Comparative analysis of neurological recovery and adverse effects in chondrodystrophic dogs with thoracolumbar intervertebral disc herniation treated with methylprednisolone versus non-steroidal anti-inflammatory drugs

William McCartney
North Dublin Orthopaedic Animal Hospital
Ciprian Andrei Ober (ciprian.ober@usamvcluj.ro)
University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca https://orcid.org/0000-0003-3997-725X
Maria Benito
Sandyford Dublin

Research Article

Keywords: anti-inflammatory, chondrodystrophic dog, disc herniation, methylprednisolone, NSAID

Posted Date: September 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-906140/v1

Abstract

Thoracolumbar intervertebral disc herniation is a common neurologic disease presented to the small-animal practitioner. The use of methylprednisolone sodium succinate (MPSS) as an adjunct to surgical decompression in cases of acute spinal cord injury following intervertebral disc extrusion is controversial. A prospective study was undertaken to compare the preoperative use of MPSS and non-steroidal anti-inflammatory drugs (NSAIDs) in 40 chondrodystrophic dogs presenting with similar signs and undergoing spinal decompressive surgery. Twenty dogs received MPSS and 20 had NSAIDs administered preoperatively. Dogs were administered with either MPSS intravenously 20 minutes before surgery (30 mg/kg) or NSAID (meloxicam 0.2mg/kg or carprofen 4 mg/kg) subcutaneously 20 minutes before surgery. Dogs were evaluated by neurologic examination of gait 24 hours postoperatively, at time of discharge and then at 8 weeks. The neurological recovery were similar in both groups, but the frequency of side effects such as vomiting (MPSS group: 90% versus NSAIDs group: 55%), and anorexia within the first three days (present in all 20 dogs pretreated with MPSS) was significantly different, with complications being more prevalent in the MPSS group. Side effects were significantly more evident with MPSS treatment group –including vomiting and anorexia during the first 3 days after surgery– than with NSAID treatment group, with a neurological recovery similar in both groups.

Introduction

Medical and surgical treatments for intervertebral disc herniation have been described extensively (Griffin et al. 2009a, b). One of the effects of acute spinal cord injury (SCI) is reduction in blood flow to the neural tissue. As reperfusion occurs, highly reactive free radicals are liberated. These free radicals induce lipid peroxidation and damage to the cellular plasma membrane. Ischemia/reperfusion injury is key in irreversible tissue loss following spinal cord trauma and ischemia (Sharp and Wheeler 2005). The potentially beneficial mechanism of action of glucocorticoids in SCI is inhibition of this lipid peroxidation as well as hydrolysis of lipids, processes that lead to damage of both neuronal and microvascular membranes (Bracken et al. 1997). This inhibition is postulated to be due to the steroids' high lipid solubility and ability to intercalate into artificial membranes between the hydrophobic polyunsaturated fatty acids of the membrane phospholipids and limit the chain reaction of lipid peroxidation throughout the phospholipid bilayer (Demoupoulis et al. 1980; Hall 1992; Hall and Springer 2004). In addition to the primary action of glucocorticoids at physiologic doses, some formulations, such as methylprednisolone sodium succinate (MPSS) can exert a number of other actions on the spinal cord, including maintenance of tissue blood flow, maintenance of aerobic energy metabolism, improved reversal of intracellular calcium accumulation, reduction of neurofilament degradation, and enhanced neuronal excitability and synaptic transmission (Bracken et al. 1990; Hall 1992; Bracken et al. 1997). Another effect of methylprednisolone is inhibition of phospholipase A2 formation, inhibiting arachidonic acid release as well as prostaglandin F2α and thromboxane A2, which can produce anti-inflammatory effects (Fingeroth and Thomas 2015). Use of MPSS evolved during the 1990s, through the results obtained from the National Acute Spinal Cord Injury Studies –NASCIS II and III–, as a standard treatment in acute spinal

