

# Debates prós e contras

## Trauma medular

**Uso  
Corticosteroides**



**Não uso  
Corticosteroides**

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# Estado da arte

- Não existem evidências científicas que justifiquem o uso de corticosteroides em trauma medular de animais de companhia
- Existe apenas um estudo em humanos utilizando o protocolo NACISIS – *National acute spinal cord injury study que demonstra*

# Estado da arte

- Protocolo NACISIS\*:
  - 30 mg/Kg IV de succinato sódico de metilprednisolona (SSMP) nas primeiras 8 horas pós-trauma
  - Seguindo-se infusão constante de SSMP a 5,4 mg/Kg/hora durante 24 horas



*Bracken MB, Shepard MJ, Collins WF, et al. A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal-cord injury. Results of the Second National Acute Spinal Cord Injury Study. N Engl J Med 1990;322(20):1405–11*

# Estado da arte

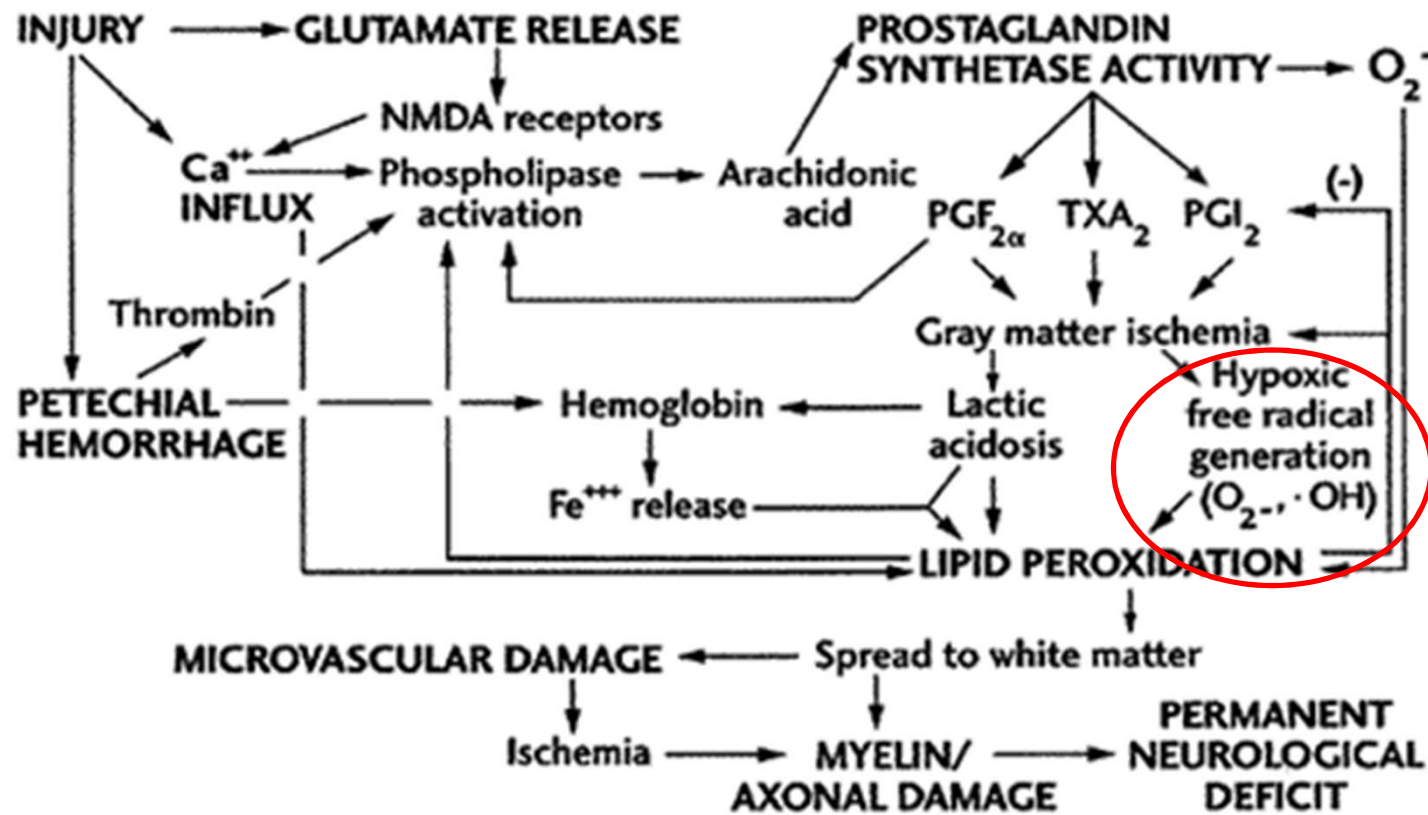
- Protocolo NACISIS:

Bracken MB, Shepard MJ, Collins WF, et al. A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal-cord injury. Results of the Second National Acute Spinal Cord Injury Study. N Engl J Med 1990;322(20):1405–11.

