

Subcutaneous administration of ciclosporin in 11 allergic cats – a pilot open-label uncontrolled clinical trial

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Background – Oral ciclosporin has been reported to be efficacious for feline inflammatory skin diseases; however, cats are often difficult to medicate orally.

Hypothesis/Objective – To evaluate the efficacy and tolerability of subcutaneous ciclosporin administered to cats with allergic skin disease.

Animals – Eleven client-owned cats with nonseasonal clinical signs.

Methods – Prospective open label trial. Ciclosporin 50 mg/mL solution for injection (Sandimmune®, Novartis; NJ, USA) was administered subcutaneously for 60 days with initial doses ranging from 2.5 mg/kg once daily (one cat) to every other day (five cats) and 5 mg/kg once daily (four cats) to every other day (one cat). Dosages were adjusted monthly if needed based on clinical response. Clinical response was assessed using a modified FeDESI (feline Dermatitis Extent and Severity Index) and PVAS (pruritus Visual Analog Scale) between days (D) 0, 30 and 60.

Results – Six cats completed the study and four of five cats withdrawn from the study were included in an intention-to-treat analysis. There was significant decrease in FeDESI and PVAS scores between D0 and D30, D0 and D60 and D30 and D60 ($P < 0.05$) in all ten cats.

Conclusions and clinical importance – Ciclosporin administered subcutaneously at initial doses of 2.5–5 mg/kg, once daily to alternate days, appears to be an efficacious therapy for feline allergic dermatitis and may be an alternative therapy for cats that cannot be treated orally. Randomized and controlled long term studies which include a larger number of cats are needed to confirm these findings.

Introduction

Feline dermatoses, including allergic diseases, are often challenging to manage. Topical therapies are frequently not well tolerated by cats, may pose risk of systemic adverse effects due to drug ingestion and are typically used as adjunctive therapies.¹ Antihistamines and essential fatty acids are treatment options but the success rate is variable and often low.¹ Oral and injectable glucocorticoids are quite effective but have the potential for severe long-term adverse effects, including diabetes mellitus.¹ Oclacitinib maleate may be an alternative treatment for cats with allergic skin disease, although in one pilot study only five of 12 (41.6%) cats with nonflea- and nonfood-induced hypersensitivity dermatitis treated

with oclacitinib, at the doses recommended for dogs, showed good improvement after 30 days of therapy.²

Several studies have investigated the use of oral ciclosporin A (CsA) in cats with various skin disorders; the efficacy and safety of CsA for the treatment of feline allergic dermatoses has been reported in double-blinded and randomized controlled trials.^{3–9} Additionally, CsA has been reported in retrospective and case series reports to be effective for other feline dermatological conditions including eosinophilic granuloma complex, urticaria pigmentosa, plasmacytic stomatitis, acquired alopecia (pseudopelade), pemphigus complex, idiopathic pruritus and dirty face syndrome of Persian cats.^{7–9} Mild adverse effects have been reported with oral CsA administration in cats, including hypersalivation, headshaking, vomiting, soft faeces, diarrhoea and gingival hyperplasia.^{10,11} Given the reported efficacy and minimal adverse effects, oral CsA appears to be a valid therapeutic approach for the long-term control of feline allergic skin diseases. However, cats are often difficult to medicate orally which could interfere with the efficacy of CsA and result in treatment discontinuation by the owners. In addition, oral CsA

Abbreviations: CsA, ciclosporin; sCsA, subcutaneous injected ciclosporin.

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was shown to have low and variable bioavailability in cats, possibly contributing to lack of efficacy in some cases.¹²

A pharmacokinetic study reported that subcutaneous CsA (sCsA) bioavailability was very good in cats.¹³ Hence, the use of injectable CsA could provide an alternative therapy for feline dermatoses because it may be more efficacious compared to oral CsA, and better accepted by some cats and owners compared to oral administration. To the best of the authors' knowledge, there are no reports investigating the use of sCsA in feline dermatological conditions. The aim of this pilot open-label trial was to evaluate the efficacy and tolerability of sCsA in a small group of cats with allergic skin disease.

Materials and methods

Enrolment

The study was designed as an open label clinical trial without a control group. Client-owned cats greater than one year of age, of any sex or breed, and with a history and clinical signs compatible with non-seasonal allergic skin disease of at least one year duration, were included in the study. Owners provided written informed consent and were advised of their right to withdraw from the trial at any time. Parasitic disorders, dermatophytosis and flea bite hypersensitivity were excluded as indicated by standard procedures including skin scrapings, trichoscopy, fungal culture and antiparasitic treatment trials. Elimination diet trials and serum and/or intradermal allergen testing were not required for enrolment. Cats were not included in the study if they had received treatment with injectable glucocorticoids within the previous eight weeks, oral glucocorticoids or CsA within the previous four weeks, and antihistamines during two weeks prior to enrolment. Cats with secondary bacterial or yeast skin infection received appropriate treatment before enrolment. Allergen-specific immunotherapy was allowed if treatment had been initiated at least one year prior to enrolment. The study protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of the University of Minnesota.

