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Original Article
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Efficacy of hydrolyzed soy dog food and homemade food with original protein in the control of food-induced atopic dermatitis in dogs[1]

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ABSTRACT.- Vandresen G. & Farias M.R. 2018. **Efficacy of hydrolyzed soy dog food and homemade food with original protein in the control of food-induced atopic dermatitis in dogs**. *Pesquisa Veterinária Brasileira 38(7):1389-1393*. Escola de Ciências Agrárias e Medicina Veterinária, Pontifícia Universidade Católica do Paraná, Rodovia BR-376 Km 14, Costeira, São José dos Pinhais, PR 83010-500, Brazil. E-mail: grazivan@gmail.com

Trophoallergens are specific components of food or its ingredients, able to precipitate the atopic eczema at 19.6% to 30% of the dogs with atopic dermatitis (AD). This study evaluated the efficacy of hydrolyzed soy dog food and homemade food with unusual protein in the control of chronic pruritus in dogs with AD. For this, twenty-eight dogs with AD were selected. AD diagnosis was based on Favrot's criteria. The animals were separated in two groups; one group consumed hydrolyzed soy dog food while the other group consumed homemade food with protein sources and original carbohydrates. They were evaluated every two weeks by the Rybnicek and CADLI scale over 60 days. Animals in the group that consumed hydrolyzed soy dog food presented a reduced score of pruritus (Rybnicek scale) on days +15, +30, +45 and +60 (P<0.01) compared to day 0. While the dogs in the homemade food group have not presented a significant difference (P>0.05) in 60 days of treatment. When evaluated by the Canine Atopic Dermatitis Lesion Index (CADLI), dogs treated with soy hydrolyzed dog food had a partial improvement on days +45 (P<0.05) and +60 (P<0.01) compared to day 0, while the dogs in the second group did not show improvements (P>0.05) in 60 days of treatment. In conclusion, soy hydrolyzed dog food has proved effective to partially control clinical signs of food-induced atopic dermatitis; however, it is not effective for the complete control of the disease.

INDEX TERMS: Soy dog food, homemade food, original protein, food induction, atopic dermatitis, dogs, allergy, food allergy, exclusion diet, pruritus, trophoallergens.

RESUMO.- [**Eficácia da ração de soja hidrolisada e da comida caseira com proteína original no controle da dermatite atópica induzida por alimentos em cães**.] Os trofoalérgenos são componentes específicos do alimento ou de seus ingredientes, capazes de precipitar o eczema atópico em 19,6% a 30% dos cães com dermatite atópica (DA). O presente estudo teve como objetivo avaliar a eficácia da ração de soja hidrolisada e da comida caseira com proteína não usual no controle do prurido crônico em cães com DA. Para isso foram utilizados vinte e oito cães com DA. O diagnóstico de DA foi baseado nos critérios de Favrot. Os animais foram separados em dois grupos, um grupo consumindo ração hidrolisada de soja e o outro grupo comida caseira com fontes de proteína e carboidratos originais. Estes foram avaliados quinzenalmente pela escala de Rybnicek e CADLI durante 60 dias. Os animais do grupo alimentado com ração hidrolisada de soja apresentaram uma minimização no escore de prurido (escala de Rybnicek) nos dias +15, +30, +45 e +60 (P<0,01) em relação ao dia 0. Já os cães do grupo alimentado com comida caseira não apresentaram diferença significativa (P>0,05) nos 60 dias de tratamento. Quando avaliados pelo índice de CADLl os cães tratados com ração hidrolisada de soja tiveram uma melhora parcial nos dias, +45 (P<0,05) e +60 (P<0,01) em relação ao dia 0, enquanto que os cães do segundo grupo não obtiveram melhora (P>0,05) nos 60 dias

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de tratamento. A ração hidrolisada de soja se mostrou efetiva para controlar parcialmente os sinais clínicos da dermatite atópica induzida por alimentos, no entanto, não é eficaz para o controle total da doença.

TERMOS DE INDEXAÇÃO: Ração de soja hidrolisada, comida caseira, proteína original, dermatite atópica, cães, alergia alimentar, dieta de exclusão, prurido, trofoalérgenos.