injury (Sayer et al. 2006), and remains a drug used worldwide for ASCI. The potential beneficial effect of high-dose MPSS was initially reported in a series of NASCIS trials in 1990s (Bracken et al. 1990; Bracken et al. 1997). Following the publication of the NASCIS trials, the pre-operative treatment was adopted worldwide; and, MPSS treatment became the standard of care in human adults (Caruso et al. 2017). However, the subsequent debate over the efficacy and safety of high-dose MPSS treatment (Sayer et al. 2006; Short et al. 2000) has led to serious differences of opinion in the medical community, and variations in practice (Rozet 2008). The increased overall complication rate was observed after high-dose MPSS treatment (Matsumoto et al. 2001; Suberviola et al. 2008; Ito et al. 2009). Pneumonia, infection, and gastrointestinal bleeding are the most common complications reported in human patients receiving high-dose MPSS (Matsumoto et al. 2001; Chikuda et al. 2014). In any case, MPSS, as a steroid, is the only US FDA approved drug for the treatment of spinal cord injury in humans (Mirzaei et al. 2020). The results of the human NASCIS trials cannot be directly extrapolated to our veterinary patients. When examined closely, the benefit perceived in humans was very slight, with the result being minimal motor improvement. It is hard to discern what function that would correlate to in our patients, and if that effect would even be perceptible (in some humans there was increased digital motor function; such a benefit in dogs would be clinically insignificant) (Fingeroth and Thomas 2015). Currently there is a lack of studies comparing MPSS and NSAIDs in the treatment of dogs with acute SCI, thus, this study details the preoperative use of MPSS in a cohort of similar dogs undergoing spinal decompressive surgery and compares the use of MPSS to NSAIDs.

Materials And Methods

Design and setting

All animal procedures were in accordance with the national Research Council Guide for the Care and Use of Laboratory Animals using protocols approved by the Institutional Animal Care and Use Committee at the University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, Romania. All the methods in the study was carried out in accordance with the ARRIVE guidelines. Prospective study of 40 consecutive cases of IVDD treated preoperatively with MPSS and NSAIDs that have undergone spinal decompressive surgery at a single private hospital. Twenty cases were selected for every group. Dogs with confirmed IVDH were included in this study. Data on nature and progression of signs, patient signalment, history and duration of paralysis, preoperative neurologic status, cross-sectional imaging findings, surgical details, details of drugs used for anesthesia and pain management, and postoperative care were recorded. Dogs were evaluated by neurologic examination of gait 24 hours postoperatively, at time of discharge and then at 8 weeks (using modified Frankel score system). Inclusion criteria for the trial were: chondrodystrophic dogs weighing < 20 kg, aged with acute onset of hindlimb paralysis with intact deep pain sensation (within 72h of admission), no contrary prior treatment with corticosteroids or with non-steroidal anti-inflammatory drugs (NSAIDs) before referral if appropriate but continuation of same class as relevant, no clinically relevant systemic comorbidity and diagnosis of acute TL-IVDH that was treated surgically (Fig. 1). The diagnosis was established by myelography and MRI scan (Siemens Magneton 0.3

T). T1-weighted (T1W), T2-weighted (T2W), 3D T2, short tau inversion recovery (STIR), and contrast studies were performed. Findings to confirm disc extrusions were: extradural compressive material hyperintense to the spinal cord parenchyma on T2W, signal voids in epidural space associated with the compression, suggesting the presence of hemoglobin breakdown products (T2W), increased conspicuity of intervertebral disc-associated extradural compression with STIR and enhanced herniated intervertebral disc material on T1W after administration of gadolinium-based contrast medium. No hyperintensity of the spine was recorded to be compared with the length of L2.

Perioperative management

Dogs were administered with either MPSS (n = 20) intravenously 20 minutes before surgery (30 mg/kg) or NSAID (n = 20) (meloxicam 0.2mg/kg or carprofen 4 mg/kg) subcutaneously 20 minutes before surgery. This was in combination with 30 minutes preoperative antibiotics (cephalexin 25mg/kg) and analgesia (buprenorphine 0.02mg/kg or methadone 0.6mg/kg). Premedication consisted of medetomidine and either methadone or buprenorphine. Induction was performed with propofol and anesthesia was maintained with isoflurane in oxygen. Methadone or buprenorphine injections were given for three days postoperative plus either prednisolone (2 mg/kg for 3 days then 1 mg/kg for four days) or NSAID (carprofen 2 mg/kg or meloxicam 0,1 mg/kg) orally for seven days. All dogs underwent a single site hemilaminectomy.

