

Investigation on the effects of ciclosporin (Atopica) on intradermal test reactivity and allergen-specific immunoglobulin (IgE) serology in atopic dogs

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Source of Funding

This study was funded by a grant from the American College of Veterinary Dermatology.

Conflict of Interest

No conflict of interest has been declared.

Abstract

The ability to use ciclosporin (Atopica®: Novartis Animal Health, Greensboro, NC, USA) prior to intradermal testing (IDT) would help avoid exacerbation of clinical disease that can be associated with drug withdrawal. This study evaluated the effects of 30 days of administration of ciclosporin at a dose of 5 mg/kg once daily on IDT reactivity (immediate phase reactions) in a group of dogs with atopic dermatitis (AD) with initial positive IDT reactions. 16 dogs diagnosed with AD were included in the study. Eight dogs (group A) were treated with ciclosporin orally at 5 mg/kg once daily for 30 days. Eight dogs (group P) were treated with a placebo orally once daily for 30 days. IDT was performed at day 0 and day 30 on all dogs enrolled using a standardized panel of 45 aqueous allergens (Greer Laboratories, Lenoir, NC, USA) appropriate to our geographical region. IDT reactivity was assessed by both subjective and objective methods at 15 min post-intradermal injection. Serum for allergen-specific immunoglobulin (IgE) serology was obtained at day 0 and day 30. The study was designed as a double-blinded, placebo-controlled, cross-over study. Data were analysed using a split-plot analysis of variance with the grouping factor of treatment and the repeat factor of time (SAS System for Windows). At week 4, ciclosporin did not have a statistically significant effect on IDT reactivity or serology results. It therefore appears that, no withdrawal is recommended to evaluate immediate phase reactions.

Accepted 19 June 2009

Introduction

Canine atopic dermatitis (AD) is a genetically predisposed inflammatory and pruritic allergic skin disease that is associated with immunoglobulin E (IgE) antibodies to environmental allergens. Both human and canine AD, however, are very complex and multifaceted diseases, and IgE may only represent an epiphenomena rather than a primary immunological aberration.¹

The exact incidence of canine AD is not known, but has been reported to range from 3–15%.^{2–4} Owing to the variable efficacy and adverse effects of current therapies for AD, there is ongoing research to identify new treatment options. The clinical benefit of oral ciclosporin (CsA) for the treatment of human AD was documented in 1987.⁵ The efficacy of oral CsA in reducing skin lesions and pruritus of canine AD was first reported in a small open trial in 2001.⁶ Since then, several studies^{7–11} have shown that CsA is efficacious in the treatment of dogs with AD. Furthermore, CsA does not act on glucocorticoid receptors^{12,13} (and is therefore an option for tachyphylaxis associated with long-term glucocorticoid use), is given once daily (which increases owner compliance), lacks major side effects, does not require routine blood monitoring,¹⁴ and can be used with drugs that inhibit the cytochrome P450 enzyme system to decrease expense¹⁵ (Editors' note: this is off-label use and may be prohibited in some countries). In contrast to humans, dogs generally appear to tolerate CsA well without many adverse effects. Renal impairment and hypertension are often seen even at low doses in humans, but these effects are not observed in dogs.¹⁶ Adverse effects occur in approximately 20% of treated dogs, and primarily consist of gastrointestinal signs such as vomiting and diarrhoea.¹⁵ Other reported side effects include papillomatosis, hirsutism, gingival hyperplasia and secondary infections, but these are rare at therapeutic doses.¹⁷ Randomized, blinded, multicenter studies have established that 5 mg/kg per day is an effective induction dose to control clinical signs.^{7,8} Once in remission, it has been shown that the daily dosage or dosage interval can be decreased to control clinical signs in most dogs.¹⁸ Another important use for CsA is to alleviate clinical signs associated with drug withdrawal prior to IDT.

In veterinary medicine, Atopica® (Novartis Animal Health, Greensboro, NC, USA) is the approved micro-emulsion formulation. It is designed to improve bioavailability and decrease the inter-individual variability of drug absorption. In dogs, this offers 35% bioavailability

compared with 20–25% with the vegetable oil formulation.¹⁶ As CsA in this formulation (Atopica®) is becoming increasingly popular, knowledge of its effect on IDT reactivity is important. In the authors' and other clinicians' experience CsA does not seem to have a negative effect on the results of IDT in atopic dogs,^{19–22} although this has not been demonstrated in a controlled study. Therefore, the purpose of the present study is to evaluate the effects of 30 days treatment with CsA at 5 mg/kg orally once daily on IDT reactivity (immediate phase reactions) and allergen-specific IgE serology in a group of dogs with AD with known positive IDT reactions.