INTRODUCTION

Atopic dermatitis (AD) is a genetically predisposed inflammatory, chronic, pruritic, recurrent dermatopathy which clinical onset are related to the production of class IgE antibodies, in particular against environmental antigens such as dust mites and pollen (Hensel et al. 2015). However, recently studies suggest that non-environmental allergens, like food, are also accountable for the AD pathogenesis in dogs (Pucheu-Haston et al. 2015). This condition is denominated as Food-Induced Atopic Dermatitis (FIAD), which clinical signs can include pruritus (initially responsive to corticosteroids), that affects distal members, face, ventral abdomen, pinnas and areas of flexure of the skin. However, not all dogs with FIAD can show these signs or can demonstrate additional 'non-classical' signs related to AD, as the poor response to corticosteroids, perianal pruritus, seborrhea, atypical age of onset and gastrointestinal disorders.

Therefore, all animals with AD that presents chronic and perennial pruritus, which does not stabilizes with the control of the recurrent infections, must be subject to one or more food challenge: the recovery of the physical barrier function of the epidermis, and exclusion or minimization of the contact of the skin with primary irritants (elimination test to determine and eliminate allergens that can cause atopic eczema from diet (Olivry et al. 2007).

By knowledge of the allergenic potential of large proteins, the use of hydrolyzed and ultra-hydrolyzed molecules has begun decades ago to control allergic reaction to food (Olivry & Bizikova 2010). The goal of protein hydrolysis is breaking the peptide bonds of the amino acid chains and generating smaller fragments of the molecule in order to reduce its allergenicity and increase its digestibility (Ricci et al. 2010).

Studies evaluating food with hydrolyzed proteins in dogs allergic to food have been described in the international literature. However, there are few studies presenting the use of hydrolyzed dog food compared to homemade food with original protein to control chronic pruritus and tegumental injuries in dogs diagnosed with AD.

The present study aimed to evaluate the efficacy of hydrolyzed soy dog food and homemade food with original protein in the control of food-induced atopic dermatitis in dogs.

MATERIALS AND METHODS

A non-randomized longitudinal study was conducted. To this end, were selected 28 dogs with atopic dermatitis covering at least six of the eight criteria set by Favrot et al. (2010), characterized by chronic, enduring and alesional pruritus initial responsive to corticosteroids at the distal portion of the forelimb, pinna and ear canals, and have not presented pruritus in the lumbosacral region and edges of the pinnas. These animals were intradomiciliated, and its clinical signs began before three years of age or later.

In the project, were included only dogs whose pruritus intensity did not minimize significantly with the pyoderma control, malasseziosis, infestation of ectoparasites, or in contact with primary irritants. Animals requiring regular or intermittent use of drug therapies like antibiotics and corticosteroid were excluded from the study.

The 28 animals were separated in two groups. The first group was composed of 14 dogs, which were fed with hydrolyzed soy dog food (SH Group). In this group, were included only dogs that never regularly ate food with soy protein. The food was given free of charge to the dog owners every fifteen days, and its administration complied with the daily amount indicated on the manufacturer's package according to the animal weight (Table 1).

The second group was composed of 14 dogs too, and was fed with homemade food with original protein (DC Group). For each dog it was established a unique dietary protocol with one original

Table 1. Daily amount of hydrolyzed soy food recommended according to manufacturer and its ingredients

Dog weight (kg)	Thin (g)	Normal (g)	Overweight (g)
2	65	55	40
3	90	70	55
4	110	90	65
5	130	105	80
6	150	120	90
7	165	135	100
8	185	145	110
9	200	160	120
10	215	175	130
11	235	185	140
13	265	210	160
15	290	235	175
17	320	255	190
19	345	275	210
21	375	300	225
23	400	320	240
25	425	340	255
27	450	360	270
30	485	385	290
35	540	435	325
40	595	475	360
50	700	560	420
60	800	640	480
70	900	720	540
80	990	790	595

