubation and maintenance of anesthesia with isoflurane (Isoflurane, BioChimico) volatilized in oxygen using a vaporizer in Patients 2, 3, 4, 5, and 6; in Patient 1, the same protocols were followed until the orotracheal intubation, and then the animal was maintained in propofol infusion at 0.2mL/kg/min. In Patients 1 and 2, the dorsal metatarsal artery was cannulated for invasive mean arterial blood pressure (MAP) monitoring using a pressure transducer attached to the Brain4care BCM2000 monitor. The skin over the cerebelomedullary cistern (CMC) and lumbar spine was clipped and aseptically prepared. The dogs were placed in left lateral recumbency with the head flexed at 90° relative to the neck. CSF was collected from the CMC in all dogs and was immediately sent to the clinical pathology laboratory for analysis. Subsequently, using the Brain4care stereotactic holder, the non-invasive sensor was placed over the skin of the parietal region for subsequent monitoring of the NI-ICP with the Brain4care BCMM 2000 monitor.

In the three dogs subjected to SP monitoring, two spinal needles were introduced into the lumbar subarachnoid space (LSS), one between L5 and L6 and the other between L4 and L5 (Fig.1 and 2). In dogs subjected only to NI-ICP monitoring, a single needle was introduced at L5-L6 to inject the contrast medium. They were inserted at the cranial aspect of the dorsal spinous process, perpendicular to the spine in the midline, until it reached the floor of the vertebral canal (Dewey et al. 2015). In Patient 3, lumbar CSF was collected and sent for analysis. The volumes of CSF collected from the CMC and LSS, ranged from 0.2mL to 3mL (mean = 0.25mL/kg). After verifying that the lumbar needle was properly inserted, a syringe containing the contrast medium iohexol (Omnipaque 300, GE Healthcare) was connected for contrast injection, and the second spinal needle was connected to an extension tube filled with sterile saline to a disposable pressure transducer (TruWave; Edwards Lifesciences) for SP monitoring. NI-ICP and SP monitoring was performed simultaneously (Fig.2 and 3). After recording the NI-ICP and the subarachnoid pressure (SP) for 1 min (M1), the contrast medium was injected at 0.35-0.4mL/kg, with the duration of application of 1.5-3min. The NI-ICP and the SP were monitored again, simultaneously, during the injection of contrast medium (M2), and then immediately after (M3), for another minute. In dogs submitted only to NI-ICP monitoring, the recording was also performed at M1, M2, and M3.

Evaluation of radiographic images. At the end of the contrast medium injection, the needles were removed. Radiographs of the spine were taken with a digital radiography device (CR 30-Xm, AGFA) in the ventrodorsal (VD), laterolateral (LL), and left and right oblique lateral projections, when necessary, to identify spinal cord lesions in the extradural, intradural/extramedullary, or intramedullary spaces that could explain the observed neurological signs. After the procedure, the patients were kept under observation with their heads elevated until they were awake, and they were maintained on intravenous fluid therapy for 24 hours, with isotonic crystalloid solution (5-10mL/kg/h) to facilitate diuresis and elimination of the contrast medium and to minimize the occurrence of epileptic seizures.

Data analysis. A memory card with the collected data was then removed from the monitor and inserted into a notebook so that the data obtained could be sent remotely to the Brain4care Analytics website[5] for analysis by a software (LabView®). The parameters associated with the ICP pulse waveforms were obtained based on the percussion wave (P1) and tidal wave (P2) classification schemes (P1>P2 or P2>P1) and P2:P1 ratios (Fig.4) (Fan et al. 2008, Bahr Arias et al. 2022).

Statistical analysis. To verify whether the Brain4care monitor was able to detect the increase in NI-ICP and SP induced by the contrast injection, the mean P2:P1 ratio values were analyzed at each monitoring time point (M1, M2, and M3) (Fig.5). The mean P2:P1 ratio was obtained within each 1-min monitoring interval. The Shapiro-Wilk test was used in the three dogs submitted to SP monitoring. After normal distribution was verified, ANOVA and Tukey's test were performed to compare the means of the P2:P1 ratio in M1-M2, M2-M3, and M1-M3 moments. Means and standard deviations were calculated for each moment. In the six dogs submitted to NI-ICP monitoring, due to the absence of normal distribution evidenced by the Shapiro-Wilk test, the Kruskal-Wallis test was used, followed by the Dunn test with p-value adjusted by the Benjamin Hocberg method for comparison of the three moments, M1-M2, M2-M3, and M1-M3. The median and quartiles 1 and 3 were calculated for each time point. Pearson's correlation coefficient was calculated for the three monitoring moments to verify the degree of the linear relationship between NI-ICP monitoring and SP. Statistical analysis was performed using R software (R Development Core Team 2011), and the significance level was set at 5%. The SP and NI-ICP waves obtained at the three monitoring times were compared using the GNU Octave program, version 5.2.0 Copyright (C) 2020 for Linux (Eaton et al. 2019).