Materials and methods

Animals and experimental design

Sixteen dogs diagnosed with canine AD were included in this study, which was performed from July to November (Table 1). The inclusion criteria were a diagnosis of canine AD based on suggestive history, compatible clinical signs and the systematic rule out of other pruritic skin diseases, including the use of a home-cooked elimination diet trial for 8 weeks, and empirical treatment for fleas, *Sarcoptes* and other ectoparasites where appropriate. All the dogs had positive immediate reactions on IDT that corresponded with the history and clinical signs.

Dogs with concurrent flea allergy dermatitis or cutaneous adverse food reactions were excluded from the study. Animals with a pre-existing systemic disease or animals that could not suspend therapy due to severity of AD were also excluded. Dogs with secondary bacterial or yeast skin and/or ear infections were initially treated with an appropriate systemic and/or topical antimicrobial agent, allowing a 9-day withdrawal period prior to testing. All the medications were free of any glucocorticoids and nonsteroidal anti-inflammatory drugs. In addition, systemic ketoconazole was excluded to prevent increased serum CsA levels due to suppression of the cytochrome P450 enzyme system.

The following drug withdrawal periods prior to testing were observed: 90 days for all repositol corticosteroids; 30 days for all other injectable, oral and topical corticosteroids; 7 days for all antihistamines, essential fatty acid supplements, and nonsteroidal anti-inflammatory drugs; and no bathing for 7 days prior to examination. In addition, all dogs enrolled in the study had never been treated with CsA or this had been withdrawn for at least 30 days. The study was approved by the Michigan State University All-University Committee on Animal Care (AUCAC) and all clients participated with informed consent.

The 16 dogs were randomly assigned to two treatment groups. Eight dogs (group A) were treated using CsA (Atopica®) orally at 5 mg/kg once daily for 30 days, and eight dogs (group P) were treated with a placebo orally once daily for 30 days. IDT were performed and assessed at day 0 and day 30 on all dogs using a standardized panel of 45 aqueous allergens²³ (Greer Laboratories, Lenoir, NC, USA) appropriate to our geographical region. The same investigator performed all of the intradermal testing, and was blinded to each treatment group. In addition, serum for the measurement of a 48-allergen-specific IgE panel [Allercept® Northeast Regional Allergen Panel (ANRAP), Heska Corp, Loveland, CO, USA] was obtained at day 0 and day 30.²³

Intradermal testing (IDT) reactivity was assessed by both subjective and objective methods. Subjective grading was determined by assessing the degree of erythema, induration, and wheal diameter at 15 min post-intradermal injection. A positive reaction on IDT was a reaction that scored 2 + or higher on a scale from 0–4 +. 0 was the score given to the negative control (saline) and 4 + was the score given to the positive control (histamine). Objective grading was determined by measuring the horizontal and vertical dimensions of the wheals with a transparent ruler (in millimetres), with the wheal diameter reported as the mean of these two measurements. A reaction was considered positive if it was more than or equal to 0.5 ×

(the mean diameter) of the histamine reaction. This standardized and consistent method of measurement was used because the frequency with which the saline wheal was immeasurable was greater than the frequency with which it was measurable.

Statistics

Based on a standard deviation of 2.5 mm in wheal diameter, 16 dogs were determined to be sufficient to provide an 80% power to detect a difference of 3 mm at $P < 0.05$. Data were analysed by means of a split-plot analysis of variance with the grouping factor of treatment and the repeat factor of time. All data were analysed using least squares analysis of variance (LS_{ANOVA}), with all main effects and interactions included in the model. Differences among treatments and times were analysed using orthogonal contrast analysis. Testing for heterogeneity of regression was conducted to evaluate time trends between treatments. The analysis was performed at the highest significant order of regression. Because the IDT scores were not normally distributed, they were log transformed prior to analysis. Means and SE were calculated using the untransformed data. However, all P values are representative of the log transformed data. Because the number of allergens and the strength of allergen reaction for each animal were not consistent, all data were also analysed using dust mite only to attempt to standardize reactions. All analyses were performed using the statistical software package SAS System for Windows, version 8.2 (SAS Institute, Cary, NC, USA). A level of $P < 0.05$ was considered significant.