lngredients: Broken rice, *roy* hydrolyzed protein', pork fat, chicken fat, beet pulp, zeoltte, *w y* refinecl oil', fish refinecl oil, fructo ligo saccharides, borage oil, Marigold extract, dicalciumphosphate, potassium chloride, calcium carbonate, sodium chloride, (common salt), monocalcium phosphate, monosodium phosphate, vitamins (A, E, 03, C, 81, B2, 86, B12, PP), biotin, pantothenic acid, folie acid, choline chloride, inosttol, copper amino acid chelate, copper sulfate, iron sulfate, manganeseamino acid chelate, manganese oxide, calcium iodate, zinc amino acid chelate, zinc oxide, sodium selenite, chicken liver, taurine, tyrosine, OL-methionine, L-fysine, antioxidant (BHA). Soy hydrofyzed proteu1 and soy refined oil producecl from genetically modified soy by *Agrobacterium* sp.

protein, according the complete history of patient previous protein exposure. To this study were used as protein source lamb or duck meat or white fish associated with a carbohydrates source such as brown rice or potatoes.

Food was prepared by this study team fortnightly, and distributed free of charge to the owners.

The carbohydrates (brown rice or potato) were boiled in water, adding a tablespoon of canola oil and without the addition of seasoning or condiments as additives, colorings, preservatives commonly found in industrial products. The protein sources (lamb or duck meat, white fish) were ground and also cooked only in water. After prepared, the food was fractionated according to the animal weight, stored in plastic bags and frozen (Fig.1). The protein and carbohydrate amount was provided as the daily dietary needs by each animal weight, as shown in Table 2, in a ratio of 1:1.

Each animal was subjected to dermatological clinical examination, and lesional score established by CADLI index on days 0, 15, 30, 45 and 60, during the feeding with hydrolyzed soy dog food and homemade food. Pruritus was evaluated fortnightly, and its score established by the Rybnicek (Rybnicek et al. 2009), scale between days 0 and 60. At the end of the 60 days, all the animals were challenged with its previous food, and its pruritus and lesion scores reassessed after a week according to scales CADLI and Rybnicek. The dogs that had relapses on the clinical signs were diagnosed with food-induced atopic dermatitis (FIAD). Those dogs that did not respond to the diet were diagnosed with AD *stricto sensu* or atopic dermatitis *like.*

Fig.1. Homemade food prepared with brown rice and lamb protein, fractionated in 1:1 for a dog of 22lbs (10kg) and packed in plastic bag for later freezing and distribution.

Table 2. Amounts required per homemade food serving during the exclusion diet with original protein used in dogs with adverse reactions to food

Weight (kg)*	Protein source (g)*	Carbohydrates (g)*
3	100	150
4	125	160
5	150	200
10	230	250
15	310	350
20	380	500
25	450	600
30	500	600
40	700	700
50	800	900

* The servings are offered twice a day to the dogs.

Statistical analysis. All data of this present study were demonstrated in medians and standard deviation. Due to the establishment of scores to assess the degree of injury and pruritus on the dogs included on the study, a median within groups and between groups were analyzed by Kruskal-Wallis and a non-parametric test followed by Mood's median test. A significance level was adopted for the observed values of 5% ($P \leq 0.05$).

RESULTS

The hydrolyzed soy dog food as well as homemade food had been well accepted by all animals in the study on the palatability, and there was no problem in the administration. Additionally, were not observed tegumental or gastroenteric signs in each group throughout the study.

Among the 28 animals with atopic dermatitis evaluated, 15 (54%) achieved a complete or partial improvement of clinical signs with exclusion diets, and relapsed after oral challenge, resulting in the diagnosis of food-induced atopic dermatitis (FIAD).

Of the 14 dogs belonging to the SH group, eight dogs (57%) were diagnosed with FIAD, five of these (63%) achieved partial improvement, and three (38%) had clinical improvement greater than 80%.

In DC group, seven of 14 dogs (50%) had improvement of clinical signs during the 60 days of study, and worse after re-exposure to previous food, being diagnosed with FIAD. Of these seven, one (13%) had improvement above to 80% of the clinical condition.

Relative to CADLI index, the eight dogs with FIAD fed with hydrolyzed soy dog food had a significant lesion involution as of days +45($P \leq 0.05$) and +60 ($P \leq 0.01$) compared to day 0. However, in the Rybnicek analysis, these animals had a significant reduction of the pruritus score from the day +15 until day +60 ($P \leq 0.01$) compared to day 0.

