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Original article

Evaluation of a hydrolysed salmon and pea hypoallergenic diet application in dogs and cats with cutaneous adverse food reaction

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Abstract

Cutaneous adverse food reaction (CAFR) is a common disease, affecting about 1-2% of dogs and cats. Diagnosis of the CAFR is made through elimination diet coupled with diet challenge, as methods like skin tests, patch tests, basophil degranulation tests and assessment of IgG and IgE serum levels are not sensitive enough. A partially hydrolysed salmon and pea hypoallergenic diet was evaluated in the diagnosis and treatment of CAFR in dogs and cats.

The diet was used in the treatment of 13 dogs and 12 cats for 10 weeks. The Pruritus Visual Analog Scale (PVAS; dogs and cats), Canine Atopic Dermatitis Extent and Severity Index (CADESI-04; dogs) and the Scoring Feline Allergic Dermatitis (SCORFAD; cats) were used for effectiveness evaluation.

In dogs, a significant decrease was reported in both CADESI-04 (from 17.3 ± 7.5 to 10.15 ± 7.4 ; p=0.028) and PVAS (from 7 ± 1.3 to 4.76 ± 1.8 ; p=0.003) after four weeks of treatment. Also in cats, both the PVAS (from 6.75 ± 1.8 to 4 ± 2.3 ; p=0.006) and SCORFAD (from 4.16 ± 1.9 to 2.58 ± 1.2 ; p=0.029) decreased significantly after four weeks. After eight weeks, a significant improvement was observed in almost all the animals. Evaluated diet was useful in the treatment of the CAFR in dogs and cats.

Key words: cats, cutaneous adverse food reaction, dogs, hypoallergenic diet

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Introduction

Cutaneous adverse food reactions (CAFRs) are one of the most common dermatological problems in dogs and cats. Published studies place it as the second or third (after atopic dermatitis and allergic flea dermatitis) skin hypersensitivity disease. Its cases represent about 1 to 2% of all diseases and about 24% of skin diseases in dogs. In cats, however, prevalence is less than 1% of all diseases and 3 to 6% of dermatological problems (Olivry and Mueller 2016). Adverse food reactions involve immunological (food allergies) and non-immunological (food intolerance) processes (Anderson 1986). The mechanism of reaction development relies on IgE-dependent immediate hypersensitivity and delayed hypersensitivity (type IV), as well as type III hypersensitivity (Scott et al. 2001, Martin et al. 2004). Allergens inducing sensitization are mainly glycoproteins. In dogs, they most often derive from beef, dairy products, chicken, and wheat (Scott et al. 2001, Chesney 2002, Martin et al. 2004, R. S. Mueller et al. 2016). In cats, allergies are caused by the ingestion of beef, fish and chicken (Olivry and Mueller 2016). Adverse reaction to more than one antigen in an individual is common. This phenomenon occurs in about 40% of dogs and about 50% of cats (Guilford 1996, Guilford et al. 2001). A clinical manifestation of the CAFR is atopic dermatitis (food-induced atopic dermatitis) (White and Sequoia 1989, Scott et al. 2001). In case of cats, there are four syndromes described as the cutaneous signs of food allergies: self-induced alopecia, head-and-neck ulcerative dermatitis, eosinophilic dermatitis and miliary dermatitis (White and Sequoia 1989, Wills and Harvey 1994, Scott et al. 2001).

Diagnosis of the disease is time-consuming. Proper elimination diet should be implemented for a minimum period of nine-ten weeks, followed by food challenge, which should take additional one-two weeks (Olivry and Mueller 2020). It is not possible to distinguish the disease clinically from environmentally-induced atopic dermatitis in either dogs or cats (DeBoer and Hillier, 2001, Olivry and Mueller 2016).

Serological tests involving the measurement of specific IgG and IgE antibodies in serum with western blot have not yet been clinically validated for diagnostics due to its low sensitivity (Mueller and Tsohalis 1998, Foster et al. 2003, Jackson et al. 2003, Martin et al. 2004, Ricci et al. 2010, Zimmer et al. 2011, Bethlehem et al. 2012, Favrot et al. 2017). Limited research on serological tests has been performed in cats and, similarly to dogs, it is believed that the concentration of specific antibodies is not reliable in the diagnosis of food allergies. It was reported that levels of antibodies do not differ significantly between sick and healthy cats (Belova et al. 2012).