Criteria for withdrawal

Cats could be withdrawn from the study at any time with the occurrence of any of the following: significant worsening of the clinical condition (i.e. severe increase in pruritus and/or lesional scores); development of unacceptable drug adverse effects; owner desire to withdraw; lack of owner compliance; development of secondary bacterial and/or yeast infections severe enough to require systemic treatment; use of disallowed therapy or loss of follow-up examination. The reasons for withdrawal were recorded.

Treatment

Ciclosporin 50 mg/mL injection USP (Sandimmune®, Novartis; New Jersey, NJ, USA) was administered subcutaneously by owners at home, in the interscapular region using a 22 gauge needle, upon strict guided instructions. The dose volume to be administered was marked on the syringe using Mark-A-Dose Strip (Baxter Healthcare Corporation; Zurich, Switzerland); owners were trained to draw the exact dose and requested to wipe the top of the vial with alcohol before extracting each dose. All owners were carefully educated on the importance of following the instructions strictly. In the absence of data on the ideal initial dosage and administration frequency of sCsA therapy in cats, different dosages were used [this is in part because the bioequivalence of oral modified and injectable (nonmodified) forms of ciclosporin are unknown]. Starting dosages of sCsA (D0) were 2.5 mg/kg once daily (one cat), 2.5 mg/kg every other day (five cats), 5 mg/kg once daily (four cats) and 5 mg/kg every other day (one cat). Dosages were adjusted monthly if needed based on clinical response as follows: if at least 50% reduction was seen in FeDESI and PVAS scores, the dosage was reduced and, if there was less than 50% improvement, the dosage was increased. Cats

needed to be treated for at least 60 days to allow sufficient time for evaluation of efficacy. It was recommended that cats be kept completely indoors during the study.

Assessment of treatment efficacy

Each cat was assessed by the investigators at the first visit [day 0 (D0)] and at re-evaluation visits on D30 and D60. A modified (and therefore unvalidated) FeDESI (feline Dermatitis Extent and Severity Index) was used by the investigators at each visit to estimate the extent and severity of clinical signs.¹⁴ The severity of five types of lesions was assessed including erythema, excoriations/erosions, self-induced alopecia, crusted papules (miliary dermatitis) and nodules/plaques. Lesions were evaluated at 47 different sites covering the entire body. Each lesion at each body site received a severity score defined as: 0, no lesions; 1, mild; 3, moderate; and 6, severe. The maximum score was 1,410. Owners evaluated the intensity of pruritus on D0, D30 and D60 by placing a mark on a 10 cm horizontal PVAS (pruritus Visual Analog Scale, this scale has not been validated for cats) from 0 ('not itchy or occasionally itchy as a normal cat') to 10 ('very itchy').

Safety monitoring

All cats were monitored clinically by the investigators and owners for any systemic and local injection site reactions. Additionally, in order to help monitor for potential long-term adverse effects, complete blood cell count (CBC), chemistry profile, urinalysis and urine culture were performed whenever possible on D0 and D60.

Statistical analyses

The Friedman test was used to determine if there were differences in the FeDESI scores and PVAS values at any time point. If significant differences were noted, pairwise comparisons were done using the Wilcoxon test for paired samples with Bonferroni–Holm correction for multiple comparisons. Intention-to-treat-analysis was used by carrying forward the last known observation for missing data in four of 11 cats. Cat 10 was excluded from the statistical analysis because it was withdrawn prior to D30. R 3.2.0 was used for all statistical analyses (R Core Team. R: A Language and Environment for Statistical Computing. <<http://www.R-project.org/>> R Foundation for Statistical Computing, Vienna, Austria, 2014). A *P*-value < 0.05 was considered to be statistically significant.

Results

Cats

Eleven client-owned cats diagnosed with nonseasonal allergic skin disease were enrolled. Cats were reported to be healthy, except for Case 4 which had well-controlled diabetes at the time of enrolment. There were eight domestic short hair, two domestic long hair and one Abyssinian cat. Five cats were female spayed and six were male neutered and their age ranged from two to 15 years (mean: 6.3). The cats presented variable clinical signs. Three cats (cases 1, 4 and 10) had alopecia, erythema, and crusts with or without excoriations; three cats (cases 3, 6 and 7) had miliary dermatitis and alopecia with or without erythema and excoriations; two cats (cases 5 and 11) had symmetrical alopecia; and three cats (cases 2, 8 and 9) had eosinophilic granuloma complex lesions with or without alopecia, erythema and excoriations. Demographic information and clinical data are summarized in Table S1.