RESULTS

The data regarding breed, sex, age, weight, procedures, neuroanatomical localization, CSF analysis results, contrast medium volume administered, contrast medium injection speed, total injection time of contrast medium, diagnosis, anesthetic protocols, P2:P1 ratio results, and treatment of the dogs submitted to NI-ICP and SP monitoring are summarized in Table 1. The diagnoses were meningoencephalitis of unknown origin (n=1), IVDD (n=2), vertebral neoplasm (n=1), and IVDD with hemorrhagic myelomalacia (n=2). The median age was 6.3 years, and the median weight was 6kg. The minimum duration of anesthesia was 45 min, the maximum was 75 min, and the median was 60 min.

In the six dogs submitted to NI-ICP monitoring, it was observed that, except for Dog 1, in M1, P2 was lower than P1 and/or P2:P1<0.8, whereas in M2, there was an increase in P2 relative to P1 and/or the ratio P2:P1 was ≥0.8 in all dogs.

[5] Available at <https://www.braincareanalytics.com/start> Accessed on Apr., 2020.

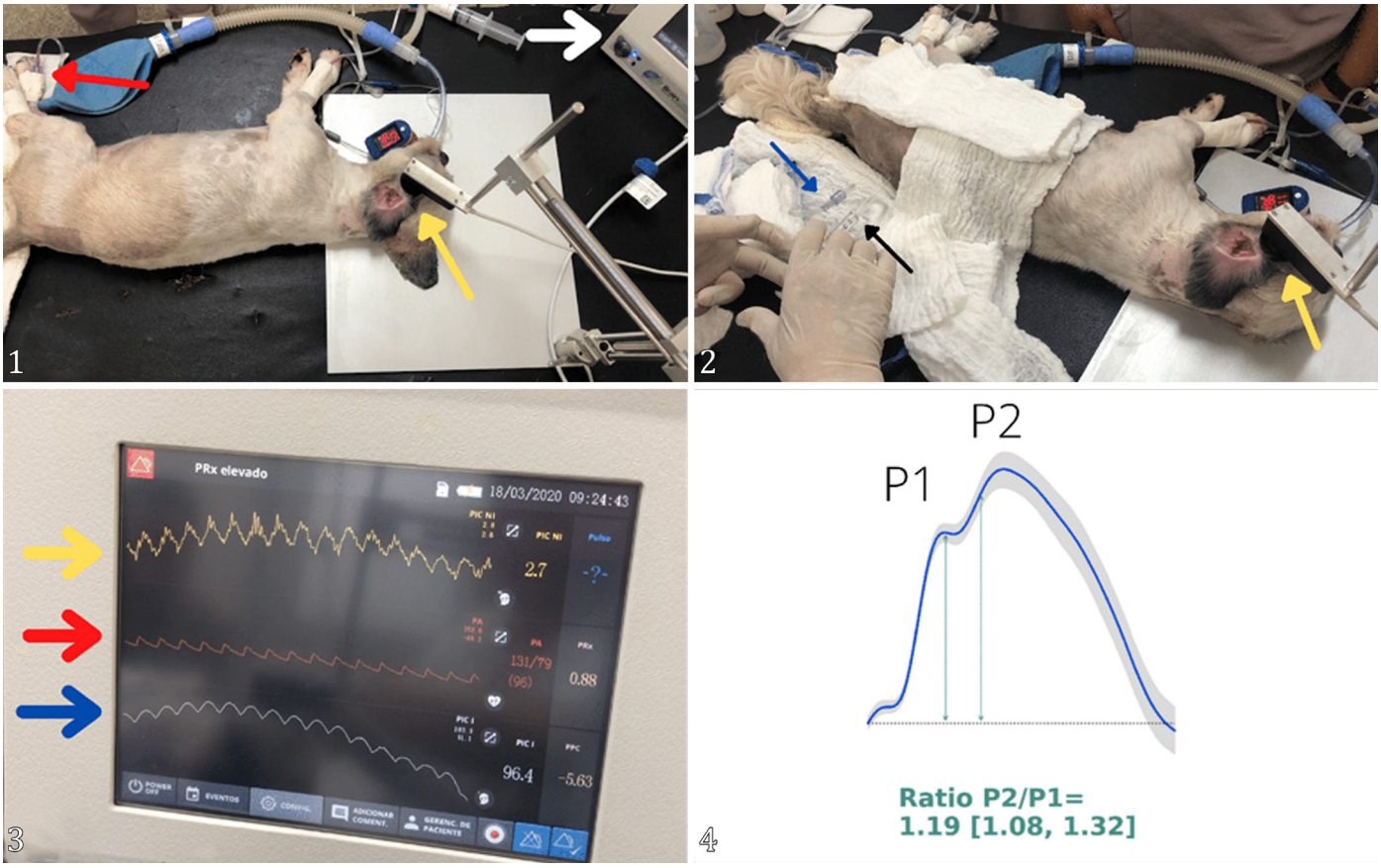

Fig.1-4. Demonstration of the non-invasive intracranial pressure (NI-ICP) and subarachnoid pressure (SP) monitored simultaneously with the Brain4care BCMM 2000 device in Dog 2 undergoing myelography. (**1**) Patient positioned in lateral recumbency and the positioning of the NI-ICP sensor over the skin on the parietal region (yellow arrow) and transmission to the monitor (white arrow). The mean arterial blood pressure (MAP) is monitored through the dorsal metatarsal artery (red arrow). (**2**) Moment during contrast injection (M2) into the lumbar subarachnoid space (LSS) with a spinal needle (black arrow) and a second spinal needle (blue arrow) for PS monitoring coupled to the transducer. (**3**) Monitor image during monitoring of NI-ICP (yellow arrow), SP (blue arrow), and MAP (red arrow). (**4**) ICP wave morphology at time M2 with P2>P1, after data processing by Labview® software. Londrina/PR, 2022.

