

Measurement of serum macrophage migration inhibitory factor (MIF) and correlation with severity and pruritus scores in client owned dogs with atopic dermatitis

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Background – Atopic dermatitis (AD) is a common inflammatory skin disease of dogs. Macrophage migration inhibitory factor (MIF) initiates pro-inflammatory cytokine release in human AD and serum concentrations are correlated with disease severity.

Hypothesis – Canine serum MIF concentrations are increased in dogs with AD and correlate with clinical lesion and pruritus scores.

Animals – Client owned dogs (n = 49) diagnosed with AD and 17 healthy, unaffected control dogs were used for the study.

Methods and materials – A commercially available MIF ELISA was optimized for the dog and serum from clinical cases used. Information regarding treatment, Canine Atopic Dermatitis Extent and Severity Index, (CADESI-4) and pruritus Visual Analog Scale (pVAS) were recorded for each dog at the time of serum collection.

Results – Dogs with AD which had not received steroid therapy and those treated with oclacitinib had significantly elevated serum MIF concentrations compared to controls. Concentrations of MIF were not significantly different in AD dogs receiving steroids compared to controls. There was no significant correlation between MIF concentrations and clinical scores (CADESI-4 or pVAS).

Conclusions and clinical importance – Serum MIF concentrations are increased in dogs with AD and MIF might be a target for therapy.

Introduction

Macrophage migration inhibition factor (MIF) is an immunoregulatory cytokine that through interactions with its receptor CD74, recruits and activates macrophages at inflammatory loci.^{1,2} The most important source of MIF is T-helper 2 cells (Th2), where MIF is essential for T-cell activation, but other sources include macrophages, eosinophils, epithelial cells, endothelial cells and keratinocytes. Macrophage MIF is released from macrophages in response to lipopolysaccharide (LPS) and from different cell types in response to proliferative or hypoxic signals.^{3,4}

MIF has many functions in the regulation of innate and acquired immunity. For example, MIF initiates inflammation by regulation of pro-inflammatory cytokines including TNF α , IL1 and IL6,⁵ and may act in part to antagonize glucocorticoid-mediated suppression of immune cell responses, modifying systemic inflammation.⁶

The role of MIF in some human dermatological conditions such as allergic dermatitis, contact dermatitis, AD, psoriasis, vitiligo, alopecia areata, pemphigus vulgaris and bullous pemphigoid has been a focus of research.^{1,7–10} In humans with AD, MIF concentrations in serum and expression in the epidermis of affected skin correlate with disease severity.^{1,3,10} Additionally, topical steroid therapy results in a reduction in serum MIF which correlates with clinical resolution.¹ MIF promoter polymorphisms are associated with increased risk for the development of AD,¹¹ and in other diseases such as rheumatoid arthritis, certain MIF polymorphisms are associated with reduced disease severity.¹² MIF also regulates delayed-type hypersensitivity (IV), and when released from eosinophils can exacerbate human allergic and inflammatory disease such as asthma and AD.^{13,14} It has been reported,¹⁵ that MIF contributes to pollen-induced

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allergic conjunctivitis and dermatitis in mice by inducing eosinophil infiltration. Further evidence for a role of MIF in the pathogenesis of AD comes from murine models. A MIF DNA vaccine was produced to immunize mice that spontaneously develop AD-like skin signs.^{16,17} Clinically, the immunized mice, which produced anti-MIF antibodies, showed reductions in hyperkeratosis, oedema, pruritus and inflammation with histologically significant reductions in dermal eosinophils and mast cells. Collectively, these studies suggest that MIF may control AD, pollen-induced allergic conjunctivitis and pollen dermatitis and could be a target for treatment.

Canine atopic dermatitis (AD) is a common, genetically predisposed, inflammatory and pruritic skin disease thought to affect $\leq 10\%$ of dogs worldwide.^{18,19} The pathogenesis of canine AD is likely to be, at least in part, associated with dysregulation of cytokine production leading to activation of Th1 cells, Th2 cells, Langerhans cells and monocytes.^{20,21} As there are many similarities between human and canine AD, it is possible that MIF may play a role in the pathogenesis of canine AD. The aim of this study was therefore to evaluate serum MIF concentrations in dogs with AD compared with a control population and assess the correlation with clinical lesion scores.

