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Treatment of the feline atopic syndrome – a systematic review

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Background – Feline allergic skin disease and asthma occur regularly in small animal practice.

Objectives – To provide evidence-based recommendations for small animal practitioners on the treatment of feline atopic syndrome (FAS).

Methods and materials – The authors reviewed the literature available before February 2020, prepared a detailed evidence-based literature review and made recommendations based on the evaluated evidence.

Results – Sixty-six papers and abstracts were identified describing treatment interventions for FAS and evaluated to establish treatment recommendations. For many treatment options, the papers were retrospective, open studies or case reports.

Conclusion and clinical relevance – In this review, there was good evidence for the efficacy of systemic glucocorticoids and ciclosporin, and limited evidence for the efficacy of topical glucocorticoids, oclacitinib and allergen-specific immunotherapy in feline atopic skin syndrome. Evidence pointed to low-to-moderate efficacy for antihistamines, fatty acids and palmitoyl ethanolamide. In feline asthma, there was good evidence for the efficacy of oral and inhaled glucocorticoids, and limited evidence of moderate efficacy for allergen-specific immunotherapy. Evidence supported low-to-moderate efficacy of mesenchymal stem cells, inhaled lidocaine and oclacitinib as treatments for feline asthma. For almost all therapeutic options (with the exception of glucocorticoids and ciclosporin), more randomised controlled trials are needed.

Introduction

Feline atopic syndrome (FAS) is the newly-proposed terminology encompassing allergic diseases of the skin, gastrointestinal and respiratory tract in the cat. Feline atopic skin syndrome (FASS) describes allergic skin disease associated with environmental allergies.[1–3] Allergic dermatitis in the cat presents with multiple cutaneous reaction patterns that all may be caused by environmental, food and/or insect allergens, as well as other diseases. Those reaction patterns include miliary dermatitis, self-induced alopecia/hypotrichosis, the eosinophilic granuloma complex (eosinophilic granuloma, eosinophilic plaque, indolent ulcer) and/or excoriations-ulcers on the head and neck.[3] Consequently, the treatment of these reaction patterns will depend on their aetiology, and other causes such as food allergy or flea bite hypersensitivity must be ruled out before diagnosing FASS. Feline asthma is a common lower airway inflammatory condition in cats with significant morbidity and occasional mortality. From a clinical and pathogenetic point of view, feline asthma is remarkably similar to the human disease. As in humans, affected cats exhibit a spontaneous and natural hyper-reactivity of the airways resulting in a reversible bronchoconstriction, airway inflammation and chronic remodelling.[4] Intradermal and serum testing for allergen-specific immunoglobulin (Ig)E is not suitable for the diagnosis of FAS. Similar to dogs, the FASS is diagnosed based on the history, clinical signs and exclusion of differential diagnoses appropriate to each case.[5] Over the last decades, different treatments have been reported for FAS variants, yet to the best of the authors' knowledge, a systematic review of all available therapeutic and

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preventive interventions has not been published. The aim of this review was therefore to summarise and review the published evidence for the various treatment options for the cutaneous and respiratory components of FAS. It was not within the remit of this paper to discuss the aetiology, pathogenesis and diagnosis of these diseases. These subjects are reviewed in other papers in this series and readers are directed to them for more information.[1–3]

Methods and materials

In order to evaluate the efficacy and safety of treatments for the two main FAS manifestations (FASS and asthma), online bibliographic databases (PUBMED and WEB OF SCIENCE) and scientific meeting proceedings were searched for relevant published studies or abstracts of sufficient detail for analysis. The bibliographies of identified studies and of main veterinary dermatology textbooks were further evaluated. Studies were analysed and their value determined based on the quality of their evidence (QOE). They were summarised and, based on the available data, a given treatment's efficacy was determined and its reported adverse effects listed. Thereafter a recommendation about each treatment option was given, with the strength of recommendation (SOR) based on the QOE (Table 1). Data evaluation and strength of recommendations were modelled after previous practice guidelines for human[6,7] and canine atopic dermatitis (cAD).[8]

Results

We found a total of 72 papers and abstracts describing treatment interventions for FAS. These included 58 clinical trials and eight case reports evaluating efficacy of treatments,[9–16] five safety and pharmacokinetic studies in healthy cats,[17–21] and one retrospective safety study (without reporting efficacy).[22] Of the 55 clinical trials, six were available only as abstracts[23–28] and 49 had been published in peer-reviewed journals. There were 48 prospective and 10 retrospective studies.[23,25,27,29–35] Of the prospective studies, 19 were open and uncontrolled[24,28,36–52] while 29 were randomised, controlled[53–59] and often blinded.[26,42,60–79] These studies included clinical trials on allergen avoidance, allergen(-specific) immunotherapy (ASIT), topical, inhaled and systemic glucocorticoids, ciclosporin, oclacitinib, bronchodilators, H1-receptor (H1R) antihistamines, essential fatty acids (EFA) and palmytoylethanolamide, antibiotics, inhaled lidocaine and mesenchymal stem cells. Thirty-three of the reports focused on the reaction patterns of FASS, while 23 studies evaluated feline asthma. Eleven of those latter studies originated from the same research group using cats experimentally sensitised to various allergens and five from another colony of cats sensitised to *Ascaris suum*. In some reports, cats with respiratory or cutaneous manifestations were included.[15,29]

Allergen avoidance

Analysis of evidence

In one retrospective study of 29 asthmatic cats[35] and one prospective study on 20 asthmatic cats,[47] avoidance of allergens was reported for individual cases. We could not find any such evidence for FASS.

Analysis of efficacy

In the above-mentioned studies, one cat sensitised to human dander improved after access to the owner's bedroom was restricted.[35] Changing from dry food to a moist diet led to the complete remission of clinical signs in three cats allergic to storage mites.[47]

Recommendations

Although allergen avoidance is common sense and should be effective (QOE 3; SOR C), it is often unfeasible in cats sensitised to environmental allergens. There is only limited evidence for the benefit of allergen avoidance in asthmatic cats,[35,47] and no such information exists for FASS.

ASIT

Analysis of evidence

Eleven reports evaluated ASIT in a total of 197 cats with FASS.[12,13,15,16,23,25,28–32] Five retrospective studies specifically evaluated ASIT in 70 cats with different reaction patterns of FASS.[23,25,30,32] Seventeen cats had miliary dermatitis, 21 had noninflammatory alopecia, 18 had eosinophilic lesions[16,25,30,32] and in one study the clinical signs were not detailed.[23] Two of these reports were abstracts in proceedings from World Congresses of Veterinary Dermatology and thus not sufficiently detailed.[23,25] Likewise, one prospective open study evaluating sublingual ASIT was a conference abstract.[28] One report described the response to ASIT in three littermates with atopic skin disease,[12] one case series described four cats with miliary dermatitis and eosinophilic granuloma,[16] and another focused on rush immunotherapy (RIT) in four atopic cats,[13] although treatment outcomes were not described in the latter report. One larger study was based on a questionnaire sent out by a laboratory after serum testing for allergen-specific IgE and subsequent orders for ASIT in 81 cats, six of which had lower respiratory tract disease.[29] The last study evaluated 45 cats with FASS, 23 of which underwent AIT.[31] Definitions of a good, moderate, partial or no response varied and often were unclear. In one study, an excellent response was described as complete remission of the patient with no concurrent medication and was seen in 26% of the

Table 1. Strength of recommendation taxonomy (SORT)

Strength of recommendation (SOR)	
A	Based on consistent and good quality patient-orientated evidence
B	Based on inconsistent or limited quality patient-orientated evidence
C	Based on consensus, usual practice, opinion, disease-orientated evidence or case series
Quality of evidence (QOE)	
1	Good quality, patient-orientated
2	Limited quality, patient-orientated
3	Other evidence (usual practice, opinion, or disease-orientated evidence)

Table 2. Responses to allergen immunotherapy in 194 cats with naturally occurring feline atopic skin syndrome (FASS)

Type of Allergen (number of cats evaluated)	Dose	Responses			References Type of study	QOE
		Good–excellent	Partial	No response		
Der f 2-pullulan-based vaccine (n = 1)	Not reported; allergens administered once weekly for six weeks, then monthly for 4.5 months		Clinical remission with cessation of topical glucocorticoids and oral oclacitinib		Martin et al. 2019[15] Case report	2
Not reported (n = 19)	Not reported; allergens administered for 6 months	SCORFAD[a] reduced from 22 to 5.7, pruritus score from 7.9 to 3.6			Foj et al. 2019[28] Abstract of case series	2
Not reported (n = 23)	Not reported; administered for > 12 months	Good in 13	Partial in 6	Poor in 4	Ravens et al. 2014[31] ReSt	2
Aqueous allergens (n = 4)	11,000–22,000 PNU every 7–35 days administered for 8–24 months	Good in 2		Poor in 2	Schnabl et al. 2006[16] Case series	2
Aqueous allergens (n = 3)	Not reported; allergens administered every 10 days for three years	2 only mild seasonal itch	1 still regular, but less frequent prednisolone		Moriello 2001[12] Case report	2
Aqueous allergens (n = 19)	20,000 PNU every three weeks	1 good (no other medications, but still mild clinical signs), 5 excellent (remission)	5 some improvement (but still concurrent medication) and 3 marked improvement (but still intermittent medication)	5	Bettenay 1998[23] ReSt	2
Not reported (n = 75)	Not reported	10 cats 100% improvement, 39 cats 75–99%	12 cats 50–75%, 6 ≤ 50%	8 cats slight improvement, 6 cats no change or deterioration	Halliwell 1997[29] ReSt	3
Phosphate Ca-bound allergens (n = 22)	Not reported	16 in remission with very mild pruritus and no medication	1 only on one glucocorticoid injection per year	2 still on regular glucocorticoids	Prost 1992[25] Case series	2
Aqueous allergens (n = 13)	10,000 PNU every four weeks	9 cats good response (>50% improvement with no other drugs)	3 moderate improvement (approximately 50% improvement with occasional other drugs)	1 poor response	McDougal 1986[30] Case series	2
Alum-precipitated allergens (n = 15)	1 mL every four weeks	Good in 10 cats		Poor in 5 cats	Reedy 1982[32] Case series	2
Mean outcomes		60%	20%	20%		

QOE quality of evidence, RCT randomised controlled trial, ReS retrospective study, SCORFAD Scoring Feline Allergic Dermatitis.

cats.[23] In the study using a survey sent out to veterinarians treating cats with ASIT after serum testing for allergen-specific IgE, lesional scores were assigned and the percentage of improvement calculated.[29] In another study, concurrent medications were not discussed;[32] in many reports concurrent medications were mentioned and details not given.

