

Ciclosporin therapy is associated with minimal changes in calcium metabolism in dogs with atopic dermatitis

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Background – Ciclosporin is widely used in the management of canine atopic dermatitis. In humans, ciclosporin therapy has been linked to disturbances in calcium metabolism and resultant skeletal disorders.

Objectives – The objective of this study was to assess calcium homeostasis in dogs before and after a 6 week course of once daily oral ciclosporin at the licensed dose (5 mg/kg).

Animals – Sixteen client-owned dogs with spontaneous atopic dermatitis.

Methods – Serum concentrations of calcium, phosphate, creatinine, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D and plasma concentrations of ionized calcium and parathyroid hormone (PTH) were measured, together with the urinary fractional excretion of calcium and phosphate. The extent of skin lesions was scored using the Canine Atopic Dermatitis Extent and Severity Index (CADESI)-03 and the degree of pruritus by the Edinburgh Pruritus Scale prior to and at the end of the study.

Results – The CADESI-03 and the Edinburgh Pruritus Scale scores decreased satisfactorily in all dogs by the end of the study. Plasma PTH concentrations were significantly increased ($P = 0.02$) following ciclosporin treatment, whereas all other biochemical parameters were not significantly different from their starting values. The increase in PTH was mild in most cases and the proportion of dogs that had a PTH concentration above the reference range was not significantly different following treatment.

Conclusions and clinical importance – This study indicates that ciclosporin has minimal impact on calcium metabolism in dogs with atopic dermatitis when used at the licensed and clinically effective dosage for 6 weeks.

Introduction

Ciclosporin is being increasingly used for the treatment of diseases of small animals.¹ It is licensed for veterinary use as a topical 0.2% ophthalmic ointment (Optimmune®; Schering-Plough Limited, Welwyn Garden City, UK) for the treatment of keratoconjunctivitis sicca in dogs, as oral 10, 25, 50 and 100 mg capsular preparations (Atopica®; Novartis Animal Health, Basel, Switzerland) for the treatment of atopic dermatitis (AD) in dogs and as a 100 mg/mL oral solution (Atopica® for Cats; Novartis Animal Health) for the treatment of allergic dermatitis in cats. Analysis of the outcomes of randomized controlled trials has indicated that oral ciclosporin is effective in reducing skin lesions and pruritus in dogs with AD.² Ciclosporin has also been used off-licence to treat a wide range of other canine conditions, including granulomatous menin-

gioencephalitis,³ anal furunculosis,^{4,5} myasthenia gravis,⁶ sebaceous adenitis,⁷ pemphigus foliaceus⁸ and sterile nodular panniculitis.⁹ Its use in veterinary dermatology has recently been reviewed by Kovalik *et al.*¹⁰ The reported adverse effects of ciclosporin administration to dogs include vomiting and diarrhoea (usually mild and resolving despite continued usage), gingival hyperplasia and hirsutism.¹¹

Ciclosporin is also widely employed to treat a diverse range of human disorders.¹² It is commonly used as an immunosuppressant agent, often in combination with other drugs, in organ transplantation, where it has a major role in preventing allograft rejection in transplant patients.¹³ Ciclosporin has also been shown to be useful for the short-term treatment of psoriasis¹⁴, AD¹⁵ and refractory chronic idiopathic urticaria.¹⁶ In humans, ciclosporin therapy is associated with a wide range of adverse effects, including renal dysfunction, hepatotoxicity, infection, gingival overgrowth and hirsutism.¹⁷ In addition, osteoporosis and osteomalacia are also commonly reported.^{17–21} The risk of bone fracture increases in many patients treated with ciclosporin after organ transplantation.^{19,22}

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After renal transplantation, osteoporosis is a clinically important problem that affects between 6 and 15% of all patients in the first year after transplantation.^{23,24} Decreases in bone mineral density are well documented and especially rapid during the early post-transplantation period, when the doses of all immunosuppressants are highest.^{19,25–28} The mechanism(s) of ciclosporin-associated bone disease in humans is ill defined, which is, in part, due to the difficulties of investigating the effects of one drug in patients who are often treated with a wide range of additional medications and who often have several concurrent medical conditions.