Methods and materials

Study design

The study had ethical approval from the institute's Veterinary Ethical Review Committee (VERC). Client owned dogs diagnosed with AD were enrolled in the study with informed consent. A diagnosis of AD was made according to accepted criteria, and after ruling out other causes of pruritus.²² Based on clinical examination and history, dogs were excluded from the study if there was evidence of any other concurrent disease process, including active secondary infection (bacterial or yeast). For the dogs with AD, current medication(s), owner-assessed pruritus Visual Analog Score (pVAS),²³ Canine Atopic Dermatitis Extent and Severity Index, 4th iteration (CADESI-4 score)²⁴ and dermatological history were recorded. Dogs were then assigned to three groups according to their current treatment: AD group 1, AD dogs that had not received any systemic or topical steroid therapy for four weeks before sampling; AD group 2, AD dogs currently receiving steroid therapy (systemic and/or topical); and AD group 3, AD dogs currently receiving oclacitinib (Apoquel®, Zoetis; Surrey, UK). Dogs receiving concurrent oclacitinib and topical steroid therapy were included in group 2 (receiving steroid therapy).

Healthy control dogs had no history or clinical signs of skin disease or any other concurrent disease. They were excluded from the study if they were receiving any medication or supplementation apart from routine vaccination, and ecto- and endoparasite control.

Serum was harvested and stored at -80°C for six months until time of analysis.

Migration inhibitory factor ELISA

A canine specific competitive MIF enzyme-linked immunosorbent assay (ELISA) was purchased and used according to manufacturer's instructions (Canine MIF ELISA MBS738733, MyBioSource Inc; San Diego, CA, USA). This ELISA kit contained a 96-well plate pre-coated with an anti-canine MIF monoclonal antibody. Optimization was achieved using various dilutions of canine serum with known standards (as supplied by the manufacturer in the ELISA kit). Undiluted serum (100 μL) was used in the final analysis with samples added to the wells of the 96-well plate in duplicate. The optical density (OD) of each standard, sample and control was determined at 450 nm using the average OD of the duplicate. The OD value was subtracted from the mean blank control to allow construction of a standard curve. The

concentration of samples was determined using the corresponding mean absorbance from the standard curve. A positive control sample from a dog with glomerulonephritis was included in the optimization,²⁵ which gave an average serum MIF concentration of 461 pg/mL (data not shown). The sensitivity of the assay was 1 pg/mL with a range of detection between 1 pg/mL and 1,000 pg/mL and an intra-assay coefficient variation of <10 . All samples were batch-thawed and tested on the same day.

Statistical analysis

Statistical analysis was performed with a commercial software package (GraphPad Prism v5; San Diego, CA, USA) and $P < 0.05$ was considered significant. Kolmogorov–Smirnov tests showed that the data were not normally distributed. A Wilcoxon–Mann–Whitney U-test was used to determine whether there was a difference between serum MIF concentrations in the control and AD groups MIF concentrations. Multigroup statistical analysis was performed using one-way ANOVA (Kruskal–Wallis test) with Dunn's multiple comparison post-tests. Pearson correlation tests were used to investigate correlation of serum MIF concentrations with CADESI-4 or pVAS.

Results

Treatment groups

Samples were obtained from 17 healthy control dogs and 49 dogs with AD. The AD group consisted of 19 dogs that had not received any topical or systemic steroid therapy (group 1), 21 dogs that were currently receiving steroid therapy which were subcategorized as receiving topical steroid only and four dogs receiving topical steroid and oclacitinib, or systemic steroid therapy ($n = 12$) or combinations of both ($n = 3$) (group 2), and nine dogs receiving once daily dosing of oclacitinib and no steroid (group 3); four group 3 dogs also received regular injections of allergen-specific immunotherapy (ASIT). Table 1 shows all other concurrent treatments used by some of the dogs in the AD groups 1–3.