A strict elimination diet trial with a novel or hydrolyzed protein source, followed by a challenge with the original diets is the recommended diagnostic procedure. Elimination diet should be implemented for a minimum period of nine-ten weeks (Rosser 2013). It can be prepared independently at home by the owner and it is based on foods that have not been given to the particular individual in the history. The second method is to use a commercially available special diet for animals with food allergies (Scott et al. 2001, Rosser 2013). Diets based on hydrolyzed protein represent a new generation of elimination diets. By hydrolyzing proteins prior to food incorporation, allergenicity is reduced (Biourge et al. 2004). Partial hydrolyzation of proteins attenuates allergenic potential through chemical and enzymatic hydrolysis, reducing molecular weight and peptide size in prepared hypoallergenic diet. The process relying on enzymatic or chemical hydrolysis, depending on the manufacturer, results in peptides under 5kDa. In comparing partially to extensively hydrolyzed diets, partially hydrolyzed are characterized by generally lower cost, protein content, osmolality and higher palatability (Alexander et al. 2010). Affordability and palatability can be important factors of successful elimination diet in dogs and cats.

The aim of the study was to evaluate the effectiveness of the partially hydrolyzed salmon and pea hypoallergenic diet (Brit Hypoallergenic Dogs, Vafo Praha, Czechia), in animals with CAFR.

Materials and Methods

Animals

A group of 19 dogs with signs of atopic dermatitis were selected for the study. In cats, 18 individuals with signs of allergic dermatitis (pruritus of the head and neck, miliary dermatitis or extensive alopecia) were selected for the study. In certain animals (five dogs and three cats), CAFR had been previously confirmed, but for various reasons related to the accidental ingestion of food containing particular antigens, their clinical symptoms had returned. In other animals, the introduction of diet was used to differentiate atopic dermatitis from food allergies, which are clinically indistinguishable. The clinical criteria of Favrot et al. (2010) (Set 2) (Favrot et al. 2010) were applied to diagnose atopic dermatitis, respectively the diagnostic criteria of Favrot et al. (2011) were used for cats, meeting at least six criteria, with flea allergies excluded (Favrot et al. 2012). Study subjects were patients of the Veterinary Faculty within the University of Life Sciences in Lublin.

All of the dogs and cats that participated in this study were client-owned animals that joined the study



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during their treatment process. All of the owners were informed on their animals' participation in the study and were only involved after obtaining their written consent. A dietary history was collected and only animals with no history of eating salmon were included to the study.

Diagnostic procedures

Other pruritic diseases (fungal, parasitic, or pyodermas) were excluded before with a Wood's lamp test and microscopic examination of hair, skin scrapings and cytological examination. All qualified patients were receiving regular anti-flea prophylaxis to exclude a flea allergy at least two months before study inclusion.

Individuals not improving significantly after ten weeks of hypoallergenic diet ingestion (six dogs and six cats) were additionally evaluated with another elimination diet (Royal Canin Hypoallergenic, Royal Canin USA Inc.; St Charles, MO, USA) with no clinical improvement. These animals were later diagnosed with atopic dermatitis, *sensu stricto* (dogs), or allergic dermatitis not caused by a flea allergy/allergy to food (cats). These individuals were excluded from the study. Their treatment was successfully conducted through symptomatic antipruritic treatment. Individuals involved in study did not receive any antipruritic drugs and antibiotics during the study period.

For further statistical analysis, 13 dogs (10 females and 3 males) (three french bulldogs, three spitzs, four mongrel dogs, boxer, labrador, maltese) aged 1 to 9.75 years (median 2.25 years) and 12 cats (7 females and 5 males) (one Persian cat, one Maine coon, two Siamese, eight European shorthair) between 2 and 12 years (median 6 years) were involved.

