

# Comparative Analysis of Outcomes and Side Effects in Chondrodystrophic Dogs Treated With Preoperative Methylprednisolone Versus Non-steroidal Anti-inflammatory Drugs

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## Research Article

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# Abstract

## Background

Thoracolumbar intervertebral disc herniation is likely the most common neurologic disease presented to the small-animal practitioner. The use of methylprednisolone (MPSS) as an adjunct to surgical decompression in cases of acute spinal cord injury following intervertebral disc extrusion is controversial. A prospective preliminary 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.

## Results

Twenty dogs received MPSS and 20 had NSAIDs administered preoperatively. The outcomes 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. 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. The use of MPSS is associated with higher adverse side effects than NSAIDs.

## Conclusions

Our results shows that MPSS use is associated with higher side effects than when using NSAIDs instead. 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.

## Background

Medical and surgical treatments for intervertebral disc herniation have been described extensively [1, 2]. 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 cause damage to the plasma membrane of cells by the process of lipid peroxidation. This phenomenon is key in irreversible tissue loss following spinal cord trauma and ischemia [3]. The potentially beneficial mechanism of action of glucocorticoids in SCI is inhibition of this lipid peroxidation as well as hydrolysis, processes that lead to damage of both neuronal and microvascular membranes [4]. 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 [5-7].

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

when given at suprapharmacologic doses, 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 [4, 6, 8]. Another effect of methylprednisolone is inhibition of phospholipase A2 formation, inhibiting arachidonic acid release as well as prostaglandin F2 $\alpha$  and thromboxane A2, which can produce anti-inflammatory effects [9].

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 [10], and remains the drug used worldwide for ASCI. The beneficial effect of high-dose MPSS was initially reported in a series of NASCIS trials in the 1990s [4, 8]. MPSS is a potent and long-acting anti-inflammatory, antiallergic and immunosuppressant used in patients with spinal cord injury, in order to minimize neurological damage [11]. Following the publication of the NASCIS trials, the pre-operative treatment was adopted worldwide; thus, MPSS treatment became the standard of care in human adults [12]. However, the subsequent debate over the efficacy and safety of high-dose MPSS treatment [10, 13] has led to serious differences of opinion in the medical community, and variations in practice [14]. The increased overall complication rate was observed after high-dose MPSS treatment [15-17]. Pneumonia, infection, and gastrointestinal bleeding are the most common complications reported in human patients receiving high-dose MPSS [15, 18]. Anyway, MPSS, as a steroid, is the only approved drug for the treatment of spinal cord injury [19]. With all of the controversy surrounding the human NASCIS, it is difficult to extrapolate their results to our 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) [9].

A direct comparison between methylprednisolone and NSAIDs in dogs is currently lacking, 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.

## **Methods**

### **Aim**

To compare the preoperative use of MPSS and non-steroidal anti-inflammatory drugs in 40 chondrodystrophic dogs presenting with similar signs and undergoing spinal decompressive surgery.

### **Design and setting**

Prospective study of 40 consecutive cases of IVDD treated preoperatively with MPSS NSAIDs that have undergone spinal decompressive surgery at a private hospital. Twenty cases were randomly selected for every group. 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.

## **Case selection**

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. Inclusion criteria for the trial were: chondrodystrophic dogs weighing <20 kg, aged with acute onset of paralysis (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 (Figure 1). The diagnosis was established by myelography and MRI scan (*Siemens Magnetom 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 treatments**

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 receive 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 between groups was the medication administered. Side effects were recorded (Table 2) and compared using Fisher's test. 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

All outcomes were binary in nature, with the occurrence of each type of complications being either present or absent. As a result, 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 are considered significant when p-values are <0.05.

## Results

### Study population

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 type of medication: MPSS (group 1) or NSAIDs (group 2).

**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

### History and clinical signs

Pain sensation was present in all dogs (grade 3 or 4 modified Frankel score). Results of hematology, basic liver, and kidney biochemistry were unremarkable.