Postoperative follow-up

Drug administration was initiated once the diagnosis of IVDH was confirmed and all dogs underwent hemilaminectomy. The only difference in treatment between groups was the medication administered. Side effects were recorded (Table 2) and compared using Fisher's test. Diarrhea was considered because the loose stools were watery. Melena was established based on the dark reddish brown to black color of the feces. Vomiting was observed based on digested material eliminated. Anorexia was considered when dog totally refused to eat. Neurologic function was assessed 8 weeks postoperatively (using modified Frankel score system) to assure the outcome of the surgical procedure. Physiotherapy started from day 1 postoperative consisting of assisted standing, flexion/extension, and massage of affected limb muscles. The assisted standing water treadmill started with day 3. Bladder emptying by manual expression was performed every 8 hours.

Statistical Analysis

Fisher's exact test was used to compare between the two medication groups. Fisher's test was preferred to the Chi-square test, sometimes used for this type of data, due to the size of the two samples. All analyses compared between the two medication groups, and a summary of the analysis results are shown in Table 2 as the number and percentage of subjects with complications within each group. The differences were considered significant when p-values are < 0.05. Certain outcomes were binary (e.g., diarrhea, vomiting).

Results

Forty client-owned dogs with acute onset of thoracolumbar (T3-L3) acute intervertebral disc herniation (IVDH) Hansen type I were admitted to the clinic and examined (Table 1). Median age was 3.9 years (range, 1–7 years) at the time of surgery. There were 23 males and 17 females. Breeds were 18 Dachshunds, 7 Jack Russel Terriers, 6 Shih Tzu, 4 French Bulldogs, 2 Pugs, 1 Pembroke Welsh Corgi, 1 Pekingese, 1 Lhasa Apso. Data were collected from the cohort of animals that underwent hemilaminectomy and were preoperatively treated with two different medications: MPSS (group 1) or NSAIDs (group 2). Pain sensation was present preoperatively in all dogs (all dogs had a modified Frankel score of grades 3 or 4, similar between the two groups). Results of hematology, basic liver, and kidney biochemistry were unremarkable.

Table 1
Baseline characteristics of dogs in the study.

No.	Group 1			Group 2		
	Breed	Age (years)	Sex	Breed	Age (years)	Sex
1	Dachshund	2	F	Dachshund	3	M
2	Dachshund	5	M	Dachshund	6	F
3	Dachshund	3	M	Dachshund	3	M
4	Dachshund	7	M	Dachshund	4	M
5	Dachshund	3	M	Dachshund	2	F
6	Dachshund	5	F	Dachshund	5	M
7	Dachshund	5	F	Dachshund	6	F
8	Dachshund	3	F	Dachshund	3	M
9	Dachshund	2	M	Pembroke Welsh Corgi	6	F
10	Dachshund	4	M	Shih Tzu	3	M
11	French Bulldog	4	M	Shih Tzu	2	M
12	Pekingese	5	F	Shih Tzu	5	F
13	Pug	7	F	Jack Russel Terrier	4	F
14	Shih Tzu	2	M	Jack Russel Terrier	5	M
15	Shih Tzu	1	M	Jack Russel Terrier	3	M
16	Shih Tzu	4	F	Jack Russel Terrier	4	F
17	Lhasa Apso	7	F	French Bulldog	1	M
19	Jack Russel Terrier	6	M	French Bulldog	2	M
19	Jack Russel Terrier	3	F	French Bulldog	1	F
20	Jack Russel Terrier	5	M	Pug	7	M

Postoperative outcome and follow-up

The results indicated statistically significant differences in the occurrence of both vomiting and anorexia within the first three days between two medication groups. Both of these two complications were more prevalent in the MPSS group (Table 2). There was also some evidence that diarrhea was more common in the MPSS group – 12/20 (60%) versus 5/20 (25%) in the NSAIDs group–, although this difference was

only of borderline statistical significance (p = 0,05) (Table 2). In the MPSS group there was one death due to unknown causes, thus, the animal was eliminated from the study. A necropsy was not performed. Twenty-five dogs developed urinary tract infections, 10/20 (50%) in the MPSS group, and 15/20 (75%) in NSAIDs group without statistically significant differences (p = 0,19) (Table 2). Thirty animals – 17/20 (85%) pre-treated with MPSS and 13/20 (65%) with NSAIDs– developed melena also without statistical significant differences (p = 0,27). Further 3/20 (15%) dogs from the MPSS group suffered wound infection versus 1/20 (5%) dog from the NSAIDs group (p = 0,61). The neurological recovery was similar in both groups with no statistical differences (Table 2).

Table 2
Comparison of complications between medication groups.