Parathyroid hormone (PTH) and vitamin D play a crucial role in calcium metabolism and maintenance of skeletal structure. The active hormonal form of vitamin D, 1,25-dihydroxyvitamin D [1,25(OH)₂D] is necessary for optimal intestinal absorption of calcium and phosphorus and also exerts an inhibitory effect on PTH synthesis.²⁹ Vitamin D deficiency and secondary hyperparathyroidism can contribute not only to accelerated bone loss and increasing fragility, but also to neuromuscular impairment that may increase the risk of falls.^{30,31} Clinical trials involving older individuals at high risk for calcium and vitamin D deficiency indicate that supplementation of both can reverse secondary hyperparathyroidism, decrease bone resorption, increase bone mass and decrease fracture rates.²⁹ The seasonal decrease in vitamin D and increase in PTH concentrations during the winter months is associated with an increase in the number of fractures, independent of the increase in rate of falls.³²

Given that PTH and 1,25(OH)₂D play a pivotal role in the maintenance of skeletal tissue and that ciclosporin administration is associated with skeletal pathology in humans, a number of studies have examined the effects of ciclosporin on PTH and 1,25(OH)₂D concentrations. For example, PTH concentrations were found to be significantly increased after renal transplantation.³³ Similar results were also observed by Compston *et al.*,³⁴ who reported a highly significant increase in the plasma PTH concentration at 1–2 months after liver transplantation; likewise, Giannini *et al.*³⁵ described increased serum PTH concentrations after kidney transplantation.

Given the clinical significance of ciclosporin-associated bone disorders in humans, the effects of ciclosporin on PTH and vitamin D have been explored in animal models. Studies in ciclosporin-treated rats revealed that plasma PTH concentrations were significantly higher than those in control animals. These findings suggested that bone resorption in ciclosporin-treated rats is induced by high-turnover osteoporosis and that bone remodelling activity may be particularly activated by PTH.³⁶ It has also been reported that ciclosporin treatment causes hypercalciuria in animals. Ciclosporin treatment in rats at a dosage of 15–50 mg/kg for 7–14 days increased urine calcium excretion by 60–330%.^{37–39} It has been proposed that downregulation of renal calbindin-D28k may be involved in the pathogenesis of ciclosporin-induced hypercalciuria.^{39,40}

The primary goal of this study was to assess the effect of ciclosporin used at standard licensed therapeutic dosages on calcium metabolism in dogs with AD. We hypothesized that ciclosporin in a microemulsion formulation

administered at the recommended therapeutic dose once daily to atopic dogs would not be associated with a significant disturbance in calcium metabolism. This hypothesis was examined by measuring the concentrations of plasma ionized calcium, serum calcium and phosphate, plasma PTH and serum 25-hydroxyvitamin D [25(OH)D] and 1,25(OH)₂D, before and after 6 weeks after ciclosporin treatment at as near as possible to the licensed dosage of 5 mg/kg once daily.

Materials and methods

Investigations were performed in client-owned dogs with the owners' permission. The study was approved by The University of Edinburgh's Ethical Review Committee through the Royal (Dick) School of Veterinary Studies [R(D)SVS's] Veterinary Ethical Review Committee.

Study design and conduct

This study was undertaken in the Dermatology Unit of the R(D)SVS, The University of Edinburgh between January 2009 and January 2010. Consecutive dogs with a clinical diagnosis of AD according to well-established criteria⁴¹ were considered eligible for the study. Diagnoses physically resembling AD (e.g. ectoparasitic infestations or cutaneous adverse food reactions) were ruled out using standard diagnostic and therapeutic methods prior to inclusion in the study. Dogs with physical and laboratory evidence of secondary skin infections, e.g. bacterial pyoderma or *Malassezia* dermatitis, were treated to resolution prior to inclusion and, if needed, topical therapy was used to manage relapses that occurred during the study. In addition, dogs with AD that had received glucocorticoids and ciclosporin in the previous 12 weeks were excluded. Following a standard therapeutic cascade, the atopic dogs were treated with ciclosporin if the preparation of an allergen-specific immunotherapy vaccine was pending or if immunotherapy had been discontinued due to lack of efficacy. No other treatments were allowed. A total of 16 consecutive atopic dogs were included in the study and were given oral capsular ciclosporin at as near as possible to the licensed dosage of 5 mg/kg (range 4.4–6.0 mg/kg) once daily for 6 weeks. Dogs were maintained on the same diet throughout the study to prevent dietary influences on measured parameters.