Signalment

The control group consisted of 10 breeds and the AD group of 17 breeds, with neutered males slightly over-represented in both (Table 2). The age range of the control group was 3.1–10.1 years (median 7.5-year-old), and the age range for the AD group was 0.5–11 years (median

Table 1. List of concurrent medications administered to some of the dogs in the atopic dermatitis group

Medication	Number of dogs
Chlorhexidine gluconate/miconazole nitrate washes (Malaseb®, Dechra; Shropshire, UK)	8
TrisEDTA/climbazole wipes (CLX®, Vetruus; High Wycombe, UK)	5
Salicylic acid-based ear cleaner (Epiotic®, Virbac; Suffolk, UK)	4
Chlorhexidine digluconate gel wipes (Clorexiderm®, Vetruus; High Wycombe, UK)	1
Phytosphingosine HCl 0.05% shampoo (Douxo calm shampoo®, Ceva, Amersham, UK)	1
Ultramicronized palmitoylethanolamide (Redonyl Ultra®, Dechra; Shropshire, UK)	1

Table 2. Breeds and sexes in the control and atopic dermatitis (AD) groups

Control breeds	Sex	Breeds with AD	Sex
Border terrier (2)	Male entire (1)	Beagle (1)	Male entire (4)
Boxer (1)	Male neutered (9)	Border terrier (1)	Male neutered (25)
Collie cross (2)	Female entire (0)	Boxer (2)	Female entire (4)
Cocker spaniel (2)	Female neutered (7)	Bulldog (4)	Female neutered (16)
Greyhound (1)		Bullmastiff (1)	
Jack Russell terrier (2)		Cavalier King Charles spaniel (2)	
Labrador retriever (2)		Cocker spaniel (5)	
Lurcher (2)		Collie and collie crosses (3)	
Rottweiler (1)		Clumber spaniel (1)	
West Highland white terrier (2)		Dogues de Bordeaux (1)	
		Golden retriever (6)	
		German shepherd dog (3)	
		Rottweiler (1)	
		Labrador retriever (7)	
		Staffordshire bull terrier (4)	
		Rottweiler (1)	
		West Highland white terrier (4)	

The number of dogs of each breed is included in brackets.

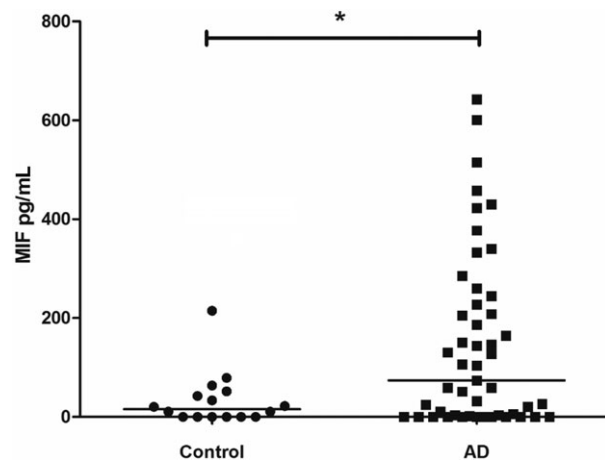


Figure 1. Serum macrophage inhibitory factor (MIF) concentrations of 17 unaffected control dogs and 49 dogs with atopic dermatitis. Horizontal black line represents median value (* $P < 0.05$).

4.2-year-old). There was no significant difference between the two groups ($P = 0.16$). The three most common breeds for the AD dogs were the Labrador retriever ($n = 7$), golden retriever ($n = 6$) and cocker spaniel ($n = 5$).

Serum MIF concentrations

Control dogs had a serum MIF concentration range of 0–214 pg/mL (median 15.63 pg/mL). The dogs with AD had a MIF concentration range of 0–642 pg/mL (median 73.89 pg/mL), which was significantly higher than the control dogs ($P < 0.029$) (Figure 1). There was a significant difference between the three combined treatment groups and control group ($P < 0.0001$). When further analysis of the AD groups 1–3 was made using Dunn's multiple comparison post-test analysis, there was a significant increase in the serum MIF concentrations in groups 1 ($P < 0.001$) and 3 ($P < 0.01$), compared to controls, but not with group 2 compared to the controls ($P > 0.05$) (Figure 2 and Table 3).