Five studies evaluated cats with respiratory disease/asthma. In an older retrospective study, veteriarians submitting feline serum specimens for allergen-specific IgE testing were asked to complete a follow-up questionnaire, six cats with respiratory clinical signs undergoing ASIT were included.[29] One study focussed on ASIT as treatment for 12 asthmatic cats showing sensitization to aeroallergens based on intradermal testing.[47] Three studies were performed in an experimental model of feline asthma in which cats were sensitised to Bermuda grass and house dust mites.[59,65,76] In the first randomised controlled trial (RCT), intranasal or subcutaneous RIT were compared.[59] In a second study using the same model, cats received RIT with an allergen that they were not sensitised to or with only one of the two allergens they were sensitised to.[76] The third study evaluated the influence of oral and inhaled glucocorticoids on the outcome of RIT.[65] In one conference abstract, a cat with cutaneous and respiratory sign was treated with ASIT using a recombinant Der f 2-based vaccine.[15]

Analysis of efficacy

The results of ASIT for FASS were reported in 210 cats (Table 2). The reported efficacy was between 45 and 75%, similar to what is reported for dogs.[80,81] One of the studies did not evaluate treatment outcome, and looked only at the safety of RIT in four cats with FASS.[13]

Results of ASIT in 80 cats with asthma are listed in Table 3. In one study a complete remission of clinical signs was observed in eight of 12 cats with naturally occurring asthma (67%) in which symptomatic therapy with glucocorticoids could be discontinued on ASIT. Four cats still required pharmacotherapy, including inhaled corticosteroids and bronchodilators.[47] In a retrospective study, veterinarians treating 12 cats with suspected feline asthma reported a good response via questionnaire.[29]

Three studies evaluated ASIT in cats with experimentally induced asthma.[59,65,76] In the first RCT, intranasal or subcutaneous RIT improved clinical signs and dampened eosinophilic inflammation of the airways.[59] However, intranasal RIT had fewer adverse effects and a decreased interleukin (IL)-4/interferon-gamma ratio in the bronchoalveolar lavage fluid (BALF).[59] In the second study, airway eosinophilia decreased and the percentage of regulatory T cells and IL-10-producing cells increased in cats treated with RIT compared to controls independent of their sensitisation status and content of the allergen extract, indicating nonspecific effects. However, only matched allergens could potentially induce an immunological cure.[76] In the same model of feline asthma, cats given oral prednisolone at 10 mg once daily over the first six months of ASIT showed an increased percentage of eosinophils in the BALF after nine months of ASIT by contrast with inhaled fluticasone at 220 mcg twice daily.[65]

Adverse effects

Adverse effects were not mentioned in ten reports.[12,23,25,29–32,59,65,76] After RIT, two of four cats showed increased pruritus and in two of four a dermal alopecic nodule developed one week after initiation of therapy.[13]

Recommendations

ASIT seems to be an efficacious therapy for FASS (QOE 2; SOR B). However, some studies were presented only as abstracts with very limited information,[23,25] none of the studies were controlled or randomised, and all were characterised by unclear outcome measures, making final assessment difficult. By contrast, there is evidence of moderate-to-good efficacy of ASIT in naturally occurring feline asthma (QOE 2; SOR B) and moderate efficacy of RIT in cats with experimental asthma (QOE 1; SOR A). Adverse effects seem to be rare (QOE 1; SOR A). More studies on ASIT in cats are needed urgently.

Systemic glucocorticoids

Analysis of evidence

Three prospective double-blinded RCTs evaluated systemic glucocorticoid treatment in cats with FASS.[60,62,64] One prospective study looked at the diabetogenic potential of prednisolone and dexamethasone in healthy cats.[56] The three clinical trials included 63 cats: 11 treated with prednisolone, 36 with methylprednisolone and 16 with triamcinolone. The treatment regimens used dosages of 1 mg/kg once daily of prednisolone, 0.77 mg/kg twice daily (20 cats) to 1.4 mg/kg once daily (16 cats) of methylprednisolone, and 0.18 mg/kg once daily of triamcinolone acetonide for 28[62,64] to 84[60] days. The latter study used daily treatment for ≤14 days to achieve remission and then tapered treatment resulting in final alternate day dosages of 0.54 mg/kg methylprednisolone and 0.08 mg/kg triamcinolone.[60] Pruritus was assessed using a 0–10 Visual Analog Scale[82] (pVAS) in two studies[60,62] and a 0–5 Linear Analog Scale in one.[64] Lesion scores were assessed using the Canine Atopic Dermatitis Extent and Severity Index, 2nd iteration (CADESI-02),[64,83] a Feline

Table 3. Responses to allergen immunotherapy in 82 cats with naturally occuring and experimental asthma

Type of Allergen (number of cats evaluated)	Dosage	Responses	References Type of study	QOE
Alum-precipitated allergens (n = 12, EX)	200 mcg weekly Bermuda grass allergen SC or intranasally for six months	Respiratory scores and eosinophil % in BALF decreased,	Lee-Fowler et al. 2009[59] *RCT*	1
Alum-precipitated allergens (n = 18, EX)	200 mcg weekly Bermuda grass allergen SC for nine months, additional oral or inhaled glucocorticoids for the first six months (n = 6 each)	Decrease in eosinophil% and IL-5 in BALF	Chang et al. 2013[26] *RCT*	1
Alum-precipitated allergens (n = 36, EX)	200 mcg/week for six months	Decrease in eosinophil% and lymphocyte proliferation stimulation index, increase in CD4 + CD25+ FoxP3 + T cells	Reinero et al. 2012[76] *RCT*	1
Allergens adsorbed on Calcium phosphate gel (n = 12)	1 mL every 28 days for six to nine months	Remission in 8/12 cats	Prost 2008[47] *Case series*	2
Not reported (n = 4)	Not reported	Mean percentage clinical improvement 89.5%	Halliwell 1997[29] *ReSt*	3

BALF bronchoalveolar lavage fluid, EX experimental asthma, NO naturally occuring asthma, QOE quality of evidence, ReSt retrospective study, RCT randomised controlled trial, SC subcutaneously.

Erythema, Excoriation and Alopecia score (FEEAS; a modified CADESI-03 score omitting lichenification),[60] and a Scoring Feline Allergic Dermatitis (SCORFAD) scale.[62] Only the SCORFAD scale had been validated for pruritic and eosinophilic skin lesions in cats.[84,85] One study[62] included a validated Quality of Life (QoL) score.[86] The cats presented with pruritus and a variety of the recognised reaction patterns associated with FASS. Most cats presented with more than one type of lesion. The seasonality of the clinical signs was not recorded.

One cross-over RCT compared oral prednisolone at 10 mg/day with inhaled flunisolide at 250 μg twice daily in six cats with feline asthma experimentally sensitised to Bermuda grass.[66] Another cross-over RCT treated six cats sensitised to *A. suum* with either oral prednisolone at 1 mg/kg twice daily, 500 mcg of inhaled fluticasone proprionate twice daily, or a combination of inhaled fluticasone propionate and salbutamol at 500 mcg and 50 mcg, respectively, for four consecutive days.[71] A study with 14 client-owned cats with lower airway disease assessed airway function before and after prednisolone therapy.[48]

Analysis of efficacy

Treatment outcome data were available for 63 cases with FASS (see Table 4). Cats that responded to treatment were reported to do so within 7–14 days. There was no association between the responses to treatment and the type of lesions.

Although prednisolone decreased allergen-specific IgE and the percentage of eosinophils in the BALF of cats experimentally sensitised to Bermuda grass, it did not improve airway hyper-reactivity in response to methacholine.[66] In the *A. suum*-sensitised cats there were no significant differences in respiratory rate or Penh [an estimate of airflow limitation measured by conventional barometric whole body plethysmography (BWBP)] between the treatment groups.[71] Allergen-induced airway hyperresponsiveness was significantly inhibited by the oral prednisolone, inhaled fluticasone proprionate and inhaled fluticasone propionate/salbutamol. The mean BALF eosinophil percentage was lower after oral and inhaled corticosteroid treatment and these changes were significant for groups receiving prednisolone and the combination of inhaled fluticasone propionate/salbutamol,[71] although the dose of inhaled fluticasone was fairly high. In the study with client-owned cats with lower airway disease, a significantly decreased peak to mid-expiratory flow and no significant changes in other BWBP parameters were noted after at least three weeks of therapy with prednisolone at 1.2–2 mg/kg once daily.[48]

Adverse effects

Clinical adverse effects were uncommon, with one case each of vomiting and lethargy among the 20 cats treated with methylprednisolone.[62] Clinicopathological abnormalities included increased liver enzymes in one of 16 triamcinolone- and eight of 36 methylprednisolone-treated cats.[60,62] Hyperglycaemia was seen in four, altered haematological parameters in four, and glycosuria in one of the 36 methylprednisolone-treated cats. Mean albumin and fructosamine levels significantly increased in triamcinolone- (n = 16) and methylprednisolone-treated cats (n = 16) and remained within the reference ranges.[60] Amylase was elevated above the reference range in 10 of 15 triamcinolone- and two of 14 methylprednisolone-treated cats at the end of the induction phase, and returned to normal during the every other day maintenance phase.[60] The safety study evaluated 14 cats treated with either 4.4 mg/kg once daily of prednisolone or 0.55 mg/kg once daily of dexamethasone for 56 days.[56] Dexamethasone treatment resulted in significantly increased fructosamine concentration, decreased insulin sensitivity and secretion, and increased glycosuria, although the cats did not become hyperglycaemic at any point. No adverse effects were mentioned in most of the studies evaluating asthmatic cats.[48,66,71] One study evaluated long-term effects of glucocorticoids in asthmatic cats and found adverse effects such as polyuria and polydipsia, diabetes mellitus and fungal infection in four of 34 cats.[27] A study evaluating long-term safety (at least three years) of methylprednisolone in 25 cats detected an increase of

Table 4. Responses to systemic glucocorticoid treatment in 63 cats with feline atopic skin syndrome (FASS)

Glucocorticoid‡ (number of cats evaluated)	Dosage	Response to treatment†			References	
		Pruritus	Lesion scores	QoL	Type of study	QOE
Methylprednisolone (n = 16, not all cats had an elimination diet)	1.4 mg/kg once daily for over six weeks	95% decrease§,¶	70% decrease§,¶	ND	Ganz 2012[60] RCT	1
Methylprednisolone (n = 20)	0.77 mg/kg twice daily for 28 days	67% decrease¶	69% decrease¶	21% decrease	Noli 2019[62] RCT	1
Triamcinolone (n = 16, not all cats had an elimination diet)	0.18 mg/kg once daily for over six weeks	95% decrease¶	70% decrease¶	ND	Ganz 2012[60] RCT	1
Prednisolone (n = 11)	1 mg/kg once daily for 28 days	5/11 improved 6/11 worse	6.9% ±77.8%‡	ND	Wisselink 2009[64] RCT	2

ND not determined, QoL quality of life (lower scores are better), ReSt retrospective study, RCT randomised controlled trial.