Complication	Steroid (MPSS) N (%)	NSAIDs N (%)	P-value
Vomiting	18 (90%)	11 (55%)	0.03*
Diarrhoea	12 (60%)	5 (25%)	0.05
Melena	17 (85%)	13 (65%)	0.27
Anorexia 1st 3 days	20 (100%)	11 (55%)	0.001*
Cystitis	10 (50%)	15 (75%)	0.19
Wound infection	3 (15%)	1 (5%)	0.61
Neurological recovery	14 (70%)	15 (75%)	1.00
*MPSS: methylprednisolone; NSAIDs: non-steroidal anti-inflammatory drugs. N: number *p < 0.05.*			

Discussion

The main findings in this prospective study are that dogs suffering SCI following acute intervertebral disc herniation treated surgically have similar neurological outcomes when they receive methylprednisolone versus NSAIDs, but that there was a significant difference in side effects between groups, with a higher percentage of dogs in the MPSS group having side effects than the NSAID group. Vomiting and anorexia were more prevalent in the MPSS group in our study, with statistically significant differences in the occurrence comparing with NSAID group. We considered vomiting and anorexia as consequences of gastrointestinal ulceration, because these signs were not present preoperatively. Renal function analyzes were performed only preoperatively to assure no comorbidity was present (an inclusion criteria request). We mentioned these aspects as limitations of the study. In humans, spinal cord injury is associated with increased risk of gastroduodenal ulceration, but the mechanism is not completely understood (Kewalramani 1979). Also, after high-dose MPSS treatment in patients with acute cervical spinal cord injury (Miekisiak et al. 2014), the authors observed that patients receiving high-dose MPSS had a significantly increased risk of major complications (gastrointestinal ulcer and bleeding). The treatment

was not associated with an increase in mortality. In two studies, one hundred per cent of healthy dogs who received high dose MPSS had endoscopic evidence of gastric bleeding (Rohrer et al. 1999a, b). Concurrent treatment with gastrointestinal protectant drugs did not ameliorate this adverse effect. We didn't use any gastrointestinal protectant drugs for the dogs in the study. In another study, 90% of dogs undergoing spinal surgery with adjunctive MPSS treatment had evidence of gastrointestinal bleeding assessed by faecal occult blood tests (Hanson et al. 1997). Olby et al. (2016) did not find any benefit of MPSS or polyethylene glycol in the therapy of acute, severe thoracolumbar IVDH used as adjunctive treatments administered to dogs in the first 24 hours of onset of paralysis. Boag et al. (2001) found that dachshunds with acute intervertebral disc disease treated with decompressive surgery and receiving MPSS had a significantly higher incidence of postoperative gastrointestinal complications rate, an increased use of gastrointestinal protectants, and also financial costs. We consider gastrointestinal bleeding and/or ulceration to be responsible for vomiting, anorexia and melena, with vomiting and anorexia significantly more prevalent comparing with NSAID group in our study.

Urinary bladder dysfunction is an important and common problem in perioperative cases of thoracolumbar IVDD (Kerwin et al. 2018). It was not possible to accurately determine preoperatively the urinary status of the population of dogs in our study due to the acute nature of the condition and the short amount of time spent in the hospital before the surgery. Ten dogs in MPSS group and 15 in NSAID group developed cystitis postoperative without statistically significant differences between groups. This is was somehow surprising for us and not very consistent with what has been reported in the literature. In a study conducted on 161 dogs with surgically confirmed IVDD (Levine et al. 2008), dexamethasone group dogs was 11.4 times as likely to have a urinary tract infection and 3.5 times as likely to have diarrhea, compared with other glucocorticoid and nontreatment group dogs. No differences in neurologic function at discharge or rre-evaluation were detected among groups. In another study (Mari et al. 2019) there was a strong significant association between not administering NSAIDs after diagnosis and a higher risk of faecal incontinence. In that study dogs that were administered NSAIDs (81 cases) were compared to dogs that did not receive NSAIDs (106 cases). In the latter group both dogs that did not receive any anti-inflammatory treatment (93 cases) and dogs that received corticosteroids (13 cases) were included. When dogs that received corticosteroids to dogs that did not were compared, no significant association with faecal incontinence was found (Mari et al. 2019). In any case, the low number of cases receiving corticosteroids and the lack of randomization, any direct comparison between the effect of these 2 classes of anti-inflammatory drugs on the occurrence of urinary infection or feacal incontinence was difficult to establish. Neurological grade at referral was also a predictor of urinary and faecal incontinence. This suggested that further prospective randomized studies are necessary to investigate NSAIDs treatment in dogs with acute nucleus pulposus extrusion.