There were two dogs in AD group 2 receiving only daily topical steroid therapy; serum MIF concentrations for

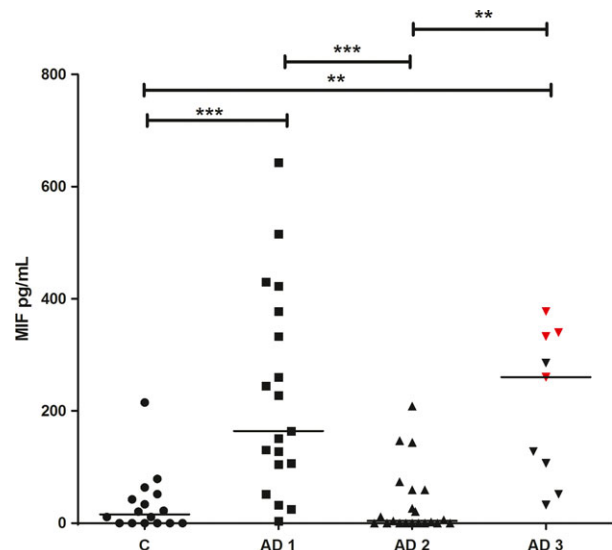


Figure 2. Serum macrophage inhibitory factor (MIF) concentrations of 17 unaffected control dogs compared to dogs with atopic dermatitis (AD) separated into three groups according to treatment. AD group 1 were not receiving steroids ($n = 19$), AD group 2 received steroid therapy ($n = 21$) and AD group 3 were receiving oclacitinib ($n = 9$). Horizontal black lines represent median values. For the AD group, the red data points identify four dogs on concurrent oclacitinib and injectable immunotherapy. An asterisk above the groups represents statistical significance (** $P < 0.01$, *** $P < 0.001$). C control group.

these dogs were 11.3 and 0 pg/mL. Four of the dogs in AD group 2 were receiving at least twice weekly topical 0.0584% hydrocortisone aceponate, as well as daily oclacitinib at the time of sampling. Serum MIF concentrations for these four dogs were 0 pg/mL. No dogs were receiving systemic steroid therapy and oclacitinib or systemic steroid therapy and ASIT.

The AD group 3 contained four dogs receiving regular (every three to four weeks) injectable ASIT for at least six months (Greer aqueous allergens; Lenoir, GA, USA). These dogs also were receiving daily oclacitinib at the time of sampling and all had serum MIF concentrations greater than the control dogs (Figure 2, red data points).

Table 3. Summary of treatment groups and serum macrophage inhibitory factor (MIF) values including number of dogs in each group, median values and MIF range

Treatment group	Number of dogs	Median serum MIF (pg/mL)	Serum MIF range (pg/mL)
Control	17	15.63	3.65–215.0
AD group 1	19	104.4	0–642.5
AD group 2 (steroid)	21	3.98	0–208.4
Topical	2	5.65	0–11.3
Systemic	12	2.21	0–208.4
Topical and systemic	3	1.1	0–147
Topical and oclacitinib	4	0	0
AD group 3 (oclacitinib)	9	260.2	32.4–377.5
Oclacitinib only	5	78.6	32.4–285.4
Oclacitinib and allergen-specific immunotherapy	4	336.3	260.1–377.5

AD atopic dermatitis.

CADESI-4 and pVAS correlation

CADESI-4 data were available for 39 of 49 cases and pVAS data were available for 38 of 49 cases. There was no significant correlation between serum MIF

concentrations in the AD group and CADESI-4 (Figure 3a) or pVAS scores (Figure 3b) ($r = 0.04$, $P = 0.78$ and $r = 0.24$, $P = 0.78$ for CADESI-4 and pVAS, respectively). There also was no significant correlation when comparing the serum MIF concentration of each treatment group to CADESI-4 or pVAS (Figure 4).

Discussion

Dogs diagnosed with AD had increased serum MIF concentrations compared to control dogs in our study. This difference was not observed in dogs that had been