†See text for the definitions of the responses to treatment.

‡Mean improvement ± standard deviation.

§13 of 16 cats achieved remission.

¶Two of three cats that failed to achieve remission responded to higher doses of glucocorticoid.

††Three of 20 cats worsened.

‡‡14 of 16 cats achieved remission.

triglycerides, amylase and monocytes, yet changes remained within the reference interval.[87]

Recommendations

Systemic glucocorticoids are rapid and effective in most cats with FASS (QOE 1; SOR A). Treatment with 1.4–1.5 mg/kg once daily of methylprednisolone-induced remission in 33 of 36 cats within 14 days. The similar response to 0.18 mg/kg once daily of triamcinolone acetonide suggests that this drug has seven-fold greater potency than methylprednisolone. It is therefore likely that equipotent doses of other glucocorticoids will be likewise effective (QOE 3; SOR C). By contrast, 1 mg/kg once daily of prednisolone (approximately 50% of the above dosages) was much less effective. Once in remission, treatment can be tapered to the lowest and least frequent dosage that maintains remission (QOE 1; SOR A). On average, this equated to 20–25% of the starting dosage. Once-daily treatment is advised (QOE 1; SOR A). There was no difference in the efficacy of methylprednisolone at 0.77 mg/kg twice daily and 1.4 mg/kg once daily. One study noted that twice-daily dosing reduced QoL scores.[62] Systemic glucocorticoids at these doses were well-tolerated, although all of the studies were short-term. However, altered haematology, serum biochemistry and urinalysis parameters were frequent (particularly markers of glucose metabolism). Regular monitoring of cats on a long-term treatment with systemic glucocorticoids is therefore warranted, especially with more diabetogenic drugs such as dexamethasone (QOE 1, SOR A).

In feline asthma, there is good evidence for clinical efficacy of oral glucocorticoids (QOE 1; SOR A) although most of this evidence is based on experimentally sensitised cats.

Topical and inhaled glucocorticoids

Analysis of evidence

There was one prospective open and uncontrolled clinical trial of topical 0.0584% hydrocortisone aceponate (HCA, Cortavance, Virbac; Carros, France) in 10 cats with perennial pruritus and lesions consistent with FASS.[43] The cats were treated with two sprays per 10 x 10 cm area of affected skin from 10 cm away daily for 28 days, followed by every other day dosing up to Day (D).[43] The outcome measures included a pVAS,[82] a validated Feline Dermatitis Extent and Severity Index lesion score (FeDESI),[84] and a five point categorical score for efficacy, tolerance and ease-of-administration.

Four studies evaluated the use of inhaled glucocorticoids in an experimental model of feline asthma.[65,66,68,71] In one study, inhaled flunisolide at 250 μg twice daily was compared with oral prednisolone at 10 mg once daily in six cats.[66] In the second blinded cross-over RCT the effect of three different dosages of inhaled fluticasone propionate delivered by a metered-dose inhaler was investigated in six cats with experimentally induced allergic airway inflammation.[68] A third cross-over RCT treated six cats sensitised to *A. suum* with either prednisolone (1 mg/kg twice daily), inhaled fluticasone propionate (500 mcg twice daily), or a combination of inhaled fluticasone propionate and salbutamol (500 mcg/50 mcg twice daily) for four consecutive days.[71] In another study, sensitised cats underwent RIT and for the first six months concurrently received either oral prednisolone at 10 mg/kg/day/cat or 220 mcg twice-daily inhaled fluticasone/cat.[65] One study investigated the effects of 400 mcg of inhaled budesonide twice daily on 37 cats with naturally occurring asthma and chronic bronchitis in a retrospective study using client questionnaires.[34]

Analysis of efficacy

Three cats were withdrawn from the HCA study; two were lost to follow-up and one was removed owing to poor efficacy.[43] Using an intention-to-treat analysis, there was a 77% reduction in FeDESI score and 76% reduction in pruritus by D56. Over 50% of the improvement was seen by D14. Ease-of-administration, tolerance and efficacy assessments were good-to-excellent in the seven cats that completed the study. Of these cats, six of seven could be maintained on every other day treatment and one required daily therapy.

Although inhaled flunisolide decreased allergen-specific IgE and the number of eosinophils in the BALF of cats experimentally sensitised to Bermuda grass (Table 5),[66,68] it did not improve airway hyper-reactivity to methacholine.[66] Fluticasone dosages of 44, 110 or 220 mcg twice daily for three weeks did not suppress the hypothalamic–pituitary–adrenal axis.[68] In the same experimental model, inhaled fluticasone did not influence the outcome of RIT in contrast to oral glucocorticoids (where airway eosinophilia was significantly increased after nine months of RIT), although the dose of prednisolone was very high.[65] In the study with the six cats sensitised to *A. suum*, inhaled fluticasone propionate, or a fluticasone propionate and salbutamol combination, resulted in significantly decreased allergen-induced airway hyper-responsiveness. The mean BALF eosinophil percentage was significantly lower after the inhaled combination of fluticasone and salbutamol.[71] In the study of naturally occurring asthma or chronic bronchitis treated with budesonide, close to a third of the cats were asymptomatic with therapy, almost as many improved (Table 5).[34] BWBP parameters had improved in the 19 cats where pre- and post-examinations were available.[34]

Adverse effects

In the study using HCA in cats with FASS, no adverse events were noted and there were no haematological, biochemical or urine abnormalities in samples from four of the cats.[43] Four cats would not tolerate the spray and the solution was applied directly using cotton wool. There was no association between the response to treatment and lesion type. In studies evaluating feline asthma, clinical adverse effects to inhaled glucocorticoids were either not seen[34,65] or not mentioned.[66,68,71] Inhaled budesonide therapy was associated with hypothalamic–pituitary–adrenal axis suppression in one study.[34]

Recommendations

Topical 0.0584% HCA was rapidly effective in seven of 10 cats (QOE2; SOR B). It is likely that other topical

Table 5. Responses to inhaled glucocorticoids in 67 cats with asthma

Inhaled glucocorticoid (number of cats evaluated)	Dosage	Response	Reference Type of study	QOE
Budesonide (n = 43)	400 mcg twice daily for less than two months	Clinical improvement in 23/43, lower basal Penh, higher PCPenh300	Galler 2013 *ReSt*	2
Fluticasone (n = 6)	220 mcg twice daily for six months concurrent to ASIT	Decrease in BALF eosinophils and airway inflammation	Chang 2013[26] *RCT*	1
Fluticasone (n = 6)	500 mcg twice daily for one month	Decrease in airway hyperresponsiveness	Leemans 2012[71] *RCT*	1
Fluticasone (n = 6)	44 mcg twice daily, 110 mcg twice daily and 220 mcg twice daily in a cross-over design	Reduction of airway eosinophilia	Cohn 2010[68] *RCT*	1
Flunisolide (n = 6)	250 mcg twice daily for two weeks	Decrease in BALF eosinophils	Reinero 2005[66] *RCT*	1

ASIT allergen (-specific) immunotherapy, BALF bronchoalveolar lavage fluid, Penh enhanced pause, QOE quality of evidence, RCT randomised controlled trial, ReSt retrospective study.

glucocorticoids also will be effective depending on the type and formulation of glucocorticoid (QOE 3; SOR C) and topical treatment should be considered for FASS whenever feasible (QOE 3; SOR C). This is likely to have fewer adverse effects than systemic glucocorticoid treatment. However, these products are not licenced for cats, systemic absorption is possible and regular clinical monitoring is advised. There is good evidence that inhaled glucocorticoids are beneficial for cats with asthma (QOE 1; SOR A). No clinical adverse effects were reported, although again monitoring of cats on long-term treatment is advised. Hypothalamic–pituitary–adrenal axis suppression was documented with high doses of inhaled flunisolide and budesonide.