Ciclosporin dose and frequency of administration

Doses of sCsA on D0 ranged from 2.5 to 5 mg/kg daily to every other day. At D30, the dosages of the eight cats in

the study were 2.5 mg/kg every third day (two cats), 5 mg/kg once daily (two cats) and 5 mg/kg every other day (four cats). Only six of 11 cats completed the study and their dosages included 2.5 mg/kg every third day (one cat), 5 mg/kg every 36 to 48 h (one cat), 5 mg/kg every other day (three cats) and 5 mg/kg every third day (one cat), (Table S1).

Withdrawal

Five (45.45%) cats (cases 7, 8, 9, 10 and 11) were withdrawn from the study per owners' requests prior to trial completion (D60). One cat (Case 8) was withdrawn due to behaviour changes reported by the owner and lack of response to therapy. Two cats (cases 9 and 11), although improved, were withdrawn because of adverse effects at injection sites reported by the owners. Two cats (cases 7 and 10) were withdrawn because the owners were not comfortable to continue administering the injections. Table S1 shows details of withdrawal times and reasons for each cat.

Assessment of skin lesions (FeDESI)

The Friedman test showed a significant ($P = 0.0002$) impact of therapy on skin lesions. Pairwise analyses showed significant skin lesion improvement between D0 and D30 ($P = 0.008$), D0 and D60 ($P = 0.006$) and D30 and D60 ($P = 0.02$). Figure 1 and Table S2 show the individual scores. Figure S1 and Figure S2 show pictures of two cats that completed the study.

Assessment of pruritus (PVAS)

The Friedman test showed a significant ($P = 0.0003$) impact of therapy on pruritus. Pairwise analyses showed significant pruritus decrease between D0 and D30 ($P = 0.028$), D0 and D60 ($P = 0.026$) and D30 and D60 ($P = 0.034$). Figure 1 and Table S2 show the individual scores.

Adverse effects and laboratory tests

A total of six (54.5%) cats (4, 5, 6, 8, 9 and 11) developed adverse effects reported by the owners. Five cats (4, 5, 6, 9 and 11) developed lesions associated with the injection sites, seven to 10 days after starting therapy (Table S1). Owners described the lesions as focal hair loss, crusts, abscesses or swellings with or without oozing. These resolved in three of five cats (cases 4, 5 and 11) after changing the injection site, reviewing injection administration instructions or discontinuing therapy. Cases 4 and 11 had focal alopecia at the injection sites observed by the investigators on D30 and presumed to be sequelae of previous lesions. One cat (Case 8) developed behaviour changes and another cat (Case 9) was licking the injection site and twitching her back after each injection. None of the cats developed systemic signs during the study duration or follow-up period. In one cat (Case 4) the pre-diagnosed diabetes mellitus remained clinically controlled during the follow-up period. Table S1 shows details on adverse events for each cat. Ten (90.9%) cats had chemistry profiles, complete CBC, urinalyses and urine cultures before starting sCsA therapy. Six (60%) cats had these tests repeated on D60. There were no significant abnormalities reported at any time for any of the cats.

Follow-up of cats after completion of the study

Six cats (cases 1, 2, 3, 4, 5 and 6) continued to receive sCsA therapy beyond D60, with therapy duration ranging from three to 18 months (mean: 9.8 months). The maintenance sCsA dose for these cases ranged from 2.5 to 5 mg/kg every two to three days. Any further attempt to taper the frequency of injections failed with recurrence of pruritus with or without skin lesions and alopecia. No adverse reactions were reported during the follow-up visits. Table S1 provides further details on treatment duration.