Detrimental wound-healing effect and increased infection with the use of glucocorticosteroids both in humans and dogs were observed (Nishida et al. 2016; Levine et al. 2007).

There were no statistical significant differences regarding neurological recoveries of dogs in our groups. Recently, it has been shown that MPSS therapy in 50 dogs with surgically treated Hansen type-I

thoracolumbar intervertebral disk herniation (TL-IVDH) significantly reduced the swelling of the spinal cord, although failed to provide any significant advance in recovery rate or length in time (Nishida et al. 2016). A study evaluating 233 dogs treated medically for presumptive thoracolumbar intervertebral disc herniation showed successful treatment (complete or substantial improvement without recurrence) in 55% of the dogs, with recurrence of paraspinal hyperesthesia, ataxia, or weakness in 31%; 14% of dogs were classified as therapeutic failures (decline in or lack of improvement after completion of medical therapy, or necessity for surgery or euthanasia within 1 month) (Levine et al. 2007). In that study, owners completed proxy quality of life scores for their dogs. Although duration of cage rest was not associated with outcome, administration of corticosteroids was negatively associated with both outcome and quality of life in a multivariate model that controlled for initial severity of spinal cord injury. Administration of NSAIDs was more likely to result in improved quality of life scores. The small population of dogs in our groups together with lack of any specific quality of life questionnaire for owner do not allow us to draw any major conclusion regarding quality of recovery.

Temporal effects of steroid administration limits how results of human trials can be extrapolating to veterinary patients. The human studies routinely showed either no benefit or worsened outcomes when patients received steroids more than 8h after spinal cord injury. Unfortunately for veterinarians, it is not always possible to identify the precise time of onset of disc-induced spinal cord injury in our patients, so we may find ourselves treating dogs with steroids well beyond any time frame where they might have had any potential benefit. Until we have prospective, blinded, large-scale studies in our patients with naturally occurring spinal cord injury, we cannot advocate using high-dose MPSS in our patients (Fingeroth and Thomas 2015).

Many veterinary clinicians continue to use corticosteroids such as prednisone or dexamethasone routinely at lower, anti-inflammatory doses for the management of canine IVDE (Moore et al. 2016). The question of whether treatment with non-steroidal anti-inflammatories (NSAIDs) or steroids is most appropriate represents a somewhat polarizing issue in veterinary medicine and is highly clinician-dependent (Moore et al. 2020).

Limitations of the study reported here included a small population in the two groups, lack of a control group and subjective assessment of anorexia and melena in treated dogs. Future studies with larger groups, ensuring that vomiting and anorexia are clearly due to anti-inflammatory drugs, with dogs having additional risk factors for gastrointestinal injury and bleeding, such as older age and presence of comorbidities, would better represent the clinical population of dogs receiving MPSS and NSAIDs. Any conclusions made in this study cannot be solely attributed to a single dose of MPSS preoperatively. Although such additional studies are warranted, our study results lead us to believe that the benefit of pre-operatively treatment with MPSS in chondrodystrophic does not support the use of this drug over NSAIDs prior to spinal surgery.

We have shown results supporting that MPSS use is associated with higher side effects than when using NSAIDs instead when using for IVDD in dogs. Side effects are significantly more evident with MPSS –

including vomiting and anorexia during the first 3 days after surgery– than with NSAID, with an outcome recovery similar in both groups.

Declarations

Authors' Contributions McCartney W performed all surgeries and wrote the draft of the study. Ober C contributed to conceptualization, writing, editing, and critically revision of the manuscript. Menito Maria contributed to the interpretation of the data and design of the study.

Funding This research received no external funding

Data Availability The data sets in this study are available from the corresponding author on reasonable request. All data and materials are available for publication.

Ethical Approval This study was conducted at the University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, Romania with approval of the Ethics Committee of the University (No. 267/12.07.2021). All animal procedures were in accordance with the national Research Council Guide for the Care and Use of Laboratory Animals using protocols approved by the Institutional Animal Care and Use Committee at the University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, Romania.

Data Availability Statement: Data obtained is available upon request to the corresponding author.

Consent to Participate All authors read and approved the manuscript.

Consent to Publish All authors read and approved the manuscript.