Bracken MB, Shepard MJ, Holford TR, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA 1997; 277(20):1597–604.

# Estado da arte

- SSMP actua inibindo a peroxidação dos lípidos membranários pela remoção de radicais livres de oxigênio
  - Fase aguda da lesão secundária
- Controvérsia quanto às conclusões:
  - benefícios mínimos
  - Elevada prevalência de complicações
    - Pneumonia
    - sepsis



# Estado da arte

- 2 ensaios clínicos em medicina veterinária:
  - Utilizando modelo canino
  - Falharam em demonstrar um efeito benéfico na utilização de metilprednisolona
  - Utilizaram doses do protocolo NACISIS

# Estado da arte

VETERINARY  
SURGERY



Coates JR, Sorjonen DC, Simpson ST, et al. Clinicopathologic effects of a 21-aminosteroid compound (U74389G) and high-dose methylprednisolone on spinal cord function after simulated spinal cord trauma. Vet Surg 1995;24:128–39.

- Ensaio clínico:
  - Poder estatístico fraco
  - n=4
  - Comparou metilprednisolona com 21-aminosteroide
  - Não foi um ensaio duplamente cego
    - Observador
    - Tratador



# Estado da arte

## PubMed

Search: Rabinowitz RS, Eck JC, Harper CM Jr, et al

U.S. National Library of Medicine  
National Institutes of Health



Display Settings  Abstract

[Spine \(Phila Pa 1976\)](#), 2008 Oct 1;33(21):2260-8.

### **Urgent surgical decompression compared to methylprednisolone for the treatment of acute spinal cord injury: a randomized prospective study in beagle dogs.**

[Rabinowitz RS](#), [Eck JC](#), [Harper CM Jr](#), [Larson DR](#), [Jimenez MA](#), [Parisi JE](#), [Friedman JA](#), [Yaszemski MJ](#), [Currier BL](#).

Barrington Orthopaedic Associates, Hoffman Estates, IL, USA.

#### **Abstract**

**STUDY DESIGN:** Experimental dog model of acute spinal cord injury.

**OBJECTIVE:** To compare the relative value of methylprednisolone, surgical decompression, or both for the treatment of traumatic spinal cord injury.

**SUMMARY OF BACKGROUND DATA:** Acute spinal cord injury results from both primary damage to the spinal cord at the time of the initial injury as well as a deleterious secondary cascade of events, which leads to further damage. Surgical decompression is known to improve clinical outcomes, but the timing of surgical decompression remains controversial.

**METHODS:** A nylon tie was used to constrict the spinal cord in 18 adult male beagle dogs. The animals were then prospectively randomized to 3 groups: 1) surgical decompression at 6 hours and intravenous methylprednisolone; 2) surgical decompression at 6 hours and intravenous saline; and 3) intravenous methylprednisolone without surgical decompression. Each animal was evaluated by somatosensory-evoked potentials, daily neurologic assessment, and histologic examination at 2 weeks following injury.

**RESULTS:** Immediately following spinal cord constriction, all animals were paraplegic, incontinent, and the somatosensory-evoked potentials were abolished. Surgical decompression 6 hours after injury, with or without methylprednisolone, led to significantly better neurologic function at 2 weeks than methylprednisolone alone.

**CONCLUSION:** In the setting of acute and persistent spinal cord compression in beagle dogs, surgical decompression 6 hours after injury, with or without methylprednisolone, is more effective for improving neurologic recovery than methylprednisolone alone.

# Estado da arte

- Poder estatístico fraco
- $n=6$
- Seguimento apenas até as 2 semanas
- Não foi um ensaio duplamente cego
  - Observador
  - Tratador

# Ensaaios clinicos



# Ensaaios clínicos

- Pontos fracos dos estudos apresentados:
  - Ausência de controlos com placebo
  - Ausência de ensaios clínicos duplamente cegos
  - Grupos experimentais com  $n$  muito reduzido
    - Ideal  $n \geq 30$
    - Número de replicados para cada variável ou observação deve ser superior a 2
  - Ausência de avaliação funcional a longo prazo
    - Falta padronização na avaliação funcional

# Ensaaios clinicos

- Pontos fracos dos estudos apresentados:
  - Modelo de execução da lesão medular diferente entre ensaios
  - Ausência de avaliação funcional a longo prazo
    - Falta padronização na avaliação funcional
  - Grupos devem ser homogêneos
    - Reduz variabilidade intragrupo
  - Evitar controlos históricos

