BMC Veterinary Research

RESEARCH

Open Access

Amantadine as a therapeutic option for neuropathic pain in dogs with degenerative lumbosacral stenosis

Chiara Caterino[1*], Giovanni Della Valle[1], Federica Aragosa[1*], Stefano Cavalli[1], Francesco Lamagna[1] and Gerardo Fatone[1]

Abstract

Background Degenerative lumbosacral stenosis is a multifactorial condition with no consensus on optimal therapeutic management. In mildly affected dogs, treatment often includes analgesics and non-steroidal anti-inflammatory drugs, which may be insufficient for effective pain control. This study aimed to evaluate the efficacy of amantadine in managing chronic neuropathic pain associated with this pathology in dogs, using ground reaction forces (GRFs) analysis, including Peak Vertical Force (PVF), Vertical Impulse (VI), and stance time (ST), and to evaluate whether the co-administration of amantadine improves the efficacy of meloxicam in patients who have shown a refractory response to meloxicam alone.

Methods Client-owned dogs (≥ 12 months old, ≥ 20 kg) with a confirmed diagnosis of degenerative lumbosacral stenosis were enrolled in a randomized trial. Subjects were assigned to two treatment groups: Group A received meloxicam (0.2 mg/kg PO SID loading dose, followed by 0.1 mg/kg SID for 6 days) plus amantadine (3 mg/kg PO SID for 21 days); Group B received amantadine alone (3 mg/kg PO BID for 21 days). Gait analysis was performed using a force platform at baseline (T0), after 7 days (T1), and after 21 days (T2).

Results Twenty dogs met the inclusion criteria and completed the study. At enrollment, the two groups (10 animals each) were homogeneous. After 21 days, both groups showed significant increases in PVF%BW ($p < 0.0001$) and VI%BW ($p = 0.0064$ in Group A; $p = 0.0023$ in Group B). For VI%BW, Group A demonstrated a significant improvement between T0 and T1 ($p = 0.0120$), and T0 and T2 ($p = 0.0083$), but not between T1 and T2 ($p = 0.4040$). Group B showed significant increases between T0 and T2 ($p = 0.0012$), and T1 and T2 ($p = 0.0034$), but not between T0 and T1 ($p = 0.7788$). Regarding PVF%BW, both groups exhibited significant differences across all time points, showing progressive improvement over time.

Conclusion The results suggest that amantadine, either alone or in combination with meloxicam, improves GRFs in dogs with degenerative lumbosacral stenosis and, may be a valuable component of its multimodal therapy, though additional research is necessary to validate these findings.

*Correspondence:
Chiara Caterino
chiara.caterino@unina.it
Federica Aragosa
federica.aragosa@unina.it

Full list of author information is available at the end of the article

Keywords Degenerative lumbosacral stenosis, Force plate gait analysis, Canine, NMDA, Neuropathic pain

Background

Degenerative lumbosacral stenosis (DLSS), also referred to as cauda equina syndrome or lumbosacral compression, is an acquired multifactorial condition frequently observed in dogs. This condition is notably common in large male dogs [1], with certain breeds, such as German Shepherds, military dogs, and working dogs appearing to have a higher predisposition [2–6].

DLSS leads to chronic pain and neurological issues due to the compression of the seventh lumbar (L7) nerve roots, local blood vessels, and the cauda equina. Clinical signs range from pain in the lumbosacral region and difficulty jumping or climbing stairs to different degrees of neurological deficits, such as abnormal tail carriage, unilateral or bilateral pelvic limb lameness, nerve root sign, ataxia in hindlimbs, paraparesis, and, in severe cases, urinary and faecal incontinence [1, 6–8].

The compression also leads to demyelination and inflammation of nerve roots [9] and the pain resulting from such pathology manifests as neuropathic pain since it is caused by a lesion which leads to damage and dysfunction of the somatosensory system, in particular the spinal cord and peripheral nerves [10, 11].

To date, there is no consensus regarding the treatment modalities [12]. It has been suggested that management of DLSS in mildly affected dogs without moderate to severe neurological deficits should consist of using analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) and lifestyle adjustments [13] such as strengthening the core muscles through physiotherapy [14]. According to veterinary literature, conservative treatment has been effective in 55% of dogs treated, but in 32% of cases, clinical signs returned after discontinuation [8]. Alternative treatments, such as epidural steroid injections, have shown promising outcomes in a median follow-up of 48 months [15]. Long-term use side effects (e.g., duodenal ulcers, acute renal failure, increased enzyme activities) reduce the safety usage of NSAIDs [16]. In addition, neuropathic pain is often refractory to traditional analgesic medications [9].

Surgical management of DLSS has been more extensively reported, with clinical improvement identified in 67–97% of cases [1, 17–21] and may be indicated in dogs that do not respond to conservative management [14]. Nevertheless, there is no evidence or objective evaluation on which to base the decision to choose surgery over conservative management [14].

Amantadine is an antiviral drug, dopamine agonist and non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist. In human medicine, it was initially used to treat influenza A encephalopathy; currently, due to its anti-inflammatory, neurotrophic and dopaminergic effects, it is used in the treatment of conditions such as Parkinson's disease, Huntington's chorea and depression. It has also been shown to be effective in the treatment of neuropathic pain [22]. Moreover, amantadine may decrease central sensitization and opioid tolerance in some patients and may enhance the effects of NSAIDs, gabapentin and opioids [23]. Based on a pharmacokinetic study performed in greyhound dogs, the suggested dosing is 3–5 mg/kg Q12-h [23–26]. In veterinary medicine, a single case report study reported the use of amantadine for treating neuropathic pain in a dog [27]; in addition, a randomized, placebo-controlled trial showed significant improvement in pain scores related to osteoarthritis for dogs which received amantadine in conjunction with meloxicam compared to placebo [23]. To the Authors' best knowledge, no study has been performed to evaluate objectively the effectiveness of amantadine in a conservative treatment for neuropathic pain due to DLSS in dogs. Our hypothesis was that amantadine might be a valid treatment for neuropathic pain caused by DLSS and that improvement could be observed during clinical evaluation and objectively assessed through kinematic data from the force platform.