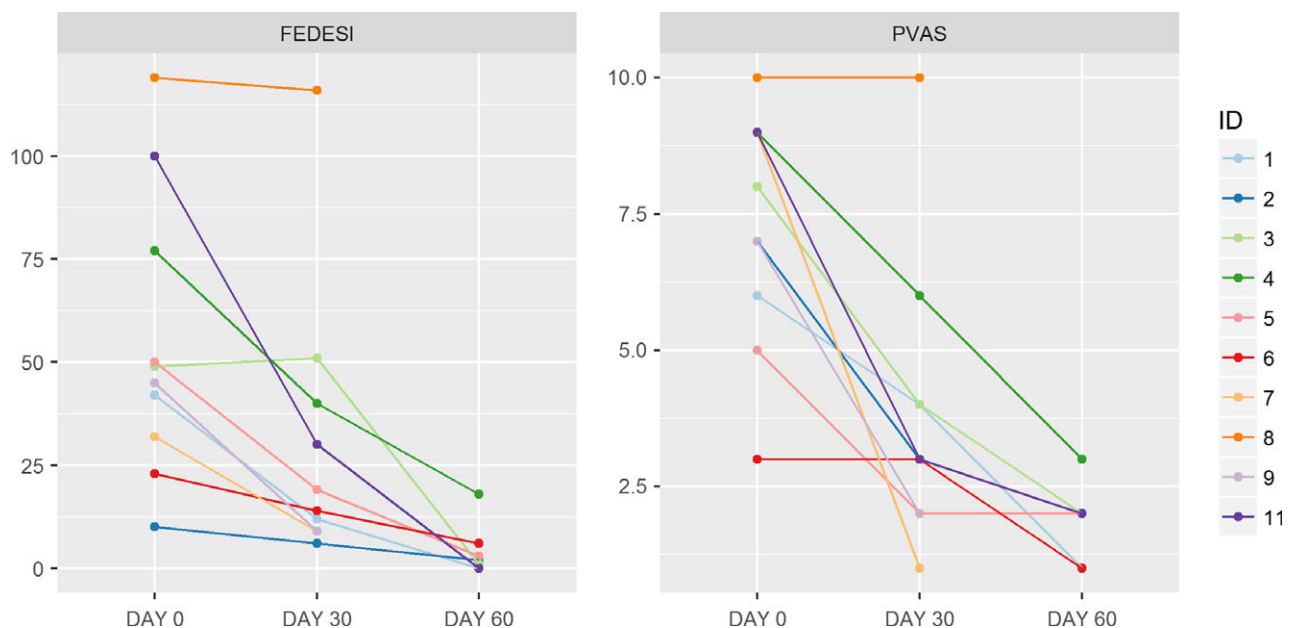


Figure 1. Feline Dermatitis Extent and Severity Index and pruritus Visual Analog Scale (range 0-10) scores on days (D) 0, 30 and 60 in 10 cats with allergic skin disease (Cat 10 not included).

Discussion

In this study, sCsA therapy resulted in significant improvement of pruritus and skin lesions in cats with allergic dermatitis. FeDESI scores and PVAS values reduced by at least 50% in five and six of the 10 cats evaluated on D30, respectively. In all six cats that continued therapy until D60, a reduction of at least 60% in FeDESI and PVAS compared to D0 was noted. These findings support previous studies showing that oral CsA is efficacious for the treatment of inflammatory skin diseases in cats;^{4–7} and suggest that the subcutaneous route of administration might be an alternative to oral dosing for noncompliant cats or those with intractable gastrointestinal signs.

Double-blind controlled trials have shown that 7 mg/kg/day doses of oral modified CsA are more efficacious compared to 2.5 and 5 mg/kg/day.^{5,6} However, the initial dosage of 2.5 to 5 mg/kg, once a day to every other day, used in this study was adequate to control the clinical signs of the treated cats suggesting that lower dosages can be given when administering CsA subcutaneously. This could be explained by differences in the pharmacokinetics of oral versus subcutaneous ciclosporin.^{12,13} Previous studies indicated that alternate day maintenance dose of oral CsA is adequate to control allergic signs in cats.⁷ Likewise, it appears that a maintenance dose of sCsA of 2.5–5.0 mg/kg every 36–72 h may be suitable to control feline allergic skin diseases. The authors used various dose regimens because the ultimate study goal was to determine treatment efficacy; hence, dosages were adjusted according to each cat's response. Due to the small number of cats that completed the study, a correlation between decreases in FeDESI and/or PVAS scores and CsA dosages could not be determined.

To date, SCORFAD (scoring feline allergic dermatitis) is the only validated scoring system used in cats.^{15,16} We used a modified FeDESI because SCORFAD was not available at the time of this study. However, the lesions added in the FeDESI modified by the authors (i.e. crusted papules and nodules/plaques) were similar to the ones added to SCORFAD.

A total of six (54.5%) cats developed adverse effects believed to be related to therapy, with the most common adverse reaction being injection site lesions in five cats. The lesions resolved after modifying the injection method or discontinuing therapy. One cat developed behaviour changes (i.e. "not being himself") which resolved after therapy was discontinued. The high percentage of adverse effects noted in this relatively short study is of concern and should alert clinicians to educate owners of the potential adverse effects and closely monitor all cats receiving this treatment modality.

Systemic adverse effects were not noted in the present study. There were no significant laboratory abnormalities in any of the six cats that had CBC and chemistry profiles performed at 60 days post-therapy. In addition, no adverse events were reported by owners of the five cats that continued to receive sCsA for up to 18 months.