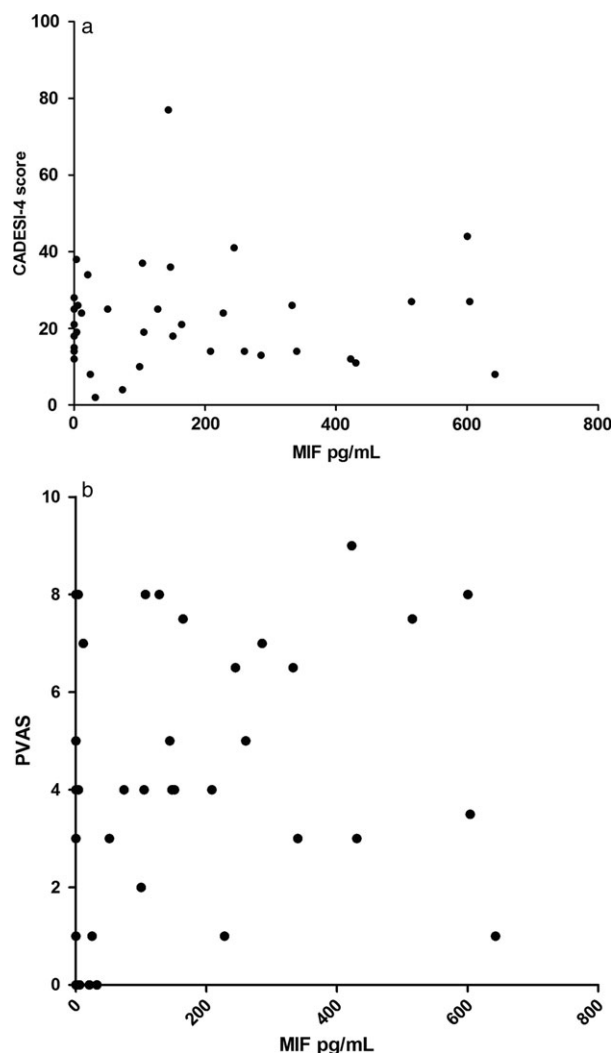


Figure 3. (a) Correlation between serum macrophage inhibitory factor (MIF) concentrations in dogs with atopic dermatitis and Canine Atopic Dermatitis Extent and Severity Index, 4th iteration (CADESI-4) score. ($n = 39$, $r = 0.04$, $P = 0.78$). (b) Correlation between serum MIF concentrations in dogs with AD and pruritus Visual Analog Scale (pVAS) score. ($n = 38$, $r = 0.24$, $P = 0.78$).

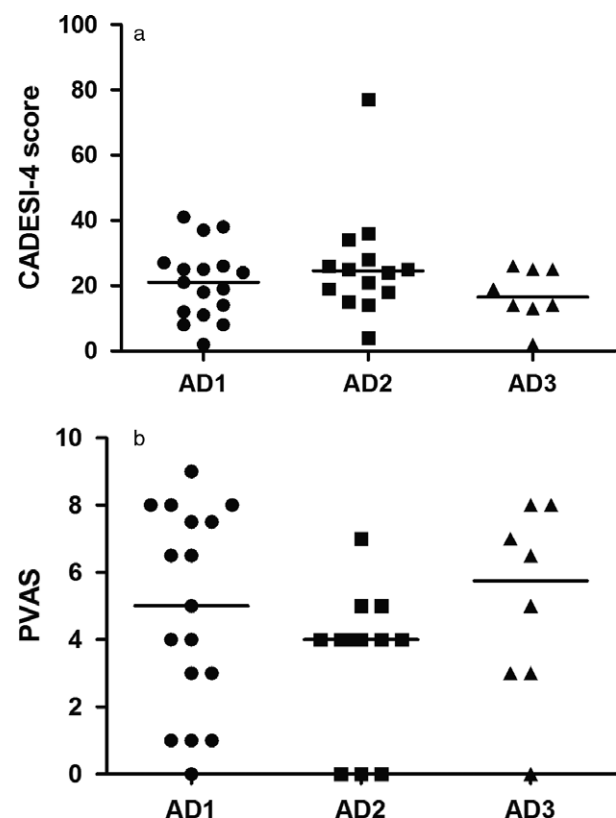


Figure 4. Individual Canine Atopic Dermatitis Extent and Severity Index, 4th iteration (CADESI-4) (a) and pruritus Visual Analog Scale (pVAS) (b) scores, for each of the groups with atopic dermatitis. AD group 1 were not receiving steroids, AD group 2 were receiving steroid therapy and AD group 3 were receiving oclacitinib. Horizontal black line represents median value.

treated with steroids, suggesting that glucocorticoids reduce serum MIF concentrations. This needs to be confirmed in a longitudinal study of individual dogs before and after treatment but is consistent with the known ability of glucocorticoids to suppress MIF production in activated T cells.²⁶ Measurement of serum TNF α also would be useful because it is known that there is interplay between TNF α and MIF, with reductions in MIF correlated with TNF α reductions.^{1,27}

The high serum MIF concentrations in dogs receiving oclacitinib are perhaps not surprising. Oclacitinib selectively inhibits Janus-kinase (JAK) enzymes, particularly JAK1-dependent cytokine receptor complexes and is not directly involved in T-cell inhibition. Because Th2 cells are the main source of serum MIF and neither MIF production or secretion involves JAK pathways,²⁸ oclacitinib would not be expected to reduce serum MIF concentrations.²⁹ We identified four dogs in AD group 2 receiving topical steroid therapy and concurrent oclacitinib which all had unmeasurable serum MIF concentrations. This probably reflects the actions of topical steroid therapy antagonizing serum MIF rather than the oclacitinib.