Ciclosporin

Analysis of evidence

Ciclosporin use in FASS was evaluated in two double-blinded, placebo-controlled studies,[42,77] one double-blinded, prednisolone-controlled study,[64] three prospective open studies,[40,46,88] one safety and tolerability study,[18] and three retrospective case series.[22,31,33] In two studies, specific clinical presentations were not mentioned,[22,64] while the other studies[31,33,40,46,77] included cats with excoriations as a consequence of pruritus (n = 185), self-induced alopecia (n = 181), eosinophilic granuloma (n = 112) and miliary dermatitis (n = 100). Most cats presented with more than one lesion type. There is one case report of a cat with asthma, congestive heart failure and diabetes mellitus treated successfully with ciclosporin.[14] Two other studies evaluated the effect of ciclosporin on mast cell degranulation and airway remodelling in a colony of cats sensitised to *A. suum*.[74,89] In older studies, a human product of ciclosporin was used (Neoral, Novartis; Basel, Switzerland),[33,40,64] whereas in newer studies, the veterinary product was administered (Atopica, Novartis) and in one study both products were used.[31]

Analysis of efficacy

Two double-blinded, placebo-controlled studies,[42,77] one double-blinded, prednisolone-controlled study,[64] three prospective open studies,[40,46,88] and two retrospective case series,[31,33] reported the treatment outcome in 328 cases of FASS. In general, ciclosporin was effective in 40–100% of the cats. However, scoring systems for the lesions varied. Many studies used a validated score such as the SCORFAD,[42,46,88] and others used the Feline Eosinophilic Granuloma, Eosinophilic Plaque, Extension and Severity Index (FEGEPESI),[40] or a score devised as a total lesion score (TLS) describing the extent and severity on a scale from 0 to 4 for each of the major reaction patterns seen in FASS.[77] One study[64] used a CADESI-02 score validated for cAD.[90,91] Owner-assessed pruritus was evaluated in most studies using a pVAS,[40,46,77,88] yet one study used a scale from 1 to 5,[64] and another used a scale from 1 to 10.[33] The latter study also evaluated the lesions on a 1–10 scale .[33] Only two studies used owner global assessments.[42,77] Finally, one retrospective study did not consider pruritus or lesions, and rather evaluated the owners' impressions of various treatments.[31] One study[88] was a follow-up of a double-blinded, placebo-controlled study and evaluated tapering schedules for ciclosporin in cats.[42] During the final four weeks of that particular study, 63%, 22% and 15% of 157 cats could be maintained on twice-weekly, every other day or daily treatment, respectively.[42] Likewise, in another open study ciclosporin could be tapered to every other day in 15% and twice weekly in 57% of the cats.[46] Results of the various studies are listed in Table 6.

Ciclosporin did not affect mast cell degranulation or the early asthmatic response in *A. suum*-sensitised cats with induced asthma.[74] However, in another study by the same group, ciclosporin was shown to reduce airway reactivity and remodelling after chronic antigen challenge in cats sensitised to *A. suum*.[89] Ciclosporin also was used in a cat with feline asthma and concurrent congestive heart failure and diabetes mellitus at a dosage of 4 mg/kg twice daily.[14] Clinical signs and airway eosinophilia resolved completely within three weeks of therapy. However, thereafter the ciclosporin was replaced with inhaled fluticasone and long-term effects of the ciclosporin could not be evaluated.[14]

Adverse effects

In all studies, gastrointestinal signs were the most common adverse effects. In one study, vomiting, diarrhoea

Table 6. Responses to ciclosporin treatment in 328 feline atopic skin syndrome (FASS) cases

Type of ciclosporin (number of cats evaluated)	Dosage	Responses†			References Type of study	QOE
		Lesions	Pruritus	Global Assessment		
Ciclosporin microemulsion liquid (Novartis) (n = 144)	7 mg/kg once daily for 42 days	Mean (SD) 7.3 (3.0) to 2.5 (2.8)	Mean (SD) 69 (22) to 28 (28)	69% successful response	Roberts et al. 2016[42] *RCT*	1
Neoral capsules or ciclosporin microemulsion liquid (Novartis) (n = 10)	Only mentioned in three cats: 2–4 mg/kg once daily	Good response in all cats		N/A	Ravens et al. 2014[31] *ReSt*	2
Ciclosporin microemulsion liquid (Novartis) (n = 65)	7 mg/kg once daily for four weeks	Mean (SD) 7.3 (3.5) decreased to 2.3 (2.7) in first 28 days	Mean (SD) 66 (23) decreased to 26 (29)	N/A	Steffan et al. 2013[46] *RCT*	1
Ciclosporin microemulsion liquid (Novartis) (n = 32)	2.5 mg/kg once daily for six weeks	Mean (SD) 6.8 (2.8) decreased to 1.8 (1.5); 15 improvement > 50%	Mean (SD) 69 (23) decreased to 46 (36), 13 improvement > 50%	Mean (SD) 1.8 (1.5)‡	King et al 2012[77] *RCT*	1
Ciclosporin microemulsion liquid (Novartis) (n = 33)	7 mg/kg once daily for six weeks	Mean (SD) 7.7 (3.9) decreased to 2.9 (2.7); 23 improvement > 50%	Mean (SD) 66 (21) decreased to 31 (30), 21 improvement > 50%	Mean (SD) 1.4 (1.4)‡	King et al. 2012[77] *RCT*	1
Neoral capsules (Novartis) (n = 18)	5 mg/kg daily for 28 days	Improvement by 38% (SD 45%), 13/18 improvement by > 25%	Pruritus improved in 61%	N/A	Wisselink et al. 2009[64] *RCT*	2
Neoral capsules (Novartis) (n = 10)	4–8 mg/kg once daily for 30 days	FEGEPESI decreased from 7.5 to 3.6, 5 improvement > 50%	Decreased from 8.5 to 4.6, 4 improvement > 50%	N/A	Noli et al. 2006[40] *Case series*	2
Neoral capsules or solution (n = 16)	6.4–12.3 mg/kg per day for 90 days	All cats but 1 cured (1 euthanasia)	All cats but 1 in clinical remission (1 euthanasia)	N/A	Vercelli et al. 2006[33] *ReSt*	2

FEGEPESI Feline Eosinophilic Granuloma, Eosinophilic Plaque, Extension and Severity Index, QOE quality of evidence, RCT randomised controlled trial, ReSt retrospective study.

† See text for details of the outcome measures.

‡ 0 = excellent, 1 = good, 2 = acceptable, 3 = poor, 4 = bad.

and/or anorexia was noted in 12 of 50 and weight loss in eight of 50 cats.[22] Gingival hyperplasia, a known adverse effect in dogs, occurred once.[22] In one study, vomiting occurred in 26 of 65 and diarrhoea in 13 of 65 cats.[46] In another study, diarrhoea was more common (in five of 18) than intermittent vomiting (three of 18).[64] In one study,[77] the neutrophil and eosinophil cell count decreased significantly in the high-dose group, and still was within the reference range. An elevation in total bilirubin, urea and glucose also was seen in the high-dose group, yet again all values were within the reference range. Nonsignificant weight loss was seen in the first three weeks, and reversed in the second three weeks of the study when the medication, initially mixed with food, was given separately orally.[77] Cryptococcosis and toxoplasmosis developed in one and two of ten cats, respectively, in one retrospective study.[31] In a larger study, 10 of 144 cats receiving ciclosporin had a positive *Toxoplasma* titre.[42] Other adverse effects included anorexia, lethargy, sneezing and weight loss, at least one of which occurred on daily ciclosporin in 80% of cases in one report.[46] Increased appetite and polydipsia (in one cat each) were seen in another study.[64] In one study none of the 32 cats on glucocorticoids or ciclosporin for at least six months showed subclinical bacteriuria, when urine obtained by cystocentesis was evaluated.[92] Although not reported in any of the cited studies, acute bullous keratopathy was significantly associated with systemic administration of ciclosporin in cats in a larger study evaluating 12 patients that had developed this disease in a population of 70,167 cats.[93]

Recommendations

Based on the available evidence in a large number of cats with FASS, ciclosporin at a dose of 7 mg/kg once daily is efficacious in the treatment of reaction patterns caused by FASS (QOE 1; SOR A). In more than half of the cats, ciclosporin could be tapered from daily to twice-weekly administration.[46,88] By contrast, there is insufficient evidence to recommend ciclosporin for feline asthma. As reported in dogs,[94] gastrointestinal adverse effects are the most common. There is evidence that cats that get infected with *Toxoplasma gondii* while receiving ciclosporin daily develop much more severe clinical signs,[17] or even die.[9,11,17] By contrast, shedding of oocysts or recurrence of clinical signs was not seen in cats already infected with *Toxoplasma* before ciclosporin administration.[17] Consequently, *Toxoplasma* antibody titres may be recommended before ciclosporin therapy and may

influence the treatment decision in seronegative cats with access to outdoors or fed raw meat (QOE2; SOR B).

Oclacitinib

Analysis of evidence

One case report,[10] two open prospective studies[24,41] and one methylprednisolone-controlled double-blinded study[62] reported the efficacy of oclacitinib for FASS. These included 68 cats, 48 of whom were treated with oclacitinib. In one abstract, details of the improvements were not given.[24] The outcome measures of the other two prospective studies were a clinician-assessed lesional score, the SCORFAD and an owner-based pVAS.[41,62] One study did not specify the lesion type,[62] and the other studies included 19 cats with excoriations on the head and neck, eight cats with self-induced alopecia, four cats with eosinophilic granuloma and one cat with miliary dermatitis.[10,24,41] Most cats presented with more than one lesion type. Seasonality was not recorded for any cat. In a randomised, placebo-controlled study, 24 cats with induced asthma experimentally sensitised to Bermuda grass received oclacitinib at 0.5 or 1.0 mg/kg twice daily for four weeks and airway inflammation was monitored.[26] In addition, a more recent study documented a more rapid elimination of oclacitinib in the cat versus the dog, and recommended a shorter dose interval and/or higher doses of oclacitinib in cats compared to dogs.[19]

Analysis of efficacy

Treatment outcome data were available for all 48 cats with FASS (see Table 7). Cats that responded to treatment were reported to do so within one month. Overall, a good response was reported at a dosage of 1 mg/kg once or twice daily. One third of the cats had a good-to-excellent response in one study.[41] In one case report with long-term follow-up, the cat achieved long-term clinical remission while on therapy.[10]

In the study evaluating the two doses of oclacitinib (0.5 or 1.0 mg/kg twice daily) in cats with experimental asthma, the percentage of eosinophils in BALF was significantly decreased compared to placebo with no difference between the two dosages.[26] There was no significant difference between treatment groups in the effective concentration of methacholine that induced a 200% increase over baseline airway resistance.[26]

Adverse effects

Adverse effects were not specifically recorded in two studies,[24,41] although in one study owners reported the drug to be clinically well-tolerated by all cats.[41] In another study, at least half of the cats were monitored with complete blood counts and serum biochemistry with neutropenia seen in two, thrombocytopenia in one, increased blood ureanitrogen and creatinine in four, and increased alanine aminotransferase in three cats.[62] In the case report monthly serum biochemistries and complete blood counts for 10 months did not show any changes.[10] In a recent placebo-controlled safety study, oclacitinib was administered at 1 and 2 mg/kg twice daily for 28 days.[95] Vomiting and soft stools were noted in two of 10 cats each in the high-dose group. A small increase in fructosamine concentrations was observed for both treated groups compared with placebo; however, values remained within the normal reference range. There were no differences in individual parameters in complete blood counts and biochemistry panels. In the study of cats with experimental asthma, no adverse effects were noted in the four weeks of treatment.[26]