Cats receiving oral therapeutic doses of CsA appear to be at higher risk of developing clinical toxoplasmosis if they become infected while receiving CsA,^{17,18} but

activation of *Toxoplasma gondii* in chronically infected cats is also possible.¹⁹ Toxoplasmosis titres were not performed in this study; however, owners were asked to maintain their cats exclusively indoors. Considering the potential risks for severe and possible fatal *T. gondii* infection during treatment with CsA, it is wise to perform titres before initiating therapy and educate clients to maintain the cats completely indoors and to avoid raw meat diets and hunting behaviours.

Although injectable CsA therapy may improve compliance and clinical outcome in cats that do not accept or tolerate oral therapy, it is important to realize that some cats and owners may not accept frequent injections administered at home, as observed in two of the five cats that dropped out of the study. Additionally, injections may pose a risk of injury for owners and cats that demonstrate nervous or aggressive behaviour.

There are several limitations to this study including the small number of cats, the short study duration, the use of different CsA doses and administration frequencies, and the lack of a control group and blinded evaluations which could have influenced the investigators' and owners' outcome measurements.

To the best of the authors' knowledge, this is the first report evaluating sCsA in cats with allergic dermatoses. Double-blind, randomized and controlled long-term clinical trials with larger numbers of cats are needed to confirm these findings and to evaluate the optimal dosage and safety profile of sCsA, before recommending its use in daily practice.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Figure S1. (a) Cat 3. Before subcutaneous ciclosporin therapy showing self-inflicted multifocal alopecia on dorsum, lateral thorax and front legs. (b) Cat 3. Sixty days post-subcutaneous ciclosporin therapy showing complete hair regrowth.

Figure S2. (a). Cat 4. Before subcutaneous ciclosporin therapy showing extensive alopecia, erythema, crusts and excoriations on the face. (b) Cat 4. 60 days post-subcutaneous ciclosporin therapy showing almost complete hair regrowth and resolution of skin lesions.

Table S1. Demographic, clinical data and follow-up period of 11 cats with allergic skin disease.

Table S2. Feline Dermatitis Extent and Severity Index and pruritus Visual Analog Scale (range 0–10) scores on days (D) 0, 30 and 60 in 11 cats with allergic skin disease.

Résumé

Contexte – La cyclosporine orale est rapportée comme efficace pour les dermatoses inflammatoires félines ; cependant, les chats sont souvent difficiles à traiter oralement.

Hypothèse/Objectif – Évaluer l'efficacité et la tolérance de la ciclosporine sous-cutanée administrée aux chats atteints de dermatoses allergiques.

Sujets – Onze chats de propriétaires présentant des signes cliniques non saisonniers.

Méthodes – Essai prospectif ouvert. Une solution de cyclosporine à 50 mg/mL injectable (Sandimmune®, Novartis; NJ, USA) a été administrée en sous cutanée pendant 60 jours à des doses initiales allant de 2.5 mg/kg une fois par jour (un chat) à un jour sur deux (cinq chats) et 5 mg/kg une fois par jour (quatre chats) à un jour sur deux (un chat). Les doses ont été ajustées chaque mois si besoin en fonction de la réponse clinique. Celle-ci a été évaluée par un FeDESI modifié (Feline Dermatitis Extent and Severity Index) et un PVAS (Pruritus Visual Analog Scale) entre les jours (D) 0, 30 et 60.

Résultats – Six chats ont finalisés l'étude et quatre des chats étant sortis de l'étude ont été inclus dans une analyse d'intention de traitement. Il y avait une diminution significative du FeDESI et du PVAS entre D0 et D30, D0 et D60 et D30 et D60 pour tous les dix chats ($P < 0.05$).

Conclusions et importance clinique – La cyclosporine administrée en sous-cutané aux doses initiales de 2,5 à 5 mg/kg une fois par jour à un jour sur deux, semble efficace pour les dermatites allergiques félines et pourrait être une alternative pour les chats ne pouvant être traités oralement. Des études contrôlées et randomisées incluant un plus grand nombre de chats sont nécessaires pour confirmer ces données.

Resumen

Introducción – Ha sido publicado que la ciclosporina oral es eficaz para las enfermedades inflamatorias de la piel en gatos; sin embargo, los gatos son a menudo difíciles de medicar por vía oral.

Hipótesis/Objetivo – Evaluar la eficacia y tolerabilidad de la ciclosporina subcutánea administrada a gatos con enfermedad alérgica cutánea.

Animales – Once gatos de propietarios privados con signos clínicos no estacionales.

