



Focal spinal hyperesthesia as a prognostic factor in paraplegic dogs without deep pain perception¹

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ABSTRACT. Wrzesinski M.R., Ripplinger A., Schwab M.L., Ferrarin D.A., Rauber J.S., Beckmann D.V., Schamall R.F. & Mazzanti A. 2022. **Focal spinal hyperesthesia as a prognostic factor in paraplegic dogs without deep pain perception.** *Pesquisa Veterinária Brasileira* 42:e06929, 2022. Serviço de Neurologia e Neurocirurgia Veterinária, Departamento de Clínica de Pequenos Animais, Universidade Federal de Santa Maria, Prédio 97, Camobi, Santa Maria, RS 97105-900, Brazil. E-mail: alexamazza@yahoo.com.br

Intervertebral disc extrusion (IVDE) is the most common cause of spinal cord compression in dogs, whose prognosis is variable and depends on several factors, with deep pain perception (DPP) being the main parameter used. Investigations of new prognostic factors are studied to assist in the estimation of functional recovery. Thus, this study aimed to evaluate whether spinal hyperesthesia (SH) at the compression site can be used as a prognostic factor for the functional recovery of dogs with acute IVDE (Hansen type I), without DPP being subjected to thoracolumbar hemilaminectomy. Decompression surgery was performed on the same day or the day after admission. The duration of the loss of DPP until surgery performance ranged from 1 to 60 days, with a median of 4.5 days for the group of dogs with SH and 5.5 days for those without SH. Among the 68 dogs included in this retrospective study, 73.5% (50/68) showed SH, and 26.5% (18/68) were not identified. Recovery was satisfactory in 60% (30/50) of dogs with SH and in 27.7% (5/18) of dogs without SH, demonstrating that paraplegic dogs without DPP but with SH were 3.9 times more likely to recover when compared to dogs in the same condition, but with no SH. No studies have evaluated SH by palpation of the spine as a prognostic factor, which reinforces the relevance of the present study. The results of this study imply that SH in paraplegic dogs affected by thoracolumbar IVDE, without the presence of DPP, can be used as a possible prognostic indicator of functional recovery.

INDEX TERMS: Focal spinal hyperesthesia, paraplegia, dogs, pain perception, intervertebral disc disease, spinal cord, dog diseases, nociception, neurology.

RESUMO. [Hiperestesia espinhal focal como fator prognóstico em cães paraplégicos sem percepção de dor profunda.] A extrusão do disco intervertebral (EDIV) é a

causa mais comum de lesão compressiva na medula espinhal de cães, cujo prognóstico é variável e depende de diversos fatores, sendo a percepção de dor profunda (PDP) o principal parâmetro utilizado. Pesquisas de novos fatores prognósticos são estudados com intuito de auxiliar na estimativa mais precisa de recuperação funcional. Com isso, o objetivo do estudo foi avaliar se a hiperestesia espinhal (HE) no local da compressão, pode ser utilizada como um fator prognóstico para recuperação funcional de cães com extrusão aguda do disco intervertebral (Hansen tipo I), sem a presença de PDP submetidos a hemilaminectomia toracolombar. A cirurgia descompressiva ocorreu no mesmo dia ou no dia seguinte ao atendimento. A duração da perda de dor profunda até a realização da cirurgia variou de 1 a 60 dias, com uma mediana de 4,5 dias para o grupo de cães com e 5,5 dias para aqueles

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sem hiperestesia espinhal. Dos 68 cães incluídos nesse estudo retrospectivo, 73,5% (50/68) apresentavam HE e, em 26,5% (18/68) a dor não foi identificada. A recuperação foi satisfatória nos cães com HE em 60% (30/50) e, sem HE, em 27,7% (5/18) dos casos, demonstrando que os cães paraplégicos sem PDP, mas com presença de hiperestesia espinhal tem 3,9 vezes mais chances de recuperação quando comparado com cães na mesma condição, mas sem HE. Não foram encontrados trabalhos que avaliaram a HE mediante a palpação da coluna vertebral como um fator prognóstico, o que reforça a relevância do presente estudo. Os resultados do presente trabalho sugerem que a HE em cães paraplégicos acometidos por EDIV toracolombar sem presença de PDP pode ser utilizada como um possível indicador prognóstico de recuperação funcional.

