

Noninvasive evaluation of vascular endothelial growth factor-A (VEGF-A) protein concentrations in the stratum corneum and serum of healthy and atopic dogs

Danielle Cobiella, Dunbar Gram and Domenico Santoro 

Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, 2015 SW 16th Avenue, Gainesville, FL 32610, USA

Correspondence: Domenico Santoro, Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, 2015 SW 16th Avenue, Gainesville, FL 32610, USA. E-mail: dsantoro@ufl.edu

Background – Vascular endothelial growth factor (VEGF) is a cytokine involved primarily in angiogenesis. In human atopic dermatitis (AD), VEGF has been detected in the stratum corneum and blood.

Objective – To evaluate VEGF-A expression in the serum and stratum corneum of healthy and atopic dogs, and its possible correlation with disease severity in atopic dogs.

Animal – Fifteen atopic and 15 healthy, privately owned dogs.

Methods and materials – The severity of clinical signs associated with AD was evaluated with the Canine Atopic Dermatitis Extent and Severity Index (CADESI-04). For all dogs, a single blood sample was performed and serum collected. Tape stripping (15 times) was performed on the left periocular area (lesional skin). A commercially available canine-specific VEGF-A enzyme-linked immunosorbent assay was performed with all samples.

Results – Vascular endothelial growth factor-A was undetectable in the serum. In the stratum corneum, there was no significant difference in VEGF-A concentrations between healthy (mean 89.4 ± 59.5 pg/ml) and atopic dogs (mean 100.3 ± 77.1 pg/ml) ($P = 0.71$). There was no correlation between stratum corneum VEGF-A concentrations and CADESI-04 scores.

Conclusions and clinical importance – The role of VEGF in canine AD is unclear. Because of many variants, VEGF-C and VEGF-D or VEGF-A isotopes should be explored in the skin to better evaluate the role of VEGF in canine atopy. Full-thickness skin biopsy, molecular biology and histopathological investigation may be necessary to further assess cutaneous VEGF expression.

Introduction

Canine atopic dermatitis (cAD) is a common chronic pruritic skin disease in dogs which can be difficult to manage.¹ Studies identifying key cytokines involved in AD have been critical in gaining a better understanding of its pathogenesis.² There has been growing interest in the role of vascular endothelial growth factor-A (VEGF-A) in chronic inflammatory human skin diseases, including AD.^{3–7} Studies have concentrated on the pro-inflammatory action of VEGF and its ability to increase erythema,⁸ leucocyte trafficking and extravasation,⁹ and endothelial adhesion molecules on cutaneous blood vessels.⁹ Furthermore, VEGF-A has been regarded as an important cytokine involved in angiogenesis, vascular permeability, wound healing and tumour development.^{10–12} Historically, it has been thought that VEGF-A is synthesized and released primarily from endothelial cells and

fibroblasts.^{10,13} However, epithelial cells, especially keratinocytes, in humans,¹⁴ mice¹⁵ and dogs¹⁶ have been associated with VEGF-A secretion. Furthermore, pro-inflammatory cytokines have been shown to induce release of VEGF from human keratinocytes [interleukin (IL)-1, IL-6 and interferon (IFN)- γ]⁴ and mast cells (IL-9).⁵

In humans, VEGF-A has been shown to be increased markedly in the serum⁶ and lesional stratum corneum of atopic patients.^{3,7} A significant increase in VEGF protein expression was seen in the serum of atopic patients and stratum corneum of lesional atopic skin compared with healthy and nonlesional atopic skin.³ However, there was no difference between VEGF concentrations in the stratum corneum of nonlesional atopic skin compared with healthy control skin.³ A positive correlation was reported between the severity of atopic lesions and protein expression of VEGF-A in the plasma,¹⁷ serum⁶ and in the stratum corneum of lesional skin.^{6,7} In dogs, although VEGF-A has been identified in healthy canine epidermis,¹⁸ there have been no published studies analyzing the presence and role of VEGF-A in canine inflammatory skin diseases.