Métodos – estudio clínico prospectivo abierto. Una solución inyectable de Ciclosporina 50 mg/ml (Sandimmune®, Novartis, NJ, EE.UU.) se administró por vía subcutánea durante 60 días con dosis iniciales que iban desde 2,5 mg/kg una vez al día (un gato) o a días alternos (cinco gatos) y 5 mg/kg una vez al día (cuatro gatos) o en días alternos (un gato). Las dosis se ajustaron mensualmente cuando fue necesario en base a la respuesta clínica. La respuesta clínica se evaluó usando un FeDESI modificado (índice de extensión y severidad de la dermatitis felina) y PVAS (escala analógica visual del prurito) entre los días (D) 0, 30 y 60.

Resultados – Seis gatos completaron el estudio y cuatro de los cinco gatos excluidos del estudio se incluyeron en un análisis de intención de tratar. Hubo una disminución significativa en las puntuaciones de FeDESI y PVAS entre D0 y D30, D0 y D60 y D30 y D60 ($P < 0.05$) en todos los gatos.

Conclusiones e importancia clínica – La ciclosporina administrada por vía subcutánea a dosis iniciales de 2,5–5 mg/kg, una vez al día o en días alternos, parece ser una terapia eficaz para la dermatitis alérgica felina y puede ser una terapia alternativa para gatos que no pueden ser tratados por vía oral. Se necesitan

estudios al azar y controlados a largo plazo que incluyan un mayor número de gatos para confirmar estos hallazgos.

Zusammenfassung

Hintergrund – Es wurde bereits beschrieben, dass Ciclosporin *per os* bei entzündlichen Erkrankungen der Katzen wirksam ist; Katzen sind jedoch bei der Verabreichung von Medikamenten oft schwierig.

Hypothese/Ziele – Eine Evaluierung der Wirksamkeit und Toleranz von subkutan verabreichtem Ciclosporin, welches Katzen mit allergischen Hautkrankheiten verabreicht wurde.

Tiere – Elf private Katzen mit nicht-saisonalen klinischen Zeichen.

Methoden – Es handelt sich um einen offenen prospektiven Versuch. Es wurde Ciclosporinlösung bei einer Dosierung von 50mg/ml zur Injektion (Sandimmune®, Novartis; NJ, USA) 60 Tage lang subkutan verabreicht, wobei die Initialdosis zwischen 2,5 mg/kg einmal täglich (eine Katze) bis jeden zweiten Tag (fünf Katzen) und 5mg/kg einmal täglich (vier Katzen) bis jeden zweiten Tag (eine Katze) reichte. Die Dosierungen wurden basierend auf der klinischen Reaktion monatlich angepasst. Die klinische Reaktion wurde mittels modifiziertem FeDESI (feline Dermatitis Extent and Severity Index) und PVAS (Pruritus Visual Analog Scale) zwischen den Tagen (D) 0, 30 und 60 ermittelt.

Ergebnisse – Sechs Katzen beendeten die Studie und vier der fünf Katzen, die aus der Studie genommen wurden, wurden in eine Intention-to-treat Analyse inkludiert. Es bestand eine signifikante Verminderung des FeDESI und der PVAS Werte zwischen D0 und D30, D0 und D60 und D30 und D60 ($P < 0,05$) bei allen zehn Katzen.

Schlussfolgerungen und klinische Bedeutung – Subkutan verabreichtes Ciclosporin bei einer Anfangsdosis von 2,5-5mg/kg einmal täglich bis zu jedem zweiten Tag scheint eine wirksame Therapie für die allergische Dermatitis der Katzen zu sein und könnte eine alternative Therapie für Katzen darstellen, die *per os* nicht behandelt werden können. Randomisierte und kontrollierte Langzeitstudien, die eine größere Anzahl an Katzen inkludieren, sind nötig um diese Ergebnisse zu bestätigen.

要約

背景 – 経口シクロスポリンは、猫の炎症性皮膚疾患に有効であると報告されているが、猫は経口投与が困難ことが多い。

仮説/目的 – アレルギー性皮膚疾患を有する猫に対するシクロスポリンの皮下投与の有効性及び許容性を評価すること。

供与動物 – 非季節性の臨床症状を呈する11頭の飼い猫。

方法 – 前向き非盲検試験。注射用シクロスポリン50 mg/mL(Sandimmune、Novartis、ニュージャージー州、米国)を2.5 mg/kgで1日1回(1頭)か隔日(5頭)あるいは5 mg/kgで1日1回(4頭)か隔日(1頭)を初期用量として60日間投与した。投与量は、治療応答性に基づいて必要に応じて毎月調整した。治療反応性は、0日目(D)、30日目および60日目の改変FeDESI(猫の皮膚炎範囲および重症度指数)およびPVAS(痒み視覚アナログスケール)を比較して評価した。

