Clinical and immunological responses of dust mite sensitive, atopic dogs to treatment with sublingual immunotherapy (SLIT)

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Background – Sublingual immunotherapy (SLIT) has been reported to be beneficial in people with atopic dermatitis (AD) and dust mite sensitivity. Evaluation of this therapy has not been reported in spontaneous canine AD.

Objectives – The objective of this study was to preliminarily evaluate the effectiveness of an established SLIT protocol, as used in human patients, in dogs with AD.

Animals – Ten dust mite sensitive dogs with spontaneous AD.

Methods – Dogs underwent a 6 month open trial of SLIT concurrently with decreasing dose oral methylprednisolone. Clinical evaluations and quantitative serum anti-mite IgE and IgG levels were performed every 2 months.

Results – Mean methylprednisolone use from the first 2 months of the study to the final 2 months declined from 10.2 to 4.3 mg/kg/2 months (P < 0.001, Student’s paired t-test); at 6 months, four dogs required no oral corticosteroid administration. Over the course of the study, median Canine Atopic Dermatitis Extent and Severity Index (CADESI)-03 scores declined from 76.5 to 59; median pruritus scores declined from 65 to 37 (P < 0.02 and P < 0.01, respectively; Wilcoxon signed-rank test). Pre- and post-SLIT intradermal test scores for mite allergen were not significantly different over time. Median Dermatophagoides farinae (DF)-specific IgE levels declined significantly from 150.2 x 10^3 AU/mL to 3.6 x 10^3 AU/mL (P < 0.05). Concurrently, median DF-specific IgG levels increased from 18.5 x 10^6 AU/mL to 3923.4 x 10^6 AU/mL (P < 0.05; Wilcoxon signed-rank tests).

Conclusions and clinical importance – SLIT treatment produced clinical improvement in dogs with dust mite-associated AD and was associated with serological changes supporting this improvement. Further studies in larger numbers of dogs and those with polysensitization are warranted.

Introduction

Sublingual immunotherapy (SLIT) is a form of allergen-specific immunotherapy (ASIT) treatment for allergic diseases, in which allergen extracts are administered into the oral cavity instead of by injection. It has been a prominent treatment modality for allergic diseases in people, particularly in Europe where this method is often favoured over injection ASIT, and where registered products have been available for years. Although early efficacy studies reported conflicting results, recent meta-analyses have led such authorities as the World Allergy Association, the Cochrane Collaboration and the Johns Hopkins University Evidence-Based Practice Center to conclude that SLIT is a safe and efficacious treatment. In 2014 the first two SLIT products received United States regulatory approval for treatment of human allergies (Oralair®, Staltergenes, Norwell, MA, USA and Grastek®, Merck, Whitehouse Station, NJ, USA).

The major uses of SLIT in human beings (and the majority of studies) have been for allergic respiratory diseases such as allergic rhinoconjunctivitis or asthma, but it has also found use in atopic dermatitis (AD). In one trial of SLIT in mite-sensitive people with AD, 59% of patients showed significant improvement of their clinical signs with an average of 46% reduction in standardized clinical score. In mite-sensitive children with AD, SLIT produced a significant drop in clinical score as well as a decrease in other medications necessary for control,
with mild to moderately affected patients benefiting the most.5

Sublingual immunotherapy has not been evaluated as a treatment for dogs with spontaneously occurring AD. In this pilot study, our preliminary objective was to evaluate the efficacy of SLIT in a group of dogs with AD, using a protocol based on established treatment for human beings. We monitored both clinical criteria and selected immunological determinations to assess the value of SLIT and its potential for further study in dogs.

Materials and methods

This study involved client owned dogs presented to our institution. The study protocol was reviewed and approved by the institution’s Animal Care and Use Committee prior to commencing the trial and all owners gave informed consent for participation in the trial.