In M3 there was a reduction in P2 and the ratio P2:P1 in all of them except for Dog 1. Using the Kruskal-Wallis statistical test and Dunn's test with *p*-value adjusted by Benjamin Hocberg's method, there was a difference between M1 and M2 moments (p=0.033) but not between M1 and M3 (p=0.17) and between M2 and M3 (p=0.32) (Fig.5 and 6, Table 1). In the three dogs that underwent SP monitoring, there was a difference between moments M1 and M2 (p=0.003). In these same dogs, there was a similarity between the results of SP and NI-ICP at M1, M2, and M3 (Fig.7 and 8, Table 1 and 2). The Pearson correlation coefficient showed a strong positive correlation (r=0.76, p=0.018) between NI-ICP and SP.

DISCUSSION

The Brain4care non-invasive ICP monitor captured and recorded in real-time the ICP wave dynamics before, during, and after contrast medium injection into the subarachnoid space in dogs with myelopathies undergoing myelography. The ICP waves captured by the non-invasive sensor were similar to those captured invasively in the lumbar subarachnoid space. The evaluation of the P2:P1 ratio provided useful information for understanding brain compliance and non-invasive monitoring of ICP in dogs.

A way to study ICP is by inducing its increase through the injection of saline solution (Ivan & Choo 1982, Cabella et al. 2016) or contrast medium (Arany-Tóth et al. 2012, 2013, Minto et al. 2021) into the subarachnoid space. The methodology used was similar to that described in a study of dogs affected by neurological disorders undergoing myelography to calculate the safe volume of contrast medium to be injected and the cerebral perfusion pressure (CPP) (Arany-Tóth et al. 2012, 2013). In the present study, the needles were placed in the lumbar region to avoid injury to the brainstem if movement occurred during invasive subarachnoid pressure monitoring in the CMC (Feliu-Pascual et al. 2008). Because this study aimed to simultaneously monitor NI-ICP and SP, manipulation of the spinal needles in the CMC during monitoring could cause artifacts and difficult signal uptake by the sensor (Cabella et al. 2016, Vilela et al. 2016). In addition, there is greater accuracy in identifying thoracolumbar lesions when myelography is performed by lumbar puncture (Dewey et al. 2015).