Therefore, the aims of this clinical trial were to assess the efficacy of amantadine alone within a therapeutic protocol for managing neuropathic pain in dogs affected by degenerative lumbosacral stenosis through the analysis of ground reaction forces (GRFs), including Peak of Vertical Force (PVF), Vertical Impulse (VI), and stance time (ST) and to evaluate whether the co-administration of amantadine improves the efficacy of meloxicam in patients who have shown a refractory response to meloxicam alone.

Results

Twenty dogs met the inclusion criteria: 13 were male (4 neutered), and 7 were female (5 sterilised). Ten dogs were assigned to each group. None of the enrolled dogs showed signs of clinically relevant pain in the two weeks preceding the start of the study, as assessed by the CMPS-SF following owner-reported signs of discomfort. Consequently, all dogs which met the inclusion criteria, completed the study. Table 1 shows the distribution of the breeds and sex in each group. The mean BW was 37.57 ± 11.42 kg and 31.68 ± 7.37 kg for groups A and B, respectively. The mean age was 9 ± 3 years and 9 ± 1.5 years for groups A and B, respectively. Normalized kinetic variables were not normally distributed. At T0, no statistical difference for GFRs and BW between the two

Table 1 Distribution of study population for breed and sex. M = male, MN = male neuterd; F = female, FS = female sterilized

	GROUP A				GROUP B				
BREED	**M**	**MN**	**F**	**FS**	**M**	**MN**	**F**	**FS**	**TOTAL**
German Shepherd	1	1	1	1			1		5
Mix breed				3	4	2			9
Golden Retriever					1	1			2
Cane Corso Italiano	1								1
Labrador Retriever		2							2
Irish Setter								1	1
Total	10				10				20

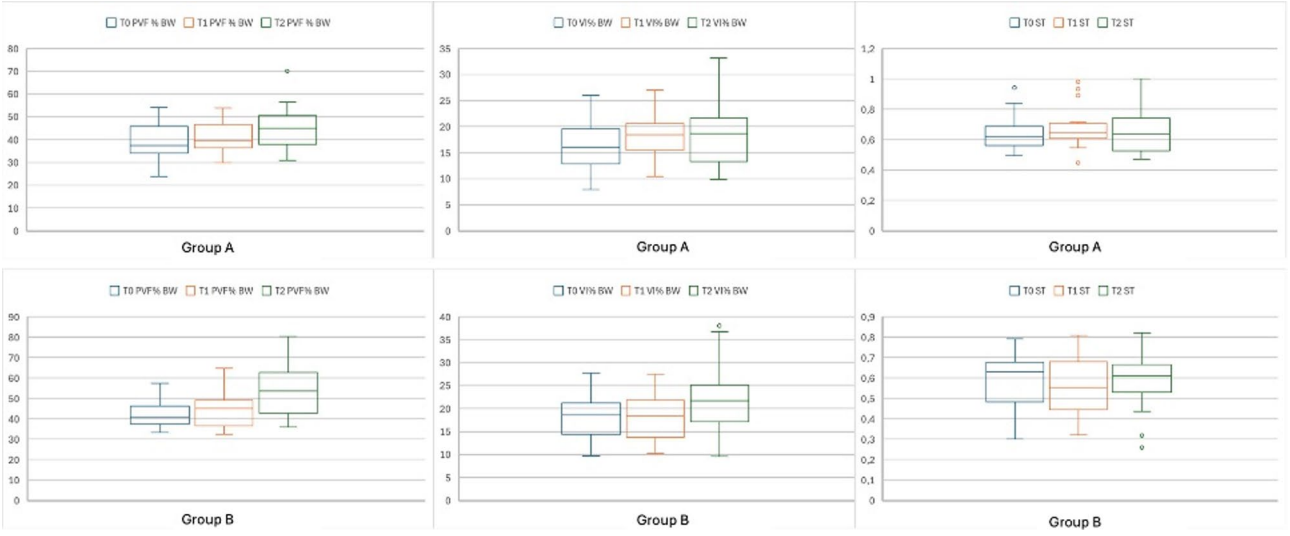

Fig. 1 Box-and-whisker plot of peak vertical force, vertical impulse, and stance time across time points (T0, T1, T2) in groups **A** and **B**

groups was present. Fig. 1 shows GRFs values over time controls.

In group A, Wilcoxon signed rank test between T0 and T2 showed a statistically significant increase in VI%BW (p-value = 0.0064) and PVF%BW (p-value < 0.0001).

For group B, the statistical comparison between T0 and T2 showed, like group A, a statistically significant increase in VI%BW (p-value = 0.0023) and PVF%BW (p-value < 0.0001). There was no statistically significant increase in ST.

In both groups, the increase in VI%BW and PVF%BW over time differed significantly in the groups (p-value < 0.0001). In group A for VI%BW, there was a statistically significant difference between T0 and T1 (p-value = 0.0120), T0 and T2 (p-value = 0.0083), but not between T1 and T2 (p-value = 0.4040). For group B, there was a statistically significant difference between T0 and T2 (p-value = 0.0012), and between T1 and T2 (p-value = 0.0034). Still, there was no statistically significant difference between T0 and T1 (p-value = 0.7788). Regarding PVF%BW, in group A, there was a statistically significant difference between T0 and T1 (p-value = 0.0172), T0 and T2 (p-value = 0.0003), and between T1 and T2 (p-value = 0.0026). In group B, there was a statistically significant difference between T0 and T1 (p-value = 0.0161), T0 and T2 (p-value < 0.0001) and between T1 and T2 (p-value = 0.0001). Table 2 shows the results.