Recommendations

Oclacitinib at a dosage of approximately 1 mg/kg once or twice daily was an efficacious treatment option for FASS (QOE1; SOR A). Based on the small number of cats and the short duration of most studies as well as the lack of long-term safety data and the off-label use of the drug, cats receiving oclacitinib should be monitored closely until

Table 7. Responses to oclacitinib treatment in 48 cats with feline atopic skin syndrome (FASS)

Dose (number of cats evaluated)	Global efficacy by owner			SCORFAD; MEAN (SD)	pVAS; mean (SD)	References Type of study	QOE
	Good–excellent–marked	Fair	Poor				
0.7–1.2 mg/kg twice daily for 28 days (n = 20)	11	4	5	6.2 (2.3) and 2.4 (2) before and after; >50% in 12	7.5 (1.5) and 3.4 (3) before and after; >50% in 15/20; >2 cm in 11	Noli et al. 2019[62] *RCT*	1
1 mg/kg twice daily for 14 days, then once daily for 300 days, then twice daily (n = 1)	N/A	N/A	N/A	Remission after 30 days, relapse after 300 days on once daily, and then remission again on twice daily		Fernandes et al. 2019[10] *Case reports*	2
0.5–0.8 mg/kg twice daily for 14 days, then once daily for 14 days (n = 15)	N/A	N/A	N/A	10 improved†	10 improved†	Pandolfi et al. 2016[24] *Case series*	2
0.4–0.6 mg/kg twice daily for 14 days, then once daily for 14 days (n = 12)	4	3	5	4.9 (2.4) and 3.6 (3) before and after	8.5 (1.6) and 7 (2.5) before and after	Ortalda et al. 2015[41] *Case series*	Twice daily

pVAS pruritus Visual Analog Scale, QOE quality of evidence, RCT randomised controlled trial, ReSt Retrospective study, SCORFAD Scoring Feline Allergic Dermatitis.

† No further details were given in the abstract.

more data are available. There also is only limited evidence for the use of oclacitinib in asthmatic cats (QOE2; SOR B) and, to the best of the authors' knowledge, no study has evaluated this drug in naturally occurring feline asthma.

Bronchodilators

Analysis of evidence

One study evaluated salbutamol, ipratropium bromide and the combination of those two drugs in cats sensitised to ovalbumin and to *A. suum* compared to control cats.[69] In another study, the same drugs were used in a double-blinded, placebo-controlled cross-over design in *A. suum*-sensitised cats.[70] In a clinical study including 19 cats with naturally occuring bronchial disease, therapy with low-dose prednisolone was supplemented with propentofylline in 10 cats.[57]

Analysis of efficacy

In the first study, cats sensitised to ovalbumin (n = 6), to *A. suum* (n = 6) and nonsensitised control cats (n = 6) were evaluated.[69] Salbutamol (100 mcg, two puffs), ipratropium bromide (20 mcg, two puffs) or a combination of salbutamol and ipratropium bromide (120 mcg/20 mcg, two puffs) were administrated to the conscious cats by use of a pressurized metered-dose inhaler and a spacing chamber connected through an inspiratory valve to a facemask. Salbutamol/ipratropium bromide reduced BAL-induced bronchoconstriction in the cats sensitised to *A. suum*, and not in the cats sensitised to ovalbumin or control cats. By contrast, salbutamol or ipratropium bromide alone did not lead to any significant changes.[69] In the cross-over study with five cats sensitised to *A. suum*, enhanced pause, an estimator of airflow limitation measured by BWBP, was repeatedly assessed within 120 min following the administration of each treatment protocol.[70] Responses to inhaled medications were evaluated by calculating the area under the time–response curves (AUC) from 0 to 60 or 120 min after drug administration ($AUC_{0–60}$, $AUC_{0–120}$), as well as the times required for half-recovery or for returning to nearly basal conditions. There was no difference in time-related bronchodilating effects between 100 mcg salbutamol, 20 mcg ipratropium bromide, a combination of the two treatments, and the nontreated control.[70] Cats treated with a combination of propentophylline and prednisolone significantly improved in their auscultation scores, respiratory pattern scores and radiological bronchial markings score over the observation period, and they coughed less and were more active at the end of the study compared to the cats treated with prednisolone alone.[57]

Adverse effects

No adverse reactions occurred in one study,[69] adverse effects were not mentioned in two.[57,70]

Recommendations

Although bronchodilators are frequently recommended for the treatment of feline asthma,[96,97] the two evaluated studies provided no evidence supporting the use of bronchodilators in asthmatic cats (QOE2; SOR B). Moreover, both trials were with cats experimentally sensitised in the laboratory and studies evaluating bronchodilators in cats with naturally occurring asthma are lacking. Despite this, inhaled bronchodilators are recommended for management of acute asthmatic episodes and for long-term treatment of feline asthma alongside inhaled steroids (QOE3; SOR C). Clearly, further studies on the efficacy of bronchodilators are needed.

H1-receptor blocking antihistamines

Analysis of evidence

There were seven open and uncontrolled studies reporting the efficacy of H1R-antihistamines in FASS; six were prospective[36–38,44,45,51] and one was retrospective.[31] One study was prospective, double-blinded and placebo-controlled.[63] These included 164 cats: 37 treated with chlorphenamine/chlorpheniramine maleate (11 received concurrent omega three of six essential fatty acids),[37,44] 10 with clemastine fumarate,[38] 20 with cyproheptadine hydrochloride,[45] 51 with cetirizine[36,63] and 46 with loratidine.[31,51] The outcome measures varied with the five prospective studies using owner-assessed pVAS (reductions of 0–25% poor, 26–50% fair, 51–75% good and 76–100% excellent in four studies; and ≤25% mild, 25–50% moderate and ≥50% marked in one study). The retrospective study defined a "good" response as a marked reduction or resolution of clinical lesions and reduction or discontinuation of ongoing symptomatic medications, a "partial" as a reduction in clinical lesions with ongoing antipruritic drugs, and "no response" with no apparent change to lesions, pruritus and/or symptomatic medications. The cats presented with pruritus and a variety of the recognised reaction patterns associated with FASS. Most cats presented with more than one type of lesion. Seasonality was recorded for 99 cats, with 90 having perennial disease and nine seasonal disease. Two studies evaluated cetirizine and cyproheptadine in a model of feline asthma.[66,67] Unfortunately, only two studies reported pharmacokinetic data of antihistamines in cats.[20,21] Oral cyproheptadine was well-absorbed and had a half life of approximately 12 h.[20] Cetirizine was well-absorbed after oral administration, with higher plasma concentrations than seen in humans and a half-life compatible with once-daily dosing.[21]

Analysis of efficacy

Treatment outcome data were available for 164 cats with FASS (see Table 8). Cats that responded to treatment were reported to do so within three to 10 days of starting treatment and to relapse within two to three days of stopping. There was no association between the responses to treatment and the type of lesions or seasonality.

A retrospective study[31] (QOE 3) reviewed type 1 antihistamine treatment in 31 cats. However, with the exception of cetirizine (n = 19) and loratidine (n = 18) (outcomes included in Table 6), specific treatments and outcomes were not reported. Most cats received more than one antihistamine with variable and inconsistent results. Overall, a good response was reported in two of 31, a partial response in 20 of 31, and a poor response in nine of 31 cats.[31]

When used in a model of feline asthma, antihistamines such as cetirizine and cyproheptadine did not alter percentage of eosinophils in BALF, or serotonin and histamine concentrations in plasma or BALF.[66,67]

Adverse effects

Most of the antihistamines were reported to be well-tolerated. Adverse effects included sedation in two of 37 cats treated with chlorphenamine and diarrhoea in one of 10 cats given clemastine. However, adverse effects were reported in 11 of 20 cats treated with cyproheptadine; three cats were withdrawn from treatment (one with vomiting, two with polyphagia) and adverse effects were reported in another eight cats (vomiting in one, polyphagia in four and altered behaviour/vocalisation in four).

Recommendations

Oral antihistamines could provide a small and limited benefit in some cats with FASS and this is not likely to result in good-to-excellent response in most cases (QOE 2; SOR B). The available evidence supports the use of chlorphenamine as a first-line H1R-antihistamine (QOE 2; SOR B). The mode of action of these drugs in cats is unknown yet, based on recommendations in cAD,[8] it is likely that they will be most effective in early and/or mild disease and when given proactively rather than reactively to manage an acute exacerbation (QOE3; SOR C). It is also possible that the sedative effect of first generation H1R-antihistamines may alleviate stress-associated triggers in FASS (QOE3; SOR C). The high frequency of adverse effects to cyproheptadine is of concern (QOE2; SOR B). There is no evidence supporting the use of antihistamines in cats with asthma (QOE2; SOR B).