It has been proven that the ICP and pressure in the subarachnoid space of the CMC are approximately the same if there is no obstruction of CSF flow (Löfgren & Zwetnow 1973, Ivan & Choo 1982, Klarica et al. 2005, Arany-Tóth et al. 2012, 2013). In one experimental study in dogs, the epidural

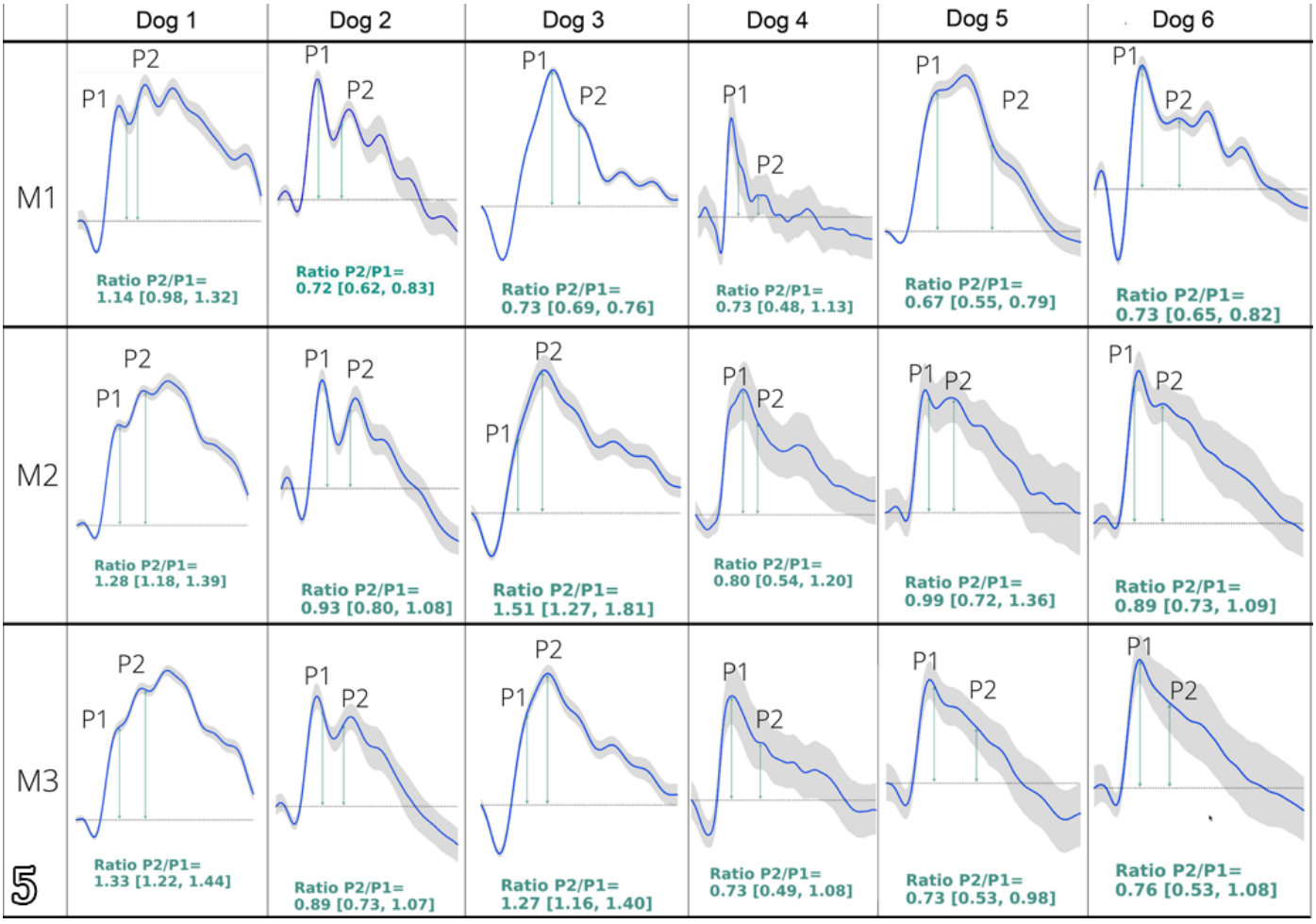

Fig.5. Graphics obtained after data insertion in the Labview® software, representing the relationship of the non-invasive intracranial pressure (NI-ICP) waves of the six dogs submitted to NI-ICP monitoring at moments M1, M2, and M3 and the P2:P1 ratio. Londrina/PR, 2022.