TERMOS DE INDEXAÇÃO: Hiperestesia espinhal focal, cães, paraplegia, percepção de dor, doença do disco intervertebral, medula espinhal, doenças de cães, nocicepção, neurologia.

INTRODUCTION

Intervertebral disc disease (IVDD) is a term widely used in veterinary medicine that covers several injuries that affect the intervertebral disc. These lesions are distinct and have been discovered and studied concurrently with advances in diagnostic technologies (Fenn & Olby 2020).

A classification system for the different types of IVDD was mentioned by Fenn & Olby (2020), in which they described the types of IVDD in intervertebral disc extrusion (IVDE) (Hansen type I), intervertebral disc protrusion (Hansen type II), hydrated nucleus pulposus extrusion, non-compressive acute nucleus pulposus extrusion, fibrocartilaginous embolic myelopathy, and intradural/intramedullary IVDE.

Among the types of IVDD, IVDE is the most common cause of compressive spinal cord injury in dogs (Fenn & Olby 2020). The prognosis for dogs with this condition and treated surgically is variable, depending on several factors (Olby et al. 2020). In recent decades, studies evaluating the prognostic factors for walking recovery have been published (Fenn & Olby 2020). These studies used clinical parameters (Davis & Brown 2002, Ferreira et al. 2002, Ruddle et al. 2006, Jeffery et al. 2016), imaging examinations (Duval et al. 1996, Ito et al. 2005, Costa et al. 2020), biomarkers (Levine et al. 2010, Roerig et al. 2013, Nishida et al. 2014, Olby et al. 2019), and electrophysiological tests (Hu et al. 2018, Siedenburger et al. 2018) to attempt to predict the recovery of these dogs.

Deep pain perception (DPP) is the main clinical prognostic factor used (Fenn & Olby 2020). Age, breed, onset and duration of clinical signs, extrusion location, and use of corticosteroids are other clinical parameters investigated; however, consistent results have not been demonstrated to justify their use as prognostic factors (Jeffery et al. 2016, Fenn & Olby 2020).

In animals that do not have DPP, the prognosis for functional recovery varies from 30% to 75% in different studies (Scott 1997, Olby et al. 2003, Ruddle et al. 2006, Jeffery et al. 2016, Olby et al. 2020). The cause of the high recovery variation in patients with IVDE without DPP remains unclear. However, in a study by Olby et al. (2003), who evaluated the return to walking in the long term (> six months) of 87 dogs with acute-onset paraplegia without DPP due to IVDE or trauma, the possibility of different degrees of spinal cord involvement and

that this could influence DPP recovery or the ability to return to walking were reported. Based on this, the investigation of other clinical parameters that can be associated with the absence of DPP is necessary to pursue a more accurate prognosis.

DPP is transmitted to the cerebral cortex by type C unmyelinated fibers, and it is believed that the transmission occurs mainly through the ascending reticular formation in the spinoreticular tract and through other pathways found in all spinal cord funiculi (Olby et al. 2003, Thomson & Hahn 2012, Uemura 2015). Therefore, for a spinal cord injury to cause a loss of DPP caudal to the lesion, there must be extensive injury to all spinal cord tracts. Thus, clinically, the loss of DPP is a sign of poor prognosis in animals with severe spinal cord injuries (De Lahunta et al. 2015, Uemura 2015).

Focal spinal hyperesthesia (SH) seen in dogs with IVDE is also transmitted by type C fibers (Uemura 2015). However, unlike DPP, no studies have considered the absence of SH at the compression site as a prognostic factor in dogs with IVDE, even though both have similar transmission pathways to the cortex, arranged in a variety of spinal cord tracts (Thomson & Hahn 2012, Uemura 2015).

Therefore, this retrospective study aimed to assess whether SH at the compression site, assessed by palpation of the spine, can be used as a prognostic factor for the functional recovery of paraplegic dogs without DPP caused by acute IVDE (Hansen type I).