Patient criteria

Ten predominantly mite-sensitive, atopic dogs were selected for entry into this uncontrolled, open trial. All dogs had undergone standard diagnostic evaluation and fulfilled criteria for the clinical diagnosis of AD, with no component of food sensitivity, no fleas or other parasites and year-round clinical signs with no observed seasonal variability. This clinical presentation is relatively common in our geographic area. Both our standard intradermal testing (IDT) panel and serum allergen-specific IgE testing (Heska Allercept; Loveland, CO, USA) were performed at entry and all dogs were shown to be positive to Dermatophagoides pteronyssinus and/or Tyrophagus putrescentiae. A maximum of one additional positive test result for a grass, tree or weed pollen was allowed, although in each case this result was considered likely to be minor or inconsequential because of lack of seasonal worsening.

Dogs were required to have been symptomatic for at least 1 year and to be symptomatic at the start of the study, as documented by a Canine Atopic Dermatitis Extent and Severity Index, version 3 (CADESI-03) score7 of 25 or greater on the first visit, a Pruritus Visual Analog Scale (PVAS) score8 of >60 on the first visit, or both.

Excluded were pregnant or lactating bitches, dogs with concurrent disease unrelated to AD and dogs that had previously undergone any ASIT regimen. If drug therapy had been used, minimum withdrawal times prior to entry were: ciclosporin 4 weeks; oral corticosteroids 6 weeks depending on drug; antihistamines 4–6 weeks; and fatty acid supplements. Flea and heartworm control/preventive products were continued throughout the study. Specifically disallowed products were: systemic antibiotics and/or antifungal medications; nonsteroidal ophthalmic preparations; topical products containing corticosteroids including antibacterial or antifungal shampoos, sprays, creams or lotions; and vitamins and/or essential fatty acid supplements. Fea and heartworm control/preventive products were continued throughout the study. Specifically disallowed medications included: corticosteroids of any type other than oral methylprednisolone; antihistamines; and sedatives or tranquilizers.

Evaluations

Evaluations were performed at entry into the study, and at 2, 4 and 6 months of treatment. If corticosteroid tablets were necessary during maintenance treatment, they were discontinued for 14 days prior to each evaluation. At each evaluation the following were collected:

- Clinical examination score, as CADESI-03 scoring5 by the investigator;
- Pruritus score, as PVAS8 scored by the owner. Owners were instructed to assign the PVAS score based upon the degree of pruritus observed in the week prior to the evaluation. This represented a period during which the dog was not receiving corticosteroid treatment, although if improvement was perceived, this could have been related to recent corticosteroid use.
- The number of methylprednisolone tablets administered since the previous visit, if any, as recorded in the daily log by the owner;
- Blood sample, with serum separated and stored at –20°C;

At the final study visit (6 months), IDT was repeated. Owners were also asked for their global subjective assessment on the overall level of improvement in their pet after the course of treatment, on a scale from 0 to 100% improvement.

Laboratory determinations

Sera were assayed for presence of D. farinae (Df)-specific IgE using a commercial allergen-specific IgE assay (Greer Laboratories; Lenoir, NC, USA) modified for quantitative determination. A known strongly positive sample was selected as a reference standard and arbitrarily assigned a concentration of 100,000 Assay Units (AU)/mL. Df-specific

Figure 1. Administration method of sublingual immunotherapy (SLIT) treatment by hooking the small plastic dispensing nozzle over the lower arcade of teeth so that the solution is dispensed sublingually.

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IgE. The standard was prepared in three-fold serial dilutions and included on each plate along with appropriately diluted patient samples. The assay was then conducted according to standard procedure. Results from serial dilutions of the reference standard were plotted as optical density versus concentration in AU/mL to create a standard curve. Concentrations in unknown samples were then calculated according to this standard curve and expressed in AU/mL.

Samples were also assayed for Df-specific IgG in a similar fashion. In this case, a sample strongly positive for Df-specific IgG was selected as the reference standard, assigned a concentration of 100,000 AU/mL, and similarly diluted to create a standard curve for each plate. The assay was otherwise conducted by standard methods, except that the secondary antibody was biotinylated mouse anti-canine IgG heavy chain (Jackson Immunoresearch; West Grove, PA, USA). Concentrations of Df-specific IgG were expressed in AU/mL.

Individual serum samples from various patients and time points were identified only by code numbers, intermixed and assayed in a blind fashion in a single assay run.