Essential fatty acids and palmitoylethanolamide

Analysis of evidence

Treatment outcome data were available for 37 cats with FASS (see Table 9). In one prospective, double-blinded, placebo-controlled study 15 cats either received evening primrose oil (EPO) or olive oil as the placebo for 12 weeks.[61] There was one prospective, double-blinded, placebo-controlled study evaluating 15 cats with FASS,[61] two randomised studies with 11[54] and 14[53] atopic cats, one prospective study with 10 cats with FASS (and 18 cats with food allergy, flea bite hypersensitivity or miliary dermatitis, self-induced alopecia or eosinophilic granuloma without further diagnostic work-up)[39] and 12 cats with miliary dermatitis,[55] respectively. In another study, healthy cats were given essential fatty acids as a supplement to a standard diet.[98] In some studies, cytological evaluation, fungal cultures, skin scrapings, flea control and elimination diets were performed as needed before inclusion to confirm the diagnosis of FASS.[53,54,61] In others, cats showed clinical features of FASS, and differential diagnoses were not[55] or not always[39] evaluated. In three studies, only cats with miliary dermatitis (n = 30) were included.[53–55] In an open label study, 15 cats with nonflea-associated FASS were given 10 mg/kg ultramicronised palmitoylethanolamide (PEAum) twice daily for 30 days. The outcome measures were a clinical assessment (pruritus, erythema, alopecia, and extent of eosinophilic plaques and granulomas) and evaluation of mast cell numbers in skin biopsies.[50] One double-blinded, placebo-controlled randomised trial assessed the efficacy of PEAum in maintaining remission in cats with nonseasonal pruritus and FASS (described as nonflea-associated hypersensitivity dermatitis with a variety of reaction patterns).[99] The cats initially were stabilised with two weeks of methylprednisolone (4–6 mg/cat/day) and then maintained on PEAum (n = 21; approximately 15 mg/kg/day)

Table 8. Responses to antihistamine treatment in 164 cats with feline atopic skin syndrome (FASS)

Antihistamine (number of cats evaluated)	Dose	Responses† Good–excellent–marked	Partial–moderate–fair	Poor–mild	References Type of study	QOE
Loratidine (n = 46)	5 mg/cat once daily for 14 days	4%	17%[e]	79%	Ravens et al 2014[31] *ReSt* Scott et al 2015[51] *Case series*	3 2
Cetirizine (n = 19)	1 mg/kg once daily for 28 days	0%	11%	89%	Wildermuth et al 2013[63] *RCT*	1
Cetirizine§ (n = 32)	5 mg/cat once daily for 14 days	9%	16%	75%¶	Griffin et al 2012[36] *Case series*	2
Cyproheptadine HCl (n = 20)	2 mg/cat twice daily for 14 days	45%	0	55%	Scott et al 1998[45] *Case series*	2
Chlorpheniramine (n = 37)	2 mg/cat twice daily for 14 days	70%	0	30%‡	Miller and Scott 1990[37] *Case series* Scott and Miller 1995[44] *Case series*	2
Clemastine fumarate (n = 10)	0.34 mg/cat twice daily for two weeks, then 0.68 mg/cat twice daily for two weeks	50%	0	50%	Miller and Scott 1994[38] *Case series*	2
Mean outcomes		36%	6%	58%		

QOE quality of evidence, RCT randomised controlled trial, ReSt Retrospective study.

†See text for the definitions of the responses to treatment.

‡ Five of 11 nonresponders were concurrently treated with an omega3/omega6 essential fatty acid supplement.

§Median pruritus scores decreased from 5.25 to 5 (all cats) or 2.75 (responders).

¶ Includes five cats with a mild improvement; [e]all in one retrospective study.[31]

or placebo (n = 23) alone. The outcome was the time to relapse [≥2 point increase and/or score ≥ 4 in SCORFAD, ≥2 cm increase in pVAS or global assessment score of 3 (0–3 scale)]. One study assessed the preventive effects of omega-3 polyunsaturated fatty acids (omega3 PUFA) and luteolin supplementation on allergen-induced airway inflammation in eight *A. suum*-sensitised cats.[49]

Analysis of efficacy

In one prospective, double-blinded, placebo-controlled study, 15 cats either received evening primrose oil (EPO) or olive oil as the placebo for 12 weeks.[61] Mean pruritus, erythema, alopecia and overall scores did not improve significantly, nor was there a significant difference between groups. Two owners in each group considered their cats partially improved.[61] In another randomised study, 11 cats received either EPO (n = 6) or sunflower oil (n = 5) for 12 weeks. Mean overall clinical, self-trauma and crusted papule scores decreased by >50% in both groups.[54] In another study evaluating 14 cats with miliary dermatitis, seven of 14 showed good improvement after six weeks of 0.5 mL EPO/cat once daily.[53] When combined with fish oil for another six weeks, 11 of 14 cats showed a good response (the "good response" was not further defined). When given fish oil for another six weeks without the EPO, clinical signs recurred in 10 of 11 cats.[53] Five healthy cats and five cats with miliary dermatitis were administered an oil preparation with 33% omega 3 and omega 6 fatty acids in a ratio of 1:2, while five healthy cats and seven cats with miliary dermatitis were not treated.[55] Serum concentrations of eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3) increased in the treated cats and the miliary dermatitis resolved in three of five affected cats.[55] In a further study, healthy cats were given a fish oil (FO; EPA and DHA) or a flax seed oil [FSO; α-linolenic acid (ALNA, 18:3n-3)] supplement (n = 14 in each group) to a standard diet (n-6:n-3 ratio 20:1) to achieve an n-6:n-3 ratio of 5:1.[98] The supplements and diets were given for 12 weeks. Cutaneous reactions to histamine were reduced by 20–40% after FO and by 50% after FSO. FO raised leukotriene B (LTB) 5 levels and decreased the LTB4:LTB5 ratio; and FO and FSO decreased B, T-helper and total T-cell numbers, as well as proliferation to pokeweed mitogen. However, there was no effect on T-cytotoxic, natural killer and MHC class II cells, delayed type (type 4 cell-mediated) hypersensitivity, IL-2 expression or plasma IgG concentration, or concanavalin A or phytohaemagglutinin-triggered stimulation. No adverse effects were reported in any of these studies. In the uncontrolled trial of PEAum,[50] pruritus/erythema/alopecia improved in 64.3% of the cats and eosinophilic dermatitis lesions in 66.7% (three of 15 completely resolved). There was no change in mast cell numbers, although their granularity increased. No adverse effects were noted. In the RCT assessing maintenance of methylprednisolone-induced remission of FASS,[99] the mean time to relapse was significantly longer in the PEAum group (40.5 days; 13 of 19 cats relapsed) than the placebo group (22.2 days; 12 of 22 cats relapsed). Pruritus scores were significantly lower in the PEA-treated cats and there was no difference in lesion scores. Gastrointestinal effects were seen in four PEAum-treated cats (two withdrawn) and six placebo-treated cats (one withdrawn).

When eight asthmatic cats sensitised to *A. suum* received four weeks of omega-3 fatty acids (20 mg once daily) and luteolin (10 mg once daily), analysis of BALF total and differential cell counts did not reveal any significant differences between treated and untreated *A. suum*-stimulated cats.[49] However, concentrations of leukotriene A4 increased and airway responsiveness decreased after the supplement intake.[49]

Recommendations

Based on available data, there is limited evidence for moderate efficacy of EFA supplementation in cats with miliary dermatitis (QOE2; SOR B). A single study in healthy cats showed decreased reactivity to histamine with variable and moderate suppression of B- and T-cell function.[98] However, the clinical relevance of these findings remains unknown. There is moderate evidence of moderate efficacy for PEAum in FASS (QOE2; SOR B). There is insufficient evidence for the benefit of EFAs or PEAum in feline asthma.

Maropitant

Analysis of evidence

One open study evaluated maropitant at 2 mg/kg orally once daily for four weeks as treatment for cats with FASS.[52] Two randomised, placebo-controlled studies looked at the effect of maropitant on acute and chronic asthma, respectively, in experimentally sensitised cats.[78,79]

Analysis of efficacy

Maropitant decreased SCORFAD from 7.8 to 2.2 and pruritus scores from 7.1 to 2.3, respectively, in 12 cats with FASS.[52] Ten of those cats improved by >50% in lesions, and 11 of 12 by >50% in pruritus.

When administered to artificially sensitised cats with feline asthma at 2 mg/kg subcutaneously immediately after allergen challenge, maropitant did not diminish clinical scores or airway eosinophilia.[79] Likewise, there was no difference in clinical scores or airway eosinophilia when sensitised cats were administered maropitant at 2 mg/kg every 48 h for four weeks, although daily administration was not evaluated.[78]

Adverse effects

Increased salivation immediately after maropitant administration occured in two of 12 cats with FASS.[52]

Recommendations

There is limited evidence of good efficacy for maropitant in FASS (QOE2; SOR B). There is currently no evidence supporting the use of maropitant in cats with asthma (QOE1; SOR A).

Antibiotics

Analysis of evidence

There was one double-blinded, placebo-controlled study on the efficacy of oral amoxicillin-clavulanate

[Clavamox; Pfizer Animal Health (now Zoetis): Madison, NJ, USA] on eosinophilic plaques (amoxicillin-clavulanate 12–14.6 mg/kg twice daily, n = 4; placebo, n = 5) and indolent ulcers (amoxicillin-clavulanate 12–16.2 mg/kg twice daily, n = 4; placebo, n = 4).[75] All of the cats had cytological evidence of infection with neutrophils and intracellular bacteria at entry. The cats were treated for three weeks with no other treatment apart from flea control. No adverse reactions were reported. Another study evaluated the influence of doxycycline (5 mg/kg twice daily) on cats with experimentally induced asthma.[58]

Analysis of efficacy

Treatment with amoxicillin-clavulanate significantly reduced the mean lesion size of the eosinophilic plaques by 96% and indolent ulcers by 43% compared to the placebo (0% and 37% increases, respectively). There also was a decrease in the number of high-power microscope fields with cytological evidence of infection of 80% in the eosinophilic plaque group and 65% in the indolent ulcer group compared to placebo (16% decrease and 13% increase, respectively).[75] It needs to be pointed out that eosinophilic plaques, indolent ulcers and linear granulomas are reaction patterns associated with other underlying allergic and nonallergic causes, and those cats were diagnosed with secondary bacterial infections. In cats with asthma, four days of doxycycline did not influence the early or late asthmatic response.[58]

Recommendations

The small and well-conducted study in FASS provided evidence of high efficacy of amoxicillin-clavulanate in eosinophilic plaques and indolent ulcers (QOE 1, SOR A). However, it is unclear whether the improvement was the result of eliminating the bacteria from the lesions and/or immunomodulation, and whether treatment resulted in a sustained response. In addition, current antimicrobial treatment guidelines for skin infections (summarised in Brissot, 2016[100]) emphasise using topical antimicrobial therapy over systemic treatment and, where this is necessary, using the lowest tier, most narrow-spectrum drug possible for the shortest time required to clear the infection. Long-term therapy in the absence of a bacterial infection usually is discouraged, and veterinarians are advised to follow antimicrobial treatment guidelines established in their country of practice and/or in international consensus recommendations. So far, no evidence has been published supporting the use of antibiotics in feline asthma (QOE 2, SOR B).

Inhaled lidocaine.

