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Allergen specific immunotherapy (ASIT) with allergoids in canine atopic dermatitis (CAD) treatment

J. L. Gonzalez, Y. Moral

Hospital Clinico Veterinario, Facultad Veterinaria, Universidad Complutense de Madrid, Madrid, 28040, Spain

BACKGROUND

The chemical modification of allergens to allergoids allows higher immunotherapy doses to be safely administered over a short period of time compared with traditional allergen based protocols [Subiza J, et al. Allergy 2010; 65 (S92):564]. A simpler induction protocol allows for improved immunotherapy compliance. Allergoids have been successfully used to treat human allergy from more than 30 years. [Grammer LC, et al. J Allergy Clin Immunol 1986; 78 (1180-1184)]

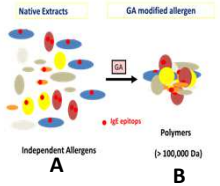

Figure 1. By glutaraldehyde treatment of native allergenic extracts (**A**) high molecular weight polymers named **Allergoids** are obtained (**B**). [Patterson R, et al. J Allergy Clin Immunol 1977; 59(4):314-9]

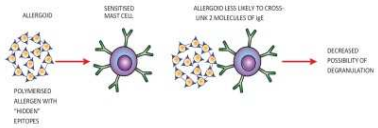

Figure 2. They have **reduced allergenicity**. A polymer comprising multiple allergens has a smaller surface area than the same number of allergen monomers, with fewer exposed epitopes which are able to cross-link mast cell bound IgE. [Patterson R, et al. J Allergy Clin Immunol 1979; 63(1):47-50.]

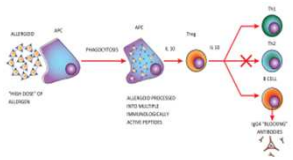

Figure 3. Also they **maintain (or have increased) immunogenicity** compared to native allergens. The use of polymerised allergens provides a safe mechanism to quickly deliver the high concentrations of allergen required to initiate immune modification. [Subiza J, et al. Clin Exp Allergy 2008; 38(6):987-994.]

MAIN OBJECTIVE

Assess field safety and efficacy of allergen specific immunotherapy in dogs with CAD using allergoids with a cluster administration scheme.

MATERIALS AND METHODS

- **Fifty three dogs with CAD** were selected of which **forty nine completed the study**. Four were lost to follow-up.

INCLUSION	EXCLUSION
Met at least 5 of the Favrot criteria	Oral glucocorticosteroids and/or antihistamines in the last 3 weeks before diagnosis
Concomitant food allergy ruled-out through elimination diet for at least 8 weeks	Depot glucocorticosteroids in the last 8 weeks before diagnosis
Positive results in IDR and/or serological IgE test	

- **Allergenic design of ASIT** (VetGoid™; Alergovet -Inmunotek, Madrid, Spain) was made taking into account: results of intradermal (Allervet™ IDR; Alergovet, Madrid, Spain) and serological tests (specific IgE) (PET ELISA™; Alergovet, Madrid, Spain), the environment and veterinary criteria. Overall, environmental allergens from the main groups (pollens, mites, and moulds) were included in the study but never more than 5 different allergoids per treatment.

Figure 4. Administration schedule of subcutaneous injections was: day 0: 0.2mL, day 7: 0.5mL (initial phase) and then one injection of 0.5 mL every 30 days thereafter (maintenance phase).

- **Data monitoring: Safety and efficacy** were registered in a clinical questionnaire every injection and evaluated at 3, 6, 9 and 12 months after the first injection. All records were included in an **individual monitoring chart** designed for this study, with two questionnaire forms: one to be fulfilled by the veterinarian and another one by the owner.
- **Parameters recorded**:
  - **Demographical data** of the animal.
  - **Clinical history and examination** results in first visit
  - **Safety:**
    - Recording of adverse reactions: pruritus increasing, inflammation at point of injection, diarrhea, onset or worsening of erythema or skin lesions, urticaria or anaphylaxis symptoms.
    - Recording times: immediately after injection, in the first hour and between them.
  - **Efficacy:**
    - Subjective evaluation of the disease (veterinary and owner): pruritus level (scaled 1 to 10), improvement in lesions, general condition of the animal and any other comment from owner.
    - Objective evaluation of key parameters: lesion evolution, medication scores, concomitant pyoderma and general condition of hair and skin.