Statistical analysis
Clinical evaluation data and mite-allergen-specific Ig data were analysed using the Wilcoxon signed-rank test or Student’s paired t-test as applicable. Mite-specific Ig data were log-transformed prior to analysis. Only differences from the beginning to the end of the study (i.e. 0 and 6 months) were evaluated. Analysis was conducted using the SPSS software package (IBM SPSS Statistics v22, IBM Corporation; Endicott, NY, USA).

Results
The 10 dogs entered into the study ranged from 1.5 to 8 years of age and included five males and five females, of various breeds including miniature poodle (1), Labrador retriever (4), Newfoundland (1), golden retriever (1), German shepherd dog (1), bichon frise (1) and great Pyrenees (1). The dogs were entered into the study over a 16 month period.

Clinical evaluations
The primary outcome measure for this trial was reduction in glucocorticoid use over time. Glucocorticoid (methylprednisolone) use was calculated for each 2 month period as the total mass (mg) of drug used over 2 months, divided by the dog’s body weight (kg). Mean glucocorticoid use declined significantly over the course of the study (Table 1), from 10.2 mg/kg/2 months for the first 2 months, to 4.3 mg/kg/2 months for the last 2 months (P < 0.001, Student’s paired t-test). At the 6 month visit, four dogs had required no glucocorticoid use during the prior 2 months.

CADESI-03 scores and PVAS from beginning to end of study for each dog are shown graphically in Figures 2 and 3. Note that these values are also shown in relation to glucocorticoid use: on the same graphs, the first 2 months’ and final 2 months’ required methylprednisolone use are annotated next to each data point.

Table 1 also shows CADESI-03 scores and PVAS over the entire 6 month treatment period. Over the course of the study, median CADESI-03 scores declined gradually and significantly, from 76.5 at study initiation to 59 at 6 months (P < 0.02, Wilcoxon signed-rank test). Over the same period, median pruritus scores (PVAS; Table 1) declined significantly from 65 to 37 (P < 0.01, Wilcoxon signed-rank test). At the final study visit, three dogs had PVAS scores of <19, implying that they were essentially itch-free. The reader should note that at least some improvement was expected regardless of the efficacy of the SLIT intervention, as owners were using concurrent glucocorticoid treatment to control clinical signs.

The owners’ global assessment of the degree of their pet’s improvement after 6 months of treatment ranged from 0% improvement (two dogs) to 100% improvement (two dogs). Eight of 10 dogs were rated as improved by their owners, with a range of 65–100% and a median improvement of 72.5%.

Pre- and post-study intradermal test scores for mite allergen varied for individuals, with no apparent pattern over time and no significant difference in median score from study beginning to end. For example, median IDT scores for D. farinae at a 1/5000 dilution were 3.5 at the beginning of the study and 3.0 at the end of the study.

SLIT treatment was generally well tolerated in these 10 dogs. Owner reported adverse effects included transient vomiting (one dog), transient lethargy and decreased appetite (one dog) and transiently increased pruritus (two dogs). None of the adverse effects required veterinary intervention.

Df-specific IgE and IgG determinations
Median levels of serum Df-specific IgE dropped substantially during the first 2 months of treatment (Figure 4), then rose following dose escalation from 2 to 4 months, then decreased again as the dose was further escalated from 4 to 6 months. This pattern was seen with most, but not all dogs. Overall, median Df-specific IgE levels dropped significantly from 150,000 AU/mL at the beginning of treatment to 4,000 AU/mL at the end (P < 0.05, Wilcoxon signed-rank test).

Df-specific IgG levels were more variable over time (Figure 5). Generally, median levels followed an inverse relationship to specific IgE levels, with an initial increase (Figure 4) followed by a decrease following dose escalation from 2 to 4 months, and a further increase dur-

Table 1. Clinical data from dogs in study at Month 0 (beginning of study) and at 2-, 4- and 6-month evaluations

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>0 months</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>CADESI-03, median (95% CI)</td>
<td>76.5 (49.0–95.4)</td>
<td>64.0 (35.6–82.6)</td>
<td>60.0 (27.3–111.5)</td>
<td>59.0* (31.0–70.6)</td>
</tr>
<tr>
<td>PVAS, median (95% CI)</td>
<td>65.0 (46.3–78.9)</td>
<td>37.5 (18.2–64.0)</td>
<td>44.5 (22.6–71.0)</td>
<td>37.0* (17.0–57.1)</td>
</tr>
<tr>
<td>Methylprednisolone use (as mg/kg/2 months), mean (95% CI)</td>
<td>–</td>
<td>10.2 (6.8–13.7)</td>
<td>4.7 (0.9–9.8)</td>
<td>4.3 (0.8–7.8)</td>
</tr>
</tbody>
</table>