Analysis of evidence

Nebulised lidocaine has received interest as a corticosteroid-sparing drug in human asthmatics, reducing airway resistance and peripheral blood eosinophilia.[101,102] It was evaluated in healthy and experimentally asthmatic cats in a cross-over study.[72] Five healthy and nine experimentally asthmatic cats received nebulised lidocaine at the dose of 2 mg/kg three times a day for two weeks in a cross-over design.[72]

Analysis of efficacy

In healthy cats, lidocaine did not significantly alter BALF eosinophilia or the concentration of methacholine increasing baseline airway resistance by 200%. There was no difference in eosinophil percentages in the BALF in asthmatic cats treated with lidocaine (36 ± 10%) or placebo (33 ± 6%). However, lidocaine significantly increased the concentration of methacholine increasing baseline airway resistance by 200% compared with placebo (10 ± 2 versus 5 ± 1 mg/mL).[72] Adverse effects were not seen with nebulized lidocaine.

Recommendations

Based on this one study, lidocaine may serve as adjunctive therapy in feline asthmatics with mild beneficial effects on airflow obstruction (QOE2; SOR B).

Mesenchymal stem cell therapy

Analysis of evidence

Adipose-derived mesenchymal stem cells (MSC) were evaluated in a small RCT in an experimental feline asthma model.[73] In this pilot study, allogenic adipose-derived MSCs were administered in five intravenous infusions at D0, D14, D28, D98 and D130 to four of six cats experimentally sensitized with Bermuda grass while two cats were treated with placebo.[73] BALF eosinophilia was evaluated at seven time points over nine months, along with blood samples to evaluate T-lymphocyte phenotype, total Bermuda grass allergen-specific lymphocyte proliferation, IL-10 production from lipopolysaccharide (LPS)-stimulated whole blood, and numbers of IL-10-producing cells. Additionally, thoracic computed tomography (CT) in conjunction with abbreviated pulmonary function testing was compared to that of healthy cats used as controls.

Analysis of efficacy

Diminished airway hyper-responsiveness was noted in all MSC-treated compared with the placebo-treated cats at D133. Lung attenuation and bronchial wall-thickening scores consistent with decreased airway remodelling were significantly reduced in MSC-treated versus untreated asthmatic cats.[73]

Recommendations

There is limited evidence of mild-to-moderate long-term efficacy of MSC in the treatment of feline asthma (QOE2; SOR B).

Discussion

To the best of the authors' knowledge, this is the first systematic review of therapeutic interventions for the feline atopic syndrome, both for FASS and feline asthma. Such reviews are standard practice in similar human and canine conditions, where the evidence is used as a base for treatment guidelines.[6,103] The data evaluated in this review have been used to provide a summary of treatment recommendations (Table 10). Clinicians should note that these recommendations do not imply that all of the listed treatments should be used in all patients, nor that they should be considered in this order.

Table 9. Responses to treatment with fatty acids in 37 cases with feline atopic skin syndrome (FASS)

Fatty acids (number of cats evaluated)	Dose	Responses[†] 36%	6%	58%	References Type of study	QOE
Evening primrose oil (n = 7)	0.5 mL/cat once daily		2/7	5/7	Logas and Kunkle 1993[61] *RCT*	1
Evening primrose oil/fish oil (n = 14)	0.5 mL/cat once daily	11/14			Harvey 1993[53] *Open study*	2
Evening primrose oil (n = 6)	0.25 mL/cat once daily for 12 weeks	Mean overall clinical scores decreased from 7 to 2.2, self trauma scores from 50 to 12 and crusted papule score from 8 to 2			Harvey 1993[54] *RCT*	2
DVM Derm Cap Liquid (n = 10)	0.2 mL/kg once daily for 14–44 days	5/10		5/10	Miller and Scott 1993[39] *Case series*	2
Mean outcomes		52%	6%	42%[‡]		

QOE quality of evidence, RCT randomised controlled trial.
[†] See text for details of the outcome measures.
[‡] In one study, only the good-to-excellent responders were mentioned[53] and it is unclear if the residual three cats were partial or poor responders and in order not overestimate the treatment benefits of EFAs we assumed that the residual cases showed a poor response.

Table 10. Summary of treatment recommendations for cats with atopic syndrome

Treatment or intervention	Recommendation	QOE	SOR
Allergen avoidance	Limited evidence of moderate efficacy in feline asthma Insufficient evidence in FASS	3	C
Allergen immunotherapy	Limited evidence of moderate (feline asthma) to good (FASS) efficacy	2	B
Systemic glucocorticoids	Satisfactory evidence of good efficacy in FAS and feline asthma	1	A
Topical glucocorticoids:	Limited evidence of good efficacy in FASS	2	B
Hydrocortisone aceponate	Satisfactory evidence of good efficacy in feline asthma	1	A
Inhaled glucocorticoids			
Ciclosporin	Satisfactory evidence of good efficacy in FASS	1	A
	Insufficient evidence in feline asthma		
Oclacitinib	Limited evidence of good efficacy in FASS	1	A
	Limited evidence of low efficacy in feline asthma	2	B
Bronchodilators	Recommended for acute asthma attacks	3	C
	Limited evidence of poor efficacy in feline asthma	2	B
	Clinical use alongside inhaled glucocorticoids	3	C
Oral H1R-antihistamines	Limited evidence of low to moderate efficacy in FASS	2	B
	Limited evidence of poor efficacy in feline asthma	2	B
Essential fatty acids	Limited evidence of moderate efficacy in FASS (miliary dermatitis)	2	B
PEAum	Limited evidence of moderate efficacy in FASS	2	B
	Insufficient evidence in feline asthma		
Maropitant	Limited evidence of good efficacy in FASS	2	B
	Good evidence of poor efficacy in feline asthma	1	A
Antibiotics	Limited evidence of good efficacy in FASS if there is confirmed infection	2	B
Doxycycline	Limited evidence of poor efficacy of doxycycline in asthma	2	B
Inhaled lidocaine	Limited evidence of low efficacy in feline asthma	2	B
Stem cell therapy	Limited evidence of low to moderate efficacy in feline asthma	2	B
	Insufficient evidence in FASS		

FAS feline atopic syndrome, FASS feline atopic skin syndrome, QOE quality of evidence, SOR strength of recommendation.

Clinical manifestations of FASS are common problems that decrease the QoL of affected cats and their owners.[62] They appear to be chronic conditions that require long-term management. It is therefore important to eliminate fleas, *Demodex gatoi*, and other ectoparasites and endoparasites, food allergens, bacterial skin infection/pyoderma, yeast overgrowth and differential diagnoses before making a final diagnosis. It also is likely that FASS and feline asthma have a multifaceted aetiology.[3] As in cAD and human asthma, treatments may need to be combined to optimise the outcome for each cat. Clinical trials usually are designed to evaluate the efficacy of a single treatment and therefore may underestimate the efficacy of combination treatment.

Treatment should be tailored to each cat, taking into account the severity, type and distribution of the lesions, and stage of the dermatitis and airway disease. It is likely that most cats will require more potent treatment (e.g. systemic glucocorticoids, topical and inhaled glucocorticoids, ciclosporin or oclacitinib) initially to induce remission. Treatment can then be tapered and/or switched to less potent treatments (e.g. ASIT, essential fatty acids and antihistamines) to maintain the remission.

These treatment recommendations should not be read as a "diktat", particularly considering the facts that many products are not approved for cats, pharmacokinetic data and dose-finding studies are lacking for most products,

and safety data beyond the studies discussed here also are not available for most drugs. Not every treatment will be effective, tolerated or suitable in every cat. It is up to the individual clinician to evaluate their patient and discuss the advantages and disadvantages of each treatment option with the owners. This will include potential adverse effects, ease-of-administration, and cost as a single treatment or in combination. The owners' preferences as well as concurrent conditions and medication also will have to be accounted for. Nevertheless, the treatments recommended in this review should be considered before moving to alternatives with less evidence of efficacy and safety in FASS or feline asthma.

The recommendations in this review were derived largely from the results of clinical trials reporting statistically significant changes in various outcome measures. Following best practice, the recommendations were based on SORT scores[7] (Table 1), which are a simple and robust way of evaluating patient-orientated outcomes. However, clinicians should note that statistically significant improvements do not necessarily mean that these are clinically significant (i.e. lead to an acceptable improvement in clinical signs and in the QoL for the patient and owner). Moreover, individual animals may have a better or worse response than the mean outcome reported in a clinical trial. In addition, most studies performed on feline asthma utilised small numbers of cats experimentally sensitised to HDN, Bermuda grass or *A. suum* and more studies are urgently needed assessing treatment options for naturally occurring feline asthma, as well as evaluating adverse effects of those therapies with long-term use.

This review highlights the limited evidence for some treatments in FAS. The analysis of the clinical trials was variously affected by small group sizes, uncontrolled studies, retrospective studies, deficient data reporting, and variable and nonvalidated outcome measures. Compared to the dog, where a rapidly increasing number of randomised, controlled trials are being published, fewer studies of lesser quality are found evaluating allergic cats and more randomised controlled trials are urgently needed. Wherever possible, the quality of clinical trials should be improved by designing double-blinded RCTs, using power calculations to determine adequate treatment cohorts, and using validated outcome measures (e.g. the SCORFAD[84,85] and pVAS[82] scales or lung function studies), similar to those published for dogs with atopic dermatitis[104] and in human asthma.[105,106] Other outcome measures relevant to the clinical significance of therapeutic interventions include a QoL score,[86] and global scores for efficacy, tolerance and ease-of-administration. Minimum datasets should include intention-to-treat data with means or medians and an appropriate measure of variance (e.g. standard deviation or 95% confidence intervals). Additional useful outcomes include the proportion of cats reaching certain clinical thresholds (e.g. >50% and >75% improvements in pruritus and lesion scores or in lung function). Statistical tests should be appropriate to the data and, where necessary, advice from a statistician should be sought during design of the study.

The recommendations in this review are derived from an evidence-based consensus supporting use of an intervention and do not imply endorsement of specific therapeutic options or products. Furthermore, these recommendations do not consider availability or licensing specifics in individual countries. Clinicians should therefore choose individual treatments based on legal and ethical standards in their own country of practice.