Competing Interests The authors declare that they have no conflicts of interest.

References

1. Boag AK, Otto CM, Drobatz KJ (2001) Complications of methylprednisolone sodium succinate therapy in dachshunds with surgically treated intervertebral disc disease. J Vet Emerg Crit Care 11:105–110. https://doi.org/10.1111/j.1476-4431.2001.tb00076.x
2. Bracken MB, Shepard MJ, Collins WF, Holford TR, Young W, Baskin DS, Eisenberg H, Flamm E, Leo-summers L, Maroon J, Marshall L, Perot P, Piepmeier J, Sonntag V, Wagner F, Wilberger J, Winn HR (1990) A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal cord injury. NEJM 322:1405–1411. doi:10.1056/NEJM199005173222001
3. Bracken MB, Shepard MJ, Holford TR, Leo-Summers L, Aldrich EF, Fazl M (1997) Administration of Methylprednisolone for 24 or 48 hours or Tirilazad Mesylate for 48 hours in the treatment of acute spinal cord injury. JAMA 277:1597–1604
4. Caruso MC, Daugherty MC, Moody SM, Falcone RA, Bierbrauer KS, Geis GL (2017) Lessons learned from administration of high-dose methylprednisolone sodium succinate for acute pediatric spinal

cord injuries. J Neurosurg Pediatr 20:567–574. doi:10.3171/2017.7.PEDS1756

5. Chikuda H, Yasunaga H, Takeshita K, Horiguchi H, Kawaguchi H, Ohe K, Fushimi K, Tanaka S (2014) Mortality and morbidity after high-dose methylprednisolone treatment in patients with acute cervical spinal cord injury: a propensity-matched analysis using a nationwide administrative database. Emerg Med J 31:201–620. doi:10.1136/emermed-2012-202058
6. Demoupoulis HB, Flamm ES, Pietronigro DD, Seligman ML (1980) The free radical pathology and the microcirculation in the major central nervous system disorders. Acta Physiol Scand
7. 492.:91–119
8. Fingeroth JM, Thomas WB (2015) Advances in intervertebral disc disease in dogs and cats. Willey-Blackwell
9. Griffin JF, Levine JM, Kerwin SC, Cole R (2009a) Canine thoracolumbar intervertebral disc disease: Diagnosis, prognosis, and treatment. Compend Contin Educ Vet 31(3):E3
10. Griffin JF, Levine JM, Kerwin SC (2009b) Canine thoracolumbar intervertebral disc disease: Pathophysiology, neurologic examination, and emergency medical therapy. Compend Contin Educ Vet 31(3):E2
11. Hall ED (1992) The neuroprotective pharmacology of methylprednisolone. J Neurosurg 76:13–22. doi:10.3171/jns.1992.76.1.0013
12. Hanson SM, Bostwick DR, Twedt DC, Smith MO (1997) Clinical evaluation of cimetidine, sucralfate and misoprostol for prevention of gastro-intestinal tract bleeding in dogs undergoing spinal surgery. Am J Vet Res 58:1320–1323
13. Hall ED, Springer JE (2004) Neuroprotection and acute spinal cord injury: a reappraisal. NeuroRx 1:80–100. doi:10.1602/neurorx.1.1.80
14. Ito Y, Sugimoto Y, Tomioka M, Kai N, Tanaka M (2009) Does high dose methylprednisolone sodium succinate really improve neurological status in patient with acute cervical cord injury?: a prospective study about neurological recovery and early complications. Spine (Phila Pa 1976) 34:2121–2124. doi:10.1097/BRS.0b013e3181b613c7
15. Kerwin SC, Levine JM, Mankin JM (2018) Thoracolumbar vertebral column. In: Johnston SA, Tobias KM (eds) Veterinary Surgery: Small Animal. St. Louis, Missouri, Elsevier; 2018
16. Kewalramani LS (1979) Neurogenic gastro-duodenal ulceration and bleeding associated with spinal cord injuries. J Trauma 19:259–265. doi:10.1097/00005373-197904000-00008
17. Levine JM, Levine GJ, Johnson SI, Kerwin SC, Hettlich BF, Fosgate GT (2007) Evaluation of the success of medical management for presumptive thoracolumbar intervertebral disc herniation in dogs. Vet Surg 36:481. doi:10.1111/j.1532-950X.2007.00295.x
18. Levine JM, Levine GJ, Boozer L, Schatzberg SJ, Platt SR, Kent M, Kerwin SC, Fosgate GT (2008) Adverse effects and outcome associated with dexamethasone administration in dogs with acute thoracolumbar intervertebral disc herniation: 161 cases (2000–2006). J Am Vet Med Assoc 232:411–417. doi:10.2460/javma.232.3.411