Results

All dogs returned for the 30-day post-treatment visit. An allergy score incorporating the mean of all positive reactions was calculated for the objective IDT results, subjective IDT results and the allergen specific IgE results to facilitate the statistical analysis. In an attempt to make the data more clinically applicable, an allergy score was subsequently formulated for the dust mite only positive reactions prior to statistical analysis.

Neither CsA nor the placebo treatment had any statistically significant effect on the mean wheal size of the positive reactions, although there was a slight decrease in the objective mean wheal size for the placebo group after 30 days (Figure 1). However, there was no statistically significant difference in the mean objective IDT reaction diameters between group A and group P over time.

Ciclosporin (CsA) and placebo treatments had no statistically significant effect on the mean subjective of the positive reaction scores, although there was a slight increase in the mean subjective score for CsA and a decrease in the mean subjective score for the placebo group after 30 days (Figure 2). However, there was no statistically significant difference in the mean subjective IDT reaction scores in groups A and P over time.

Ciclosporin (CsA) and the placebo did not have any statistically significant effect on the objective mean wheal size of the dust mite reactions, although there was a slight decrease in the objective mean wheal size for both the CsA and placebo group after 30 days (Figure 3). However, there was no statistically significant difference in the mean objective IDT reaction diameters between group A and group P over time.

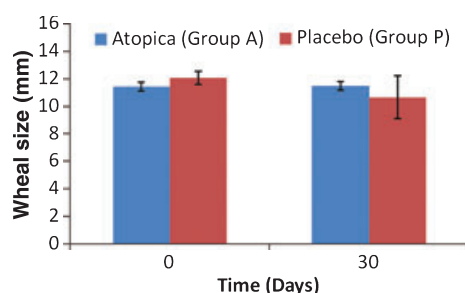
Ciclosporin (CsA) and placebo treatment did not have any statistically significant effect on the mean subjective score of the positive dust mite reactions, although there was a slight decrease in the mean subjective scores for both the CsA and placebo group after 30 days (Figure 4).

Table 1. Signalment, history, clinical signs and previous treatments of dogs included in study

Group	Signalment	History	Clinical signs	Previous treatments
A	3-year-old MN Cocker Spaniel	Warm weather seasonal pruritus since 1.5 years warm weather seasonal otitis externa since 2 years	Pruritus of face (muzzle), feet, axilla, abdomen	Commercial diet trial with Hill's Z/D Ultra for 8 weeks Prophylactic selamectin trial for scabies Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefalexin) Steroids (intermittent prednisone) Antihistamine (diphenhydramine)
A	1-year-old FS Pitbull mix	Warm weather seasonal pruritus since 5 months	Pruritus of face and feet	Commercial diet trial with Hill's Z/D Ultra for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefalexin, cefpodoxime) Steroids (prednisolone) Antihistamines (diphenhydramine, clemastine) Sentinel year round with fipronil/s-methoprene in warm weather
A	1.5-year-old MN mix	Warm weather seasonal pruritus since 6 months of age	Pruritus of face, feet and inguinal area	Commercial diet trial with Purina HA for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefalexin) Antihistamines (chlorpheniramine, cetirizine)
A	5-year-old MN mix	Warm weather seasonal pruritus since 3 years	Pruritus of face, feet and abdomen	Milbemycin oxime seasonally Commercial diet trial with Hill's Z/D Ultra for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefalexin, cefpodoxime) Antihistamines (chlorpheniramine) Sentinel year round
A	2-year-old MN mix	Warm weather seasonal pruritus since 1 years Warm weather seasonal otitis externa since 1.5 years Chronic anal gland problems	Pruritus of feet, abdomen and perianal area	Commercial diet trial with Hill's Z/D Ultra for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefpodoxime) Steroids (prednisone) Antihistamines (diphenhydramine, loratidine) Miconazole
A	2-year-old MN mix	Warm weather seasonal pruritus since 7 months of age Intermittent acute moist dermatitis on the head	Pruritus of flank, abdomen, medial thighs, face and ears	Home cooked elimination diet for 2 months Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefalexin) Ivermectin seasonally
A	1-year-old FS Bulldog	Nonseasonal pruritus with warm weather exacerbations since 6 months of age	Pruritus of face, feet and abdomen	Home cooked elimination diet for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Ivermectin seasonally
A	3-year-old FS Pekingese	Warm weather seasonal pruritus since 1.5 years	Pruritus of abdomen, ventrum, medial thighs and neck	Commercial diet trial with Hill's Z/D Ultra for 8 weeks Strict flea control with imidacloprid every 3 weeks Antibiotics (cefalexin) Steroids (prednisone, dexamethasone)
P	7-year-old FS Bassett Hound	Nonseasonal otitis externa since 2 months of age Warm weather seasonal pruritus since 1.5 years	Pruritus of face (muzzle), feet, axilla, abdomen	Home cooked elimination diet trial for 8 weeks Prophylactic selamectin trial for scabies Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics No steroids
P	5-year-old FS English Springer Spaniel	Warm weather seasonal progressing to non-seasonal pruritus since 2 years of age Nonseasonal otitis externa since 1 years	Pruritus of face, feet and abdomen	Home cooked elimination diet trial for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics No steroids