結果 – 6頭の猫が試験を完遂し、試験から脱落した5頭のうち4頭が、治療企図分析に含められた。10頭すべての猫において、D0とD30、D0とD60、D30とD60の間にFeDESIおよびPVASの有意な低下が認められた($P < 0.05$)。

結論および臨床的な重要性 – 初期用量2.5~5 mg/kg、1日1回から隔日の皮下投与シクロスポリンは、経口投与ができない猫に対してする猫アレルギー性皮膚炎の有効な代替治療法であると考えられる。これらの知見を立証するために、より多くの猫を対象とした長期間の無作為化コントロール研究が必要である。

摘要

背景 – 据报道,口服环孢素对猫炎症性皮肤病有效。然而,猫经常难以接受口服药物治疗。

假设/目的 – 评估环孢素皮下给药,对过敏性皮肤病患猫的疗效,以及猫的耐受性。

动物 – 11只非季节性临床症状的私家猫。

方法 – 预期性开放性试验。皮下注射环孢素50mg/ml溶液(Sandimmune, Novartis; NJ, USA)共60天,初始剂量(一只猫)每天一次2.5 mg/kg, (五只猫)两天一次2.5 mg/kg; (四只猫)每天一次5 mg/kg, (一只猫)两天一次5 mg/kg。根据临床反应,每月调整剂量。使用改良的FeDESI(猫皮炎程度和严重指数)和PVAS(瘙痒视觉模拟量表),在第0天、30天和60天评估临床反应。

结果 – 六只猫完成了研究,退出的五只猫中,有四只被纳入意向性治疗分析。所有10只猫中D0和D30,D0和D60,D30和D60($P < 0.05$)的FeDESI和PVAS评分均显著降低。

结论和临床意义 – 皮下注射环孢素,初始剂量为2.5-5 mg/kg, 每天一次至两天一次,似乎对猫过敏性皮炎治疗有效,可以替代口服治疗。还需要对大量的猫进行随机和对照性长期研究,以证实这些结论。

Resumo

Contexto – O uso de ciclosporina por via oral tem sido relatado como eficaz para dermatopatias inflamatórias felinas; entretanto, gatos frequentemente são difíceis de serem medicados por via oral.

Hipótese/Objetivo – Avaliar a eficácia e a tolerância de ciclosporina aplicada por via subcutânea para gatos com doença alérgica.

Animais – Onze gatos de proprietários com sinais clínicos não sazonais.

Métodos – Ensaio clínico aberto prospectivo. A solução para injeção de ciclosporina 50mg/mL (Sandimmune®, Novartis; NJ, USA) foi administrada por via subcutânea por 60 dias com doses iniciais variando de 2,5 mg/kg uma vez ao dia (um gato) ou em dias alternados (cinco gatos) e 5 mg/kg uma vez ao dia (quatro gatos) ou em dias alternados (um gato). As dosagens foram ajustadas mensalmente de acordo com a necessidade, baseado na resposta clínica. Esta foi avaliada utilizando um FeDESI (*Feline Dermatitis Extent and Severity Index*) modificado e a PVAS (*Pruritus Visual Analog Scale*) entre os dias (D) 0, 30 e 60.

Resultados – Seis gatos completaram o estudo e quadro dos cinco gatos que não concluíram o estudo foram incluídos em uma análise de intenção de tratar. Houve um decréscimo significativo nos escores de FeDESI e PVAS entre D0 e D30, D0 e D60 e D30 e D60 ($P < 0.05$) em todos os dez gatos.

Conclusões e importância clínica – A ciclosporina administrada por via subcutânea em doses iniciais de 2,5-5 mg/kg, uma vez ao dia ou em dias alternados, parece ser uma terapia eficaz para dermatopatias alérgicas em felinos e pode ser uma alternativa de terapia para gatos que não podem ser tratados por via oral. Estudos controlados e randomizados a longo prazo que incluam um número maior de animais são necessários para confirmar estes resultados.









