Feline Environmental Allergy Treatment and Control

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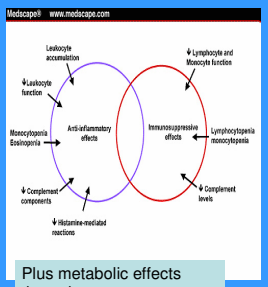
NFNFHD
Main Stream and Novel

- Corticosteroids
- Cyclosporine
- Fatty acids and antihistamines
- Allergen avoidance
- Infection control
- Control of other allergies
- Allergen specific immunotherapy
- Maropitant (Cerenia ®)
- Oclacitinib (Apoquel ®)
- Palmitoylethanolamide (PEA)
- Regional and history based immunotherapy

Corticosteroids



Plus metabolic effects through receptors on most tissues

Corticosteroids in Cats

- Cats have less glucocorticoid receptors with lower binding affinity than dogs
- Prednisolone 1-2 mg per kilogram SID initially (no advantage in division) then taper to maintenance after 7-12 days
- Subset of cats need dexamethasone 0.1-0.2mg/kg – longer T1/2
- Long-term use risks:
  - Diabetes (True hyperglycaemia -fructosamine studies)
  - Immunosuppression- HERPES !
  - Feline Cushing's Liver etc ALP variable
  - Hypertension and heart failure

Long term daily or every second day corticosteroids in cats represents Worst in Class treatment

Hemodynamic effects of methylprednisolone acetate administration in cats.

Ploryngam T et al , (2006)

- 12 cats, 5mg/kg methylprednisolone acetate (MPA)
- Substantial increase in serum glucose concentration at 3 to 6 days after administration.
- Plasma volume increased substantially (> 40% in 3 cats)
- Analogous to the plasma volume expansion that accompanies uncontrolled diabetes mellitus in humans.

Off Label Topical Steroids

- Betamethasone/Fusidic acid (Isaderm ®)
- Hydrocortisone aceponate 0.584 mg/ml (Cortavance®)
- 5% hydrocortisone /neomycin (Neotopic® etc)
- Human 1% hydrocortisone +/- clotrimazole (Hydrozole®)

Skin thinning risk –irreversible
Potency
Duration and frequency
Individual factors

Short term use. If using long term, use least potent with greatest interval

What are SAFER long term dose rates for glucocorticoids in cats

- UNKNOWN
- SUBJECT TO INDIVIDUAL VARIATIONS

ANECDOTAL
Prednisolone 0.5mg/kg 2-3x week
Methyl prednisolone acetate 3x year

Must be monitored

Cyclosporine

Inhibits cytokine production, especially interleukin-2 (Native T cell differentiation)

- Lag period of about 2-4 weeks….steroids needed
- 70%+ of cases get 70-85% better within 6 weeks
- Hepato/nephrotoxic side effects generally not recognized in cats.
- 5-7mg/kg then slow tapering to maintenance every 2-3 days
- Must be FIV/FeLV –ve and free of infectious or neoplastic disease

Cyclosporine risk issues

Lower than continuous corticosteroids

- Vomiting (mostly transient)
- Opportunistic infections
  - Latent and New
  - Viral, fungal, bacterial, protozoal
- Neoplasia
- Idiosyncratic

Cyclosporine and Feline Toxoplasmosis

- Geographically variable
- New infections and re-activation of latent. Sero-negative cats at risk
- No evidence of re-shedding of oocysts. Only shed for a few weeks
- Cats that hyper-absorb cyclosporine at higher risk

•Prevent new infections
Cook meat
Stop hunting
Eliminate rodents
•FIV/FeLV –ve
•Confirmed atopic
•30 day CsA blood level
EDTA sample whole blood
24 hours post pill
Should be 200-500ng/ml and not in 1000's

Cyclosporine

- **Perceived failures?**

•Trialed for < 6 weeks
•Hypo-absobtion
•Infection
•Owner expectations and compliance
•Tapering failures.
Something other that NFNFHD dermatitis
•One those that don't respond

Use with corticosteroids
•Off label
•Often done if monotherapy ineffective
•Minimise dose and Monitor