The aims of this study were: (i) to evaluate the presence of VEGF-A in the stratum corneum of healthy and lesional skin of atopic dogs; (ii) to evaluate the presence of VEGF-A in the serum of healthy and atopic dogs; and (iii) to determine if there is a correlation between VEGF-A

Accepted 19 August 2019

Source of Funding: This study was funded by the University of Florida Resident Research Grant.

Conflict of Interest: No conflicts of interest have been declared. This study was presented at the North American Veterinary Dermatology Forum, 2019, Austin, Texas. Vet Dermatol 2019; 30: 303 (Abstract).

concentrations (serum and/or stratum corneum) and the severity of clinical signs in atopic dogs.

Methods and materials

Animal welfare documentation

All dogs were recruited at the authors' institution with approval from the Institutional Animal Care and Use Committee (IACUC) #201710104 and a signed owner consent form approved by the Veterinary Hospital Research Review Committee (VHRR # 2018-008).

Study population

Naturally affected atopic and healthy, privately owned dogs were enrolled in the study. Dogs were between 1 and 10 years old and weighed >5 kg. At the time of enrolment, healthy dogs had no history or signs of skin disease and were clinically normal. In the atopic group, cAD was diagnosed based on published guidelines¹⁹ and dogs had seasonal signs of pruritus or underwent a diet trial for at least eight weeks without improvement. All dogs received monthly flea prevention and had negative skin scrapes for both sarcoptic and demodectic mange.

Exclusion criteria

Pregnant and lactating dogs were excluded from the study. Dogs with clinical evidence or a history of malignant neoplasia, metabolic/endocrine disease, parasite infestation or contact or food allergy were excluded. Dogs with active bacterial/yeast infections diagnosed according to guidelines were excluded and treated with antimicrobial medication(s). All dogs followed drug withdrawal periods for oral and topical antibiotics and antifungal medications (four weeks), corticosteroids (12 weeks for long-acting injectable, four weeks for oral, three weeks for topical), antihistamines (two weeks), ciclosporin (four weeks), lokivetmab (eight weeks) and oclacitinib (one week). Dogs receiving allergen-specific immunotherapy for less than one year before enrolment also were excluded from the study.

Clinical assessment

The severity of the clinical signs was scored for 20 body sites using the CADESI-4 system.²⁰ The skin lesions (erythema, lichenification and excoriation/alopecia) were scored on a scale between 0 and 3 (0, none; 1, mild; 2, moderate; 3, severe) with a maximum score of 180.

Stratum corneum sampling

Stratum corneum samples were collected using a tape-stripping technique as described previously.⁷ Briefly, the hair was parted and the stratum corneum was sampled using adhesive tape (Scotch® Tape, 3M; St Paul, MN, USA) gently pressed directly onto the skin 15 consecutive times using the same tape. The anatomical site chosen for sampling in both healthy and atopic dogs was the left periorbital area, as representative of a commonly affected area in AD.¹⁹ For each dog, two tape samples were collected and stored at -80°C until use. Before storage, each tape was trimmed to 1×1 cm. A single piece of unused 1×1 cm tape was used as a control.

Stratum corneum protein extraction

Stratum corneum extracts were obtained using methods described previously.⁷ Briefly, each tape was immersed in 1 mL of *n*-hexane for 1 min, then placed in a conical vial containing 1 mL of extraction buffer (0.1 M Tris-HCL pH 8, 0.14 M NaCl, 0.1% Tween-20). The conical vial containing the tape and extraction buffer was placed on a gentle rocker for 30 min and subsequently centrifuged three times at 92g for 10 min at room temperature. The tape was removed after the first centrifugation. Between each centrifugation, the supernatant was discarded and a pellet was obtained and resuspended. After three washes, the final pellet was resuspended and the resulting supernatant was obtained and used for VEGF-A and total protein

quantification. The amount of total proteins in each sample was measured using a commercial bovine serum albumin (BSA) protein assay kit (Pierce™ BCA Protein Assay Kit, Thermo Scientific; Rockford, IL, USA) following the manufacturer's instructions.

Serum collection

Six millilitres of venous whole blood was collected from each dog via jugular venipuncture, placed in a serum separator tube and allowed to clot for 2 h at 4°C , and then centrifuged at 4°C for 20 min at 2,000g. The serum was removed and placed in a fresh tube and stored at -80°C until analysis.