Dogs underwent a standard assessment of calcium homeostasis, which involved measurement of 12 h fasting plasma ionized calcium, serum calcium, phosphate and creatinine, plasma PTH and serum 25(OH)D and 1,25(OH)₂D concentrations prior to ciclosporin administration and then again after 6 weeks of treatment, together with a trough (24 h after the last administration) serum ciclosporin concentration.^{5,42} In addition, 12 h fasting free-catch urine samples were collected before and after treatment and the urinary creatinine, calcium and phosphate concentrations were determined.

The venous blood samples for measurement of serum calcium, phosphate, creatinine, ciclosporin, 25(OH)D and 1,25(OH)₂D were collected into plain tubes and allowed to clot at room temperature before centrifugation and harvesting of serum. Samples for plasma ionized calcium determinations were collected into lithium heparin tubes. Samples for PTH determinations were harvested into ice-cold EDTA tubes. Plasma samples were centrifuged immediately and were stored at –20°C within 7 min and at –80°C within 1 h of sampling until shipment for analysis in a cold pack. The plasma PTH concentrations were measured using a two-site immunoradiometric assay (The Diagnostic Systems Laboratory, Webster, TX, USA). The PTH intra- and interassay coefficients of variation were <3.5 and <5.2%, respectively.

Serum samples for measurement of 25(OH)D and 1,25(OH)₂D were frozen within 2 h of collection and were stored at –70°C before being sent on dry ice to the laboratory for analysis, which was carried out in batch mode as described in detail elsewhere.^{43,44} Briefly, samples were extracted using acetonitrile and applied to C18 Silica Sep-paks (Waters, Elstree, UK). Separation of metabolites was by

straight-phase high-performance liquid chromatography (Waters Associates, Milford, MA, USA) using a Hewlett-Packard Zorbax-Sil Column (Hichrom, Reading, UK) eluted with hexane:propan-2-ol:methanol (92:4:4). Serum 25(OH)D₂ and 25(OH)D₃ were measured separately by application to a second Zorbax-Sil Column eluted with hexane:propan-2-ol (98:2), quantified by ultraviolet absorbance at 265 nm and corrected for recovery [sensitivity 2 ng/mL (5 nmol/L); intra- and interassay coefficients of variation of 3.0 and 4.2%, respectively].⁴⁵ Results are expressed as total 25(OH)D. Following separation by high-performance liquid chromatography, 1,25(OH)₂D (1,25(OH)₂D₂ + 1,25(OH)₂D₃) were quantified by radio-immunoassay as described in detail elsewhere [sensitivity 1.25 pg (3 pmol), intra- and interassay coefficients of variation of 7.8 and 10.5%, respectively].⁴⁴ The assay laboratory is accredited to ISO 9001:2000 and ISO 13485:2003 and participates successfully in the vitamin D external quality assessment scheme (DEQAS).

The serum ciclosporin concentrations were determined by tandem mass spectrometry in batch mode. The sensitivity of the method was 25 µg/L, and the intra-assay coefficient of variation was between 4.8 and 7.1% over the 25–2000 µg/L detection range.