Table 2 Pairwise comparisons of VI%BW and PVF%BW over time in groups A and B

Variable	Group	T0 vs. T1	T0 vs. T2	T1 vs. T2
VI%BW	A	$p = 0.0120$	$p = 0.0083$	$p = 0.4040$
	B	$p = 0.7788$	$p = 0.0012$	$p = 0.0034$
PVF%BW	A	$p = 0.0172$	$p = 0.0003$	$p = 0.0026$
	B	$p = 0.0161$	$p < 0.0001$	$p = 0.0001$

The achieved statistical power for PVF was 0.89, indicating a high likelihood of detecting a true effect. For VI, the power reached 0.72, suggesting a moderate probability of identifying significant differences. In contrast, the power for ST was lower at 0.47, reflecting a reduced ability to detect subtle changes over time in this variable. These results reflect the variability and magnitude of observed differences between groups across time points, with stronger effects seen in PVF and VI compared to ST.

Discussion

In this clinical trial, we aimed to assess the efficacy of amantadine within a therapeutic protocol for managing neuropathic pain in dogs affected by degenerative lumbosacral stenosis through the analysis of ground reaction forces (GRFs), including Peak of Vertical Force (PVF), Vertical Impulse (VI), and stance time (ST). Results from our study supported our hypothesis that amantadine might be a valid treatment for neuropathic pain caused by DLSS.

The mechanism of action of amantadine is rather unique compared to other N-methyl-D-aspartate receptor antagonists. Instead of blocking ion channels, amantadine acts as an antagonist of particular gates. Studies reveal that amantadine's main mechanism is related to the acceleration of ion channel closure, and its interactions with the receptor make it particularly effective in inhibiting NMDA responses during the prolonged depolarisations that accompany neurological insults, as occurs in chronic pain [23, 28].

Our study population is aligned with those previously reported in the literature regarding age and sex predisposition, with our sample mainly consisting of adult dogs (mean age of 9 ± 3 years and 9 ± 1.5 years) with the male dogs overrepresented (14/20) [2, 14]. We observed that the largest proportion of dogs were large mix-breeds (9 out 20), followed by German Shepherd (5 out 20). Such a proportion is justified by the higher prevalence of mixed-breed dogs in our geographical area. The enrolled mixed-breed dogs were nonetheless large-sized, mesomorphic, meaning they had a thoracic index (thoracic width × 100 / thoracic depth) ranging from 60 to 89 [29] and exhibited physical traits resembling those of Labrador Retrievers or shepherd-type dogs. In German Sheperd dogs has been described a more sagittal orientation of the articular process joints at L5-6 and L6-7 and a larger angle difference (tropism) between lumbar and LS articular process joints than in other dog breeds [30].

Force-plate analysis has been used in several studies as a method to objectively compare the clinical outcome of different surgical techniques, medications and nutraceuticals [31, 32]. In addition, since the enrolled dogs were all mesomorphic, the comparison between GRFs could be considered reliable [33]. At T0, there were no statistically significant difference between the GRFs of Group A and Group B meaning that at T0, the groups were considered homogeneous. Despite the possibility of different imaging findings between the enrolled dogs, it has been reported a poor association between clinical signs, pathology, and imaging findings. Therefore, some patients conservatively treated could show clinical improvement even in the case of persistent compression [34–36]. Regarding the GRFs, PVF and VI are considered reliable indexes to objectively evaluate the limbs' function: PVF, the maximum force exerted perpendicularly to the recording surface during the stance phase, usually decreases due to lameness, meaning less weight bearing and duration on the limping limb. Consequently, VI, which is calculated as the area under the vertical force curve using time, decreases in lame dogs. Both groups had a statistically significant difference between T0 and T2. In particular, in group A, we detected a statistically significant difference in values of PVF%BW between T0-T1, T0-T2 and T1-T2. Not in the same way, we detected a statistically significant difference for the values of VI%BW only between T0-T1 and T0-T2. Hence, a major improvement in VI%BW was registered after 7 days of treatment. In our opinion, the absence of statistical difference between T1-T2, could be explained by a terminal half-life of oral amantadine in dogs, which is 4.96 h (4.11–6.59 h) [25], therefore even if there was no longer an increase, amantadine helped those dogs to maintain the same values. Interestingly, PVF%BW increased over time, meaning there was an increase in the exerted force on the limbs. Similarly, in group B, there was a statistical difference between PVF%BW at T0 -T1, T0-T2 and T1-T2, showing an increase in pressure, not associated with a statistically significant increase of VI%BW between T0 and T1. Since the consistency among the time to maximum concentration in humans and dogs [37–39], we hypothesized that the steady-state level of amantadine reported to be reached in 4–7 days of treatment in humans [40], could be assumed as the same in dogs. Therefore, dogs showed an increase in the perpendicular force exerted (PVF) after seven days. In addition, in our opinion, amantadine could enhance the efficacy of the meloxicam acting on other receptors. Since the enrolled canine patients did not exhibit severe degrees of lameness, given the etiopathogenesis of the condition—which, in the most severe cases, leads to limb dragging—the ST value never varied statistically. Although no statistically significant changes in stance time (ST) were observed across the study period, the concurrent increases in both PVF and VI suggest an improvement in limb loading without alterations in temporal gait parameters. This pattern indicates that the treated dogs were able to generate higher vertical forces over a similar contact time, reflecting more effective use of the affected limb. The lack of significant variation in ST may be attributed to the absence of severe claudication and to the fact that improvements in limb function were expressed primarily through increased force output rather than modifications in limb contact duration. These findings are consistent with previous studies where therapeutic response in dogs with mild to moderate orthopedic or neurologic conditions was predominantly associated with PVF and VI changes, rather than ST adjustments [41, 42].