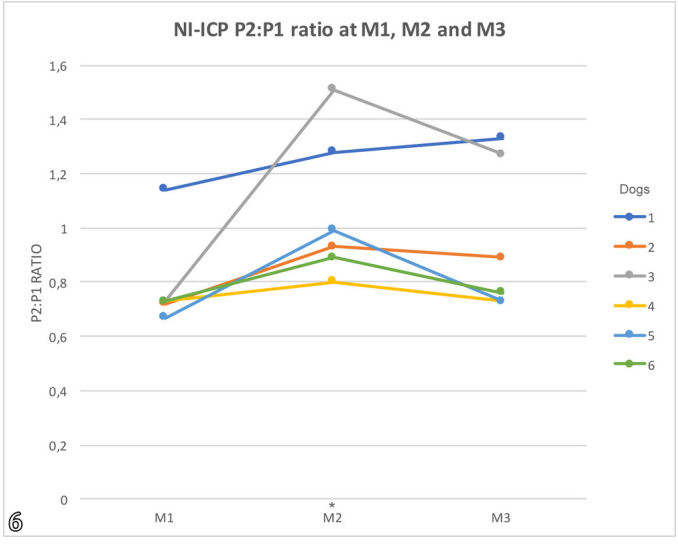

Fig.6. P2:P1 ratio in the six dogs submitted to non-invasive intracranial pressure (NI-ICP) monitoring at the three monitoring times. p=0.033 between M1 and M2 (asterisk). Londrina/PR, 2022.

ICP was compared with the subarachnoid pressure of the cisterna magna. There was a high correlation between the values obtained (Ivan & Choo 1982). Due to the importance of evaluating the effectiveness of non-invasive methods of ICP monitoring by comparing them with invasive methods, which are considered the "gold standard" (Ilie et al. 2015, Maissan et al. 2015, Cabella et al. 2016, Giannasi et al. 2020), it was chosen in the present study to monitor lumbar SP while performing myelography. Although the occurrence of histopathological changes due to needle insertion has been described, the technique is considered effective (Kunz et al. 2015). It has a low risk of clinical complications, as previously observed in another study (Kishimoto et al. 2004).

Although ICP monitoring is traditionally performed by observing the numerical values of the pressure in mmHg, wave morphology provides important information about the dynamics of ICP by analyzing its amplitude and frequency (Ballestero et al. 2017, Frigieri et al. 2018). ICP pulse waveforms generally have three characteristic peaks referred to as P1, P2, and P3, which reflect the cardiac cycle and represent the arterial pulse pressure transmitted to the CSF. The P1 peak represents the arterial pulse, P2 is the rebound after the initial arterial percussion, and P3 reflects the aortic valve closure and under normal intracranial physiological state

P1>P2>P3 (Fan et al. 2008). Thus, before contrast medium injection, it was observed through SP and NI-ICP in Dogs 2 and 3 and NI-ICP in Dogs 4, 5, and 6 that the P1 peak was higher than P2, indicating normal brain compliance (Fan et al. 2008), although P2 was increased in Dog 1.

The increase in the P2 peak in Dog 1 may be due to the granulomatous meningoencephalitis (GME) that was suspected as a possible cause of the observed neurological signs. There are reports of increased ICP in patients with meningoencephalitis that may have compromised brain compliance (Cornelis et al. 2016), which probably justifies the permanence of ICP waveform alteration at M3, with a return to normal waveforms only at the second minute of M3. A similar pattern was observed during the monitoring of SP in dogs subjected to myelography 2 min after contrast injection (Arany-Tóth et al. 2013). The difference observed in NI-ICP monitoring between moments M1 and M2 and the similarity observed at moments M1 and M3 indicate that the device could detect the elevation of ICP in response to contrast injection and the decrease in M3, probably due to the reestablishment of brain compliance (Fan et al. 2008), which is similar to another study performed in dogs monitored during myelography (Arany-Tóth et al. 2013). During the injection of contrast medium into the subarachnoid space, the P2 peak increased at all three monitoring times for SP (Dogs 1 and 3) and NI-ICP in all dogs. In Patients 2, 4, 5, and 6, although P1 remained higher than P2, the P2:P1 ratio was ≥0.8, probably indicating increased ICP (Fan et al. 2008).

There are three possible reasons why the NI-ICP waveforms differed from the SP waveforms in these patients. First, compression by the IVDD caused a blockage of the contrast medium flow towards the intracranial subarachnoid space since chondrodystrophic dogs with IVDD may suffer varying degrees of spinal compression (Klarica et al. 2005, Kunz et al. 2015). Dogs 4 and 6 had grade V thoracolumbar syndrome, clinical signs, and CSF analysis compatible with hemorrhagic myelomalacia (Lu et al. 2002). Thus, it is likely that the severity and degree of spinal cord compression and tissue destruction in these dogs may have hindered contrast flow, resulting in lower ICP elevation, similar to the observation that the degree of neurological injury can lead to increased intrathecal pressure in brachycephalic dogs affected by disc herniation (Kunz et al. 2015). In a study performed on cats, a separation was created by surgery between the brain and spinal subarachnoid space. Mannitol was then administered, and it was found that when this split exists, the ventricular ICP increases instead of falling, proving that the spinal subarachnoid space contributes to the decrease in intracranial CSF pressure (Klarica et al. 2005).