Table 1. (Continued)

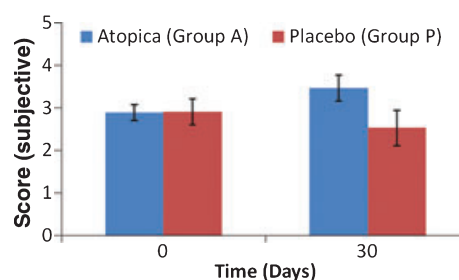
Group	Signalment	History	Clinical signs	Previous treatments
P	8-year-old FS Silky Terrier	Warm weather seasonal progressively worsening pruritus since 4 years Warm weather seasonal progressively worsening otitis externa since 4 years	Pruritus of abdomen, ventrum, axillae and face	Home cooked elimination diet trial for 8 weeks Multiple commercial diet trials Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefalexin, cefpodoxime) No steroids
P	3-year-old MN MN Pitbull	Nonseasonal progressively worsening pruritus with warm weather exacerbations since 2 years	Pruritus of face (neck), feet, axilla, inguinal region	Home cooked elimination diet trial for 8 weeks Multiple commercial diet trials Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefalexin) Steroids (triamcinolone, prednisone)
P	2-year-old MN Golden Retriever	Warm weather seasonal pruritus since 1 year	Pruritus of face, feet and abdomen	Commercial diet trial with Hill's Z/D Ultra for 8 weeks Strict flea control with imidacloprid every 3 weeks Antibiotics (cefalexin) Steroids (prednisone) Antihistamines (diphenhydramine)
P	2-year-old FS PitBull mix	Mild warm weather seasonal pruritus since 1 years	Pruritus of carpi, tarsi and feet	Commercial diet trial with Hill's Z/D Ultra for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics (cefpodoxime) Steroids (prednisone) Antihistamines (chlorpheniramine, hydroxyzine)
P	7-year-old MN American Pitbull	Nonseasonal progressively worsening pruritus with warm weather exacerbations since 2 years	Pruritus of face and feet	Home cooked elimination diet trial for 8 weeks. Strict flea control with fipronil/s-methoprene every 3 weeks Antibiotics Steroids Antihistamines
P	8-year-old MN Welsh Corgi	Nonseasonal progressively worsening pruritus with warm weather exacerbations since 3 years	Pruritus of face, feet and axillae	Home cooked elimination diet trial for 8 weeks Strict flea control with fipronil/s-methoprene every 3 weeks Antihistamines (diphenhydramine, clemastine) Steroids (prednisone)

**Figure 1.** Comparison of the mean objective wheal size for all positive allergen reactions on IDT between group A (Atopica) and group P (Placebo).

However, there was no statistically significant difference in the mean subjective IDT reaction scores between group A and group P over time.

Neither CsA nor placebo treatment had any statistically significant effect on the mean ELISA score of the positive reactions (EA units), although there was a slight decrease in the mean ELISA scores for both the CsA and placebo groups after 30 days (Figure 5). However, there was no statistically significant difference in the mean ELISA scores between group A and group P over time.

Ciclosporin (CsA) and placebo treatment did not have any statistically significant effect on the mean ELISA

**Figure 2.** Comparison of the mean subjective score for all positive allergen reactions on IDT between group A (Atopica) and group P (Placebo).

score of the positive reactions to dust mites (EA units), although there was a slight increase in the mean ELISA scores for both the CsA and placebo group after 30 days (Figure 6). However, there was no statistically significant difference in the mean ELISA scores between group A and group P over time.