Although seven dogs with FIAD belonging to DC group had partial improvement in its pruritus and lesion scores, it were not significant over 60 days of treatment by CADLI index ($P>0.05$) and Rybnicek scale ($P>0.05$).

When we compare the groups DC and SH of diagnosed animals with FIAD, by CADLI index were not observed a significant difference between the eight dogs fed with hydrolyzed soy dog food (SH) and the seven dogs fed with homemade food (DC) over the 60 days of diet (Fig.2).

Whereas by Rybnicek scale, relative to the comparison among groups, were observed statistically significant differences at the beginning of evaluations (day 0) and at the very end (day 60), with the hydrolyzed soy dog food being more effective on the pruritus reduction at the end of the 60 days ($P \leq 0.01$) (Fig.3).

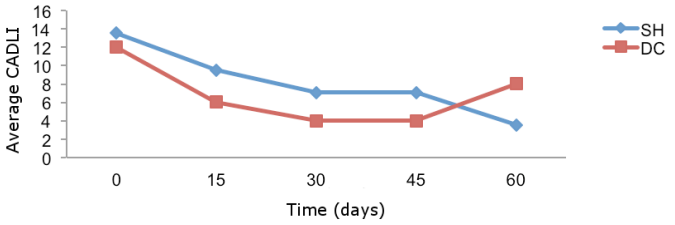

Fig.2. Medians comparison by CADLI scale (canine atopic dermatitis lesion index) among dogs diagnosed with FIAD (Food induced atopic dermatitis) of SH (hydrolyzed soy) and DC (homemade diet) groups.

Weight (kg)	Protein source (g)	Carbohydrates (g)
3	100	150
4	125	160
5	150	200
10	230	250
15	310	350
20	380	500
25	450	600
30	500	600
40	700	700
50	800	900

*The servings are offered twice a day to the dogs.

Fig.3. Comparison between pruritus score medians established by Rybnicek scale among dogs diagnosed with FIAD (Food induced atopic dermatitits) of SH (hydrolyzed soy) and DC (homemade diet) groups, where significant differences were observed on day +60 ($p \leq 0.01$).

DISCUSSION

Prospective studies have reported that food-induced atopic dermatitis (FIAD) can occur at 19.6% to 30% of cases (Marsella 2006, Farias 2007). Loeffer et al. (2006) reports that 40% of dogs with AD have the disease precipitated by food. However, Chesney (2002) observed in 33% of dogs, and Favrot et al. (2010), in 23%.

The occurrence of FIAD in 54% of dogs found in this study may be related to the fact that animals with AD included in the study are all intradomiciliated and exposed to a wide variety of food proteins. That can make trophoallergens important agents for exacerbation of their clinical signs, as observed in humans, where the more diverse and premature exposure to dietary protein is, the greater the risk of developing adverse reactions to food (Sicherer & Sampson 2014).

Homemade diets are seen as the best method of diagnosis of trophoallergens hypersensitivity in dogs (Proverbio et al. 2010), as they may be free of preservatives or additives, what is rarely found in commercial diets (Kennis 2006). Additionally, it is possible to maintain greater control over the protein source offered to the animal, with homemade diets without the risk of contamination with other trophoallergens (Rosser 2014).

However, in this study, there was no statistical difference between the two groups in identifying FIAD, which corroborates the findings of Osborn (2006), which demonstrated that the most important when selecting a diet is to choose an original protein source.

The clinical improvement of dogs fed with hydrolyzed soy dog food in this study can be attributed to exclusive exposure to a unique original protein source, since soy protein is not commonly found in commercial pet food, as currently occurs with wheat, corn and rice, which are widely used. Thus, these animals were not sensitized to this new protein source.

Among 8 animals with FIAD, a significant improvement in pruritus was observed from the 15th day, and the improvement of lesions as of 45th day, in comparison to day zero. This shows that many clinical signs of FIAD are related to pruritus such as abrasions, self-induced alopecia, crusting, secondary infection, and once controlled, there was a significant minimization of clinical lesions.