Vascular endothelial growth factor-A ELISA

The amount of VEGF-A in the stratum corneum extracts and in the serum was measured with a commercially available enzyme-linked immunosorbent assay (ELISA) specific for canine VEGF-A isoform 164 (RayBio®, Inc.; Norcross, GA, USA) (detection limit 6 pg/mL) following the manufacturers' instructions (ELC-VEGF-2). The ELISA was validated using canine plasma, serum and cell culture supernatants by the manufacturer. Each sample was run in duplicate and the mean was extrapolated and analyzed statistically for each group. Total protein and VEGF-A concentrations were analyzed by Cytation1 (BioTek; Winooski, VT, USA). To allow for standardization for differences in amount of protein extracted between dogs, VEGF-A concentrations were calculated as absolute numbers (expressed as pg/mL), and, after normalization, expressed as percentages of the total protein in each sample.

Statistical analysis

Based on a previous study in human patients,⁷ the mean and standard deviation were obtained and a minimum number of 14 dogs was extrapolated for the study ($\alpha = 0.05$; power = 0.8). Thus, a total of 15 dogs per group were elected for this study. Data collection was tested for normality using the Kolmogorov–Smirnov test ($\alpha = 0.05$). Population characteristics (age, sex and weight) were compared between the two groups using unpaired Student's *t*-test (age and weight) and Fischer exact test (sex). The amount of serum and stratum corneum VEGF-A between healthy and atopic dogs was compared using the Wilcoxon–Mann–Whitney U-test. The correlation between CADESI-04 and VEGF-A concentrations was tested using the Spearman correlation test and a correlation matrix was extrapolated; *P*-values ≤ 0.05 were considered significant. GraphPad PRISM 6 software (GraphPad Software Inc.; La Jolla, CA, USA) was used to compare all statistical data.

Results

Canine population

Healthy dogs included eight spayed female, six neutered male and an intact male. Healthy dogs were 5 ± 2.5 (mean $\pm$ standard deviation) years old and weighed 25.8 ± 13.6 kg. Healthy dog breeds included mixed breed dog ($n = 4$), German shepherd dog ($n = 3$), golden retriever ($n = 2$), whippet ($n = 1$), Welsh corgi ($n = 1$), Boxer ($n = 1$), shih tzu ($n = 1$), cane corso ($n = 1$) and American Staffordshire terrier ($n = 1$). Atopic dogs included eight spayed female, five neutered male and two male intact dogs. Atopic dogs were 6.8 ± 2.4 years old and weighed 28.6 ± 11.8 kg, with a mean CADESI-04 score of 31.1 ± 12.1 . Atopic dog breeds included mixed breed dogs ($n = 3$), Labrador retriever ($n = 3$), Boxer ($n = 2$), West Highland white terrier ($n = 2$), American Staffordshire terrier ($n = 2$), cocker spaniel ($n = 1$), German shepherd dog ($n = 1$) and golden retriever ($n = 1$). There were no differences in sex, age and weight between the two groups ($P > 0.05$).

Protein and VEGF-A in the stratum corneum

Concentrations of VEGF-A were detected in the stratum corneum of healthy (mean 89.4 ± 59.5 pg/mL) and atopic dogs (mean 100.3 ± 77.1 pg/mL). A significant difference between the two groups was not present ($P = 0.71$) (Figure 1). In order to account for the variation in protein isolation in the different dogs, the total protein expression was measured via the BSA protein assay. The protein amount equivalent extracted from the stratum corneum of healthy (median 94.8 µg/mL; range 90.2 – 104.9 µg/mL) and atopic (median 95.3 µg/mL; range 90.2 – 111.6 µg/mL) dogs was very similar ($P = 0.5$). Then the amount of VEGF-A was calculated as the percentage of VEGF-A in the total protein. Likewise, for the VEGF-A values, a significant difference between the two groups was not present ($P = 0.79$); the median percentage of VEGF-A in healthy skin was $9 \times 10^{-5}\%$ (range 0 – $2.2 \times 10^{-4}\%$) and $1 \times 10^{-4}\%$ (range 0 – $3.2 \times 10^{-4}\%$) in atopic skin.