Discussion

Treatment with CsA at 5 mg/kg once daily for 30 days did not have any significant effect on immediate IDT reactions or the allergen-specific IgE (ANRAP) levels when

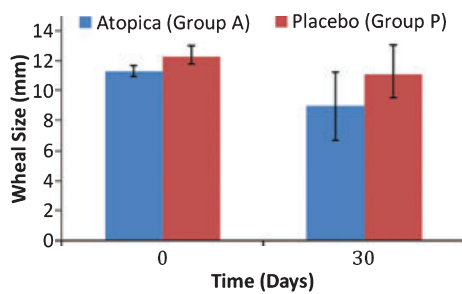


Figure 3. Comparison of the mean objective wheal size for the dust mite allergen reactions on IDT between group A (Atopica) and group P (Placebo).

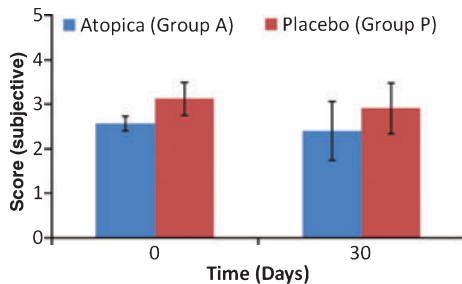


Figure 4. Comparison of the mean subjective score for dust mite allergen reactions on IDT between group A (Atopica) and group P (Placebo).

including all positive reactions or evaluating the dust mite positive reactions alone. The rationale for examining the dust mite only reaction scores was that exposure to these allergens was fairly constant over the 30-day treatment periods compared to other environmental allergens. Some dogs, in contrast, were tested at the end of their pollen season and then re-tested after pollination had ceased. This could have resulted in dogs with an initial positive reaction to pollens on both IDT or ANRAP being negative 1 month later, unrelated to the use of either the CsA or placebo.²³ One dog had significant reactions on both the initial IDT and ANRAP, but there was a significant reduction in the number of positive reactions to pollens (but not house dust mites) 30 days later. This corresponded to the expected pollen exposure for this patient. The data from this dog probably accounts for the nonsignificant reduction in mean scores following placebo compared to CsA treatment (Figures 1, 2 and 5). The mean scores for the dust mite only reactions were, in contrast, comparable between each group (Figures 3, 4 and 6).

Ciclosporin (CsA) effectively inhibits the activation of many key cells involved in cutaneous allergic inflammation, such as mast cells, eosinophils, lymphocytes, Langerhans' cells and keratinocytes.^{24–26} More specifically, CsA inhibits mast cell degranulation, survival and cytokine production in rodents, humans and dogs.²⁷ CsA also inhibits eosinophil function and survival, and inhibits most functions of T-lymphocytes, especially lymphocyte activation and proliferation.²⁷ As a result, IgE-mediated mast cell degranulation and immediate phase inflammatory reactions should, theoretically, be reduced following CsA administration. Nevertheless, previous studies¹⁹ failed to demonstrate that CsA inhibited IDT reactivity in dogs with AD. A pilot study²⁰ observed no significant reduction in

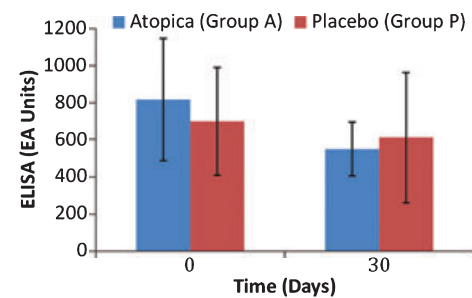


Figure 5. Comparison of the ELISA scores (EA units) for all positive reactions for both group A (Atopica) and group P (Placebo).