We hypothesized that paraplegic dogs without DPP that manifest SH upon palpation of the spine at the compression site have a limited degree of spinal cord injury, without cranial and caudal extension, increasing the possibility of functional recovery. Conversely, dogs without SH present with more severe symptoms, including perilesional lesions, reducing the prognosis of functional recovery.

MATERIALS AND METHODS

The files of the "Serviço de Neurologia e Neurocirurgia Veterinária" (Veterinary Neurology and Neurosurgery Service) of the veterinary university hospital of "Universidade de Santa Maria" (UFSM) from January 2006 to November 2020 were reviewed. Dogs with a diagnosis of thoracolumbar IVDE (Hansen type I) (T3-L3), with no DPP in the pelvic limbs and tail, and that underwent thoracolumbar hemilaminectomy were included. Surgery was performed on the same day or at the latest on the day after the dog's admission.

Only dogs with complete data on clinical history, clinical signs, neurological tests, and results of complementary tests, such as simple radiography, myelography, computed tomography, or magnetic resonance, and with a definitive diagnosis confirmed by the finding of disc material at surgery were selected and analyzed by histopathological examination. Information on breed, age, weight, sex, time of DPP absence, presence or absence of focal SH, medication use prior to care, and recovery were collected from clinical records.

Dogs in which the SH was located in a region other than the compression site, dogs that showed SH in the entire length of the spine, or in more than one site beyond the compression site were excluded. Dogs that presented bone changes cranial or caudal to the compression site that could cause pain, or in which spinal palpation was difficult due to the patient's behavior, were also excluded from the study.

The neurological assessment of dogs included general observation (level of consciousness and behavior), analysis of posture and gait,

assessment of cranial nerves, assessment of postural reactions, spinal segmental reflexes, SH through spinal palpation, and assessment of DPP (Thomas & Dewey 2003).

The SH assessment was performed by deep palpation of the paravertebral musculature, applying direct dorsoventral pressure with the fingers, relatively close (index and middle/thumb and index) between the spinous processes, starting in the cranial thoracic region and advancing in the caudal direction until reaching the lumbosacral region (Fig.1 and 3). The manifestation of hyperesthesia, such as vocalization, moaning, muscle tension, and mydriasis, was considered positive (Thomas & Dewey 2003).

The assessment of DPP was performed with the aid of hemostatic forceps, applied to the phalanges of the medial and lateral fingers of the pelvic limbs and to the tail (Fig.2 and 4). The absence of DPP was considered if the patient did not present a conscious response such as vocalization, moaning, looking around, or attempting to bite (Ruddle et al. 2006, Jeffery et al. 2016, Gallucci et al. 2017).

The time of DPP loss was considered from the moment the tutors reported paraplegia until the time of surgery (Scott & Mckee 1999, Ito et al. 2005, Laitinen & Puerto 2005, Loughin et al. 2005).

Functional recovery was classified as satisfactory for those who recovered DPP and returned to walking without falls or assistance (Olby et al. 2003, Jeffery et al. 2016). It was considered unsatisfactory when the initial neurological signs (before surgery) remained unchanged or when the dogs recovered DPP but did not return to walking (Duval et al. 1996, Olby et al. 2003). Cases of dogs that developed spinal walking, as defined by Gallucci et al. (2017) and Lewis et al. (2020), were considered unsatisfactory.

To assess functional recovery, a minimum follow-up period of three months after decompression surgery was defined, as recommended by Olby et al. (2003). Follow-up information was obtained from the information contained in the clinical return forms.