Value in Methylprednisolone Use row indicates total drug use in mg/kg for the entire 2 month period prior to the evaluation. (Significant difference from Month 0 at *P < 0.02 and †P < 0.01, Wilcoxon signed-rank test; significant difference from Month 2 at †P < 0.001, Student’s paired t-test). CADESI-03, canine atopic dermatitis extent and severity index, version 3; PVAS, pruritus visual analog scale; CI, confidence interval.
ing the final 2 months of treatment. Overall, median Df-specific IgG levels increased significantly over the course of treatment, from $18 \times 10^9$ AU/mL at entry to $3,293 \times 10^6$ AU/mL at the end ($P < 0.05$, Wilcoxon signed-rank test).

The reader should note that the vertical axes in Figures 2 and 3 are on a logarithmic scale and thus tend to visually under-represent the magnitude of the changes seen; for example, a change in median IgG or IgE levels from approximately 6 to 8 on either graph is a two-log (100X) change.

**Discussion**

The present study, although small and uncontrolled, provides initial evidence that SLIT treatment is well tolerated and can produce both immunological changes and clinical
benefit in mite-sensitive dogs with spontaneous AD. Although owner expectations of success and placebo effect were doubtless factors in perceived clinical benefit, they were unlikely to be factors in the notable, objective serological changes measured over time in these dogs.

The clinical observations made during this trial must be viewed in light of the concurrent corticosteroid treatment used. Methylprednisolone tablets were mandated at a prescribed dose for the first 15 days of the trial, after which owners were allowed to adjust the dose upwards or downwards (including discontinuation) in an amount sufficient to keep the pet comfortable. Thus, it would be expected that both CADESI-03 and PVAS scores would decrease over the course of the study, if only from the corticosteroid treatment alone, and decreases in CADESI and PVAS have limited relevance to the efficacy of SLIT. The investigators believe that the most important clinical endpoint to consider is the amount of concurrent corticosteroid treatment used, especially during the periods from 2 to 4 months and from 4 to 6 months (Table 1; Figures 2 and 3). The fact that 4 of 10 owners were able to completely discontinue corticosteroids between 4 and 6 months was notable to both the investigators and the owners.

Although the number of dogs in this study was too small to preclude more detailed statistical analysis, we could empirically observe no indication that such factors as age of dog, breed, severity of disease or allergen test results related in any way to the treatment success.

SLIT therapy generally produced increases in allergen-specific IgE and decreases in allergen-specific IgG over time, with changes occurring between timepoints at which allergen doses were escalated. This relationship has been observed in ASIT with people, and it is thought to reflect a change from a Th2-polarized to a Th1-polarized response to allergen, which in turn is thought to be in part responsible for clinical benefit of ASIT.10,11 It should be noted, however, that changes in IgE and IgG in the present study did not completely parallel clinical response; reduction in mite-specific IgE levels (or increases in mite-specific IgG levels) was not always associated with clinical improvement. This may be a reflection of the multifactorial pathogenesis of AD in dogs and the relative importance of Th2/Th1 responses in any given patient.

Closer inspection of Figure 5 suggests two patterns of response for mite-specific IgG; four dogs had an initial boost of IgG at 2 months, followed by decrease at 4 and 6 months (Pattern 1). Six dogs had a minimal increase of IgG at 2 and 4 months, but by 6 months had a very large increase (Pattern 2). Interestingly, the four dogs exhibiting Pattern 1 were among the least favourable responders, with owner global improvement scores of 0%, 0%, 65% and 70%. Dogs exhibiting Pattern 2 (and finishing the study with the highest mite-specific IgG levels) generally had the best clinical response. Thus, in this limited study, it appeared that development of high mite-specific IgG levels during SLIT could be an indicator of clinical response, and this observation deserves further study.