Supporting Information

Table S1. Demographic, clinical data and follow-up period of 11 cats with allergic skin disease

Cat	Age (years)	Sex	Breed	Lesions and distribution	Concurrent medications	Ciclosporin D0 dose	Ciclosporin D30 dose	Ciclosporin D60 dose	Adverse effects reported by owners and/or reasons for withdrawal	Therapy duration (months)
1	10	FS	DSH	Alopecia and excoriations on pinnae, neck and legs	ASIT (≥ 12 months)	2.5 mg/kg every other day	5 mg/kg every other day	5 mg/kg every other day	No adverse effects	18
2	6	FS	DLH	Indolent ulcer on upper lips and granuloma on tongue, excoriations and erythema on ventral neck and right flank	None	2.5 mg/kg every other day	2.5 mg/kg every third day	2.5 mg/kg every third day	No adverse effects	6
3	3	MN	DSH	Alopecia, scaling and miliary dermatitis on dorsum, ventral thorax and abdomen extending to front legs, sparing the head and neck	None	2.5 mg/kg once daily	5 mg/kg once daily	5 mg/kg every other day	No adverse effects	6
4	7	MN	DLH	Alopecia, erythema, crusts and excoriations on face, periocular areas, chin and alopecia on ventral abdomen and perianal area; otitis externa and bacterial overgrowth	ASIT (≥ 12 months) Otomax [®]	5 mg/kg once daily	5 mg/kg every other day	5 mg/kg every third day	Abscess or swelling at site of injection - resolved with change in administration	15
5	4	MN	DSH	Symmetrical alopecia on dorsal and ventral neck, ventral thorax, ventral abdomen, inguinal areas, flanks and limbs	ASIT (≥ 12 months) Hy-Lyt Spray [®]	5 mg/kg once daily	5 mg/kg every other day	5 mg/kg every other day	Dry crust developed once at injection site - resolved with change in administration	4
6	15	FS	DSH	Miliary dermatitis, erythema and alopecia on dorsal and ventral neck and rear limbs	Otomax [®]	5 mg/kg once daily	5 mg/kg once daily	5 mg/kg every 36-48 h	Hair loss and scabs at injection site, treatment discontinued after 3 months due to injection site reaction – did not improve changing administration of injection at home	3

7	3	MN	DSH	Miliary dermatitis, alopecia and excoriations on head, pinnae, ventral abdomen, inguinal areas, dorsum, flanks and perianal areas	None	5 mg/kg every other day	5 mg/kg every other day	NA	No adverse effects Attempted to reduce dose but did not work - owner did not want to continue giving frequent injections	2 Withdrawn prior to D60
8	8	MN	DSH	Eosinophilic plaque, generalized alopecia and erythema, excoriations	None	2.5 mg/kg every other day	NA	NA	Behaviour changes ('cat not being himself' per owner) and lack of efficacy	1 Withdrawn at D30
9	2	FS	DSH	Indolent ulcer on lower lip, eosinophilic plaque on right foot and linear granulomas on hind legs	None	5 mg/kg once daily	NA	NA	Mild hair loss at injection site associated with licking for a few minutes after injections - did not resolve with change in administration of injections	1 Withdrawn prior to D30
10	4	MN	Abyssinian	Erythema, alopecia and excoriations on face, chin, inguinal areas, and rear paws (interdigital spaces)	None	2.5 mg/kg every other day	NA	NA	No adverse effects Received only one injection, aggressive cat, owner was not comfortable giving injections at home	1 Withdrawn after 1 injection
11	7	FS	DSH	Symmetrical alopecia on trunk extending to front and rear legs	None	2.5 mg/kg every other day	2.5 mg/kg every third day	NA	Oozing/exudate at injection site - resolved after stopping therapy, however, owner did not want to continue therapy	1 Withdrawn prior to D60

ASIT, allergen specific immunotherapy (subcutaneous); DLH, domestic longhair; DSH, domestic shorthair; FS, female spayed; MN, male neutered, NA, not applicable; Hy-Lyt Spray® contains water, sodium lactate, mineral oil, PVP, polysorbate 60, safflower oil, diazolidinyl urea, lanolin oil, methyparaben, PSG-8 dilaurate, oleth-2, propylparaben, propylene glycol, iodopropynyl, butylcarbamate, fragrance, sodium dehydracatate. Otomax® contains betamethasone valerate, clotrimazole and gentamicin sulfate.

Table S2. Feline Dermatitis Extent and Severity Index and Pruritus Visual Analog Scale (range 0-10) scores on Days 0, 30 and 60 in 11 cats with allergic skin disease

Cat	FEDESI D0	PVAS D0	FEDESI D30	PVAS D30	FEDESI D60	PVAS D60
1	42	6	12	4	0	1
2	10	7	6	3	2	2
3	49	8	51	4	1	2
4	77	9	40	6	18	3
5	50	5	19	2	3	2
6	23	3	14	3	6	1
7	32	9	9	1	NA	NA
8	119	10	116	10	NA	NA
9	45	7	9	2	NA	NA
10	25	6	NA	NA	NA	NA
11	100	9	30	3	NA	NA

FeDESI, Feline Dermatitis Extent and Severity Index; PVAS, Pruritus Visual Analog Scale; D, Days NA, not available