After describing the nature of the study the owner was provided (free of charge) with an elimination diet based on partially hydrolyzed salmon and pea hypoallergenic diet (Brit Hypoallergenic). Before the beginning of diet administration the owner was instructed to feed this diet exclusively over the subsequent ten weeks. Care was taken to explain the importance of excluding all other food sources, including treats, snacks etc. Compliance was assessed by owner-interview at each of control visits.

After complete recovery, recognized by lack of pruritus and resolving of skin lesions assessed by clinician, animals were subjected to their usual diet. Relapse (erythema, mild pruritus) of disease signs after this challenge confirmed CAFR diagnosis. Observed time of relapse following re-challenge was between two days to two weeks.

Methods

To assess the effectiveness of the diet in dogs, the Pruritus Visual Analog Scale (PVAS) and Canine Atopic Dermatitis Extent and Severity Index (CADESI) were used.

The CADESI-04 system was used to grade the skin lesions (Olivry et al. 2014). The severity of pruritus was assessed according to the numerical scale of the PVAS (0-10) (Hill et al. 2007, Rybníček et al. 2009). The CADESI and PVAS assessments were performed in the dogs before treatment (T0), and 5 times after a two-week interval (after two, four, six, eight and ten weeks of study).

In cats, clinical evaluation was performed at the same intervals as in the dog group. The severity of pruritus was assessed according to the same methodology with the PVAS numerical scale. The severity of skin lesions was assessed with the Scoring Feline Allergic Dermatitis (SCORFAD) system, calculated according to the method given by Steffan et al. 2012 (Steffan et al. 2012).

The effectiveness of treatment was evaluated by assessing the number of individuals who reported a more than 50% reduction of pruritus (assessed with the PVAS) and clinical symptoms (assessed using the CADESI-04 or SCORFAD).

The procedures used were non-invasive and, in accordance with the regulations in Poland, were classified as routine medical and veterinary procedures, which do not require the consent of an ethics committee.

Statistical analysis

The normality of distribution was examined using the Shapiro-Wilk test. Results were compared to assessment scores from involvement of study for each individual. Statistical significance between the results was calculated using a Mann-Whitney U rank test. In all cases Bonferroni correction was made. The values at p<0.05 were considered significant. All calculations were made with the use of Statistica 10 software (Statsoft, Tulsa, OK, USA).

Results

Dogs included in the statistical analysis on the day before the onset of diet administration were characterized by the CADESI and PVAS, with mean values±standard deviation of 17.3±7.5 and 7±1.3, respectively. During the elimination diet, there was a gradual improvement in the clinical signs of the animals based on a decrease in the intensity of pruritus and a decrease in the CADESI-04 scores. After just two

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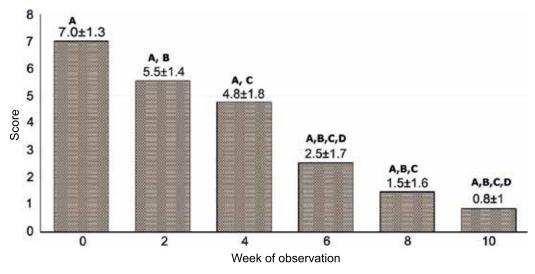


Fig. 1. Pruritus Visual Analog Scale (PVAS) values in dogs in individual weeks of observation. A,B,C,D – statistically significant differences.

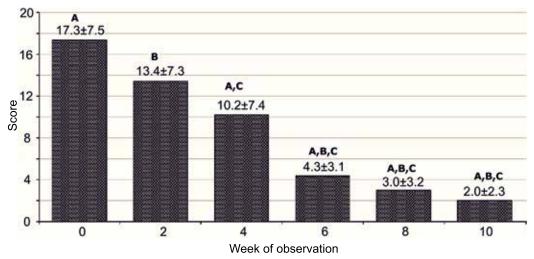


Fig. 2. Canine Atopic Dermatitis Extent and Severity Index (CADESI-04) values in dogs in individual weeks of observation. **A,B,C** statistically significant differences.

