Antipruritic therapy 2019

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Corticosteroids are extremely useful drugs for the management and of many dermatologic disorders. Unfortunately, they are often times misused. The purpose of the presentation is to dispel common myths about corticosteroids and understand the pituitary adrenal axis to improve the quality of life of our patients. Additionally, differences between dogs and cats will be discussed.

All corticosteroids are not created equally. The potency and duration of effect must be taken into account for each individual for maximum effect and minimal side effects.

Drug	Glucocorticoid potency	Equivalent dosage (mg)	Duration of Effect (hr)	Alternate day?
Short-Acting				
Cortisone	0.8	25	<12	–
Hydrocortisone	1	20	<12	–
Intermediate				
Prednisone	4	5	24-36	Yes
Prednisolone	4	5	24-36	Yes
Methylprednisolone	5	4	24-36	Yes
Long-Acting				
Flumethasone	15	1.3	36-48	No
Triamcinolone	40	0.5	36-48	No
Dexamethasone	40	0.5	36-54	No
Betamethasone	50	0.4	36-54	No

Only those products that are short-acting or intermediate are appropriate for alternate day dosing of anti-inflammatory or autoimmune disorders. Potency must also be considered when a topical product is selected. Long acting topical steroids will suppress the pituitary adrenal axis and are more likely to cause skin and hair follicle atrophy.

Glucocorticoids exhibit a myriad of early and late phase anti-inflammatory effects. The short term effects include mast cell stabilization, reduction in capillary permeability, and reduced leukocyte migration and function. These are the beneficial effects that are so important in treating Type I hypersensitivity reactions. The ultimate effect is to alter protein transcription. These proteins may be induced or inhibited and include lipocortin 1, cytokines, inducible nitric oxide synthetase (iNOS), and phospholipase A2, to name a few. By directly inhibiting phospholipase, the arachadonic acid cascade is blocked leading to a decrease in the pro-inflammatory mediators. Prostaglandins, thromboxanes, and leukotrienes are all decreased. Glucocorticoids may directly block cyclooxygenases further contributing to the anti-inflammatory effects. Alterations in protein synthesis may take hours to days for the necessary effect to take place.

There are several predictable effects of glucocorticoids that are not necessarily beneficial. Hyperglycemia results from gluconeogenesis and from insulin antagonism by blocking insulin from getting into cells. The physiologic reason is to protect glucose dependent brain functions. Glucocorticoids are catabolic in effect. Skeletal muscle and collagen breakdown result in muscle wasting, thin and hypotonic skin, and fragile blood vessels. These side effects may result from topical or parenteral administration. The catabolic effects on lipids result in the redistribution of fat. Glucocorticoids inhibit antidiuretic hormone and contribute to the polyuria/polydipsia seen in dogs. This may be due to both the glucocorticoid and mineralocorticoid effects of steroids.

Injectable glucocorticoids have variable actions of onset because of the carrier molecules. These esters must be hydrolyzed to release the active free form of the drug. Water soluble esters such as sodium succinate or sodium phosphate and are more rapidly hydrolyzed. These forms may be given intravenously and are indicated for acute conditions. The repositol forms are water insoluble. Carrier esters such as acetate or acetonide are more slowly hydrolyzed resulting in a prolonged effect. Not all glucocorticoids are labeled as "depo" so one must be aware of the carrier molecule to avoid unwanted effects.

Oral steroids are well absorbed and as fast in onset of the anti-inflammatory effects as injectable glucocorticoids. Giving an injection to "get things started" is not necessary and will lead to steroid overdose if tablets are given for a controlled effect. Prednisone is converted to prednisolone and can be interchanged for most dogs. There are some individual dogs that using prednisolone may be more effective. The dosage for anti-inflammatory effects is 0.5 mg/kg b.i.d. or can be given 1.0 mg/kg/day. Once a clinical remission is achieved, the dosage may be tapered to an alternate day therapy. This will allow the pituitary-adrenal axis to rebound. Immune suppressive dosages of these drugs begin at 2mg/kg/day. Methylprednisolone (medrol®) is also an intermediate acting glucocorticoid that is good for alternate day therapy. It is slightly more potent than prednisone or prednisolone (4mg methylprednisolone = 5mg pred.) and is usually associated with less PU/PD in dogs. It is the preferred glucocorticoid for cats (author bias). The dosage for anti-inflammatory effects in cats is twice the dosage of dogs. This is due to fewer receptors and less affinity than dogs. In general, a 10# cat would receive 4mg of methylprednisolone twice daily until remission. Cats in general are more tolerant of corticosteroids than dogs and may do well with injectable forms.