The second hypothesis points to the contrast infusion rate since, in other studies in dogs, a significant increase in ICP has been reported after injection of substances, such as saline solution at 1.94mL/min (Ivan & Choo 1982) and contrast medium at 4.1mL/min (Arany-Tóth et al. 2013), into the subarachnoid space. However, the injection rates in the present study, obtained by manual injection, were lower than those in previous studies, except for Dog 3, in which a greater elevation of ICP was observed at an infusion rate of 2mL/min. Nonetheless, this rate is within what would be recommended for dogs, which is 2-3mL/min (Dewey et al. 2015). Therefore, it is expected that in dogs with lower contrast injection rates, the existing compensatory mechanisms related to the Monroe–Kellie doctrine may have been responsible for the smallest change in the ICP waves observed (Kawoos et al. 2015). This phenomenon can also be illustrated similarly to the cerebral compliance mechanism by the pressure-volume relationship; thus, in this case, the compensatory reserve may not have been exhausted, keeping ICP waveforms normal (Fan et al. 2008). In addition to the contrast injection rate, the volume, anatomy of each animal, and existing disorders may influence ICP dynamics (Löfgren & Zwetnow 1973). The doses of contrast medium used in the present study were 0.35-0.4mL/kg, recommended in dogs (Arany-Tóth et al. 2012, 2013, Dewey et al. 2015). The total volume was also less than 8mL/dog since volumes greater than this limit may increase the risk of epileptic seizures after the end of the procedure (Dewey et al. 2015), which was not observed in the present study.

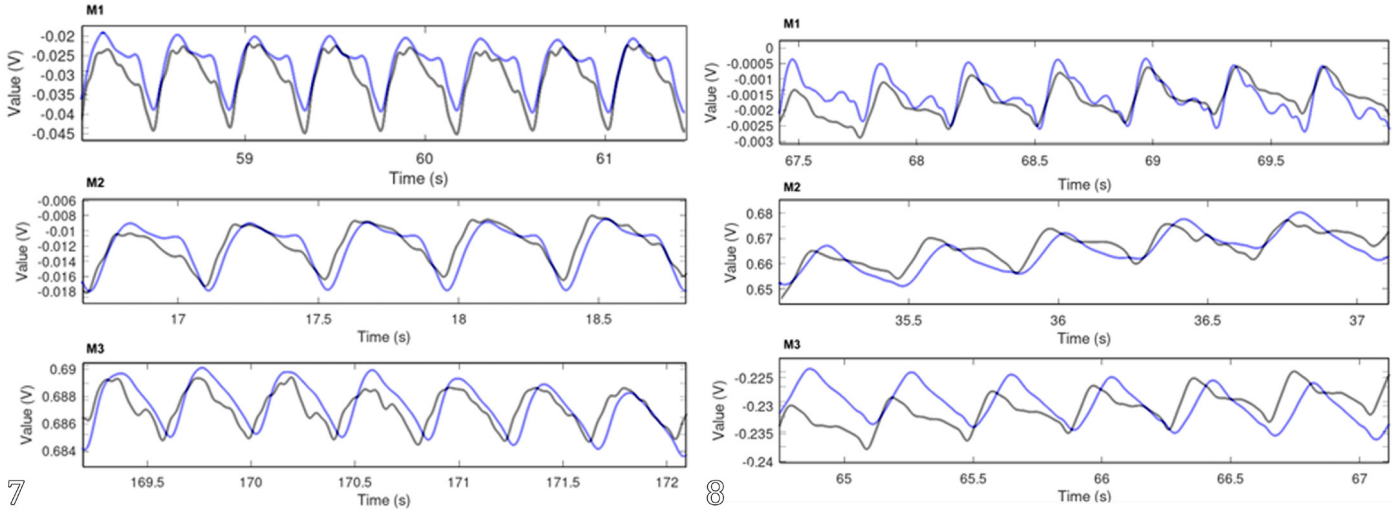

Fig.7-8. Representation of the morphology of the non-invasive intracranial pressure (NI-ICP) (blue line) and subarachnoid pressure (SP) (black line) waves of (**7**) Dog 1 (**8**) and Dog 3, with a significant similarity between the waves, at moments M1, M2 and M3. Londrina/PR, 2022.