Essential fatty acids and antihistamines

Unlikely to be effective as monotherapy

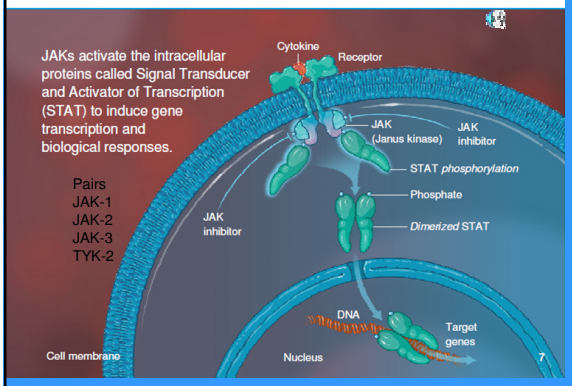
- Omega-3 and omega-6 fatty acids may reduce pruritus.
- Optimal 3:6 ratio unknown
- 1ml / 3kg in divided doses daily?
- A lag period of 6-12 weeks

Antihistamines

- Old and often uncontrolled and some conflicting studies.
- May be synergism between fatty acid therapy and antihistamines
- Chlorpheniramine registered 2-4mg/cat 2x day
- Certirizine 1mg/kg sid off label

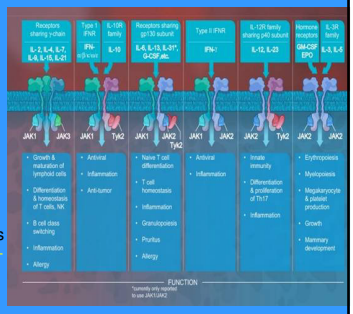
Oclacitinib (Apoquel) off label in cats

JAK Signaling Summary



Oclacitinib and JAK 1

- Oclacitinib has a high specificity for JAK-1 complex. Lower affinity for JAK-2. Little/no affinity for JAK-3 and Tyk-2
- Sparing non-JAK-1 pairings should maintain normal haematopoiesis.
- Pairings involving JAK-1 transduce the major receptors for inflammatory cytokines. IL-31
- Some degree of immune function degradation



Oclacitinib (Apoquel) off label in cats

What we know

- JAK-STAT pathway NOT the only mechanism of feline pruritus (see later). Role of IL-31 in cats unclear
- Short term studies (< 3 months)
- Good bioavailability (87%)
- Short half life 2.3 hrs
- Dog dose 0.4-0.6mg/mg 2x day for 14 days -> once day only 4/12 good/excellent

A double-blinded, randomized, methylprednisolone-controlled study on the efficacy of oclacitinib in the management of pruritus in cats with nonflea nonfood-induced hypersensitivity dermatitis
Chiara Noli* , Irina Matricoti† and Carlo Schievano‡
Vet Dermatol 2019; 30: 110

- 40 cats FIV/FeLV –ve confirmed as environmentally allergic. Divided into 2 groups of 20. 28 Day study
- < 4kg 2.7mg Apoquel 2x day or 2.0 mg methylprednisolone once day >4kg 5.4mg Apoquel 2x day or 4.0 mg methylprednisolone once day (= 5mg pred)
- Mild urea/creatinine increases in 4 oclacitinib cats. No other blood changes
- NO SIGNIFICANT DIFFERENCE BETWEEN GROUPS
  Pruritus Lesion Quality of life scores

Summary of experience and anecdotes

- Dose is of the order of 1mg/kg 2x day. Lower doses unlikely to be effective
- Indicated in cyclosporine failure or intolerance where excess steroids are needed
- Blood profile and FIV/FeLV before treatment. Renal exclusion?
- Monitor white cells and renal function at 8 weeks then 3 monthly
- Off label consent

Maropitant (Cerinia) off label in cats

What we know

- Registered for short term use in cats by injection as an anti-emeric
- Good safety profile
- Injection dose 1mg/kg
- Oral bioavailability 50% , T/12 13-17 hours, duration of action 24 hours
- Selective NK-1 receptor antagonist.
- Substance-P (a neuropeptide) binds to NK-1 receptors in nerve tissue, on immune cells, mast cells and keratinocytes, triggering the release of multiple proinflammatory molecules.
- Substance-P is pruritagenic in humans and mice and in humans and cats NK-1 inhibitors are anti-pruritic.

J Feline Med Surg. 2019 Oct;21(10):967-972. Maina E, Fontaine J.

Use of maropitant for the control of pruritus in non-flea, non-food-induced feline hypersensitivity dermatitis: an open-label, uncontrolled pilot study.

- 12 cats. Non-seasonal environmental allergy.
- Maropitant 2mg/kg once a day orally for 4 weeks
- All cats significantly reduced pruritus scores, all bar 1, decreased lesion score
- The efficacy and the tolerability of the treatment were judged as excellent or good by 83.3% of owners.
- No side effects other than, in a few cases, short-time, self-limiting sialorrhoea.