19. Mari L, Behr S, Shea A, Dominguez E, Ricco C, Alcoverro E (2019) Predictors of urinary or fecal incontinence in dogs with thoracolumbar acute non-compressive nucleus pulposus extrusion. J Vet Intern Med 33:2693–2700. doi:10.1111/jvim.15626
20. Matsumoto T, Tamaki T, Kawakami M, Yoshida M, Ando M, Yamada H (2001) Early complications of high-dose methylprednisolone sodium succinate treatment in the follow-up of acute cervical spinal cord injury. Spine (Phila Pa 1976) 26:426–430. doi:10.1097/00007632-200102150-00020
21. Miekisiak G, Kloc W, Janusz W, Kaczmarczyk J, Latka D, Zarzycki D (2014) Current use of methylprednisolone for acute spinal cord injury in Poland: survey study. Eur J Orthop Surg Traumatol Suppl 1:S269–S273. doi:10.1007/s00590-014-1422-3
22. Mirzaei F, Meshkini A, Habibi B, Pharm A, Salehpour F, Rafei E, Fathi W, Alavi SHN, Majdi A, Aghasan SR, Alavi SAN (2020) Ceftriaxone plus methylprednisolone combination therapy versus methylprednisolone monotherapy in patients with acute spinal cord injury: A Randomized, Triple-Blind Clinical Trial. Int J Spine Surg 14(5):706–712. doi:10.14444/7102. Epub 2020 Oct 19
23. Moore SA, Early PJ, Hettlich BF (2016) Practice patterns in the management of acute intervertebral disc herniation in dogs. J Small Anim Pract 57:409–415. doi:10.1111/jsap.12496
24. Moore SA, Tipold A, Olby N, Stein V, Granger N, Canine Spinal Cord Injury Consortium (CANSORT SCI) (2020) Current Approaches to the Management of Acute Thoracolumbar Disc Extrusion in Dogs. Front Vet Sci 7:610. doi:10.3389/fvets.2020.00610
25. Nishida H, Tanaka H, Kitamura M, Inaba T, Nakayama M (2016) Methylprednisolone sodium succinate reduces spinal cord swelling but does not affect recovery of dogs with surgically treated thoracolumbar intervertebral disk herniation. Jpn J Vet Res 64:191–196
26. Olby NJ, Muguet-Chanoit AC, Lim JH, Davidian M, Mariani CL, Freeman AC, Platt SR, Humphrey J, Kent M, Giovanella C, Longshore R, Early PJ, Muñana KR (2016) A Placebo-Controlled, Prospective, Randomized Clinical Trial of Polyethylene Glycol and Methylprednisolone Sodium Succinate in Dogs with Intervertebral Disk Herniation. J Vet Intern Med 30:206–214. doi:10.1111/jvim.13657
27. Rohrer CR, Hill RC, Fischer A, Fox LE, Schaer M, Ginn PE, Casanova JM, Burrows CF (1999a) Gastric hemorrhage in dogs given high doses of methylprednisolone sodium succinate. Am J Vet Res 60:977–981
28. Rohrer CR, Hill RC, Fischer A, Fox LE, Schaer M, Ginn PE, Preast VA, Burrows CF (1999b) Efficacy of misoprostol in prevention of gastric hemorrhage in dogs treated with high doses of methylprednisolone sodium succinate. Am J Vet Res 60:982–985
29. Rozet I (2008) Methylprednisolone in acute spinal cord injury: is there any other ethical choice? J Neurosurg Anesthesiol 20:137–139. doi:10.1097/01.ana.0000314441.63823.b0
30. Sayer FT, Kronvall E, Nilsson OG (2006) Methylprednisolone treatment in acute spinal cord injury: the myth challenged through a structured analysis of published literature. Spine J 6:335–343. doi:10.1016/j.spinee.2005.11.001
31. Sharp NJ, Wheeler SJ (2005) Small Animal Spinal Disorders. Elsevier Limited, Philadelphia

