How to Use (and Avoid Misuse of) Glucocorticoids in Neurology and Neurosurgery Cases

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The use of glucocorticoids (GCs) in veterinary neurological practice is highly controversial. Glucocorticoid medications may result in beneficial effects in many cases of neurological disease, however adverse effects may be potentially life threatening and appropriate cases selection is important. There is very little if any clinical data in the veterinary literature, based on well designed prospective studies, relating to the use of GCs in neurological practice. As such many recommendations have been based on anecdotal reports, extrapolation from experimental data, and human studies. As veterinarians, one of our major objectives should be to make sure we do not harm our patients. Glucocorticoids are not benign medications, and their use should be undertaken only after careful thought.

There are several commonly used preparations of GCs, including prednisolone, prednisone, dexamethasone, and methylprednisolone. Glucocorticoid receptors respond similarly to different preparations; however, the amount required and the duration of action varies.

CNS trauma

This is a controversial area in both human and veterinary medicine. Glucocorticoids are not used for their anti-inflammatory properties in these cases. The mechanism of action is thought to involve inhibition of pathways responsible for secondary events following trauma such as lipid peroxidation and destabilization of cell membranes.

Brain Trauma. Glucocorticoids are NOT specifically indicated in the treatment of acute head trauma in humans. The beneficial effects of GCs in cases of acute trauma are theoretically due to their inhibition of so-called secondary mechanisms of injury such as stabilization of lysosomal membranes and inhibition of lipid peroxidation. Based on available experimental and clinical data, the Brain Trauma Foundation/Association of Neurological Surgeons guidelines1 do NOT recommend the use of any GCs in patients with severe head injury. In fact, corticosteroids are contraindicated in severe traumatic brain injuries of humans.

There is no clinical data available to comment on veterinary patients, therefore human recommendations are generally followed.

Spinal Cord Trauma. Most veterinarians will encounter patients with acutely injured spinal cord as a result of either automobile trauma, falls or acute intervertebral disc herniation. Use of GCs in spinal cord trauma is controversial. Only high dose methylprednisolone sodium succinate (MPSS) has "possibly been shown" to have any potential benefit in humans, and the significance of this improvement and whether it really exists is debated. The adverse effects, however, are well documented and include: gastrointestinal perforation/hemorrhage, increased infection rates (e.g., pneumonia), hypotension and vomiting.

Experimentally and in human clinical trials the incorrect dose or incorrect timing of doses can result in worsening of clinical outcome, yet veterinary dosages have been extrapolated from the human and experimental literature. The most appropriate dose of MPSS, or whether it may be beneficial or detrimental, has not been determined in dogs. A significant amount of experimental data exists for cats; however there is no data to support the use of any GCs in any small animal clinical patients.

At best, high dose methyl prednisolone sodium succinate therapy in small animals should be considered an experimental treatment of unproven benefit. At worst it may have deleterious effects both on neural tissue and other organ systems (GI, hypotension, prolonged bleeding, infection). Recently published guidelines in human medicine concluded that (MPSS treatment)…."should be undertaken only with the knowledge that the evidence suggesting harmful side effects is more consistent than any suggestion of clinical benefit." High doses of dexamethasone in dogs with acute spinal cord trauma has been be associated with an increased incidence of fatal colonic perforation and other gastrointestinal side effects. We currently do not recommend using high dose MPSS as it is a treatment that has been shown to have minimal benefits (if any) in any species clinically, is of unproven efficacy in veterinary patients, yet has known, proven deleterious adverse effects.

Degenerative intervertebral disc disease

Use of corticosteroids in the treatment of mild to moderate type I disc disease is widespread in veterinary practice. The benefit of corticosteroids is anecdotal and unproven. For animals with apparent pain, with or without neurological deficits, the use of non-steroidal anti-inflammatory drugs, or better still strict cage confinement, may well be a safer and more appropriate approach to case management. If anti-inflammatory/analgesic drugs of any type are used, it is essential to ensure that animals are strictly confined to prevent exacerbation of the underlying pathology due to an increased willingness to move.

Animals with chronic type II disc protrusions or other chronic compressive myelopathies may show improvement of neurological status following anti-inflammatory doses of GCs based on anecdotal information. Treatment may be effective for several weeks to months, however the underlying disease process is not addressed and progression is likely to occur. The mechanism of action is unknown.