The use of maropitant in the management of pruritis in cats to reduce clinical signs and spare the use of corticosteroids and or cyclosporine
Yet to be published S Jaspers, E Spierings, R Hilton and A Witham

- 25 cats. 6 met full criteria to be diagnosed as non-seasonal environmental allergy. Others presumed but not confirmed
- Retrospective analysis, single centre
- Compounded Maropitant 2mg/kg once a day orally 11 out of 12 days ongoing
- A significant majority but not all were able to reduce reliance on immunosuppressive drugs. Some able to stop their other drugs entirely.
- Results similar to Maina and Fontaine (2019)
- No significant adverse events attributed to maropitant

Summary of experience and anecdotes

- Maropitant at 2mg/kg orally daily for 11 out of 12 days ongoing has significant anti-pruritic effects in a significant proportion of pruritic cats but not all.
- Benefit as a drug sparing agent and possible monotherapy in some cases
- Correctly compounded oral maropitant probably as effective in cats as the dog-registered tablets
- Useful in acute control phase and in chronic maintenance of pruritic cats
- Effect MAY be augmented by 2mg chlorpheniramine 2x day
- Off label consent

Palmitoylethanolamide (PEA)

What we know

- Canibinoid
- Anti-pruritic and anti-inflammatory benefits in dogs and humans
- Ultramicronised more effective
- Good safety profile, Registered in EU/UK. Compounded in Australia
- Anti-inflammatory, down-modulates skin mast cells, keratinocytes, macrophages and pro-inflammatory T cells
- 10mg/kg daily for 30 days improved pruritus, erythema, alopecia and lesions of the eosinophilic granuloma complex in 2/3 of patients (Scarampella *et al*., 2001)

Palmitoylethanolamide (PEA)

(Noli et al 2019) Placebo controlled study of 57 non-flea allergic cats

- Ultramicronised suspension 10-15mg/kg daily
- Methylprednislone course reducing 28 days plus PEA or placebo
- Responders followed to point of relapse without steroid plus PEA or placebo
- Mean time to relapse 40.5 days PEA group vs 22 days for placebo group
- Pruritus
  - Significantly lower in steroid plus PEA group
  - Increased in all groups after 28 days steroid but less in PEA group compared to placebo
- No difference between groups in lesion scores
- No significant PEA related adverse events

Conclusion – potentially valuable drug-sparing therapy

Allergen Specific Immunotherapy (ASIT) in the cat

Results similar to dogs in reducing total drug dependence can be achieved when appropriate allergens identified

After 8-12 months:
- 20-25% Full remission
- 35-40% Significant improvement but needing some medication
- 35-40% Fail

Similar subcutaneous injection protocol as per dogs

Mechanisms T-reg up-regulate, Th2->Th1 shift, blocking antibody ????

If successful, maintain for life

The devil is in the testing and allergen identification

Role of IgE in feline non-flea allergy is unclear

- Half of the cats with a clinical diagnosis of Non-Flea/Non-Food HD negative in IgE testing and, vice versa, a large number non allergic cats were positive for environmental allergens. (Belova et al 2012)
- No significant differences in anti-dust mite IgE in allergic and non-allergic 100+ cats (Taglinger et al 2005)

The devil is in the testing and allergen identification

Cat intradermal testing Why are many tests negative?

- **Thin skin**
- **Stress induced endogenous cortisol**
- **Uncertain role of IgE**
- **Higher allergen thresholds?**
- **Weak reactions specificity** FERRER-CAÑALS et al 2009
- **Fluorescein?**
- **Steroid withholding issues**

Discussion point – Is there a case for history and regional based immunotherapy in cats?

Evidence from dogs

- Random allergen vaccines no better than placebo
- Unbiased combined allergen vaccines gave results comparable to those based in testing (Garfield 1992)
- Irrelevant allergens do not induce hypersensitivity (Cordner and Lessard 1992)
- Regional canine vaccines outcome similar to that based on testing (Plant and Neradilek 2017)

GIVEN -All immunotherapy vaccines need to be based on the patient history

Selection of a cat history and regional based vaccine- unproven in cats

- Regional candidates
- Seasonality
- Indoor/outdoor exposure
- Cross reaction coverage

Allergen avoidance – Difficult to identify and implement

- House dust mite levels are much higher in bedrooms
- Disposal of old bedding
- Covers
- Insecticidal and IGR sprays
- Indoor / outdoor limiting

Thank you and any questions

✓ References where available on request