32. Short DJ, El Masry WS, Jones PW (2000) High dose methylprednisolone in the management of acute spinal cord injury –a systematic review from a clinical perspective. Spinal Cord 38:273–286. doi:10.1038/sj.sc.3100986
33. Suberviola B, González-Castro A, Llorca J, Ortiz-Melón F, Miñambres E (2008) Early complications of high-dose methylprednisolone in acute spinal cord injury patients. Injury 39:748–752. doi:10.1016/j.injury.2007.12.005

Figures

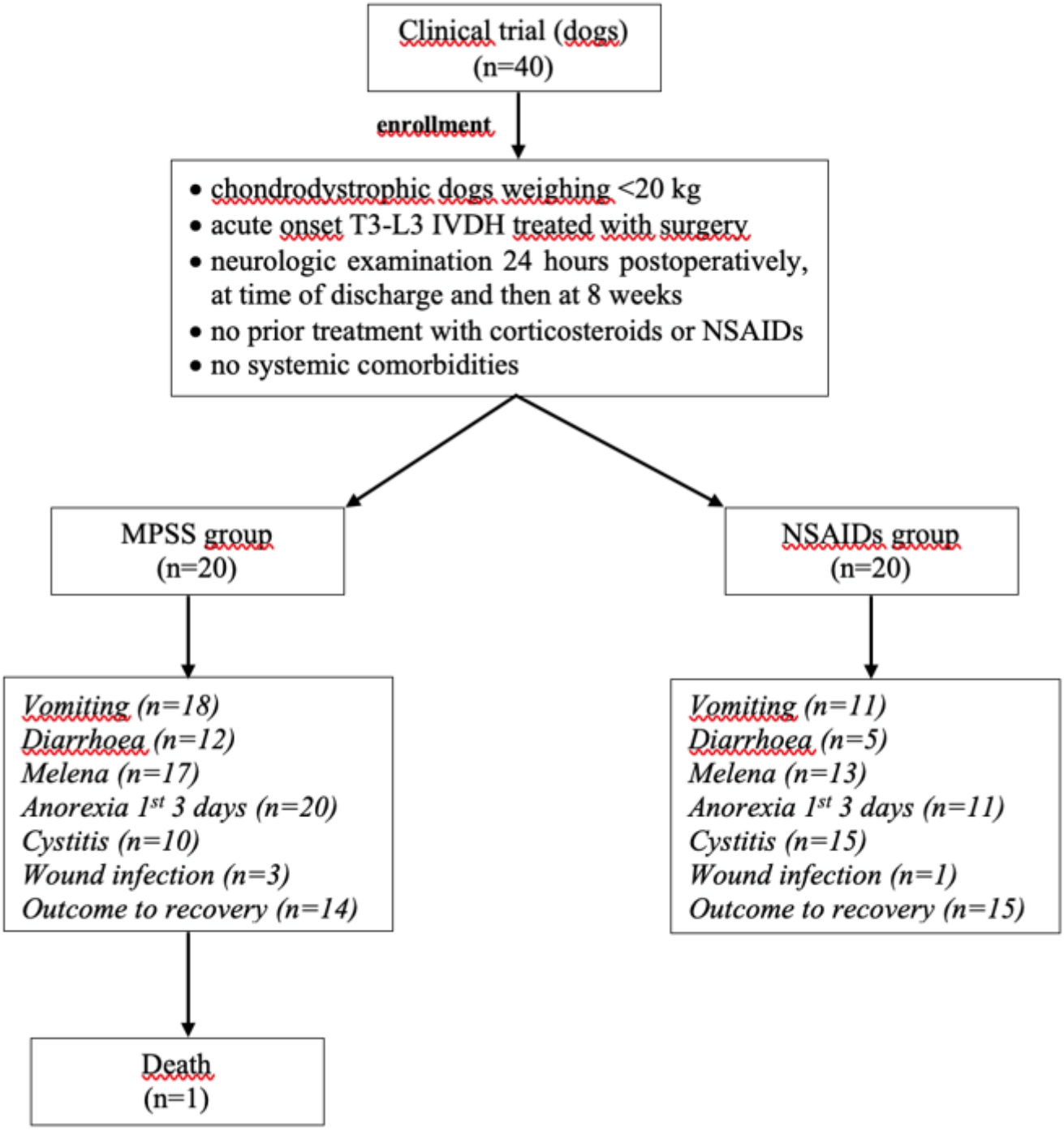

Figure 1

Consort flow diagram. This flowchart illustrates the recruitment, study groups and complications.