The overall changes from the beginning to the end of the study in DP-specific IgE and IgG are consistent with prior published observations, yet the up and down directional changes over smaller time intervals (i.e. 0–2 to 4–6 months) are difficult to explain. It is possible that varying environmental exposure over the course of the study could have influenced these results. Alternatively, it is possible that these ‘zig-zag’ changes were artefacts of the assay itself. In most ELISA assays, antibodies of different subclasses may compete for the limited amount of allergen coated on the well. Large changes in one antibody subclass can compete for allergen, resulting in artificially lowered measured levels of another subclass. Indeed, it was recognized over 30 years ago that IgG antibodies produced during allergen immunotherapy could artificially lower detectable concentrations of IgE in a radioallergosorbent assay.12 In any event, studies of serial, quantitative, allergen-specific IgE and IgG determinations in dogs with AD being treated with any form of ASIT are lacking in dogs, and our results indicate the need for additional study.

Intradermal test results in these 10 dogs did not change notably over the course of 6 months. This is in line with reports in the human allergy literature, where it is common to find changes in serum allergen-specific IgE during SLIT treatment, but IDT results often remain unchanged despite clinical benefit.13

Other investigations of orally administered ASIT in dogs are limited. One study of an orally administered house dust mite preparation to dogs with experimentally induced dust mite sensitivity failed to show clinical benefit, however, in that study the allergen was fed orally in cream cheese rather than being applied to the oral mucosa at frequent intervals.14 A further study by the same investigators with allergen extracts applied to the mucosa of experimentally sensitized laboratory beagles showed only slight clinical response, but significant increases in cytokines such as TGFβ and IL-10, which have been associated with successful ASIT.15

We conclude that SLIT treatment may represent a useful and effective treatment option for canine AD. Further studies are warranted to establish efficacy in a larger group of dogs, establish efficacy for polysensitized (i.e. dust mites plus pollen or mould spores) patients, optimize treatment protocols and investigate the possible utility of serial quantitative allergen-specific IgE and IgG assays in predicting and/or monitoring the usefulness of SLIT treatment.

Acknowledgements

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References


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Sublingual immunotherapy in atopic dogs

Resumen

Contexto – L’immunothérapie sublinguale (SLIT) a été rapportée efficace chez les patients atteints de dermatite atopique (AD) et d’hypersensibilité aux acariens de poussière. L’évaluation de ce traitement n’a pas été rapportée chez les chiens atteints de AD spontanée.

Objectifs – L’objectif de cette étude était d’évaluer de façon préliminaire l’efficacité d’un protocole de SLIT établi chez le chien atopique, comme les patients humains.

Sujets – Dix chiens sensibilisés aux acariens de poussière avec une AD spontanée.

Méthodes – Les chiens ont suivi un essai ouvert de 6 mois recevant du SLIT et une dose dégressive de méthylprednisolone orale. Les évaluations cliniques et quantitatives d’IgE anti-acarien sériques et les taux d’IgG ont été réalisés tous les 2 mois.

Résultats – La moyenne de la méthylprednisolone utilisée pendant des deux premiers mois aux deux derniers mois de l’étude a diminué de 10,2 à 4,3 mg/kg/2 mois (P < 0,001, Student’s paired t-test); à 6 mois, quatre chiens n’avaient plus besoin de corticoïdes oraux. Tout au long de l’étude le CADESI-03 (Canine Atopic Dermatitis Extent and Severity Index) moyen a diminué de 76,5 à 59; les scores d’eczéma moyen ont diminués de 65 à 37 (P< 0,02 and P< 0,01, respectivement; Wilcoxon signed-rank test). Les scores des intra-dermo-réactions pré et post-SLIT pour les allergènes d’acariens n’étaient pas significativement différents au cours du temps. Les taux moyens d’IgE spécifiques de Df (Dermatophagoides farinae) ont diminués significativement de 150,2 9 103 AU/mL à 3,6 9 103 AU/mL (P< 0,05). Dans le même temps, les taux moyens d’IgG spécifiques de DF ont augmentés de 18,5 9 106 AU/mL à 392,3 9 106 AU/mL (P< 0,05; Wilcoxon signed-rank tests).