As with any kinetic gait analysis, our methodology is subject to both environmental and subject-related sources of variability, which must be considered when interpreting the results. In our study, steps were taken to mitigate these factors—particularly by allowing each dog to explore and become familiar with the testing area and equipment prior to data collection. This acclimatization process aimed to reduce inconsistencies that can arise from stress or unfamiliarity, which are known to influence parameters such as stance time and vertical impulse [43].

Handler influence, while often considered a possible source of error, contributes only minimally to kinetic variability—typically between 0% and 7% [44]. Nevertheless, to minimize even this limited variability, each dog in our study, consistently with literature [45], was always led by the same owner, who had received standardized instructions from the clinical team regarding trial conduction.

In contrast, variability attributable to the individual dog is much greater, ranging from 14 to 69%, and is particularly impactful on peak vertical force values. Similarly, trial repetition introduces a high degree of variability, from 29 to 85% [44]. These data underscore the importance of strict control over testing conditions and repeated measures.

Gait velocity is another critical factor that influences kinetic outputs. In this study, each subject was evaluated consistently at walk. Maintaining a narrow range of speed is essential for ensuring data comparability across trials and subjects [46–48].

Overall, while some level of variability in force plate analysis is inevitable, careful methodological planning—including environmental familiarization, consistent handling, trial standardization, and velocity control—can substantially improve the reliability and interpretability of kinetic gait data.

The post hoc power analysis provided important context for interpreting the observed statistical results. The achieved power was high PVF (0.89), indicating that the study was well-powered to detect changes in this variable over time and between treatment groups. Similarly, the power for Vertical Impulse VI was acceptable (0.72), supporting confidence in the detected effects, although with a slightly increased risk of type II error. In contrast, the lower power observed for ST (0.47) suggests that the study may have been underpowered to detect meaningful differences in this parameter, potentially explaining the lack of significant findings. These results highlight the greater sensitivity of PVF and VI as outcome measures in the assessment of therapeutic efficacy in dogs with DLSS, and suggest that ST may be less responsive to change or more affected by measurement variability in this context. Future studies with larger sample sizes may be needed to clarify the role of stance time as a reliable kinetic marker. In addition to the objective gait analysis, owner-reported behavioral assessments were collected using the Canine Brief Pain Inventory (CBPI) at all study time points. Although the CBPI is validated for chronic pain assessment in dogs, it has not been specifically standardized for use in dogs with degenerative lumbosacral stenosis (DLSS). As such, these data were not included in the primary analysis. However, they are provided as supplementary material to support the interpretation of force plate data and to offer additional clinical context regarding the animals' perceived pain and functional status.

Conclusion

In conclusion, based on the data collected in our study, amantadine could be considered a useful drug in the multimodal management of neuropathic pain associated with degenerative lumbosacral stenosis in dogs. From a cost-effectiveness perspective, amantadine represents a low-cost and accessible adjunct therapy for managing chronic pain in dogs with DLSS, particularly those unresponsive to NSAIDs alone. While surgical intervention remains the treatment of choice for severe or progressive cases [6, 8, 49], it involves significantly higher costs and greater risks. In contrast, amantadine may enhance analgesic efficacy in refractory patients and potentially delay or reduce the need for surgery in selected cases. Given its favorable cost profile and ease of administration, amantadine offers a valuable therapeutic option within a multimodal conservative approach, especially for patients who are not ideal surgical candidates due to age, comorbidities, or owner limitations. This study has two main limitations. First, the absence of a meloxicam-only control group limited the possibility of directly comparing the experimental treatments to standard NSAID therapy. However, the study specifically targeted dogs that were non-responsive to meloxicam, with the aim of evaluating alternative therapeutic strategies in this refractory population. Second, the sample size was relatively small, partly due to the implementation of new European regulations during the study period, which restricted the veterinary use of the molecule under investigation and consequently limited recruitment. Further studies are needed to confirm these findings on a larger scale.

Methods

For this randomized study, the protocols and procedures were reviewed and approved by the Ethical Animal Care and Use Committee of the University of Naples "Federico II" (prot. No. PG/2023/0059191 of 22/05/2023). All procedures were performed for diagnostic and therapeutic purposes and following the European directive 2010/63/EU. Besides these procedures were carried out after informing the owners and getting their verbal consent.

The study was conducted at the Veterinary Teaching Hospital of the University of Naples "Federico II". Client-owned dogs over 1 year old and 20 kg of body weight with a diagnosis of DLSS were included in the study. Inclusion criteria were the diagnosis of DLSS and not responsiveness to NSAIDs alone. The diagnosis was based on the clinical history, neurologic examination, magnetic resonance imaging (MRI), or computed tomography (CT) studies. Reports were issued by board-certified specialists in Diagnostic Imaging and/or Neurology. Imaging findings included evidence of nerve root compression (uni- or bilateral) and/or intervertebral disc protrusion at the lumbosacral junction (L7–S1) [6, 50, 51]. Specific imaging criteria included narrowing/stenosis of lumbosacral intervertebral foramen with displacement or compression of the cauda equina or L7 nerve roots [52], and disc protrusion with or without associated spondylosis deformans [1, 53]. These findings had to correlate with the neurological deficits and clinical signs observed on physical and neurological examination to confirm diagnosis.