The home diet introduced in this study reduced pruritus and lesional index in 50% of dogs, but with rates below than observed with the hydrolyzed diet. Perhaps, this finding can be explained by cross-reactivity to IgG found in bovine muscle, which has a high homology with ovine immunoglobulins, and can promote the cross-reactivity with lamb meat (Roudebush 2013), which was used in four dogs of the seven dogs with FIAD.

Therefore, it is possible that dogs fed with lamb meat can develop cross-reactions with beef (Gaschen & Merchant 2011, Roudebush 2013) and this may have reduced the response to homemade diet in the studied dogs.

Comparing the groups of 15 dogs with FIAD, was not observed statistically significant difference in the reduction of clinical signs between the evaluated dogs fed with hydrolyzed soy dog food and homemade food with original diet. However, when comparing the effectiveness in reducing pruritus between groups, the SH group was higher than the DC group in the 60th day of observation. The improved effectiveness of hydrolyzed diet on homemade diet can be justified by the fact that the protein hydrolysis eliminates trophoallergens and allergen epitopes present in food, it may then be hydrolyzed sources less antigenic than homemade. Thus, it may also be suggested that the duration of the elimination diet should be extended, so that some animals fed with homemade food could demonstrate improvement, in relation to the established duration for hydrolyzed diets.

Rosser (2014) estimates a diagnosis failure in 25% of dogs fed with commercial diets. In this present study, 43% (6/14) of dogs not responded satisfactorily to elimination diet with hydrolyzed dog food, possibly because they were dogs with AD triggered by environmental allergens (atopic dermatitis *stricto sensu*) or atopic dermatitis *like.*

On the other hand, an insufficient degree of enzymatic hydrolysis may facilitate the maintenance of immune reactivity to food proteins (Cave 2006), since the hydrolyzed diets commercially available in Brazil have a protein molecular weight between 7 and 10kDa, and the minimum molecular mass for the single bonds in mast cell IgE receptors to occur varies between 0.97kDa and 1.4kDa (Cave 2006).

In addition, prior sensitization to chicken proteins may have triggered the allergic reaction and maintenance of clinical signs, since the dog food used in this study, although hydrolyzed soy, have chicken liver in its composition.

Also, the presence of additives such as palatability agents, colorants, flavorings and preservatives in processed food, although not yet recognized as important allergens for dogs and cats, may have pro-inflammatory effects and worsen the clinical signs of AD (Sicherer & Sampson 2014).

Because it is a balanced food, the 14 dogs fed with hydrolyzed diet maintained their body scores throughout the study. It is documented a reduced growth in children chronically fed with hydrolyzed formulas, associated to low levels of serum albumin and urea increased, when compared to a feeding by intact protein (Cave 2006). These data suggest the need to carry out further analysis work about the side effects in long-term use of protein hydrolysates in veterinary medicine.

Although the palatability can be affected by the protein hydrolysis process, the dogs of this study had no resistance in its administration, which corroborates with studies presented by Olivry & Bizikova (2010), where 80% of dogs had good acceptance related to prescription of hydrolyzed diets. There were no gastroenteric signs during the elimination diet, what can be explained by the high digestibility and uptake of hydrolyzed proteins (Cave 2006).

The diet dropout rate in this study was zero, which contradicts other authors who reported a dropout rate in 36% of cases over a study of 6 to 8 weeks making use of a homemade elimination diet (Tapp et al. 2002).

In general, there are many reasons for the failure of the diet, among them, we can mention the cost of some original protein sources and that often is difficult to find it, besides the time consuming prepare. It is possible that the low dropout rate observed in this study may be related to the fact of homemade food have been delivered ready and free to the dogs owners, which does not allow a trust relationship with the reality of this recommendation.

CONCLUSIONS

The trophoallergens can precipitate the AD symptoms in 50% of dogs with perennial pruritus.

The hydrolyzed soy diet and homemade diet with original protein can similarly identify the animals with FIAD, but the diet with hydrolyzed dog food was able to cause a significant improvement in pruritus index in these dogs.

Both foods were well accepted as to the palatability and have not induced gastroenteric reactions in dogs with atopic dermatitis.

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