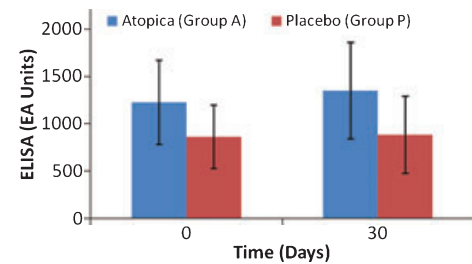


Figure 6. Comparison of the ELISA scores (EA units) for dust mite allergen reactions for both group A (Atopica) and group P (Placebo).

moderate and strong IDT reactions in six dogs with AD before and after 6 weeks of clinically effective therapy with 5 mg/kg of CsA (Neoral[®] formulation) per day. However, the interpretation of these results may have been biased, as the weak reaction scores were ignored, and when all reactions were used in analysis, CsA was shown to significantly reduce the number of IDT reactions. As none weak reaction scores were not included in the analysis of the dogs in our study, a direct comparison of these contradicting results cannot be made. Another study²¹ reported that 5 weeks treatment with CsA did not alter IDT and allergen-specific IgE serology to flea allergen in experimentally sensitized Beagles. An additional study²² of 14 human patients with severe AD found that their prick test responses were not affected by 7–16 weeks of clinically effective therapy with 5 mg/kg of CsA (Sandimmune[®]) per day. A short-term, 21-day study²¹ with CsA revealed no effect on serum allergen-specific IgE levels, although it is possible that longer treatment could have produced different results. It must also be noted that Sandimmune[®] is a different formulation from that used in this study (Atopica[®]). The absorption of CsA from the vegetable oil-based formulation (Sandimmune[®]) can be influenced by bile flow and the presence of food and gastrointestinal motility, resulting in and highly variable and potentially poor bioavailability.¹⁹ Neoral[®] is the human microemulsion formulation and is not approved in veterinary medicine. These factors must be taken into account when interpreting the results of previous studies that used these formulations.

We speculate because CsA blocks less than 100% of histamine release (~50–80%),²⁸ there is still a great enough released to produce an adequate immediate phase wheal and flare response following intradermal injection of allergens. Some of these findings may be partly explained by the fact that, *in vitro* at least, a fraction

of immunologically released histamine is also insulated from modulation by CsA.²⁸ Furthermore, studies on human and murine cells have found that CsA can potentiate IgE synthesis by both T cell-dependent and T cell-independent mechanisms²⁹ implying that CsA could paradoxically increase IgE synthesis. It would, therefore, be interesting to evaluate the effects of long-term CsA therapy on serology testing.

The lack of suppression of IDT reactivity is not associated with a lack of clinical response. In a human study evaluating CsA therapy for AD, treatment did not repress immediate phase responses to intradermal injections of an allergen of reference, IgE synthesis, or patch test reactions, even though a marked clinical improvement was reported. It was therefore concluded that the clinical response is not accompanied by an effect on the allergic response to allergens.³⁰

These data support the current clinical consensus that the use of CsA does not have a negative effect on the results of IDT or the measurement of allergen-specific IgE, and therefore withdrawal of CsA is not recommended prior to testing dogs with AD.

Acknowledgements

Special thanks to Elaine Striler for her assistance in recruiting affected dogs, performing all of the allergy testing and technical support.

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Résumé L'utilisation de ciclosporine (Atopica®: Novartis Animal Health, Greensboro, NC, USA) avant la réalisation de tests intradermiques (IDT) pourrait aider à éviter l'exacerbation des signes cliniques associés à l'arrêt thérapeutique. Cette étude a mesuré les effets de 30 jours d'administration de ciclosporine à la dose de 5 mg/kg une fois par jour sur la réactivité des IDT (réactions immédiates) dans un groupe de chiens atteints de dermatite atopique (AD) ayant des réactions initiales positives aux IDT. Seize chiens atopiques ont été inclus dans l'étude. Huit chiens (groupe A) ont été traités avec de la ciclosporine orale à la dose de 5 mg/kg par jour pendant 30 jours. Huit chiens (groupe P) ont reçu un placebo oral une fois par jour pendant 30 jours. Les IDT ont été réalisés au jour 0 et au jour 30 sur tous les chiens enrôlés avec une batterie standard de 45 allergènes aqueux (Greer Laboratories, Lenoir, NC, USA) appropriés à notre région géographique. La réactivité de test a été mesurée à la fois par des méthodes subjectives et objectives, 15 minutes après les injections intradermiques. Un dosage sérique des immunoglobulines (IgE) spécifiques d'allergènes a été réalisé à J0 et J30. L'étude était en double aveugle, contrôlée contre placebo et croisée. Les données ont été traitées par l'analyse de variance des parcelles divisées avec le traitement comme facteur de groupement et la durée comme facteur répété (SAS System for Windows). A la quatrième semaine, la ciclosporine n'avait pas d'effet statistique significatif sur la réactivité des IDT ou les résultats sérologiques. Il apparaît ainsi que de ne pas arrêter la thérapeutique est recommandé pour évaluer les réactions immédiates.