RESULTS

SAFETY: Minimal side effects were observed in 1 of all animals (n=49): an increase in pruritus after 2nd and 3rd injection.

EFFICACY: Degree, time to initial and time to maximum improvement were assessed:

DAY	0	7	30	60	90	180	270	AVERAGE
N. OF ANIMALS	0	9	33	5	1	1	0	35

Table 2. Time for onset of improvement. More than 70% of the animals started to improve within the first month, with an average of 35 days

PERIOD	30	31-60	61-90	91-180	181-270	271-360	AVERAGE
N. OF ANIMALS	0	8	37	3	1	0	87

Table 3. Time to maximum effect. The inter-injection period during which maximum improvement was observed was recorded; the average period was between two and three months.

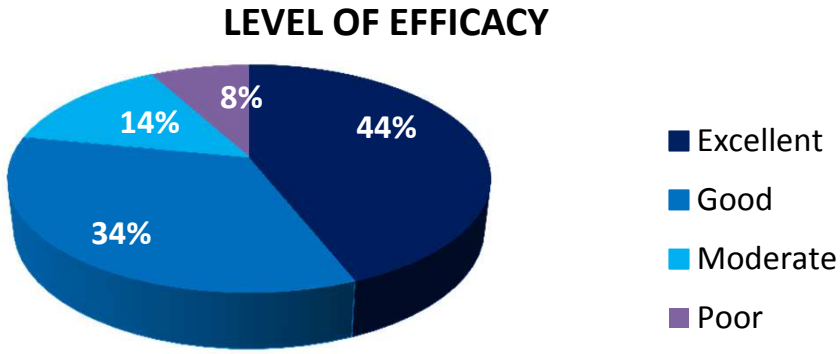

Figure 4. Efficacy analysis and distribution. The efficacy results by group were based on the following criteria: **excellent** (no signs and symptoms and no medication needed), **good** (improvement in symptoms with occasional supportive medication), **moderate** (improvement in symptoms, but continuous medication required with a dose reduction of at least 50%) and **poor** (no improvement).

Figure 5. Female, two years old, crossbreed. In first visit present intense pruritus with alopecic and ulcerative lesions around eyes and in different areas of the muzzle. The skin and serological test showed positive results to 3 mites. An ASIT was manufactured based on that, and sixty seven days after starting the treatment all lesions and pruritus have completely disappeared.

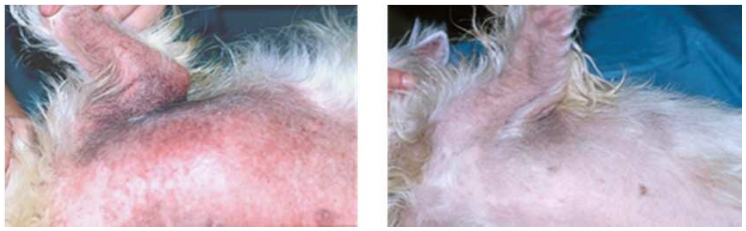

Figure 6. Male, three years old, Yorkshire terrier. In first visit presented intense pruritus and generalized erythema and alopecia, specially on ventral area and legs. Long history of repetitive otitis. The skin and serological test showed positive results to grasses and weeds pollens, and ASIT was manufactured based on them. Ninety seven days after starting treatment lesions and pruritus have disappeared with recovery of all hair.

Ninety-two percent (92%) of cases demonstrated clinical improvement following ASIT, of which 78% were excellent or good

CONCLUSIONS:

Allergoid-based ASIT is a safe, simple and effective etiologic treatment for canine atopic dermatitis.