Conclusions et importance clinique – Le traitement SLIT permet une amélioration clinique chez les chiens atopiques associés aux acariens de poussière et a été associé avec des modifications sérologiques supportant cette amélioration. D’autres études à plus grande échelle et sur des chiens polysensibilisés sont nécessaires.

Resumen

Introducción – la inmunoterapia sublingual (SLIT) es beneficiosa en personas con dermatitis atópica (AD) y sensibilidad a los ácaros del polvo. La evaluación de esta terapia no ha sido descrita en casos de dermatitis atópica canina espontánea.

Objetivos – el objetivo de este estudio fue evaluar de forma preliminar la efectividad y establecer un protocolo de SLIT, tal y como se utiliza en pacientes humanos, en perros con AD.

Animales – 10 perros sensibles a los ácaros del polvo con dermatitis atópica espontánea.

Métodos – los perros permanecieron en una prueba abierta durante seis meses de SLIT conjuntamente con una dosis decreciente de metilprednisolona. Se realizaron evaluaciones clínicas y cuantificaciones de la IgE e IgG frente a los ácaros en el suero cada dos meses.

Resultados – el uso medio de metilprednisolona durante los dos primeros meses del estudio comparado con los dos meses finales del estudio se redujo de 10,2 a 4,3 mg/kg/ 2 meses (P < 0,001, prueba t de Student pareada); a los 6 meses cuatro perros no necesitaron administración oral de corticosteroides. Durante el estudio los valores del índice de extensión y severidad de dermatitis atópica canina (CADESI)-03 disminuyeron de 76,5 a 59; los valores medios de prurito descendieron de 65 a 37 (P < 0,02 y P < 0,01,
respectivamente; prueba de rangos de Wilcoxon). Los valores de las pruebas intradérmicas anteriores y posteriores a SLIT para alérgenos de los ácaros no fue diferente a lo largo del tiempo. Los valores medios de IgE específica de IgE específica de Dermatophagoides farinae (DF) se redujeron significativamente de 150,2 por 103 AU/mL a 3,6 por 103 AU/mL ($P < 0,05$). A la misma vez, los valores medios de IgG específica se incrementaron de 18,5 por 106 AU/mL a 3923,4 por 106 AU/mL ($P < 0,05$; pruebas pareadas de Wilcoxon).

Conclusión e importancia clínica – el tratamiento con SLIT produjo una mejoría clínica en perros con dermatitis atópica asociada a ácaros del polvo y se observaron cambios serológicos que indicaban tal mejora.

Se necesitan más estudios en un mayor número de perros y también en animales polisensitizados.

Zusammenfassung

Hintergrund – Es gibt Berichte über die Behandlungserfolge der sublingualen Immuntherapie (SLIT) bei Menschen mit atopischer Dermatitis (AD) und bei Sensibilitätsreaktionen an Hausstaubmilben. Eine Evaluierung dieser Therapie ist bisher bei Hunden mit spontaner AD noch nicht beschrieben worden.

Ziele – Das Ziel dieser Studie war eine vorläufige Evaluierung der Wirksamkeit eines etablierten SLIT Protokolls, wie es für Menschen eingesetzt wird, für Hunde mit AD.

Tiere – Zehn Hausstaubmilben-allergische Hunde mit spontaner AD.

Methoden – Bei den Hunden wurde eine 6-monatige Versuchsperiode mit SLIT durchgeführt, während der die per os verabreichten Dosis an Methylprednisolon reduziert wurde. Es wurden klinische Untersuchungen durchgeführt, sowie quantitative Serum-anti-Milben IgE und IgG Werte alle 2 Monate erhoben.

Ergebnisse – Die durchschnittliche Dosis des Methylprednisolons zwischen den ersten und den letzten beiden Monaten der Studie wurde von 10,2 auf 4,3 mg/kg/2 Monate reduziert ($P < 0,001$; gepaarter Studenten t-Test); nach 6 Monaten, benötigten vier Hunde keine orale Cortisongabe mehr. Über den Verlauf der Studie sanken die medianen Canine Atopic Dermatitis Extent und Severity Index (CADESI)-03 Werte von 76,5 auf 59; die medianen Juckreizwerte sanken von 65 auf 37 ($P < 0,02$ bzw $P < 0,01$; Wilcoxon Vorzeichen Rang Test). Die pr- und post-SLIT Werte des Intradermaltests für Milbenallergen unterschieden sich mit der Zeit nicht signifikant. Die medianen Dermatophagoides farinae (DF)-spezifischen IgE Levels sanken signifikant von 150,2 9 106 AU/ml auf 3,6 9 103 AU/mL ($P < 0,05$; Wilcoxon Vorzeichen Rang Test).