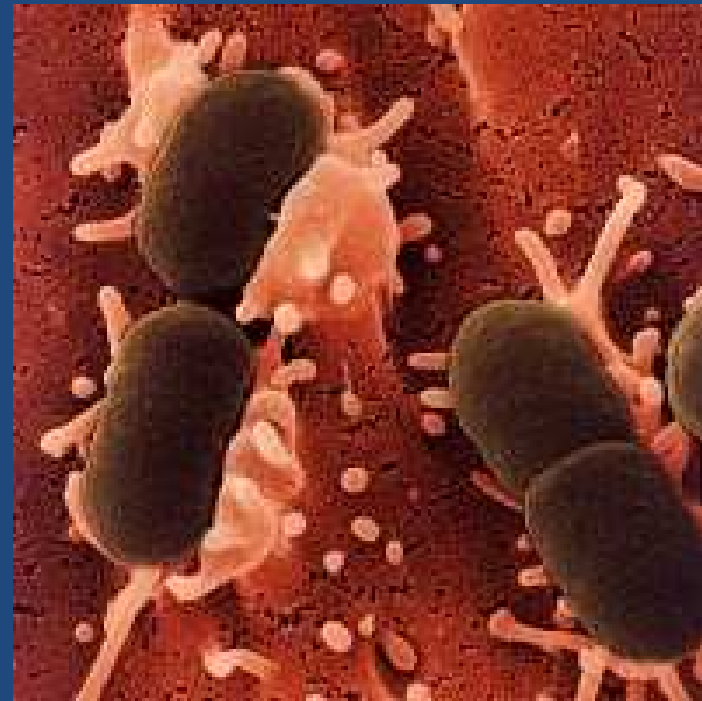
**Table 1**  
Canine clinical trials

<b>Trial</b>	<b>Type of Trial</b>	<b>Findings</b>
OFS Unit <sup>66</sup>	Blinded, placebo controlled in patients with grade 5 <sup>a</sup> IVDD	Safe, improvement in sensory function
<i>N</i> -acetylcysteine <sup>39</sup>	Blinded, placebo controlled in nonambulatory patients with IVDD	No effect
4-AP <sup>75</sup>	Phase 1	Small therapeutic range; improved sensory, motor, and bladder functions
4-AP	Blinded, placebo controlled, underway in patients with chronic grade 5 <sup>a</sup> SCI	Pending
t-Butyl derivative of 4-AP <sup>10</sup>	Phase 1	Safe; improved sensory, motor, and bladder functions
t-Butyl derivative of 4-AP	Blinded, placebo controlled, underway in patients with chronic grade 5 <sup>a</sup> SCI	Ongoing
OEC Transplants <sup>9</sup>	Phase 1	Safe
OEC Transplants	Blinded, placebo controlled, underway	Ongoing
MPSS, PEG	Blinded, placebo controlled in patients with grade 5 <sup>a</sup> IVDD	Ongoing

Adaptado de: Olby, N., 2010. The Pathogenesis and Treatment of Acute Spinal Cord Injuries in Dogs. *Veterinary Clinics of North America*. 40: 791-807



## Efeitos secundários - corticosteroides



# Efeitos secundários - corticosteroides

- Para além da sua ineficácia clínica apresentam efeitos secundários indesejáveis
- Não ocorrem apenas na terapêutica com SSMP
- Outros corticosteroides frequentemente utilizados:
  - Dexametasona IV



# Adverse effects and outcome associated with dexamethasone administration in dogs with acute thoracolumbar intervertebral disk herniation: 161 cases (2000–2006)

Jonathan M. Levine, DVM, DACVIM; Gwendolyn J. Levine, DVM; Lindsay Boozer, BSA;  
Scott J. Schatzberg, DVM, PhD, DACVIM; Simon R. Platt, DVM, DACVIM; Marc Kent, DVM, DACVIM;  
Sharon C. Kerwin, DVM, MS, DACVS; Geoffrey T. Fosgate, DVM, PhD, DACVPM



# Efeitos secundários - corticosteroides

- Doses elevadas
  - $2.25 \pm 4.28$  mg/kg
- Cães tratados com dexametasona em altas doses
  - maior prevalência de vômitos e diarreia ( $P < 0,05$ )
  - Maior prevalência de UTI ( $P < 0,05$ ), 11,4 OR

*Retrospective Study*

# Complications of Methylprednisolone Sodium Succinate Therapy in Dachshunds with Surgically Treated Intervertebral Disc Disease

Amanda K. Boag MA, VetMB, MRCVS; Cynthia M. Otto DVM, PhD, DACVECC;  
Kenneth J. Drobatz DVM, DACVECC, DACVIM