To establish non-responsiveness to meloxicam, only dogs that had previously received meloxicam at 0.1 mg/kg once daily for at least 14 consecutive days were considered for inclusion. Selection was based on persistent clinical signs of pain and dysfunction, as reported by the owners and confirmed during neurologic evaluation. Dogs showing satisfactory clinical improvement with meloxicam were excluded.

After this initial treatment period, a 14-day washout period was observed to eliminate any residual effects of the NSAID. Only at the end of this washout, and in the continued presence of clinical signs, dogs were considered non-responsive and included in the study. The baseline time point (T0) was defined as the moment immediately prior to the start of the experimental treatment, following the complete washout.

Data from the meloxicam treatment phase were not analyzed, as the aim of the study was to evaluate alternative therapeutic strategies in dogs refractory to standard NSAID monotherapy. For this reason, a meloxicam-only control group was not included.

Exclusion criteria were concomitant orthopaedic issues (i.e., moderate to severe hip dysplasia, recent history of fractures, trauma), neoplastic conditions or systemic disease with an inflammatory component, and pregnancy. Dogs with transitional lumbosacral vertebrae were also excluded in order to create a homogeneous anatomical patient group. Neurological examinations were performed by two investigators (CC and GF). Data from medical records included age, breed, weight, sex, neuter status, and duration of clinical signs. Moreover, each patient underwent a complete blood count, serum biochemistry and cardiologic evaluation to rule out concurrent disease that can mimic DLSS related pain or occult systemic disease. Before the commencement of our study, a two-week withdrawal period was required for NSAIDs and short-acting glucocorticoids and one month for long-acting oral or parental glucocorticoids and other painkillers. No other treatments for control pain were proposed, executed or accepted concurrently. The dogs were allowed to perform everyday physical activity but no physiotherapy. If owners reported signs of pain in the two weeks preceding the start of the study, the Glasgow Composite Measure Pain Scale [54] (CMPS-SF) was applied to assess clinical relevance. In case of clinically relevant pain (CMPS-SF ≥ 6/24), rescue analgesia was provided with gabapentin (10 mg/kg PO TID) or tramadol (3–5 mg/kg PO BID–TID). If gabapentin or tramadol were not sufficient or contraindicated, methadone (0.2 mg/kg IM q6–8 h as needed) was administered as an alternative. Dogs that required more than two consecutive days of rescue analgesia were excluded from baseline data collection and re-evaluated before inclusion. In addition to kinetic data, owner-reported behavioral assessments were collected using the Canine Brief Pain Inventory (CBPI) [55, 56]. The CBPI was administered at each evaluation time point (T0, T1, T2) to all enrolled dog owners. Although this tool is validated for chronic pain assessment in dogs, it has not been specifically standardized for degenerative lumbosacral stenosis (DLSS), and was therefore used as a complementary measure to support the interpretation of the objective findings. Detailed CBPI results are reported in the Supplementary Material.

Force plate gait analysis

Force plate gait analysis was performed using a computer-assisted force platform gait analysis (PASCO Capstone software version 2.2.2) before starting the study (T0) and at 7 days (T1) and 21 days (T2) of treatment in order to objectively evaluate the grade of lameness and the ground reaction forces (GRFs). Body weight (BW) was recorded at each time point. A 40 × 40 cm platform (PASPORT Force Platform, PS-2141, PASCO scientific, California, USA) was placed in a 4 m walkway to record GRFs. Before data collection, dogs were let walk freely across the walkway for at least 15 min to familiarize themselves with the environment and the operators [57]. Each trial was considered valid when the pelvic limb and the thoracic limb fully struck at the same time the surface of the plate. The dogs were walked over the pressure plate until five valid trials were achieved. The dog's velocity was registered with a dedicated detector (Motion Sensor II, CI-6742, PASCO scientific, California, USA), and only trials with a velocity of 1–1.3 m/s were accepted. Dogs were walked in both directions with a standardised starting position [58]. The computer analysis system generated the force-to-time curve. Registered kinetic GFRs were collected for both pelvic limbs, including the peak

of vertical force (PVF) and impulse (VI) and stance time (ST). PVF was defined as the maximum force exerted perpendicular to the surface during the stance phase, while VI was the calculated area under the vertical force curve. As previously described, the GRFs parameters were normalised to body weight (PVF%BW, VI%BW) [59].

Treatment

Dogs enrolled were randomly assigned to two groups using online randomization tool (https://www.randomizer.org). The list was prepared by an investigator not involved in patient evaluation or data analysis to ensure allocation concealment. Each enrolled dog was assigned a code number, and treatment allocation followed the pre-generated sequence. Group A received a combination of meloxicam for 7 days (0.1 mg/kg PO q24h after a loading dose of 0.2 mg/kg OS) and amantadine for 21 days (3 mg/kg PO q24h), Group B received amantadine only, for 21 days (3 mg/kg PO q12h). Clinical re-examinations and force gait plate analysis were performed at days 7 (T1) and 21 (T2). The individual responsible for analyzing the ground reaction forces was blinded to the treatment each patient received. This information was disclosed only after the statistical analysis had been completed. In contrast, the two operators who performed the neurological evaluations were aware of the randomized treatment assignments.

Statistical analysis

The data were imported into an electronic spreadsheet (Microsoft Excel version 16.95.1, Microsoft Corporation, Redmond, WA, USA) and analyzed using commercial statistical software (GraphPad Prism version 10.0.0 for macOS, GraphPad Software, Boston, MA, USA, www.graphpad.com). Descriptive statistics for body weight, age (in years), status (entire, neutered, castrated), were expressed as mean ± standard deviation. Data distribution for the normalized kinetic variables (PVF%BW_T0; PVF%BW_T1; PVF%BW_T2; VI%BW_T0; VI%BW_T1; VI%BW_T2; ST_T0; ST_T1; ST_T2;) was analyzed with Kolmogorov-Smirnov test. Furthermore, given the limited sample size, non-parametric tests were selected.