The response to treatment was assessed by scoring the skin lesions of all dogs on day 0 and day 42 using the Canine Atopic Dermatitis Extent and Severity Index (CADESI)-03 as previously described.⁴⁶ The owners used the Edinburgh Pruritus Scale to score the pruritus on a numerical scale (0–5) annotated with specific behavioural descriptors as described previously by our group.⁴⁷

Statistical analyses

The effect of treatment on the concentrations of calcium, ionized calcium, phosphate, 25(OH)D, 1,25(OH)₂D, PTH and urinary fractional excretion of calcium and phosphate were tested with Wilcoxon matched pairs tests. A Spearman rank correlation test was used to examine the relationship between post-treatment PTH concentrations and trough ciclosporin concentrations. Fisher's exact test was used to compare the proportion of dogs that had a PTH concentration above the reference range before and after treatment. A *P*-value of ≤0.05 was used as the criterion for statistical significance. Statistical analyses were performed using GRAPHPAD PRISM (GraphPad Software, La Jolla, CA, USA).

Results

Sixteen dogs comprising 10 breeds were enrolled in the study. Details of the dogs have previously been reported by Kovalik *et al.*⁴⁸ Briefly, 10 were male (nine castrated) and six female (five ovariectomized). Their ages ranged between 1.1 and 9.6 years (median 3.7 years) and they weighed between 5.6 and 56 kg (median 27.1 kg).

All 16 dogs completed the present study. Mild adverse effects were observed in seven dogs during ciclosporin therapy. These consisted of intermittent vomiting (two of 16; 12.5%) and soft stools (five of 16; 31%). In all

affected dogs, the vomiting resolved within 7 days of beginning ciclosporin. The soft stools persisted while the five dogs were taking ciclosporin but disappeared without medical intervention when administration was stopped.

Ciclosporin treatment reduced CADESI-03 scores by ≥25% in 16 dogs (100%) and by ≥50% in 14 of the 16 dogs (88%). Comparison of Edinburgh Pruritus Scale scores on days 0 and 42 indicated that treatment with ciclosporin reduced pruritus by ≥25% in 16 dogs (100%) and by ≥50% in 15 of 16 dogs (94%).

The median serum, plasma and urinary concentrations of the parameters measured are listed in Table 1. There were no significant differences in serum concentrations of calcium, phosphate, creatinine, 25(OH)D, 1,25(OH)₂D, plasma ionized calcium and urinary fractional excretion of calcium and phosphate before and after treatment. Plasma PTH concentrations were increased following ciclosporin treatment (pretreatment median 47.0 pg/mL, post-treatment median 71.5 pg/mL, *P* = 0.02; reference range 20–65 pg/mL; Figure 1); however, the proportion of dogs that had a PTH concentration above the reference range was not statistically different post-ciclosporin treatment (*P* = 0.47). Trough serum ciclosporin concentrations were not detectable in two samples. There was no correlation between post-treatment PTH concentrations and ciclosporin trough concentrations (*r* = −0.08, *P* = 0.78).

Discussion

The key finding of this study is that ciclosporin, when used at the manufacturer's recommended dose for the treatment of canine AD, is associated with minimal changes in calcium metabolism. Although there was a significant increase in plasma PTH concentrations following ciclosporin treatment, the additional findings that the proportion of dogs which had a PTH concentration above the reference range did not alter post-ciclosporin treatment, that there was a lack of a correlation between trough ciclosporin and PTH concentrations and that there were no significant changes in plasma ionized calcium concentrations after ciclosporin treatment collectively indicate that the overall impact of ciclosporin therapy on calcium metabolism is modest. Nonetheless, the increase in plasma PTH concentration post-ciclosporin treatment observed in this study is consistent with reports in humans, where ciclosporin was administered

Table 1. Median serum, plasma and urine pretreatment and post-treatment parameters