Neuromuscular disease

Immunosuppressive doses of GCs (1-2mg/kg PO q12h) are indicated for immune-mediated masticatory myositis, and immune-mediated polymyositis. Although there is a paucity of good clinical data documenting the use of GCs, their use in immune-mediated disease is based on sound basic principles (ie. immunosuppression) to treat an immune-mediated disease.

The use of immunosuppressive doses of GCs in myasthenia gravis is more problematic.

Although the effect on the underlying immune reaction may be beneficial, the adverse effects may be life threatening. Most dogs with myasthenia gravis that die, do so not from weakness, but from aspiration pneumonia secondary to esophageal regurgitation. Glucocorticoids will result in a polydypsic, polyphagic animal with increased susceptibility to infection.

Most animals may be managed successfully with anticholinesterase drugs alone combined with elevated feeding etc. Glucocorticoids should be used judiciously in severe cases, or those refractory to treatment. Immunosuppressive doses of GCs may cause an initial worsening of clinical signs in some cases and starting treatment at anti inflammatory doses (0.5mg/kg/day) and gradually increasing up to immunosuppressive doses (2-4mg/kg/day) has been recommended.

Inflammatory diseases

Infectious CNS Diseases

While the immunosuppressive effects of GCs may appear to contraindicate their use in infectious diseases, the anti-inflammatory effects may be beneficial if used for short periods, at low doses, when neurological signs are severe. There is no clinical based evidence to support or refute the use of GCs in small animal patients. In non-critical patients, it is probably better to treat the infectious disease process with appropriate antimicrobial drugs alone. If animals have severe CNS signs and are acutely decompensating, decreasing the imflammatory component of CNS damage may well outweigh the risks associated with the transient immunosuppressive effects of GCs. Anecdotally, anti inflammatory doses of GCs used for short periods (24-48 hours) may help to prevent the acute exacerbation of clinical signs sometimes seen after the initiation of antimicrobial therapy secondary to the widespread death of infectious organisms and subsequent inflammatory response.

Pathogen-Free Inflammatory CNS Disease

Granulomatous meningoencephalomyelitis (GME), steroid responsive meningitis-arteritis (SRMA) necrotizing meningoencephalitis (NME), and necrotizing encephalitis (NE) are inflammatory conditions of unknown etiology at this time. Immunosuppressive doses of GCs can be beneficial, especially in SRMA, and to a lesser degree with GME. NME and NE often are poorly responsive to GCs. New therapeutic approaches using anti-neoplastic drugs such as procarbazine and cytosine arabinoside may prove more effective for GME, NME and NE, in combination with GCs. Care should be taken when diagnosing cases of SRMA since CSF abnormalities (neutrophilic pleocytosis) may be extremely difficult to distinguish from cases of bacterial meningitis where immunosuppression is not indicated.

Neoplasia

Anti-inflammatory doses of GCs are a mainstay of palliative treatment for intracranial and spinal cord neoplasms. The anti inflammatory and anti-edema effects of GCs decrease the effective size of the mass within the enclosed cranial vault and can result in dramatic resolution of clinical signs for significant periods of time. Glucocorticoids may also be tumoricidal in some instances, such as in the treatment of primary or secondary CNS lymphoma.

Hydrocephalus/Syringohydromyelia

Anti-inflammatory doses of GCs may decrease CSF production, increase CSF absorption, and may be useful in the short term to ameliorate clinical signs in cases of hydrocephalus and syringohydromyelia. The mechanism of action is unknown.

Conclusion

The decision to use glucocorticoid medication in neurological patients should be based on a good understanding of the underlying pathology, positive pharmacological effects, adverse effects of the drug, and the availability of evidence to suggest that the benefits of treatment outweigh the adverse effects. Glucocorticoids can be beneficial in many circumstances, however the temptation to treat severe neurological disease with glucocorticoid medication, even in the absence of specific indications to do so, is almost universal. There are very few circumstances in veterinary neurological medicine where absolute statements can be made relating to the use of glucocorticoids, however judicious use is encouraged.

Summary

- There are no specific indications for the use of GCs in severe head trauma in humans, and probably in small animals.
- There are no proven clinical benefits of any glucocorticoid medication in acute spinal cord trauma in small animals, and benefits in humans are minimal at best.
- High doses of GCs have been associated with fatal GI adverse effects in dogs with spinal cord trauma. High doses of GCs have been associated with increased incidence of secondary infections and pneumonia.
- Think carefully before giving GCs to neurological patients. More is definitely not always better, and none at all may be the best option.

References

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