There is little difference between prednisolone and prednisone. The anti-inflammatory dosage for dogs is 0.5 mg/kg given twice daily for one week, once daily for one week, and every other day for 14 days. To make this easy to calculate, take the total number of tablets for the first week and double it. Dogs can continue to receive pred. on an every other day basis if there is a history of a prolonged seasonality problem. In some cases a switch to every third day or changing to a different product (ie. Temaril-P) may maintain the effect with a lower dosage. By using a simple chart, there are no excuses for not using oral glucocorticoids

Fill in the number of tablets in each box, along with the starting day of the week

Include at the bottom some of the common side effects. Also include what should be done if side effects are problematic. Additional notes for when to recheck may also be helpful. Have the client circle the dosage once it has been given to avoid accidentally over dosing the pet.

Temaril-P is a product that contains 2 mg of prednisolone and 5 mg of trimeperazine. The dose is 1 tablet/#20 body weight with a maximum of 3 tablets. Compared to the amount of prednisolone the dog would receive with standard dosages, temaril-P is much lower. This product is not suitable for dogs >60# and is not to be used for cats. This product works very well for uncomplicated atopy cases. It is usually unsatisfactory for dogs exhibiting flea allergy, food allergy, or scabies. It may be dispensed in a decreasing dosage similar to oral pred. Some dogs are not well managed with every other day Temaril-P. Giving the tablets twice daily, every other day, may improve clinical response.

Cyclosporine (Atopica) is effective for reducing pruritus due to atopy. It is a calcineurin inhibitor that affects both TH1 and TH2 cytokines. It is an immune suppressive agent even when used for antipruritic effect. The standard dosage for dogs is 5mg/kg qd for 30 days then reduce to eod. It is recommended to treat daily beyond 30 days until a remission is reached before decreasing to eod dosing. Some dogs will require 5-6 weeks to achieve remission. We recommend CBC and UA with culture about every 4 months. Cyclosporine should not be used if there was a history of demodicosis. I would recommend starting with name brand Atopica to see if it helps and then switch to a generic or compounded if requested. Compounded products have been demonstrated to be inaccurate with the amount of drug in the capsules.

Oclacitinib (Apoquel) is a new antipruritic agent. It functions as a Janus kinase inhibitor (JAK). It is not to be used on dogs less than one year or those with bacterial or demodex infections. Studies show that it may increase the risk of these infections. Apoquel is indicated for the use of allergic pruritus. It is initially administered twice daily

for 14 days then daily as needed. One of the benefits of this drug is that it reduces pruritus faster than glucococorticiod medications. The data show that this drug will not interfere with intradermal testing so no withdrawal period is necessary. It appears to be safe when used in conjunction with commonly used medications such as cephalexin or ketoconazole. Apoquel should not be given to cats and is not licensed or approved for this use. It has been demonstrated to not interfere with intradermal skin testing so there is no withdrawal time compared to glucocorticoid medications.

CytoPoint is a canine monoclonal IgG antibody that binds IL-31 to inhibit binding to the receptor. It is licensed for atopy in dogs only. Human articles have shown that IL-31 is the major cause of pruritus in people with cutaneous lymphoma but this product has not been studied in dogs with CTL. Cytopoint is given subcutaneously every 30 days. It is not effective for all dogs. It may or may not be effective in dogs that have been unsuccessfully treated with Apoquel. Cytopoint does not interfere with intradermal allergy testing. We have used it successfully concurrently with hyposensitization induction.