# Efeitos secundários - corticosteroides

- Neste estudo prospectivo:
  - Animais tratados com SSMP em altas doses demonstraram maior prevalência de sinais GI – vômitos e diarreia
  - 2 animais tratados com SSMP foram diagnosticados com pneumonia
    - Estudos retrospectivos em medicina humana, demonstraram um maior risco de sepsis e pneumonia\*

\* Gerndt SJ, Rodriguez JL, Pawlik JW, et al. Consequences of highdose steroid therapy for acute spinal cord injury. J Trauma: Injury Infect Crit Care 1997;42(2):279-282

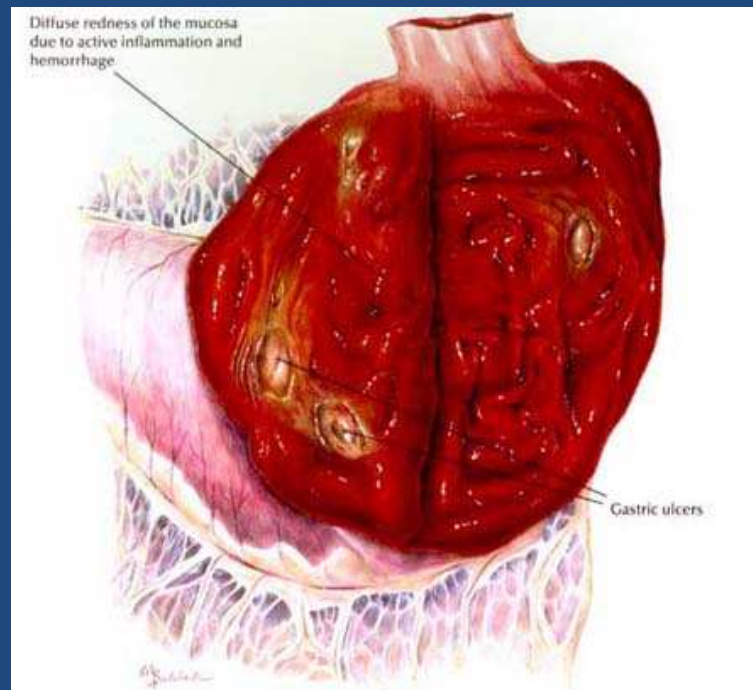
# Efeitos secundários - corticosteroides

- Neste estudo prospectivo:
  - Animais tratados com SSMP em altas doses
    - tiveram maior tempo de hospitalização
    - Custos de hospitalização mais elevados



# Efeitos secundários - corticosteroides

- Ulceração e hemorragia GI
  - efeito secundário prevalente em animais tratados com SSMP em altas doses\*



\*Rohrer CR, Hill RC, Fischer A, et al. Gastric hemorrhage in dogs given high doses of methylprednisolone sodium succinate. Am J Vet Res 1999;60(8):977-981

# Efeitos secundários - corticosteroides

- Apesar de todas as evidências:
  - Em humanos o trauma medular predispõe para ulceração GI\*

\* Kewalramani LS. Neurogenic gastro-duodenal ulceration and bleeding associated with spinal cord injuries. J Trauma 1979;19(4):259-265.

# Conclusões

- **Em pacientes com trauma medular o que fazer?**
- Monitorizar e controlar pressão arterial
  - Espinal medula perde a capacidade de autoregulação
  - Previne isquémia e lesões secundária
- Descomprimir e/ou estabilizar de forma precoce
  - Reduzir lesão primária por contusão ou concussão
  - Lavagem intensa com soro fisiológico remove aa excitatórios e MP
- Aguardar publicação de ensaios duplamente cegos de drogas promissoras
  - 4-aminopiridina
  - Polietilenoglicol



NC STATE UNIVERSITY

# COLLEGE OF VETERINARY MEDICINE

Department of  
Clinical Sciences

## Canine Spinal Cord Injury Program

### Mission Statement

"The Canine Spinal Cord Injury Program is dedicated to improving the outcome of acute and chronic spinal cord injuries in dogs."

The spinal cord conveys information to and from the brain to produce movement, sensation, urination, and defecation. Spinal cord injuries are a common problem in dogs, accounting for approximately 2% of all cases that present to the veterinarian. They are most commonly caused by disc herniations, trauma, spinal stenosis and instability, and vascular (stroke like) events. Spinal cord tissue does not regenerate effectively and therefore the consequences of an injury can be devastating. Dogs can make an excellent recovery after injury if the damage to the spinal cord is partial (incomplete) because the surviving nerves are able to take over the function of the nerves that have been lost. However, the more severe the injury, the less effective the recovery, and complete injuries, that result in transection of the spinal cord, thus cutting off all communications between the spinal cord and the brain, result in permanent paralysis.

### Canine Spinal Cord Injury Program

- [Research Team](#)
- [Clinical Trials](#)
- [The First Canine Paralympics](#)

### Contact Information

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