Table 1. Description of clinical cases. Dogs submitted to myelography in relation to breed, sex, age, site of injury, diagnosis, anesthetic protocol, volume and analysis of cerebrospinal fluid (CSF), volume and rate of contrast medium injection, myelography, P2:P1 ratio obtained by monitoring the subarachnoid pressure (SP) and non-invasive intracranial pressure (NI-ICP) at the moments before (M1), during (M2), and after (M3) injection of contrast medium into the subarachnoid space, and treatment

Dog	Signalment (kg)	Localization and grade of lesion	Final diagnosis	Anesthesia protocol	Cerebrospinal fluid			Myelography			Spinal cord compression (classification)	P2:P1						Treatment
					Volume (mL)		Analysis	Contrast				M1		M2		M3		
					CMC	LSS		Volume (mL)	Dosis (mL/kg)	Rate (mL/min)		SP	NI-ICP	SP	NI-ICP	SP	NI-ICP	
1	Spitz MN 6 y (5.3)	C, II	GME	PAM: Diazepam I: Propofol M: Infusion of Propofol	0.2	-	Normal	1.8	0.35	0.6	None	1.08	1.14	1.62	1,28	1.30	1.33	Conservative
2	Shih tzu F 5 y (4.3)	TL, IV	IVDD	PAM: Diazepam I: Propofol M: Isoflurane	1	-	Normal	1.72	0.4	0.68	T11–T12, T12–T13, L1–L2 (extradural)	0.71	0.72	1.39	0.93	1.19	0.89	HL
3	Mixed breed FN 8 y (8.6)	TL, IV	Tumor	PAM: Diazepam I: Propofol M: Isoflurane	2	0.5	Xanthocromic Neutrophilic pleocytosis PC: 128.1mg/dL	3	0.35	2	T8 (extradural)	0.74	0,73	1,46	1,51	1,20	1,27	Euthanasia
4	Shih tzu M 5y (9)	LS, V	IVDD	PAM: Diazepam I Propofol M: Isoflurane	2	-	Xanthocromic PC: 112.4mg/dL E:1.269hem/mm^3 Neutrophilic pleocytosis	3.15	0.35	1.05	L4–S3 (intraparenchymal)	-	0,73	-	0,80	-	0,73	Euthanasia
5	Lhasa apso MN 3 y (7.6)	TL, II	IVDD	PAM: Diazepam I: Propofol M: Isoflurane	2	-	Xanthocromic Albumino-cytological dissociation PC: 46.6mg/dL	2.66	0.35	0.88	T12–T13 (extradural)	-	0,67	-	0,99	-	0,73	Conservative and physical therapy
6	Teckel F 5 y (8)	TL, V	IVDD	PAM: Diazepam I: Propofol M: Isoflurane	3	-	Red Increased turbidity PC: 119.2mg/dL RBC: 3.243hem/mm^3 Neutrophilic pleocytosis	3.2	0.4	1.06	L1–L2 (extradural)	-	0,73	-	0,89	-	0,76	HL durotomy

PC = protein concentration, RBC = red blood cells, C = cervical, TL = thoracolumbar, LS = lumbosacral, IVDD = intervertebral disc disease, GME = granulomatous meningoencephalitis, PAM = pre-anesthetic medication, I = induction, M = manutention, CMC = cerebellomedullary cistern, LSS = lumbar subarachnoid space, HL = hemilaminectomy.

Table 2. Median and quartiles 1 and 3 values of the P2:P1 ratio of the *non-invasive intracranial pressure (NI-ICP)* of the six dogs with the respective values of the mean and standard deviation, as well as the P2:P1 ratio of the *subarachnoid pressure (SP)* of the three dogs at the moments before (M1), during (M2), and after (M3) contrast injection

	M1	M2	M3
NI-ICP (N=6)	0.783[a] (P25 = 0.7225; P75 = 0.730)	1.280[b] (P25 = 0.9; P75 = 1.208)	1.230[a] (P25 = 0.7375; P75 = 1.1750)
SP (N=3)	0.84 ± 0.2[a]	1.49 ± 0.112[b]	1.16 ± 0.0551[a]

[a, b] Different letters in the same line indicate statistical difference ($p<0.05$).

The third hypothesis indicates the CSF volume collected before the contrast medium's injection. The volumes ranged from 0.2mL to 3mL (mean=1.7mL), corresponding to an average of 1.17mL for every 5kg, which corresponds to the volume of cerebrospinal fluid recommended as safe to be collected from dogs. (Di Terlizzi & Platt 2009). However, the rate of CSF production in dogs is known to vary from 0.047mL/min to 0.066 mL/min, is constant, and is independent of CSF pressure and arterial pressure (De Lahunta et al. 2015). Thus, CSF production occurs at a slower rate, and there is probably no time to replace what was collected until the contrast injection, resulting in lower ICP elevation (Löfgren & Zwetnow 1973). In a study in dogs, CSF was collected before the injection of iohexol contrast, resulting in decreased ICP (Nunes et al. 2011).