### 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. Thus, 18/20 (90%) of dogs pre-treated with MPSS experienced vomiting compared to only 11/20 (55%) of the dogs pre-treated with NSAIDs ( $p=0,03$ ). However, 20/20 (100%) of animals in the MPSS group showed anorexia compared to 11/20 (55%) of dogs in the NSAID group ( $p=0,001$ ) (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 a death due to unknown causes. 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 (Table 2).. Thirty animals -17/20 (85%) pre-treated with MPSS and 13/20 (65%) with NSAIDs- developed melena also without statistical significant differences. Further 3/20 (15%) dogs from the MPSS group suffered wound infection versus 1/20 (5%) dog from the NSAIDs group. Moreover, the outcome recovery was similar in both groups with no statistical differences (Table 2).

**Table 2.** Comparison of complications between medication groups

Complication	Steroid (MPSS)	NSAIDs	P-value
	N (%)	N (%)	
Vomiting	18 (90%)	11 (55%)	0.03*
Diarrhoea	12 (60%)	5 (25%)	0.05
Melena	17 (85%)	13 (65%)	0.27
Anorexia 1 <sup>st</sup> 3 days	20 (100%)	11 (55%)	0.001*
Cystitis	10 (50%)	15 (75%)	0.19
Wound infection	3 (15%)	1 (5%)	0.61
Death	1 (5%)	0 (0%)	1.00
Outcome to 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 with disc extrusions 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 % 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

consider 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 is 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 [20]. Also, after high-dose MPSS treatment in patients with acute cervical spinal cord injury [21], the authors observed that patients receiving high-dose MPSS had a significantly increased risk of major complications (gastrointestinal ulcer and bleeding) Anyway, 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. Concurrent treatment with gastrointestinal protectant drugs did not ameliorate this adverse effect. [22, 23]. 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 [24]. Olby et al. [25] 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. [26] 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 [27]. 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 [28], 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 re-evaluation were detected among groups. In another study [28] there was a strong significant association between not administering NSAIDs after diagnosis and a higher risk of faecal incontinence. This suggested that further prospective randomized studies are necessary to investigate NSAIDs treatment in dogs with acute nucleus pulposus extrusion. 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 [28]. Anyway, 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 fecal incontinence was difficult to be established. Neurological grade at referral was also a predictor of urinary and faecal incontinence. In a recent study, the dogs with an intramedullary hyperintensity greater than 40% of the cross-sectional area of the spinal cord at the same level on transverse T2-weighted MRI images were 4 times more likely to have urinary incontinence compared to dogs with smaller lesions [29].

In the dogs in this study, were 3 cases of post-operative wound infection in MPSS group and 1 case in NSAID group. While this number was too low to permit meaningful statistical analysis, it is important to note that 3 cases were in the group treated with MPSS. Detrimental wound-healing effect and increased infection with the use of glucocorticosteroids both in humans and dogs were observed [30, 31].

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 [32]. 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) [33]. 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. 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.

A limitation in extrapolating the human trials to our patients has to do with the temporal effects of steroid administration. 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 [9].

Many veterinary clinicians continue to use corticosteroids such as prednisone or dexamethasone routinely at lower, anti-inflammatory doses for the management of canine IVDE [34]. 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 [35].

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. 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.

## Conclusions

In summary, we have shown results supporting that MPSS use is associated with higher side effects than when using NSAIDs instead. This is the first prospective study directly comparing the use of MPSS versus NSAIDs as a preoperative anti-inflammatory management. 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.

## Abbreviations

ASCI: acute spinal cord injury; IVDE: intervertebral disc extrusion; IVDH: intervertebral disk herniation; LTs: leukotrienes; MPSS: Methylprednisolone sodium succinate; NASCIS: National Acute Spinal Cord Injury Studies; NSAIDs: non-steroidal anti-inflammatory drugs; PG: prostaglandins (PGE2; PGF1; PGF2); PLA2: phospholipase A2; PMM: progressive myelomalacia; TL-IVDH: thoracolumbar intervertebral disk herniation; TXA2: thromboxane A2

## Declarations

### Ethics approval and consent to participate

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. 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. Written informed client consent to participate was obtained for each enrolled patient in this veterinary clinical trial. All the methods in the study was carried out in accordance with the ARRIVE guidelines.

### Consent for publication

Not applicable.

### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

All authors declare no conflicts of interest related to this report.

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Not applicable.

### **Author contributions**

WMC performed all surgeries and wrote the draft of the study. CO contributed to conceptualization, writing, editing, and critically revision of the manuscript. MB: contributed to the interpretation of the data and design of the study.