Parameter	Reference range	Pretreatment median (range)	Post-treatment median (range)	<i>P</i> -value
Serum calcium (mmol/L)	2.3–3.0	2.55 (2.38–2.76)	2.55 (2.28–2.65)	0.09
Plasma ionized calcium (mmol/L)	1.15–1.50	1.27 (1.11–1.40)	1.33 (1.12–1.41)	0.10
Serum phosphate (mmol/L)	0.9–2.0	1.29 (0.72–1.71)	1.19 (0.79–1.71)	0.11
Serum creatinine (µmol/L)	40.0–132.0	98.5 (79–149)	102.5 (83–143)	0.18
Urinary FE calcium (%)	0.03–0.22	0.06 (0.03–0.27)	0.07 (0.02–0.22)	0.90
Urinary FE phosphate (%)	0.4–20.1	7.6 (6.05–17.81)	7.0 (0.08–24.11)	0.72
Plasma PTH (pg/mL)	20–65	47.0 (23.0–177.0)	71.5 (24.0–193.0)	0.02
Serum 25(OH)D (ng/mL)*	19.3–43.6	28.1 (19.0–62.6)	29.0 (18.6–60.7)	0.13
Serum 1,25(OH) ₂ D (pg/mL)*	16.0–38.0	46.5 (34.00–158.0)	42.5 (20.0–72.0)	0.06

Abbreviations: FE, fractional excretion; PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D; 1,25(OH)₂D, 1,25-dihydroxyvitamin D.

*Preliminary reference range provided (Gow *et al.*⁵⁶).

post-organ transplantation.^{34,35} Compston *et al.*³⁴ demonstrated a significant increase in the plasma PTH concentrations 1–2 months after liver transplantation; likewise, Giannini *et al.*³⁵ described elevated plasma PTH concentrations in patients taking ciclosporin after kidney transplantation. In experimental models of ciclosporin-induced osteoporosis, PTH has been found to be increased before bone loss is detectable, leading to the hypothesis that plasma PTH concentrations may be a key factor associated with ciclosporin-induced bone loss.³⁶ However, the exact role of PTH in ciclosporin-induced osteoporosis remains unclear.⁴⁹ For example, Wada *et al.*³⁶ reported that PTH concentrations increased following ciclosporin administration to rats, whereas Epstein *et al.*⁴⁹ found no significant changes in PTH concentrations post-ciclosporin treatment.

Our study found no significant changes in urinary fractional excretion of calcium and phosphate. In contrast, it has been reported that ciclosporin treatment causes hypercalciuria in rodent models. Ciclosporin treatment in rats at a dosage of 15–50 mg/kg for 7–14 days increased urine calcium excretion by 60–330%.^{37–39} Approximately 60% of the filtered calcium is reabsorbed in the proximal tubule and the remainder in the medullary thick ascending

A limitation of the present study is that we investigated the effects of only a single dose of ciclosporin on calcium metabolism over a 6 week period. Additional studies are required to assess whether higher doses administered over longer periods of time have a greater impact on calcium metabolism. It remains unclear whether therapeutically effective doses of ciclosporin would have a greater effect on calcium metabolism in other species (e.g. cats).

In summary, this study indicates that ciclosporin has minimal impact on calcium metabolism in dogs with AD when used at the licensed and clinically effective dosage for 6 weeks. Although there was a significant increase in PTH concentration following ciclosporin therapy, the rise was modest in nature and was not associated with altered plasma concentrations of ionized calcium.

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Résumé

Contexte – La ciclosporine est largement utilisée dans la gestion de la dermatite atopique canine. Chez l'homme, l'utilisation de ciclosporine a été associée à des perturbations du métabolisme calcique résultant en des troubles squelettiques.

Objectifs – L'objectif de cette étude était d'évaluer l'homéostasie du calcium chez les chiens avant et après une administration quotidienne de ciclosporine orale autorisée (5 mg/kg) pendant 6 semaines.

Sujets – Seize chiens de propriétaires atteints de dermatite atopique spontanée.

Méthodes – Les concentrations sériques de calcium, de phosphate, de créatinine, de 25-hydroxyvitamine D, de 1,25-dihydroxyvitamine D et les concentrations plasmatiques de calcium ionisé et d'hormone parathyroïdienne (PTH) ont été mesurées, ainsi que la fraction urinaire excrétée du calcium et du phosphate. Les lésions cutanées ont été évaluées par le CADESI-03 (Canine Atopic Dermatitis Extent and Severity Index) et le degré de prurit par l'échelle de prurit d'Edinburgh avant et à la fin de l'étude.