The Mann-Whitney U-test was used to examine the differences between groups A and B at time T0. This was done to assess whether randomization had effectively divided the dogs into two homogeneous groups in terms of PVF%BW, VI%BW, ST, and body weight (W).

To determine whether each of the two therapies had an effect on pain control, a two-tailed Wilcoxon matched-pairs signed rank test was used to examine differences between pre- and post-treatment values (at baseline T0 and T2). Finally, to compare the differences within each therapy among the different controls, Friedman's ANOVA test for related samples was used to measure the significance of the GRF increase from T0 to T2 for both groups. The Fisher LSD test was used as a post-hoc test.

The level of statistical significance was set at $p < 0.05$.

Each dog contributed two pelvic limbs to the kinetic analysis; thus, the total number of limbs analyzed was 40 (20 limbs per group). Each limb was considered an independent statistical unit, consistent with previously validated approaches in quadrupedal gait analysis.

A post hoc power analysis was performed using G*Power software (version 3.1) to assess the sensitivity of the study to detect meaningful changes over time. The calculation was based on repeated-measures ANOVA within-between interaction. The analysis assumed a nonsphericity correction factor (ε) of 0.6, a correlation among repeated measures of 0.6, an alpha level of 0.05, and a total sample size of 40 limbs.

Effect sizes (Cohen's f) were estimated for each kinetic variable based on observed group trends and variability. For Peak Vertical Force (PVF), a medium effect size (f = 0.25) was adopted, reflecting a clear divergence between groups at T2. For Vertical Impulse (VI), the difference between groups was more modest, supporting a smaller effect size (f = 0.20). For Stance Time (ST), where minimal variation and overlapping values were observed across all time points, a small effect size (f = 0.15) was assumed.

Abbreviations

NSAIDs	Non-steroidal anti-inflammatory drugs
DLSS	Degenerative lumbosacral stenosis
GRFs	Ground reaction forces
PVF	Peak of vertical force
VI	Vertical impulse
ST	Stance time
PO	*Per os*
NMDA	N-methyl-D-aspartate
BW	Body weight
MRI	Magnetic resonance imaging
CT	Computed tomography
CMPS-SF	Composite measure pain scale- short form
CBPI	Canine brief pain inventory

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12917-025-04911-9.

Supplementary Material 1

Acknowledgements

The preliminary results were presented at the 35th ECVN/ ESVN Annual Symposium 2023, Venice, Italy and at 77th SISVet congress 2024, Parma, Italy.

Author contributions

Conceptualization, C.C. and G.F.; methodology, G.F., C.C., and G.D.V.; software, C.C., F.A., and S.C.; validation, G.F., C.C., and G.D.V.; formal analysis, C.C.; investigation, C.C., S.C., F.A., and G.D.V.; data curation, C.C., G.D.V.,; writing—original draft preparation, C.C., and G.D.V.; writing—review and editing, G.F., C.C.,F.L., G.D.V.; visualization, F.L. and G.F.; supervision, G.F. and F.L.; project administration, G.F. All authors have read and agreed to the published version of the manuscript.

Funding
No funding was received for this study.

Data availability
All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Ethical Animal Care and Use Committee of the University of Naples "Federico II" (prot. No. PG/2023/0059191 of 22/05/2023). Informed consent was obtained from the owners of the enrolled dogs.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Veterinary Medicine and Animal Productions, University of Naples "Federico II", Naples, Italy