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## **References**

1. Griffin JF, Levine JM, Kerwin SC, Cole R. Canine thoracolumbar intervertebral disc disease: Diagnosis, prognosis, and treatment. *Compend Contin Educ Vet.* 2009;31:E1.
2. Griffin JF, Levine JM, Kerwin SC. Canine thoracolumbar intervertebral disc disease: Pathophysiology, neurologic examination, and emergency medical therapy. *Compend Contin Educ Vet.* 2009;31:E1.
3. Sharp NJ, Wheeler SJ. *Small Animal Spinal Disorders.* Elsevier Limited, Philadelphia, PA; 2005.
4. Bracken MB, Shepard MJ, Holford TR, Leo-Summers L, Aldrich EF, Fazl M. Administration of Methylprednisolone for 24 or 48 hours or Tirilazad Mesylate for 48 hours in the treatment of acute spinal cord injury. *JAMA.* 1997;277:1597–1604.

5. Demoupoulis HB, Flamm ES, Pietronigro DD, Seligman ML. The free radical pathology and the microcirculation in the major central nervous system disorders. *Acta Physiol Scand.* 1980;492:91–119.
6. Hall ED. The neuroprotective pharmacology of methylprednisolone. *J Neurosurg.* 1992;76:13–22. doi: 10.3171/jns.1992.76.1.0013
7. Hall ED, Springer JE. Neuroprotection and acute spinal cord injury: a reappraisal. *NeuroRx.* 2004;1:80–100. doi: 10.1602/neurorx.1.1.80
8. Bracken MB, Shepard MJ, Collins WF, Holford TR, Young W, Baskin DS et al. A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal cord injury. *NEJM.* 1990;322:1405–1411. doi: 10.1056/NEJM199005173222001
9. Fingerroth JM, Thomas WB. 2015. *Advances in intervertebral disc disease in dogs and cats.* Willey-Blackwell; 2015
10. Sayer FT, Kronvall E, Nilsson OG. Methylprednisolone treatment in acute spinal cord injury: the myth challenged through a structured analysis of published literature. *Spine J.* 2006;6:335–43. doi: 10.1016/j.spinee.2005.11.001.
11. Tęśiorowski M, Potaczek T, Jasiewicz B, Sapa J, Zygmunt M. Methylprednisolone- acute spinal cord injury, benefits or risks?. *Postepy Hig Med Dosw (Online).* 2013;67:601–9. doi: 10.5604/17322693.1054873
12. Caruso MC, Daugherty MC, Moody SM, Falcone RA, Bierbrauer KS, Geis GL. Lessons learned from administration of high-dose methylprednisolone sodium succinate for acute pediatric spinal cord injuries. *J Neurosurg Pediatr.* 2017;20:567–74. doi: 10.3171/2017.7.PEDS1756
13. Short DJ, El Masry WS, Jones PW. High dose methylprednisolone in the management of acute spinal cord injury – a systematic review from a clinical perspective. *Spinal Cord.* 2000; 38:273–86. doi: 10.1038/sj.sc.3100986
14. Rozet I. Methylprednisolone in acute spinal cord injury: is there any other ethical choice? *J Neurosurg Anesthesiol.* 2008;20:137–9. doi: 10.1097/01.ana.0000314441.63823.b0
15. Matsumoto T, Tamaki T, Kawakami M, Yoshida M, Ando M, Yamada H. Early complications of high-dose methylprednisolone sodium succinate treatment in the follow-up of acute cervical spinal cord injury. *Spine (Phila Pa 1976).* 2001;26:426–30. doi: 10.1097/00007632-200102150-00020
16. Suberviola B, González-Castro A, Llorca J, Ortiz-Melón F, Miñambres E et al. Early complications of high-dose methylprednisolone in acute spinal cord injury patients. *Injury.* 2008;39:748–52. doi: 10.1016/j.injury.2007.12.005
17. Ito Y, Sugimoto Y, Tomioka M, Kai N, Tanaka M. 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).* 2009;34:2121–4. doi: 10.1097/BRS.0b013e3181b613c7
18. Chikuda H, Yasunaga H, Takeshita K, Horiguchi H, Kawaguchi H, Ohe K et al. 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*. 2014;31:201–6. doi: 10.1136/emered-2012-202058