In contrast to the reported association in human AD,¹ we found no significant correlation between serum MIF concentrations and the clinical lesion severity or pruritus scores. The MIF serum concentrations obtained from the dogs in this study were only taken at a single timepoint. Therefore, we cannot assess if the dogs receiving oclacitinib or steroid therapy had clinical improvement in their AD phenotype in relation to a reduction in MIF concentrations. For both human and canine AD, visual and subjective improvements in clinical lesions and scores do not always correlate with improvements in inflammatory markers and cytokines within the skin and serum. Nonlesional skin in these patients should not be considered normal, and may be associated with increased numbers of keratinocytes, which are an important source of MIF.³⁰ This may be a reason why correlation between clinical scores and MIF concentrations were not significant. Because MIF is a known pro-inflammatory mediator and is associated with many inflammatory disease processes, the elevated MIF concentrations demonstrated may be purely a marker of inflammation rather than a driver of AD.

Further evaluation of the effects of ASIT and serum MIF concentration also will need to be ascertained. In our study, four dogs receiving daily oclacitinib therapy also were receiving regular (every three or four weeks) subcutaneous injections of ASIT and had increased serum MIF concentrations compared with the control group. Although it is not currently known if MIF can modulate the T-regulatory driven immunotherapy response, MIF can promote tumour-associated T-regulatory cells.³¹ However, MIF is not thought to have any effect on IL10 or TGF β , both of which are involved in the induction of allergen tolerance. In addition, the effect of injecting foreign antigens in the form of subcutaneous ASIT will induce an innate immune response.³² Stimulation of the innate immune system by lipopolysaccharide and other ligands such as allergens causes a rapid release of MIF from cells and tissues.² This antigenic stimulation also can induce dendritic cells to increase production of IFN α , thus inducing macrophages to release MIF.^{5,33}

Combined, these reasons also may explain the elevated MIF concentrations in dogs undergoing this form of therapy. Evaluating larger cohort groups of AD dogs on immunotherapy and serially assessing their serum MIF concentrations prior to, and during immunotherapy will help to assess this further.

The serum MIF concentrations in our canine study were low compared to those reported for healthy humans (canine healthy control 0–214 pg/mL, healthy human 5,000–10,000 pg/mL)³⁴ with concentrations elevated for neonates.³⁵ On the one hand, because the assay depends upon a commercial kit and a standard, we cannot eliminate the possibility that the assay detected only a small proportion of the total circulating MIF. On the other, there are already known differences between canine and human cytokine and inflammatory profiles, with most research focusing on differences in the cytokine profiles of inflammatory bowel disease (IBD) between the two species. In human IBD, Th2 cells predominate in chronic disease, yet in dogs with IBD, the profile is of mixed Th1 and Th2 which leads to the expression of different cytokine profiles.^{36,37}

In conclusion, to the best of the authors' knowledge, we have identified for the first time that MIF is present in the serum of clinically healthy dogs as in humans, mice, pigs and rats,^{32,38} and this is the first study demonstrating elevated serum MIF in a canine inflammatory disease. We have identified that dogs with AD have significantly higher serum MIF concentrations compared to healthy dogs. Moreover, steroid treatment appears to be associated with decreased MIF concentrations to baseline levels whereas oclacitinib has little effect. Nevertheless, we could not correlate MIF concentrations with lesion or pruritus scores. The role of MIF in the pathogenesis of canine AD therefore warrants further study. This would determine the potential usefulness of MIF-targeted inhibition in canine AD.

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Résumé

Contexte – La dermatite atopique (AD) est une maladie inflammatoire cutanée fréquente chez le chien. Le MIF (Macrophage migration factor) initie le largage de cytokines pro-inflammatoires dans l'AD humaine et les concentrations sériques sont corrélées à la sévérité de l'atteinte.

Hypothèses – Les concentrations de MIF sériques canines sont augmentées chez les chiens avec AD et sont corrélées aux lésions cliniques et aux scores de prurit.