Received: 15 April 2025 / Accepted: 30 June 2025
Published online: 16 July 2025

References

1. Suwankong N, Meij B, Voorhout G, De Boer A, Hazewinkel H. Review and retrospective analysis of degenerative lumbosacral stenosis in 156 dogs treated by dorsal laminectomy. Veterinary Comp Orthop Traumatol. 2008;21(03):285–93.
2. De Risio L, Thomas WB, Sharp NJH. Degenerative lumbosacral stenosis. Veterinary Clin North America: Small Anim Pract. 2000;30(1):111–32.
3. Indrieri RJ. Lumbosacral stenosis and injury of the cauda equina. Veterinary Clin North America: Small Anim Pract. 1988;18(3):697–710.
4. Tarvin G, Prata RG. Lumbosacral stenosis in dogs. J Am Vet Med Assoc. 1980;177(2):154–9.
5. Palmer RH, Chambers JN. Canine lumbosacral diseases. Part I. Anatomy, pathophysiology, and clinical presentation. 1991.
6. Meij BP, Bergknut N. Degenerative lumbosacral stenosis in dogs. Veterinary Clinics: Small Anim Pract. 2010;40(5):983–1009.
7. De Risio L, Sharp NJH, Olby NJ, Muñana KR, Thomas WB. Predictors of outcome after dorsal decompressive laminectomy for degenerative lumbosacral stenosis in dogs: 69 cases (1987–1997). J Am Vet Med Assoc. 2001;219(5):624–8.
8. De Decker S, Wawrzenski LA, Volk HA. Clinical signs and outcome of dogs treated medically for degenerative lumbosacral stenosis: 98 cases (2004–2012). J Am Vet Med Assoc. 2014;245(4):408–13.
9. Kruger L, Light AR. Translational pain research: from mouse to man. CRC; 2009.
10. Mahnig S, Landmann G, Stockinger L, Opsommer E. Pain assessment according to the international spinal cord injury pain classification in patients with spinal cord injury referred to a multidisciplinary pain center. Spinal Cord. 2016;54(10):809–15.
11. Pedersen TR, Berendt M, Rusbridge C. Neuroanatomy of spinal nociception and pain in dogs and cats: a practical review for the veterinary clinician. Front Vet Sci. 2025;12:1534685.
12. Jeffery ND, Barker A, Harcourt-Brown T. What progress has been made in the understanding and treatment of degenerative lumbosacral stenosis in dogs during the past 30 years? Vet J. 2014;201(1):9–14.
13. Chambers JN. Optimal treatment for degenerative lumbosacral stenosis. Surgical exploration and excision of tissue; 1989.
14. Worth A, Meij B, Jeffery N. Canine degenerative lumbosacral stenosis: prevalence, impact and management strategies. Veterinary Medicine: Res Rep. 2019; 10:169–83.
15. Janssens L, Beosier Y, Daems R. Lumbosacral degenerative stenosis in the dog. Veterinary Comp Orthop Traumatol. 2009;22(06):486–91.
16. Luna SPL, Basílio AC, Steagall PVM, Machado LP, Moutinho FQ, Takahira RK, et al. Evaluation of adverse effects of long-term oral administration of carprofen, etodolac, flunixin meglumine, ketoprofen, and meloxicam in dogs. Am J Vet Res. 2007;68(3):258–64.
17. Danielsson F, Sjöström L. Surgical treatment of degenerative lumbosacral stenosis in dogs. Vet Surg. 1999;28(2):91–8.
18. Goedde T, Steffen F. Surgical treatment of lumbosacral foraminal stenosis using a lateral approach in twenty dogs with degenerative lumbosacral stenosis. Vet Surg. 2007;36(7):705–13.
19. Golini L, Kircher PR, Lewis FI, Steffen F. Transarticular fixation with cortical screws combined with dorsal laminectomy and partial discectomy as surgical treatment of degenerative lumbosacral stenosis in 17 dogs: clinical and computed tomography follow-up. Vet Surg. 2014;43(4):405–13.
20. Andrade Gomes S, Lowrie M, Targett M. Long-term outcome following lateral foraminotomy as treatment for canine degenerative lumbosacral stenosis. Vet Rec. 2018;183(11):352.
21. Hankin EJ, Jerram RM, Walker AM, King MD, Warman CGA. Transarticular facet screw stabilization and dorsal laminectomy in 26 dogs with degenerative lumbosacral stenosis with instability. Vet Surg. 2012;41(5):611–9.
22. Ma HM, Zafonte RD. Amantadine and memantine: a comprehensive review for acquired brain injury. Brain Inj. 2020;34(3):299–315.
23. Lascelles BDX, Gaynor JS, Smith ES, Roe SC, Marcellin-Little DJ, Davidson G, et al. Amantadine in a multimodal analgesic regimen for alleviation of refractory osteoarthritis pain in dogs. J Vet Intern Med. 2008;22(1):53–9.
24. KuKanich B. Outpatient oral analgesics in dogs and cats beyond nonsteroidal antiinflammatory drugs: an evidence-based approach. Veterinary Clinics: Small Anim Pract. 2013;43(5):1109–25.
25. Norkus C, Rankin D, Warner M, KuKanich B. Pharmacokinetics of oral amantadine in greyhound dogs. J Vet Pharmacol Ther. 2015;38(3):305–8.
26. Lamont LA. Adjunctive analgesic therapy in veterinary medicine. Veterinary Clin North America: Small Anim Pract. 2008;38(6):1187–203.
27. Madden M, Gurney M, Bright S. Amantadine, an N-Methyl-D-Aspartate antagonist, for treatment of chronic neuropathic pain in a dog. Veterinary Anaesth Analg. 2014;41(4):440–1.
28. Aiyer R, Mehta N, Gungor S, Gulati A. A systematic review of NMDA receptor antagonists for treatment of neuropathic pain in clinical practice. Clin J Pain. 2018;34(5):450–67.
29. Bonetti F. Tipi morfologici e costituzionali nelle razze canine. Zoognostica del Cane; Crepaldi: Bologna, Italy. 1995:63–76.
30. Seiler GS, Häni H, Busato AR, Lang J. Facet joint geometry and intervertebral disk degeneration in the L5-S1 region of the vertebral column in german shepherd dogs. Am J Vet Res. 2002;63(1):86–90.
31. Comblain F, Barthélémy N, Lefèbvre M, Schwartz C, Lesponne I, Serisier S, et al. A randomized, double-blind, prospective, placebo-controlled study of the efficacy of a diet supplemented with curcuminoids extract, hydrolyzed collagen and green tea extract in owner's dogs with osteoarthritis. BMC Vet Res. 2017;13(1):395.
32. Caterino C, Aragosa F, Della Valle G, Costanza D, Lamagna F, Piscitelli A, et al. Clinical efficacy of curcuvet and boswellic acid combined with conventional nutraceutical product: an aid to canine osteoarthritis. PLoS ONE. 2021;16(5):e0252279.
33. Della Valle G, Caterino C, Aragosa F, Balestriere C, Piscitelli A, Di Palma C et al. Relationship between ground reaction forces and morpho- metric measures in two different canine phenotypes using regression analysis. Vet Sci. 2022;9(7).
34. Fritsch EW, Heisel J, Rupp S. The failed back surgery syndrome: reasons, intraoperative findings, and long-term results: a report of 182 operative treatments. Spine (Phila Pa 1976). 1996;21(5):626–33.
35. Fraser RD, Sandhu A, Gogan WJ. Magnetic resonance imaging findings 10 years after treatment for lumbar disc herniation. Spine (Phila Pa 1976). 1995;20(6):710–4.
36. Nachemson A, Zdeblick TA, O'Brien JP. Lumbar disc disease with discogenic pain. What surgical treatment is most effective? Spine (Phila Pa 1976). 1996;21(15):1835–8.
37. Siao KT, Pypendop BH, Stanley SD, Ilkiw JE. Pharmacokinetics of amantadine in cats. J Vet Pharmacol Ther. 2011;34(6):599–604.
38. Bleidner WE, Harmon JB, Hewes WE, Lynes TE, Hermann EC. Absorption, distribution and excretion of amantadine hydrochloride. J Pharmacol Exp Ther. 1965;150(3):484–90.
39. Hayden FG, Minocha A, Spyker DA, Hoffman HE. Comparative single-dose pharmacokinetics of amantadine hydrochloride and rimantadine