19. Mirzaei F, Meshkini A, Habibi B, Pharm A, Salehpour F, Rafei E et al. Ceftriaxone plus methylprednisolone combination therapy versus methylprednisolone monotherapy in patients with acute spinal cord injury: A Randomized, Triple-Blind Clinical Trial. *J Spine Surg*. 2020; 7102. doi: 10.14444/7102.
  20. Kewalramani LS. Neurogenic gastro-duodenal ulceration and bleeding associated with spinal cord injuries. *J Trauma* 1979;19:259–65. doi: 10.1097/00005373-197904000-00008
  21. Miekisiak G, Kloc W, Janusz W, Kaczmarczyk J, Latka D, Zarzycki D. Current use of methylprednisolone for acute spinal cord injury in Poland: survey study. *Eur J Orthop Surg Traumatol*. 2014;Suppl 1:S269-273. doi: 10.1007/s00590-014-1422-3
  22. Rohrer CR, Hill RC, Fischer A, Fox LE, Schaer M, Ginn PE et al. Gastric hemorrhage in dogs given high doses of methylprednisolone sodium succinate. *Am J Vet Res*. 1999;60:977–81.
  23. Rohrer CR, Hill RC, Fischer A, Fox LE, Schaer M, Ginn PE et al. Efficacy of misoprostol in prevention of gastric hemorrhage in dogs treated with high doses of methylprednisolone sodium succinate. *Am J Vet Res* (1999) 60:982–985.
  24. Hanson SM, Bostwick DR, Twedt DC, Smith MO. Clinical evaluation of cimetidine, sucralfate and misoprostol for prevention of gastro-intestinal tract bleeding in dogs undergoing spinal surgery. *Am J Vet Res*. 1997;58:1320–1323.
  25. Olby NJ, Muguet-Chanoit AC, Lim JH, Davidian M, Mariani CL, Freeman AC et al. A Placebo-Controlled, Prospective, Randomized Clinical Trial of Polyethylene Glycol and Methylprednisolone Sodium Succinate in Dogs with Intervertebral Disk Herniation. *J Vet Intern Med*. 2016;30:206–14. doi: 10.1111/jvim.13657
  26. Boag AK, Otto CM, Drobotz KJ. Complications of methylprednisolone sodium succinate therapy in dachshunds with surgically treated intervertebral disc disease. *J Vet Emerg Crit Care*. 2001;11:105–10. <https://doi.org/10.1111/j.1476-4431.2001.tb00076.x>
  27. Kerwin SC, Levine JM, Mankin JM. "Thoracolumbar vertebral column,". In: Johnston SA, Tobias KM, editors. *Veterinary Surgery: Small Animal*. St. Louis, Missouri, Elsevier; 2018.
  28. Levine JM, Levine GJ, Boozer L, Schatzberg SJ, Platt SR, Kent M et al. 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*. 2008;232:411–7. doi: 10.2460/javma.232.3.411.
  29. Mari L, Behr S, Shea A, Dominguez E, Ricco C, Alcoverro E. Predictors of urinary or fecal incontinence in dogs with thoracolumbar acute non-compressive nucleus pulposus extrusion. *J Vet Intern Med*. 2019;33:2693–2700. doi: 10.1111/jvim.15626.
  30. Goforth P, Gudas CJ. Effects of steroids on wound healing: a review of the literature. *Foot Surg*. 1980;19:22–8

31. Amsellem P. Complications of reconstructive surgery in companion animals. *Vet Clin North Am Small Anim Pract.* 2011;41:995–1006. doi: 10.1016/j.cvsm.2011.05.005
32. Nishida H, Tanaka H, Kitamura M, Inaba T, Nakayama M. 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.* 2016;64:191–6.
33. Levine JM, Levine GJ, Johnson SI, Kerwin SC, Hettlich BF, Fosgate GT. Evaluation of the success of medical management for presumptive thoracolumbar intervertebral disc herniation in dogs. *Vet Surg.* 2007;36:481. doi: 10.1111/j.1532-950X.2007.00295.x
34. Moore SA, Early PJ, Hettlich BF. Practice patterns in the management of acute intervertebral disc herniation in dogs. *J Small Anim Pract.* 2016;57:409–15. doi: 10.1111/jsap.12496
35. Moore SA, Tipold A, Olby N, Stein V, Granger N, Canine Spinal Cord Injury Consortium (CANSORT SCI). Current Approaches to the Management of Acute Thoracolumbar Disc Extrusion in Dogs. *Front Vet Sci.* 2020; 7:610. doi: 10.3389/fvets.2020.00610.