Sujets – Des chiens de propriétaires (n = 49) ont été diagnostiqués avec AD et 17 chiens sains non atteints ont été utilisés pour l'étude.

Matériel et méthode – Un test ELISA MIF disponible dans le commerce a été optimisé pour le chien et le serum des cas cliniques utilisés. Les informations concernant le traitement, le CADESI-4 (Canine Atopic Dermatitis Extent and Severity Index) et le pVAS (pruritus Visual Analog Scale) ont été enregistrées pour chaque chien au moment de la collecte du serum.

Résultats – Les chiens avec AD qui n'avaient pas reçu de corticoïdes et ceux traités avec de l'ocloclitine avaient des concentrations sériques de MIF significativement élevées comparé aux contrôles. Les concentrations de MIF n'étaient pas significativement différents chez les chiens AD recevant des corticoïdes des

chiens contrôles. Il n'y avait pas de corrélation entre les concentrations de MIF et les scores cliniques (CADESI-4 ou pVAS).

Conclusions et importance clinique – Les concentrations sériques de MIF sont augmentées chez les chiens AD et le MIF pourrait être une cible thérapeutique.

Resumen

Introducción – la dermatitis atópica (AD) es una enfermedad inflamatoria común de la piel de los perros. El factor inhibidor de la migración de macrófagos (MIF) inicia la liberación de citoquinas proinflamatorias en la AD humana y las concentraciones séricas se correlacionan con la gravedad de la enfermedad.

Hipótesis – las concentraciones de MIF en suero canino aumentan en los perros con AD y se correlacionan con las lesiones clínicas y los valores de prurito.

Animales – se utilizaron para el estudio perros de propietarios particulares (n = 49) diagnosticados con AD y 17 perros control sanos no afectados.

Métodos y materiales – se optimizó un ELISA MIF comercial para su uso en muestras de suero canino a partir de los casos clínicos utilizados. La información sobre el tratamiento, el Índice de Extensión y Severidad de la Dermatitis Atópica Canina, (CADESI-4) y la Escala Análoga Visual de prurito (pVAS) se evaluaron para cada perro en el momento de la recolección del suero.

Resultados – los perros con AD que no recibieron tratamiento con esteroides y los tratados con oclacitinib tuvieron concentraciones séricas de MIF significativamente elevadas en comparación con los controles. Las concentraciones de MIF no fueron significativamente diferentes en los perros con AD que recibieron esteroides en comparación con los controles. No hubo una correlación significativa entre las concentraciones de MIF y las puntuaciones clínicas (CADESI-4 o pVAS).

Conclusiones e importancia clínica – las concentraciones séricas de MIF aumentan en los perros con AD y el MIF podría ser un objetivo para estrategias terapéuticas.

Zusammenfassung

Hintergrund – Die atopische Dermatitis (AD) ist eine häufige entzündliche Hauterkrankung bei Hunden. Der Makrophagen- Migrations- Inhibitions-Faktor (MIF) löst die Freisetzung von pro-entzündlichen Zytokinen bei Menschen mit AD aus und die Serumkonzentrationen korrelieren mit der Schwere der Erkrankung.

Hypothese – Die MIF Konzentrationen der Hunde sind im Serum bei Hunden mit AD erhöht und korrelieren mit den klinischen Veränderungen und den Juckreizwerten.

Tiere – Hunde in Privatbesitz (n = 49), die mit AD diagnostiziert worden waren und 17 gesunde nicht betroffene Kontrollhunde wurden für die Studie verwendet.

Methoden und Materialien – Ein kommerziell erhältlicher MIF ELISA wurde für den Hund optimiert und es wurde Serum von klinischen Fällen verwendet. Informationen bezüglich Behandlung, Canine Atopic Dermatitis Extent und Severity Index, (CADESI-4) und die Juckreiz Visual Analog Scale (pVAS) wurde für jeden Hund zum Zeitpunkt der Serumgewinnung festgehalten.

Ergebnisse – Hunde mit AD, die keine Steroidtherapie erhalten hatten und jene, die mit Oclacitinib behandelt worden waren, zeigten signifikant erhöhte Serum MIF Konzentrationen im Vergleich zu den Kontrollen. Die MIF Konzentrationen waren nicht signifikant verschieden von den AD Hunden, die Steroide erhielten im Vergleich zu den Kontrolltieren. Es gab keine signifikante Korrelation zwischen MIF Konzentrationen und klinischen Werten (CADESI-4 oder pVAS).