Résultats – Le CADESI-03 et l'échelle de prurit d'Edinburgh ont diminué de manière satisfaisante chez tous les chiens avant la fin de l'étude. Les concentrations plasmatiques de PTH étaient significativement augmentées ($P = 0.02$) à la suite du traitement de ciclosporine alors que tous les autres paramètres biochimiques n'étaient pas significativement différents de leurs valeurs initiales. L'augmentation de PTH était modérée dans la plupart des cas et la proportion de chiens ayant une concentration de PTH au-dessus des valeurs de référence n'était pas significativement différente après le traitement.

Conclusions et importance clinique – cette étude indique que la ciclosporine a un impact minimal sur le métabolisme du calcium chez les chiens atteints de dermatite atopique lorsqu'elle est utilisée à la dose autorisée et qu'elle est efficace sur le plan clinique pendant 6 semaines.

Resumen

Introducción – la ciclosporina se usa extensivamente en el manejo de la dermatitis atópica canina. En humanos, la terapia con ciclosporina ha sido asociada con alteraciones en el metabolismo del calcio resultando en anomalías del sistema esquelético.

Objetivos – los objetivos de este estudio fueron evaluar la homeostasis del calcio en perros antes y después de seis semanas de tratamiento con ciclosporina una vez al día a la dosis recomendada en la licencia (5 mg/kg).

Animales – dieciséis perros de propietarios particulares con dermatitis atópica espontánea.

Métodos – se midieron las concentraciones en suero de calcio, fósforo, creatinina, 25-hidroxivitamina D, 1,25-dihidroxivitamina D y las concentraciones en plasma de calcio iónico y hormona paratiroidea (PTH), junto con la fracción de excreción de calcio y fósforo en orina. Las lesiones de la piel se evaluaron según el índice de severidad y extensión de la dermatitis atópica canina (CADESI)-03 y el grado de prurito según la escala de prurito de Edimburgo antes y al final del estudio.

Resultados – los valores de CADESI-03 y de la escala de prurito de Edimburgo disminuyeron de forma satisfactoria en todos los perros al final del estudio. Las concentraciones en plasma de PTH estuvieron aumentadas ($P = 0.002$) tras el tratamiento con ciclosporina, mientras que el resto de parámetros no presentaron diferencias significativas con los valores iniciales. El aumento en PTH fue leve en la mayoría de los casos, y la proporción de perros de tenía una concentración de PTH por encima del rango de referencia no fue significativamente diferente tras el tratamiento.

Conclusiones e importancia clínica – este estudio indica que la ciclosporina tiene un impacto mínimo en el metabolismo del calcio en perros con dermatitis atópica cuando se usa a la dosis recomendada y clínicamente efectiva durante seis semanas.

Zusammenfassung

Hintergrund – Ciclosporin ist zur Behandlung der atopischen Dermatitis des Hundes weit verbreitet im Einsatz. Beim Menschen wird die Ciclosporintherapie mit Störungen des Calcium-Metabolismus und daraus resultierenden Skelettstörungen in Verbindung gebracht.

Ziele – Das Ziel dieser Studie war es, die Calciumhomöostase bei Hunden vor und nach einer 6 Wochen dauernden Verabreichung von Ciclosporin einmal täglich per os in der zugelassenen Dosis (5mg/kg), zu untersuchen.

Tiere – Sechzehn Hunde aus Privatbesitz mit spontaner atopischer Dermatitis wurden in die Studie aufgenommen.

Methoden – Serumkonzentrationen von Calcium, Phosphor, Kreatinin, 24-Hydroxyvitamin D, 1,25-Dihydroxyvitamin D und Plasmakonzentrationen von ionisiertem Calcium und Parathormon (PTH) wurden gemessen, gemeinsam mit dem Anteil der Calcium und Phosphor Ausscheidung über den Harntrakt. Das Ausmaß der Hautveränderungen wurde mittels Canine Atopic Dermatitis Extent and Severity Index (CADESI)-03 und das Ausmaß des Pruritus wurde mittels Edinburgh Pruritus Skala vor und am Ende der Studie beurteilt.