要約

背景 – 舌下免疫療法(SLIT)はアトピー性皮膚炎(AD)やハウスダスト過敏症のヒトで‘有効’であると報告されている。この治療法の評価は自然発症性のイヌADにおいては報告されていない。

目的 – この研究の目的はヒトの患者で使用されている既存のSLITのプロトコールの有効性をADのイヌで‘予備的に評価することである。

供与動物 – チリダニに過敏症状を示す自然発症性ADのイヌ10頭

方法 – 82–24: メチルプレドニゾロンの用量減少と同時にSLITの非盲検試験を行った。臨床評価および血清抗ダニIgEおよびIgGレベールの定を2ヶ月に行った。

結果 – 治療の開始2ヶ月から治療終了前2ヶ月までで平均ルメルブレドニゾロン用量は、10,2から4,3 mg/kg/2ヶ月まで減少し($P < 0,001$、対応のあるステージメントのt検定)。6ヶ月後には1頭のイヌが経口コルチコステロイド投与を必要とした。治療中に、平均イヌの皮膚炎指標および重症度指数(CADESI)-03スコアは76.5から59に減少し、平均秋込みスコアは65から37に減少した。それぞれP < 0.02およびP < 0.01; ヴィルコクソノンの符号付き検定)。ダニアレルゲンに対するSLIT前後の皮内反応スコアはいずれの時期でも有意差は見られなかった。平均Dermatophagoides farinae (DF)特異的IgEレベールは50.2 9 103 AU/mlから3.6 9 103 AU/mL ($P < 0.05$)に有意に減少した。同時に平均DF特異的IgGレベールは18.5 9 106 AU/mLから3923.4 9 106 AU/mL ($P < 0.05$; ヴィルコクソノンの符号付き検定)に増加し。

結論および臨床的な重要性 – SLIT療法はハウスダスト関連性ADのイヌで‘臨床的な改善を示し、この改善を支持する血清学的な変化と関連していた。より多くの数のイヌや複数の抗原に感作されたイヌにおけるさらなる研究が必要である。

概要

背景 – 舌下免疫療法(SLIT)は人と犬で抵抗の異位性皮膚炎(AD)に有効。該法による自然発症性ADの治療効果は未だ実測できていない。

目的 – 该研究的目的为初步评估SLIT治疗效果,将已制定的人类患者方案,同样用于AD患犬。

動物 – 十只犬为SLIT治疗的AD患犬。

方法 – 所有犬进行6个月开放性SLIT实验,同时逐渐减少口服甲强的松龙用量,每两个月进行一次临床评估,并测量血清中抗尘螨IgE和IgG水平。
结果 — 甲基强的松龙的平均用量，从实验开始2个月的10.2 mg/kg，下降到实验最后两个月的4.3 mg/kg（P < 0.001。学生配对t检验）；第六个月4只犬无需口服类固醇药物。研究期间，犬异位性皮炎程度和严重指数（CADESI-03）中值从76.5下降至59；瘙痒评分中值从65下降至37（分别P < 0.02和P < 0.01；威尔科克森符号等级鉴定）。SLIT前后尘螨过敏原皮内试验分数无明显变化。粉尘螨（DF）特异性IgE水平中值显著降低，从150.2 9 103 AU/mL降至3.6 9 103 AU/mL（P < 0.05）。同时DF特异性IgG水平从18.5 9 106 AU/mL增至3923.4 9 106 AU/mL（P < 0.05；威尔科克森符号等级鉴定）。

总结与临床意义 — SLIT治疗尘螨过敏的AD患犬，可见临床改善，相关的血清学变化也支持这种改善。已批准对更多多重致敏患犬开展进一步实验。