Statistical analysis was performed using the Jamovi software (1.2.27). Data on functional recovery (satisfactory/unsatisfactory) were used to process associations with age, weight, sex, breed, presence or absence of SH, and time of DPP loss. Quantitative variables such as age, weight, and time of DPP loss were subjected to the Shapiro-Wilk normality test, showing abnormal distribution. A binomial logistic regression test was used to identify the relationship between functional recovery and age, weight, and duration of



Fig.1-4. Assessment of (1,3) focal spinal hyperesthesia and (2,4) deep pain perception in paraplegic dogs caused by intervertebral disc extrusion (Hansen type I). (1,3) palpation of the paravertebral muscle applying ventral pressure with the index and middle fingers, between the spinous processes. Note the (1) presence and (3) absence of response to the stimulus. (2,4) use of a hemostatic forceps applied to the distal phalanx of the fifth finger of the pelvic limb and no reaction to the painful stimulus.

signs. To identify the relationship between recovery, breed, and the presence or absence of SH, chi-square test (χ^2) was used. Odds ratio calculation was used to compare dogs with or without SH on epaxial palpation in terms of functional recovery. In all analyses, statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

A total of 68 dogs satisfied the pre-established inclusion criteria. The results regarding the distribution of breeds, age, weight, sex, SH, time of absence of DPP, recovery, medications, data from imaging examinations, and lesion location are described in Table 1.

The most affected breed was Dachshund (49%, 33/68). Age ranged from three to 13 years, with a mean of 5.72 ± 2 years. Regarding sex, 51.5% (35/68) were female and 48.5% (33/68) were male, with an average weight of 7.47 ± 2.24 kg. Several studies have described the predisposition of chondrodystrophic breeds and the high prevalence of Dachshunds. This occurs

due to the degenerative process that occurs in these breeds, making them more prone to IVDE (Fenn & Olby 2020).

As for the functional recovery of these dogs, 51.5% (35/68) was considered satisfactory and 48.5% (33/68) unsatisfactory. This result was in line with other published studies in which the prognosis of dogs with IVDE without DPP ranged from 30% to 75% (Scott 1997, Olby et al. 2003, Ruddle et al. 2006, Jeffery et al. 2016, Olby et al. 2020).

The severity of neurological signs, especially the presence or absence of DPP, is the main prognostic factor used in clinical practice. In dogs with DPP, the prognosis is considered to be good to excellent; however, in dogs without DPP, it is uncertain (Olby et al. 2020). The wide range of recovery in dogs without DPP is yet to be clarified. However, it is suspected that primary spinal cord injury initiates a cascade of secondary events that cause spinal cord destruction at different levels and that slight differences in a compressive injury can produce significant differences in lesion severity (Jeffery et al. 2013, Lam et al. 2014).

Table 1. Distribution of dogs, age, sex, weight, presence or absence of spinal hyperesthesia, time of deep pain perception loss, functional recovery, use of drugs prior to care, image exams, and compression site of paraplegic dogs caused by intervertebral disc extrusion (Hansen type I)