Resumen La posibilidad de utilizar ciclosporina (Atopica®: Novartis Animal Health, Greensboro, NC, USA) previa a la prueba intradérmica (IDT) puede ayudar a disminuir la exacerbación de signos clínicos que pueden asociarse con la interrupción del tratamiento. Este estudio evaluó los efectos en la prueba intradérmica (fase de reacción inmediata) de la administración durante 30 días de ciclosporina a una dosis de 5 mg/kg una vez al día, en un grupo de perros con dermatitis atópica (AD) con reacciones iniciales intradérmicas positivas. Dieciséis perros diagnosticados con AD se incluyeron en el estudio. Ocho perros (grupo A) fueron tratados con ciclosporina oral a 5 mg/kg durante 30 días. Ocho perros (grupo P) fueron tratados con placebo oralmente una vez al día durante 30 días. La prueba intradérmica se desarrolló en el día 0 y a los 30 días en todos los perros del estudio utilizando un panel estándar de 45 alérgenos en solución acuosa (Laboratorios Greer, Lenoir, NC, USA) apropiada para nuestra región geográfica. La prueba intradérmica fue valorada mediante métodos subjetivos y objetivos a los 15 minutos tras la inyección intradérmica. Se obtuvo suero para la detección de IgE específicas de alérgeno en los días 0 y 30. Los datos se analizaron utilizando un análisis de varianza de áreas divididas con el factor de agrupamiento de tratamiento y el factor repetición del tiempo (sistema SAS para Windows). En la cuarta semana, la ciclosporina no tuvo un efecto estadísticamente significativo en la reactividad de la prueba intradérmica o en los resultados serológicos. Así pues no se recomienda la interrupción del tratamiento para evaluar las reacciones de fase inmediata alérgicas.

Zusammenfassung Die Möglichkeit Ciclosporin (Atopica®: Novartis Animal Health, Greensboro, NC, USA) vor dem Intradermaltest (IDT) zu verwenden, würde dabei helfen, eine Verschlechterung der klinischen Krankheit, die mit dem Absetzen der Medikamente einhergehen kann, zu vermeiden. Diese Studie untersuchte die Auswirkungen einer 30 Tage lang dauernden einmal täglichen Verabreichung von Ciclosporin bei einer Dosis von 5mg/kg auf die Reaktivität des IDT („Immediate Phase“ Reaktionen) in einer Gruppe von Hunden mit atopischer Dermatitis (AD) mit ursprünglich positiven IDT Reaktionen. Sechzehn Hunde, die mit AD diagnostiziert worden waren, wurden in die Studie aufgenommen. Acht Hunde (Gruppe A) wurden 30 Tage lang mit Ciclosporin bei einer einmal täglichen Dosis von 5mg/kg per os behandelt. Acht Hunde (Gruppe P) wurden 30 Tage lang mit einem Placebo einmal täglich per os behandelt. Ein IDT wurde am Tag null und am Tag 30 bei allen Hunden der Studie mit Hilfe eines standardisierten Panels bestehend aus 45 wässrigen Allergenen (Greer Laboratories, Lenoir, NC, USA), die unserer geografischen Region entsprechen, durchgeführt. Die IDT Reaktivität wurde 15 Minuten nach der intradermalen Injektion sowohl mit subjektiven als auch mit objektiven Methoden beurteilt. Serum für Allergen-spezifische Immunglobulin (IgE) Serologie wurde am Tag null und 30 entnommen. Die Studie wurde als doppelblinde, Placebo-kontrollierte, Cross-Over-Studie angelegt. Die Daten wurden mittels Split-Plot Design Varianzanalyse mit einem Gruppierungsfaktor Behandlung und einem Wiederholungsfaktor Zeit (SAS System for Windows) analysiert. In der Woche vier zeigte Ciclosporin keinen signifikanten Einfluss auf die IDT Reaktivität oder die Serologie Ergebnisse. Um „Immediate Phase“ Reaktionen zu beurteilen, scheint daher ein Absetzen nicht notwendig zu sein.