This systemic review of therapeutic interventions has provided evidence for treatment recommendations in FAS (Table 10). It is hoped that these will aid clinicians in designing treatment plans to improve the QoL of their patients and their owners. The review highlighted shortfalls in the quantity and quality of published data. Clinicians are therefore encouraged to publish good quality clinical trials assessing the efficacy of existing and novel treatments. Future reviews including such data will improve the strength and breadth of treatment recommendations for FAS.

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Résumé

Contexte – La maladie cutanée allergique féline et l'asthme sont fréquents en pratique vétérinaire.

Objectifs – Fournir des recommandations basées sur les preuves pour les praticiens des petits animaux de compagnie sur le traitement du syndrome atopique félin (FAS).

Matériels et méthodes – Les auteurs ont revu la littérature disponible avant février 2020, préparé une revue détaillée de la littérature basée sur les preuves et fait des recommandations à partir des niveaux de preuves.

Résultats – Soixante-six articles et résumés ont été identifiés décrivant les traitements pour FAS et évalués pour établir des recommandations de traitement. Pour de nombreuses options de traitement, les articles étaient rétrospectifs, des études ouvertes ou des cas cliniques.

Conclusion et importance clinique – Dans cette revue, il y a un bon niveau de preuve de l'efficacité des corticoïdes systémiques et de la ciclosporine, et des preuves imitées de l'efficacité des corticoïdes topiques, de l'oclacitinib et de l'immunothérapie spécifique d'allergènes dans le syndrome cutané atopique félin. Les preuves montrent une efficacité faible à modérée des antihistaminiques, des acides gras essentiels et du palmytoyléthanolamide. Dans l'asthme félin, il y a de bonnes preuves de l'efficacité des corticoïdes oraux et inhalés, et peu de preuves d'efficacité modérée pour l'immunothérapie spécifique d'allergènes. Les preuves supportent une efficacité faible à modérée des cellules souches mésenchymateuses, de la lidocaïne inhalée et de l'oclacitinib comme traitements de l'asthme félin. Pour presque toutes les options thérapeutiques (à l'exception des corticoïdes et de la ciclosporine), davantage d'études contrôlées randomisées sont nécessaires.

RESUMEN

Introducción – la enfermedad alérgica de la piel y el asma felinas ocurren regularmente en la medicina veterinaria de animales pequeños.

Objetivos – proporcionar recomendaciones basadas en evidencias para los veterinarios de pequeños animales sobre el tratamiento del síndrome atópico felino (FAS).

Métodos y materiales – los autores revisaron la literatura disponible antes de febrero de 2020, prepararon una revisión detallada de la literatura basada en evidencias y formularon recomendaciones basadas en evidencias evaluadas.

Resultados – se identificaron sesenta y seis artículos y resúmenes que describen intervenciones de tratamiento para FAS y se evaluaron para establecer recomendaciones de tratamiento. Para muchas opciones de tratamiento, los artículos eran retrospectivos, estudios abiertos o informes de casos.

Conclusión y relevancia clínica – en esta revisión, hubo pruebas sólidas de la eficacia de los glucocorticoides sistémicos y ciclosporina, y pruebas limitadas de la eficacia de los glucocorticoides tópicos, oclacitinib y la inmunoterapia específica con alérgenos en el tratamiento del síndrome de piel atópica felina. Las pruebas apuntaron a una eficacia de baja a moderada de los antihistamínicos, los ácidos grasos y la palmitoiletanolamida. En el asma felino, hubo buena evidencia de la eficacia de los glucocorticoides orales e inhalados, y evidencia limitada de eficacia moderada de la inmunoterapia específica con alérgenos. La evidencia apoyó una eficacia baja a moderada de las células madre mesenquimales, la lidocaína inhalada y el oclacitinib

como tratamientos para el asma felino. Para casi todas las opciones terapéuticas (con la excepción de glucocorticoides y ciclosporina), se necesitan más ensayos controlados aleatorios.

Zusammenfassung
Hintergrund – Allergische Hauterkrankungen der Katzen sowie Asthma treten in der Kleintierpraxis häufig auf.
Ziele – Es war das Ziel, Evidenz-basierte Empfehlungen für Kleintierpraktiker bei der Behandlung des felinen atopischen Syndroms (FAS) zu liefern.
Methoden und Materialien – Die Autoren führten eine Review der Literatur, die vor Februar 2020 zur Verfügung stand, durch und bereiteten eine detaillierte Evidenz-basierte Literatur Review vor und sprachen Empfehlungen, basierend auf der evaluierten Evidenz, aus.
Ergebnisse – Sechsundsechzig Papers und Abstracts, die Behandlungen des FAS beschrieben, wurden identifiziert und evaluiert, um Behandlungsempfehlungen zu schaffen. Für viele Behandlungsoptionen standen retrospektive Papers, offene Studien und Fallberichte zur Verfügung.
Schlussfolgerungen und klinische Bedeutung – In dieser Review ergab sich eine gute Evidenz für die Wirksamkeit der systemischen Glucokortikoide und Ciclosporin, sowie eine limitierte Evidenz für die Wirksamkeit topischer Glucokortikoide, Oclacitinib und Allergen-spezifischer Immuntherapie für das feline atopische Hautsyndrom. Die Evidenz zeigte eine niedrig-bis-moderate Wirksamkeit von Antihistaminen, essentiellen Fettsäuren und Palmitoyl Ethanolamid. Bei Katzenasthma ergab sich eine gute Evidenz für orale oder inhalierte Glucokortikoide und eine limitierte Evidenz von moderater Wirksamkeit für Allergen-spezifische Immuntherapie. Die Evidenz stützte eine niedrig-bis-moderate Wirksamkeit der mesenchymalen Stammzellen, von inhaliertem Lidocain und Oclacitinib als Behandlungen für felines Asthma. Für fast alle therapeutischen Optionen (mit Ausnahme der Glucokortikoide und Ciclosporin) sind weitere, randomisierte kontrollierte Studien nötig.

要約
背景 – のアレルギー性皮膚疾患および喘息は小動物の診療で定期的に発生する。
目的 – 研究の目的は、猫アトピー症候群 (FAS) の治療に関するエビデンスに基づく推奨事項を小動物の施術者に提供することであった。
材料と方法 – 著者は、2020年2月より前に入手可能な文献をレビューし、詳細なエビデンスに基づく文献レビューを作成し、評価されたエビデンスに基づいて推奨を行った。
結果 – FASの治療介入を説明する66の論文および要約を特定し、治療の推奨事項を確立するため評価した。多くの治療オプションについて、論文は遡及的、公開研究または症例報告であった。
結論と臨床的関連性 – 本レビューでは、全身性糖質コルチコイド製剤およびシクロスポリン製剤の有効性に関するエビデンスがあり、猫アトピー性皮膚症候群における外用糖質コルチコイド製剤、オクラシチニブ、およびアレルゲン特異的免疫療法の有効性に関するエビデンスは限定的であった。エビデンスは、抗ヒスタミン薬、脂肪酸、パルミトイルエタノールアミドの有効性が低から中程度であることを示している。ネコ喘息では、経口および吸入糖質コルチコイド製剤の有効性に関する十分なエビデンスがあり、アレルゲン特異的免疫療法に対する中程度の有効性の限定的なエビデンスがあった。エビデンスは、ネコ喘息の治療としての間葉系幹細胞、吸入リドカインおよびオクラシチニブの低から中程度の有効性を支持した。ほぼすべての治療オプション (糖質コルチコイドおよびシクロスポリン製剤を除く) については、さらにランダム化比較試験が必要である。

摘要
背景 — 猫过敏性皮肤病和哮喘在小动物临床中经常发生。
目的 — 为小动物从业者提供关于猫特应性综合征(FAS)治疗的循证建议。
方法和材料 — 作者审查了2020年2月之前的可用文献，准备了详细的循证文献综述，并根据证据评价提出建议。
结果 — 找出66篇报告FAS治疗干预的论文和摘要，并进行评价以确立治疗建议。许多关于治疗选择的论文为回顾性、开放性研究或病例报告。
结论和临床相关性 — 在本综述中，治疗猫特应性皮肤综合征，全身性糖皮质激素和环孢素的疗效证据充分，外用糖皮质激素、奥拉替尼和过敏原特异性免疫的疗效证据有限。证据表明，抗组胺药、脂肪酸和十六酰胺乙醇的疗效为低至中度。对于猫哮喘，口服和吸入糖皮质激素的疗效证据良好，过敏原特异性免疫治疗的中度疗效证据有限。证据支持间充质干细胞、吸入利多卡因和奥拉替尼治疗猫哮喘疗效为低至中度。对于几乎所有治疗选择 (糖皮质激素和环孢素除外) ，需要更多的随机对照试验。

Resumo
Contexto – A asma e a dermatopatia alérgica felina ocorrem regularmente na clínica de pequenos animais.
Objetivos – Fornecer recomendações baseadas em evidências para clínicos de pequenos animais sobre o tratamento da síndrome atópica felina (SAF).

Métodos e materiais – Os autores revisaram a literatura disponível até fevereiro de 2020, prepararam uma revisão de literatura baseada em evidências e fizeram recomendações baseadas nas evidências avaliadas.

Resultados – Sessenta e seis artigos e resumos foram identificados descrevendo o tratamento da SAF e avaliados para estabelecer as recomendações de tratamento. Para muitas opções de tratamento, os artigos foram retrospectivos, estudos abertos ou relatos de caso.

Conclusão e relevância clínica – Nessa revisão, houve boa evidência de eficácia de do uso de corticoides sistêmicos e ciclosporina, e evidência limitada da eficácia de glicocorticoides tópicos, oclacitinib e imunoterapia alérgeno-específica na síndrome atópica cutânea felina. Houve evidência de eficácia baixa a moderada para anti-histamínicos, ácidos graxos palmitoil etanolamida. Na asma felina, houve boa evidência de eficácia para glicocorticoides por via oral ou inalada, e evidência limitada de eficácia moderada para imunoterapia alérgeno-específica. As evidências demonstraram eficácia baixa a moderada para a para células-tronco mesenquimais, lidocaína inalada e oclacitinib no tratamento da asma felina. Para quase todas as opções terapêuticas (com exceção dos glicocorticoides e ciclosporina), são necessários mais estudos randomizados e controlados.