## Figures

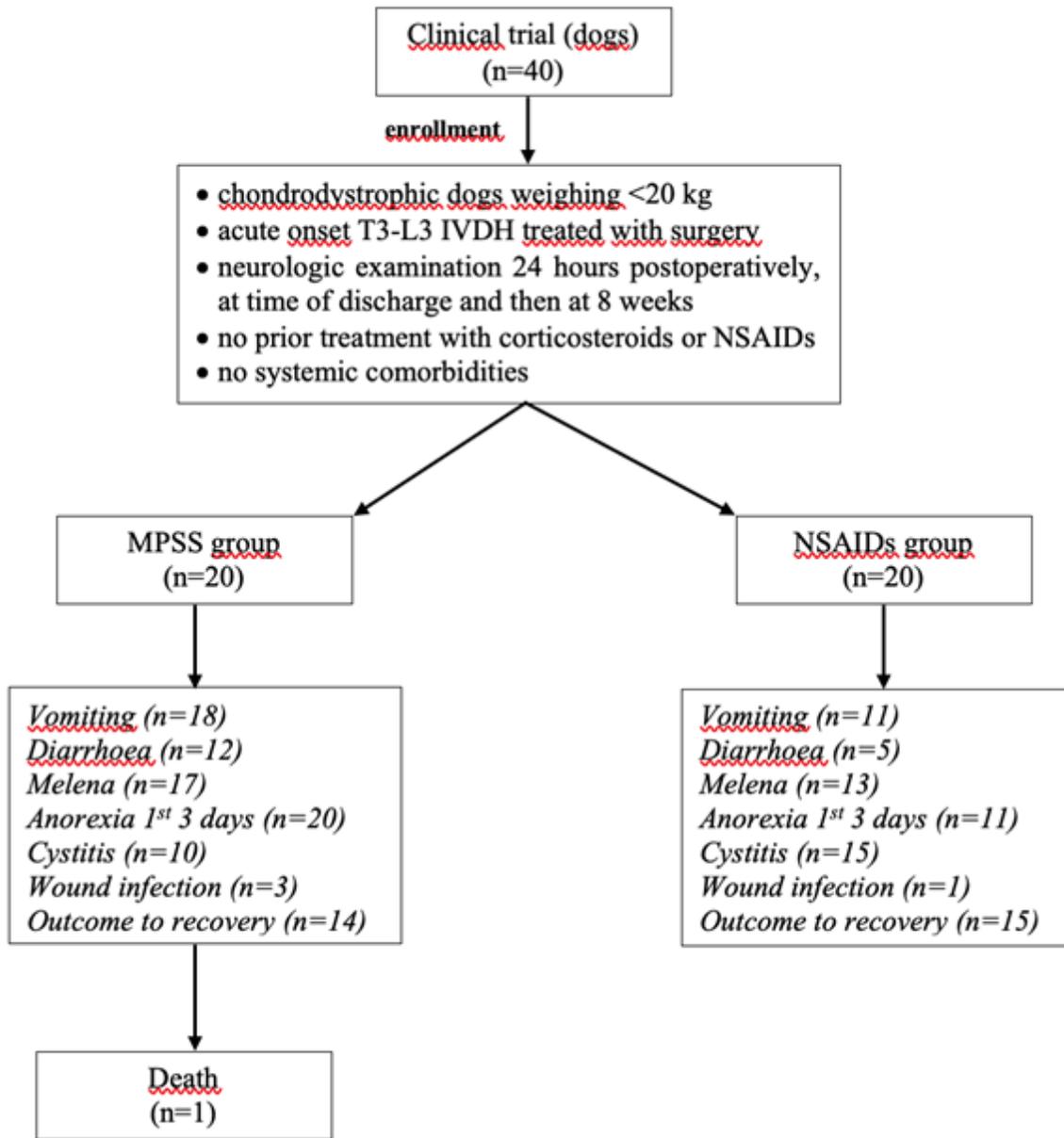


Figure 1

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