	Spinal hyperesthesia group	Group without spinal hyperesthesia	TOTAL
Dogs	50 (73.5%)	18 (26.5%)	68 (100%)
Breed	Dachshund 24 (48%) Mixed-breed 16 (32%) Shih Tzu 2 (4%) Poodle 3 (6%) Lhasa Apso 2 (4%) Yorkshire 1 (2%) Cocker Spaniel 1 (2%) Pinscher 1 (2%)	Dachshund 9 (50%) Mixed-breed 6 (33.3%) Shih Tzu 2 (11.1%) Yorkshire 1 (5.5%)	Dachshund 33 (49%) Mixed-breed 22 (32%) Shih Tzu 4 (6%) Poodle 3 (4%) Lhasa Apso 2 (3%) Yorkshire 2 (3%) Cocker Spaniel 1 (1%) Pinscher 1 (1%)
Age (years)	Min. - 3 years Max. - 13 years Average - 5.70 ± 2.04	Min. - 3 years Max. - 10 years Average - 5.78 ± 1.96	Min. - 3 years Max. - 13 years Average - 5.72 ± 2
Sex	Female 29 (58%) Male 21 (42%)	Female 6 (33.3%) Male 12 (66.6%)	Female 35 (51.5%) Male 33 (48.5%)
Weight (Kg)	Min. - 2 Max. - 13.4 Average - 7.57 ± 2.32	Min. - 4 Max. - 10.3 Average - 7.18 ± 2.01	Min. - 2 Max. - 13.4 Average - 7.47 ± 2.24
Deep pain perception loss (days)	Min. - 1 Max. - 60 Median - 4.5 ≤ 2 - n=17 3 to 7 - n=18 8 to 15 - n=8 > 15 - n=7	Min. - 1 Max. - 60 Median - 5.50 ≤ 2 - n=5 3 to 7 - n=5 8 to 15 - n=4 > 15 - n=4	Min. - 1 Max. - 60 Median - 4.50 ≤ 2 - n=22 3 to 7 - n=23 8 to 15 - n=12 > 15 - n=11
Recovery	Satisfactory - 30 (60%) Unsatisfactory - 20 (40%)	Satisfactory - 5 (27.7%) Unsatisfactory - 13 (72.3%)	Satisfactory - 35 (51.5%) Unsatisfactory - 33 (48.5%)
Drugs (analgesics and/or anti-inflammatory drugs)	n=39 Yes - 18 (46.1%) No - 21 (53.9%)	n=14 Yes - 8 (57.2%) No - 6 (42.8%)	n=53 Yes - 26 (49%) No - 27 (51%)
Image exams	MRI - 0 CT - 3 (6%) Myelography - 47 (94%)	MRI - 1 (5.5%) CT - 1 (5.5%) Myelography - 16 (89%)	MRI - 1 (1.5%) CT - 4 (5.9%) Myelography - 63 (92.6%)
Compression site	T11-T12 = 8 (16%) T12-T13 = 17 (34%) T13-L1 = 10 (20%) L1-L2 = 9 (18%) L2-L3 = 4 (8%) T13-L1-L2 = 2 (4%)	T11-T12 = 3 (16.7%) T12-T13 = 6 (33.3%) T13-L1 = 5 (27.7%) L1-L2 = 3 (16.7%) T12-T13-L1 = 1 (5.6%)	T11-T12 = 11 (16.2%) T12-T13 = 23 (33.8%) T13-L1 = 15 (22%) L1-L2 = 12 (17.6%) L2-L3 = 4 (6%) T12-T13-L1 = 1 (1.5%) T13-L1-L2 = 2 (2.9%)

Min. = minimum, Max. = maximum, MRI = magnetic resonance imaging, CT = computed tomography.

In this study, three dogs (4.4%) developed spinal walking according to the criteria defined in the methodology; two of these dogs had SH and one did not. Spinal walking is considered an involuntary motor function that can occur in dogs with complete thoracolumbar spinal cord injury (Gallucci et al. 2017, Lewis et al. 2020). This gait is developed by complex interactions that occur at the spinal cord level without supraspinal influence (Gallucci et al. 2017). Based on this information and in accordance with the objectives and hypothesis of the study, these dogs were classified as having an unsatisfactory recovery, considering that this finding does not indicate the resolution of the injury caused by IVDE in the spinal cord.

As for SH, 73.5% (50/68) of dogs had this sign, and in 26.5% (18/68), pain was not identified (Table 1). SH is the first and most common clinical sign in dogs diagnosed with IVDE. Pain is associated with inflammation and mechanical effects due to compression caused by the extruded disc in nerve roots, ganglia, ligaments, peripheral ring fibrous, meninges, and periosteum, which are highly innervated (Jeffery et al. 2013). Extrusion of the nucleus pulposus into the epidural space causes an inflammatory response, which leads to the production of chemical mediators such as glycosaminoglycans and lactic acid, resulting in hyperalgesia through peripheral sensitization (Webb 2003, De Lahunta et al. 2015).

When comparing the presence or absence of SH with functional recovery, a significant difference was noted ($p=0.038$), with a satisfactory recovery rate of dogs with SH of 60% (30/50) and 27.7% (5/18), respectively. This difference in the recovery of dogs may indicate that those with SH possibly had focal spinal cord injuries restricted to the extrusion site, with little or no perilesional involvement (cranial and caudal malacia) and reduced axonal damage, which would increase the chances of returning to walking.