weeks of administering the diet, there was a statistically significant decrease in pruritus expressed with the PVAS 5.53±1.5 (p=0.018). However, CADESI-04 did not show any statistically significant reduction at the same time; a decrease to the value of 13.38±7.3 was noted (p=0.19). After four weeks, the CADESI-04 decrease was significant, reaching 10.15 ± 7.4 (p=0.028) and the PVAS 4.76±1.8 (p=0.003). The CADESI-04 and PVAS continued to decrease during the diet, but after eight weeks this decrease reached a point where it was no longer significant and did not differ statistically (between eight and ten weeks p=0.41 for both coefficients). At the closing of observation after ten weeks of diet administration, the CADESI-04 score was at 2±2.3 and the PVAS was at 0.84±1. Detailed results regarding the PVAS and CADESI-04 in dogs are presented in Figs. 1 and 2.

The cats had a mean SCORFAD value of 4.16±1.9 and a PVAS value of 6.75±1.8 at the beginning of the

diet. During the diet, similarly as in the dogs, there was a gradual improvement in clinical conditions based on a decrease in pruritus intensity and a decrease in the SCORFAD score. The decrease of these values progressed slower than in the dogs. After two weeks of the diet, there was no significant decrease in the PVAS $(5.83\pm2.2; p=0.39)$ and SCORFAD $(3.83\pm; p=0.51)$. After four weeks, both the PVAS (4; p=0.006) and SCORFAD (2.58±1.2; p=0.029) had decreased significantly when compared to the pre-diet values. The PVAS and SCORFAD then decreased further during the whole diet period. However, after eight weeks, the decrease was insignificant and did not differ significantly (between eight and ten weeks for PVAS p=0.08, SCORFAD p=0.14). At the end of observation, after 10 weeks, both the PVAS and SCORFAD were at 0.41. Detailed results regarding the PVAS and SCORFAD in cats are presented in Figs. 3 and 4.

After two weeks of treatment, none of the dogs had



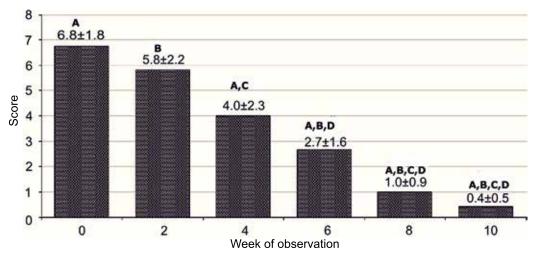


Fig. 3. PVAS values in cats in individual weeks of observation. A,B,C,D – statistically significant differences.

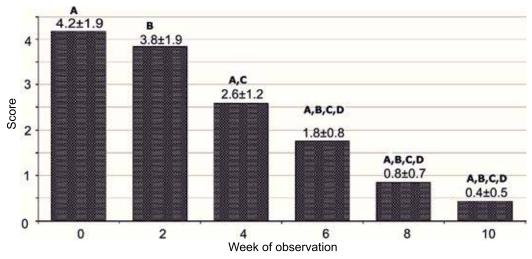


Fig. 4. Scoring Feline Allergic Dermatitis (SCORFAD) values in cats in individual weeks of observation. **A,B,C,D** – statistically significant differences.

Table 1. Number of animals with an over 50% reduction in pruritus and clinical symptoms in time.

	Weeks	0	2	4	6	8	10
Dogs	PVAS CADESI-04	0	0 2	2 7	9 12	9 13	13 13
Cats	PVAS SCORFAD	0	1 0	3 3	5 7	12 11	12 11

a decrease in pruritus by more than 50% when compared to the PVAS baseline, and in cats, in one subject only, the pruritus intensity decreased below 50%. In case of the CADESI-04 in dogs after two weeks, a decrease in the value by more than 50% was observed in two individuals. In cats, after two weeks, there were no animals where the SCORFAD had decreased significantly. Only after four weeks of treatment did a number of animals demonstrate a more significantly improved condition (for the PVAS, two dogs (10.5%) and three cats (16.6%), for the CADESI-04, seven dogs (36.8%) and three cats (16.6%)). It was only after six weeks