Schlussfolgerungen und klinische Bedeutung – Serum MIF Konzentrationen waren bei Hunden mit AD erhöht, wobei MIF ein Ziel für eine entsprechende Therapie sein könnte.

要約

背景 – アトピー性皮膚炎(AD)は犬の一般的な炎症性皮膚疾患である。マクロファージ遊走阻止因子(MIF)は人ADにおいて炎症誘発性サイトカイン放出を開始し、血清濃度が疾患の重症度と相関していることが知られている。

仮説 – 犬血清MIF濃度がAD犬で増加し、臨床病変および掻痒スコアと相関すると仮説を立てた。

被験動物 – ADと診断した飼育犬(n = 49)および罹患していない健康対照犬17頭を本研究に供した。

方法および材料 – 市販MIF ELISAを犬に最適化し、臨床例の血清を使用した。各犬に対し、治療歴、犬アトピー性皮膚炎の程度および重症度指数第 CADESI-4)ならびに掻痒視覚アナログスケール (pVAS)に関する情報を、血清収集時に記録した。

結果 – ステロイド治療を受けていないAD犬、およびオクラシニブで治療されたAD犬は、対照群と比較して血清MIF濃度が有意に上昇していた。ステロイド治療を受けたAD犬は対照群と比較し、MIF濃度に有意な差はなかった。MIF濃度と臨床スコア(CADESI-4またはpVAS)間に有意な相関関係は認めなかった。

結論と臨床的重要性 – AD犬において血清MIF濃度が上昇しており、MIFが治療ターゲットの一つとなる可能性がある。

摘要

背景 – 异位性皮炎(AD)是犬常见的炎性皮肤病。在人类AD中,巨噬细胞移行抑制因子(MIF)启动促炎细胞因子释放,并且血清浓度与疾病严重性相关。

假设 – AD患犬血清MIF浓度增加,并与临床病变和瘙痒评分相关。

动物 – 该研究采用诊断患有AD的家养犬(n = 49)和17只健康、未发病的对照犬。

方法和材料 – 使用市场上现有的最适合犬的MIF ELISA,以及来自临床病例的犬血清。在血清采集时记录每只犬的治疗情况,犬异位性皮炎严重程度指数(CADESI-4)和瘙痒评分表(pVAS)的信息。

结果 – 与对照组相比,未接受类固醇治疗的AD患犬和接受奥拉克替尼治疗的患犬血清MIF浓度显著升高;接受类固醇的AD犬的MIF浓度无显著差异。MIF浓度与临床评分(CADESI-4或pVAS)之间没有显著相关性。

结论和临床意义 – AD患犬血清MIF浓度升高,MIF可能是治疗靶点。

Resumo

Contexto – A dermatite atópica (DA) é uma doença cutânea inflamatória comum em cães. O fator inibidor de migração de macrófagos (MIF) inicia a liberação de citocinas pró-inflamatórias na DA humana e suas concentrações séricas são correlacionadas com a gravidade da doença.

Hipótese – As concentrações séricas de MIF estão aumentadas em cães com DA e correlacionam com as lesões clínicas e escore de prurido.

Animais – Cães de proprietários (n = 49) diagnosticados com DA e 17 cães saudáveis não afetados foram utilizados no estudo.

Métodos e materiais – Um kit comercial de MIF ELISA foi otimizado para cães e o soro dos casos clínicos foram utilizados. Informações sobre o tratamento, CADESI-4 (*Canine Atopic Dermatitis Severity Extent and Severity Index*) e a escala analógica visual de prurido (pVAS) foram registrados para cada cão no momento da coleta do soro.

Resultados – Cães com DA que não receberam tratamento com corticosteroides e os tratados com oclacitinib apresentaram um aumento significativo das concentrações séricas de MIF comparado aos controles. As concentrações de MIF não foram significativamente diferentes em cães com DA recebendo corticosteroides, comparado aos controles. Não houve diferença significativa entre as concentrações de MIF e os escores clínicos (CADESI-4 e pVAS).

Conclusões e importância clínica – Há aumento nas concentrações séricas de MIF em cães com DA e o MIF pode ser um bom alvo terapêutico no tratamento.