Ergebnisse – Die CADESI-03 und die Werte der Edinburgh Pruritus Skala waren bei allen Hunden am Ende der Studie in zufrieden stellender Weise abgesunken. Die PTH Konzentrationen im Plasma waren nach der Behandlung mit Ciclosporin signifikant erhöht ($P = 0.02$), während alle anderen biochemischen Parameter sich nicht signifikant von ihren Ausgangswerten unterschieden. Die Zunahme der PTH Konzentration war in den meisten Fällen gering und die Anzahl der Hunde, die eine PTH Konzentration über den Referenzwerten aufwiesen war vor und nach der Behandlung nicht signifikant verschieden.

Schlussfolgerung und klinische Bedeutung – Diese Studie zeigt, dass Ciclosporin, wenn es in der zugelassenen und klinisch wirksamen Dosis 6 Wochen lang verwendet wird, einen minimalen Einfluss auf den Calcium Metabolismus von Hunden mit atopischer Dermatitis hat.

要約

背景 – シクロスポリンは犬のアトピー性皮膚炎の管理に広く使われている。ヒトでは、シクロスポリン療法はカルシウム代謝を障害し、その結果骨疾患を生じると考えられている。

目的 – この研究の目的は、シクロスポリンの認可された用量である5 mg/kg を1日1回6週間、経口投与し、投与前と投与後の犬でカルシウム恒常性を評価することである。

供与動物 – 16 頭の自然発症性のアトピー性皮膚炎を示す飼い犬

方法 – カルシウム、リン、クレアチニン、25-ヒドロキシビタミンD、1, 25-ジヒドロキシビタミンDの血清濃度とイオン化カルシウム、上皮小体ホルモン (PTH) の血漿濃度をカルシウムとリンの尿分画排泄率とともに測定した。治療の前後に皮膚病変の範囲と程度は Canine Atopic Dermatitis Extent and Severity Index (CADESI)-03 および痒みの程度は Edinburgh Pruritus Scale を用いてスコア化した。

結果 – CADESI-03とEdinburgh Pruritus Scale はすべての犬で治療終了時に統計学的に減少した。血漿 PTH 濃度はシクロスポリン治療後に有意に上昇した ($P = 0.02$) 一方で、すべての他の生化学的なパラメーターは治療前と有意な差はなかった。PTH の上昇はほとんどの症例で軽度であり、参考値より高いPTH濃度を示した犬の割合は治療後にも有意な差がなかった。

結論と臨床的な重要性 – この試験はアトピー性皮膚炎の犬に、臨床的に有効で認可された用量を6週間使用した時に、シクロスポリンが犬のカルシウム代謝に与える影響はほとんどないことを示唆した。

摘要

背景 – 环孢素被广泛用于犬异位性皮炎的管理。人的环孢素治疗与钙代谢失调有联系，并且导致骨骼异常。

目的 – 研究是按照注册许可剂量，每日一次口服（5 mg/kg）环孢素，在服药之前和6周后评估犬的钙稳态。

动物 – 16 只家养自发性异位性皮炎患犬。

方法 – 测定血清钙、磷、肌酐、25-羟基维生素D、1, 25-二羟基维生素 D 和血浆离子钙和甲状旁腺素（PTH）浓度，连同尿中排泄的部分钙和磷。皮肤病变程度使用犬异位性皮炎程度和严重指数（CADESI）-03 进行评分，在研究前后通过爱丁堡瘙痒评分对瘙痒等级评分。

结果 – 在研究结束时，所有犬的 CADESI-03 和爱丁堡瘙痒评分都令人满意地减少。血浆 PTH 浓度随环孢素治疗显著增加 ($P = 0.02$)，而所有生化参数与其初始值相比没有显著差异。大部分病例中 PTH 轻度增加，部分犬PTH浓度超过参考范围，与治疗后的没有显著差异。

结论和临床价值 – 这项研究表明，在使用注册许可和临床有效剂量6周后，环孢素对异位性皮炎患犬的钙代谢影响很小。