Olby et al. (2003) suggested that dogs with IVDE and DPP loss have a different spectrum of spinal cord injury, which may influence sensory recovery or the ability to walk. When comparing clinical signs with histopathological findings in the spinal cord of dogs with IVDE, Henke et al. (2013) observed that, even with no statistical difference, only 33% of dogs without DPP who had a greater degree of spinal cord injury had SH. Furthermore, the results found in this study reinforced the hypothesis proposed by Olby et al. (2003) that DPP loss was frequently correlated with severe spinal cord damage, but not in all dogs, which confirms the variable recovery outcomes in dogs with thoracolumbar IVDE undergoing spinal decompressive surgery, reported in veterinary literature.

Considering that SH is transmitted to the cortex through different pathways arranged in all funiculi in the spinal cord, the greater degree and extension of the lesion affecting the tracts involved in pain transmission may explain the findings of the present study, in which patients with pain epaxial palpation are 3.9 times more likely to have a satisfactory recovery when compared to dogs without SH on epaxial palpation (Olby et al. 2003, Thomson & Hahn 2012, Uemura 2015). However, studies comparing the absence of SH with the degree of histopathological lesion in the spinal cord are needed to reinforce this hypothesis, similar to those performed by Henke et al. (2013).

Other variables can explain the absence of SH, such as the amount of extruded disc in the spinal canal, level of inflammation, individual variation in response to the stimulus between animals, evaluation of the palpation test by the examiner, and

drugs used prior to the examination (Webb 2003, De Lahunta et al. 2015, Jeffery et al. 2013). All these parameters must be considered when interpreting the results of the present study.

As for the drugs used before spinal palpation to assess SH, 49% of dogs received some type of analgesic medication, which could influence the pain response. However, as this study did not aim to assess the intensity of pain, but its presence or absence, it is believed that the use of these drugs did not interfere with the ability to perceive the induced pain, and did not change the results. Furthermore, when comparing the use of medications in the groups with or without SH, there was no statistical difference ($p=0.250$).

Other clinical parameters such as age, weight, breed, duration of clinical signs, and time from admission to surgery have already been evaluated as prognostic factors for recovery (Davis & Brown 2002; Ferreira et al. 2002, Ruddle et al. 2006, Jeffery et al. 2016). In our study, there was no correlation between recovery and breed ($p=0.632$), age ($p=0.065$), weight ($p=0.221$), compression site ($p=0.156$), and duration of clinical signs ($p=0.183$). However, a trend toward a better prognosis was observed in dogs with a shorter duration of clinical signs. Several studies have assessed the duration of signs, particularly the duration from the onset of the non-ambulatory state to surgical decompression. However, although there is some evidence that the duration of the signals can influence the speed of recovery, a consensus on the interference of the duration of the signals on the overall result has not yet been reached (Olby et al. 2020).

The main limitations of the study were related to the different sizes of the samples, the non-comparison of information from imaging examinations with the factors analyzed in this study, and the evaluation of SH and DPP. The assessment of these changes is subjective and depends on the patient's response to painful stimuli, which can often be subtle, and on the interpretation of the response, which can vary between examiners. Considering the long period of the study, different examiners (12) performed these assessments. However, the group uses a standardized methodology recommended in the literature (Thomas & Dewey 2003), which may have reduced the differences between the evaluators.

Due to the retrospective nature of the study, the determination of the duration of clinical signs and the type of drug treatment received before the appointment were taken from the clinical records, based on the information provided by the tutors. As a result, some data may be incomplete and inaccurate. However, this bias applies to all dogs in the study, and not a specific subgroup, decreasing interference when comparing groups.

Despite the limitations and the need for studies correlating with the degree of histopathological injury of spinal cord injury, the results of this study suggest that SH can be used as a possible prognostic indicator in dogs affected by thoracolumbar IVDE without DPP. Furthermore, no other studies have evaluated SH as a prognostic factor in these dogs, which reinforces the relevance of this study.

CONCLUSION

Spinal hyperesthesia (SH) in paraplegic dogs affected by thoracolumbar intervertebral disc extrusion (IVDE) without deep pain perception (DPP), when other variables are not considered, can be used as a possible prognostic indicator of functional recovery.

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Conflict of interest declaration. We have no conflict of interest to declare.

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