of treatment that most of the dogs achieved any apparent clinical improvement and showed a decrease in the CADESI-04 score of more than 50%, which occurred in 12 animals (92.3%). Pruritus assessments were also more than 50% in nine animals (69.23%). In cats, the improvement progressed more slowly because it was only after six weeks that the PVAS decreased in five cats (41.66%); in less than half of the group. Additionally, the SCORFAD decreased in seven individuals (58.33%). After eight weeks a clinical improvement was observed in both of the studied groups by more than 50%. For dogs pruritus decreased in nine indivi-



duals (75%) in the PVAS and for all animals (100%) in the CADESI-04 score. In cats, improvement was observed in the PVAS and in 11 individuals for the SCORFAD (91.66%).

The number of individuals that improved, reporting over a 50% reduction in pruritus and the severity of lesions, is presented in Table 1.

Discussion

In patients participating in diet assessment, the most important clinical factors were taken into account: the intensity of pruritus and severity of clinical changes. In order to avoid medications influence on the results of the study, we decided to withdraw pharmaceuticals, which was discussed and accepted by the owners, prior to involvement in the study. Statistically significant improvement was initially found after four weeks of the diet. After eight weeks, maximal effectiveness was achieved, and further improvement was not significant and did not differ statistically. A two-week diet period is not sufficient for owners or veterinarians to observe any improvement in the clinical condition of the animals.

The duration of elimination diets, which is necessary for the resolution of clinical symptoms, varies in the available literature. Some authors believe that as soon as three weeks after the implementation of a rigorous diet the clinical state of allergic animals could be significantly improved (Walton 1967, Anderson 1986, White 1986, Jeffers et al. 1991, Mueller and Tsohalis 1998). Such a short period would not usually be sufficient for most patients, as observed in our study. After three weeks, approximately 25% of the sick animals showed some improvement (Rosser 1993). Faster improvement occurred in patients with gastrointestinal symptoms. In these, a diet of two to four weeks would generally be sufficient to resolve symptoms (Roudebush et al. 2000). In our research, in most of the individuals a four-week period was sufficient to demonstrate apparent clinical improvement. Continuous use of the diet in animals with food allergies led to a resolution of allergic symptoms or their significant reduction after six to ten weeks from the commencement of the elimination diet, which was also observed in our study. Some cases require an extension of the diet up to as long as 13 weeks (Denis and Paradis 1994).

In CAFR diagnosis hydrolyzed hypoallergenic diets were reported as an effective method. Biourge et al. successfully used hydrolyzed diet (hydrolyzed soy) in dogs with cutaneous adverse food reactions with improvement after two months of therapy. In this case a partially hydrolyzed diet was used. It required detailed dietary history and in cases with no improvement, eva-

luation with another elimination diet is recommended (Biourge et al. 2004). Despite a higher molecular mass and length of peptides, it was assumed that the partial hydrolyzation of the investigated diet would provide a comparative clinical response to that of an extensively hydrolyzed diet. Clinical improvement of animals' state confirmed the assumption. For long-term effectiveness of therapy, palatability of the diet and financial factors needs to be taken into account. Partial hydrolyzation lowers the costs of diet for both diagnostic and therapeutic purposes maintaining favorable level of palatability.

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In our study, we decided to withdraw any animal with no improvement after ten weeks of elimination trails for ethical reasons, recommending another elimination diet. Diagnosis of environmental atopic dermatitis in those animals, sensu stricto, was later confirmed through lack of improvement with second hypoallergenic diet and successful symptomatic antipruritic therapy.

Conclusions

To conclude, a hydrolyzed salmon and pea hypoallergenic diet (Brit Hypoallergenic) is effective in both the diagnosis and treatment of food allergies in dogs and cats. This diet brings statistically significant improvement to individuals with diagnosed food allergies after about four weeks of use, and most animals recover (reduction of lesions and pruritus by over 50% of the initial value) after six weeks for dogs and eight weeks for cats. The Brit Hypoallergenic diet can be successfully used as a product for both the diagnosis and treatment of food allergies.

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