hydrochloride in young and elderly adults. Antimicrob Agents Chemother. 1985;28(2):216–21.
40. Pacifici GM, Nardini M, Ferrari P, Latini R, Fieschi C, Morselli PL. Effect of amantadine on drug-induced parkisonism: relationship between plasma levels and effect. Br J Clin Pharmacol. 1976;3(5):883–9.
41. Renberg WC, Johnston SA, Ye K, Budsberg SC. Comparison of stance time and velocity as control variables in force plate analysis of dogs. Am J Vet Res. 1999;60(7):814–9.
42. Rumph PF, Kincaid SA, Visco DM, Baird DK, Kammermann JR, West MS. Redistribution of vertical ground reaction force in dogs with experimentally induced chronic hindlimb lameness. Vet Surg. 1995;24(5):384–9.
43. Rumph PF, Steiss JE, Montgomery RD. Effects of selection and habituation on vertical ground reaction force in greyhounds. Am J Vet Res. 1997;58(11):1206–8.
44. Jevens DJ, Hauptman JG, DeCamp CE, Budsberg SC, Soutas-Little RW. Contributions to variance in force-plate analysis of gait in dogs. Am J Vet Res. 1993;54(4):612–5.
45. O'Connor BL, Visco DM, Heck DA, Myers SL, Brandt KD. Gait alterations in dogs after transection of the anterior cruciate ligament. Arthritis Rheum. 1989;32(9):1142–7.
46. Budsberg S, Rytz U, Johnston S. Effects of acceleration on ground reaction forces collected in healthy dogs at a trot. Veterinary Comp Orthop Traumatol. 1998;11(01):15–9.
47. McLaughlin RM Jr., Roush JK. Effects of subject stance time and velocity on ground reaction forces in clinically normal greyhounds at the trot. Am J Vet Res. 1994;55(12):1666–71.
48. McLaughlin R Jr., Roush JK. Effects of increasing velocity on braking and propulsion times during force plate gait analysis in greyhounds. Am J Vet Res. 1995;56(2):159–61.
49. Tanoue H, Shimada M, Ichinohe T, Kanno N, Suzuki S, Harada Y, et al. Postoperative outcomes of combined surgery comprising dorsal laminectomy, transarticular screws, pedicle screws and polymethylmethacrylate for dorsal fixation in 21 dogs with degenerative lumbosacral stenosis. J Am Vet Med Assoc. 2022;260(14):1813–9.
50. Worth AJ, Thompson DJ, Hartman AC. Degenerative lumbosacral stenosis in working dogs: current concepts and review. N Z Vet J. 2009;57(6):319–30.
51. Rossi F, Seiler G, Busato A, Wacker C, Lang J. Magnetic resonance imaging of articular process joint geometry and intervertebral disk degeneration in the caudal lumbar spine (L5-S1) of dogs with clinical signs of cauda equina compression. Vet Radiol Ultrasound. 2004;45(5):381–7.
52. Gödde T, Steffen F. Surgical treatment of lumbosacral foraminal stenosis using a lateral approach in twenty dogs with degenerative lumbosacral stenosis. Vet Surg. 2007;36(7):705–13.
53. Suwankong N, Voorhout G, Hazewinkel HA, Meij BP. Agreement between computed tomography, magnetic resonance imaging, and surgical findings in dogs with degenerative lumbosacral stenosis. J Am Vet Med Assoc. 2006;229(12):1924–9.
54. Della Rocca G, Colpo R, Reid J, Di Salvo A, Scott M. Creation and validation of the Italian version of the Glasgow composite measure pain scale-short form (ICMPS-SF). Vet Ital. 2018;54(3):251–60.
55. Brown DC, Boston R, Coyne JC, Farrar JT. A novel approach to the use of animals in studies of pain: validation of the canine brief pain inventory in canine bone cancer. Pain Med. 2009;10(1):133–42.
56. Brown DC, Bell M, Rhodes L. Power of treatment success definitions when the canine brief pain inventory is used to evaluate carprofen treatment for the control of pain and inflammation in dogs with osteoarthritis. Am J Vet Res. 2013;74(12):1467–73.
57. Hans EC, Zwarthoed B, Seliski J, Nemke B, Muir P. Variance associated with subject velocity and trial repetition during force platform gait analysis in a heterogeneous population of clinically normal dogs. Vet J. 2014;202(3):498–502.
58. Vilar JM, Morales M, Santana A, Spinella G, Rubio M, Cuervo B, et al. Controlled, blinded force platform analysis of the effect of intraarticular injection of autologous adipose-derived mesenchymal stem cells associated to PRGF-Endoret in osteoarthritic dogs. BMC Vet Res. 2013;9:1–6.
59. Voss K, Galeandro L, Wiestner T, Haessig M, Montavon PM. Relationships of body weight, body size, subject velocity, and vertical ground reaction forces in trotting dogs. Vet Surg. 2010;39(7):863–9.

Publisher's note