MAP monitoring is an important parameter for evaluating ICP dynamics. In Dogs 1 and 2, there was an increase in MAP at the time of contrast injection, reaching values of 107mmHg and 101mmHg, respectively. A similar finding was reported in a study with dogs undergoing myelography, in which 30/43 (70%) of the dogs had a mean MAP elevation of 97mmHg; in 24 of these dogs, the ICP was >61mmHg (Arany-Tóth et al. 2013). The increase in MAP, in this case, may be due to a physiological response to ICP elevation to adequately maintain cerebral circulation, known as the sympathetic phase of the Cushing reflex (Arany-Tóth et al. 2013).

Regarding the correlation of the two ICP measurement methods, even with the possibility of factors such as etiology, contrast medium administration speed, CSF collection, and the presence of artifacts interfering with ICP monitoring (Cabella et al. 2016, Vilela et al. 2016), the amplitude of the curves obtained through subarachnoid and non-invasive monitoring was similar at the three monitoring moments. The Pearson coefficient values were similar to those observed in other studies that used the Brain4care monitor simultaneously with intraparenchymal monitoring in mice (Cabella et al. 2016, Vilela et al. 2016). Although simultaneous monitoring of SP and NI-ICP was not possible in all dogs, the NI-ICP waves obtained at times M1, M2, and M3, as well as the values of the P2:P1 ratio, were similar to those observed through invasive monitoring into the subarachnoid space.

The evaluation of ICP expressed as a number may provide incomplete information because the value obtained in mmHg represents an average value, which indicates the absolute pressure difference between the exterior and interior of the skull cavity over a period of time. The intracranial pressure-volume reserve capacity is best described by observing ICP waveforms and an increase in ICP waveform occurs when there is an increase in intracranial pressure (Fan et al. 2008). In the present study, although the comparison of the ICP waves with the numerical value was not performed, it was found that the evaluation of the waves, as well as the P2:P1 ratio, provided important information about brain compliance, similar to studies in humans with meningoencephalitis, hydrocephalus, and TBI, among other conditions (Cardim et al. 2016, Ballestero et al. 2017, Bollela et al. 2017, Frigieri et al. 2018). Through the evolution of monitoring techniques, real-time data acquisition, and analysis, there is a tendency for the type of technology used in this study to be used for monitoring critically ill patients without the complications of invasive techniques (Kawoos et al. 2015).

The limitations of the study were the inability to monitor the CPP and MAP of all dogs, which could have provided more information about brain compliance, especially regarding CPP, as observed in dogs undergoing myelography, in which a significant drop in CPP was found during ICP elevation (Arany-Tóth et al. 2013). Another limitation was the small number of cases examined. However, this difficulty follows the pattern of other recent studies (Ilie et al. 2015, Sturges et al. 2019, Hori et al. 2020), which have provided information on effective methods of ICP monitoring in dogs. In addition to the difficulties already observed in another study with dogs using the same device (Bahr Arias et al. 2022), different breed conformations of the skull can also make it difficult to determine the correct location for sensor placement.

Invasive ICP monitoring methods in dogs are still rarely used in clinical practice (Kolecka et al. 2019, Seki et al. 2019), and risks regarding their use persist (Kawoos et al. 2015). Thus, non-invasive methods have been proposed to avoid these risks and complications. Ideally, they should be compared with invasive methods to demonstrate their effectiveness (Cabella et al. 2016, Giannasi et al. 2020), as performed in the present study.

CONCLUSION

Based on this study, the non-invasive Brain4care monitor detected the contrast injection-induced increase in intracranial pressure (ICP) in dogs with meningoencephalitis of unknown origin, vertebral neoplasm and intervertebral disc disease with and without hemorrhagic myelomalacia. The non-invasive intracranial pressure (NI-ICP) showed strong correlation with invasive lumbar subarachnoid pressure (SP) monitoring at all three monitoring time points.

Acknowledgments.- The authors would like to acknowledge "Coordenação de Aperfeiçoamento de Pessoal de Nível Superior" (CAPES) for the scholarship to N.L.F.C. Rocha. Part of this study was presented at the 33rd ESVN-ECVN Symposium Online, 16-18 September 2021.

Conflict of interest statement.- The authors declare having no conflicting interests

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