Correlation of CADESI-04 and the stratum corneum

There was no significant correlation between the CADESI-04 scores and the stratum corneum VEGF-A concentrations. The correlation coefficient (CC) was -0.015 with $P = 0.97$ (Figure 2).

Vascular endothelial growth factor-A in the serum

Vascular endothelial growth factor-A expression in the serum of healthy and atopic dogs was below detection limits (<6 pg/mL).

Discussion

To the best of the authors' knowledge, this is the first study evaluating VEGF-A protein concentrations in the skin and blood of atopic dogs. The VEGF-A values from the serum were below detection limits. Detectable concentrations of VEGF-A values were present in the stratum corneum of healthy and atopic dogs; however, no significant difference was found between the two groups. There was no correlation between CADESI-4 scores and VEGF-A concentrations in the stratum corneum of atopic dogs. As expected, VEGF-A represented a very small percentage of total protein within the stratum corneum for both healthy and atopic dogs.

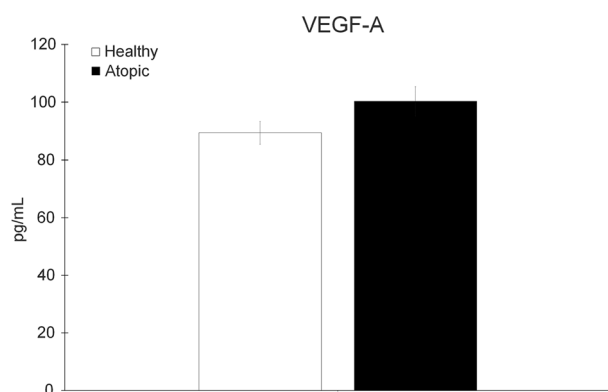


Figure 1. Protein concentrations for canine vascular endothelial growth factor-A (VEGF-A) in the stratum corneum of healthy and atopic dogs.

Bars indicate standard errors of the mean.

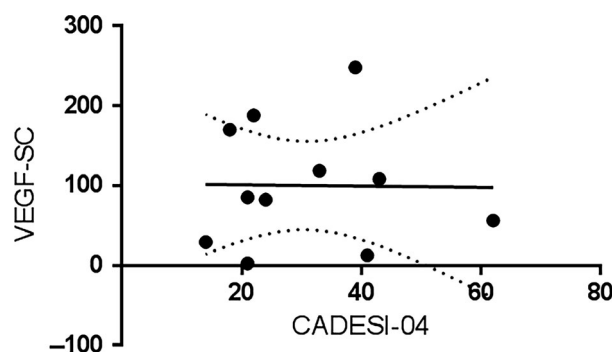


Figure 2. Correlation between Canine Atopic Dermatitis Extent and Severity Index, 4th iteration (CADESI-04) score and stratum corneum vascular endothelial growth factor (VEGF) in the periocular region of atopic dogs.

VEGF-SC, VEGF in the stratum corneum

Most of the published information regarding VEGF-A and inflammatory skin conditions derives from human studies.^{3,6,7} No studies have been published on the role of VEGF-A in inflamed canine skin. One study reported the presence of VEGF isoforms and the receptor VEGFR-1 in all tissues tested (liver, lungs, kidneys, heart, adrenal glands, thyroid, intestine, bladder, spleen and skin) in six healthy beagle dogs, with the highest concentrations in the lungs and heart.¹⁸ VEGF and its receptor were moderately to strongly evident in epidermis, sebaceous glands, apocrine glands, erector pili muscles and hair follicles.¹⁹ It was reported that in wounded canine skin, VEGF-A was heavily expressed by keratinocytes under stimulation by tumour necrosis factor (TNF)- α , TGF- β , IL-6 and endothelial growth factor.¹⁶ VEGF-A has been evaluated in the serum of healthy dogs and dogs with neoplasia with conflicting results (not detected in lymphoma cases; detected in dogs with soft tissue sarcoma).^{21,22} To the best of the author's knowledge, there have been no published studies evaluating VEGF-A in the serum of atopic dogs.

Given reports of VEGF-A in canine and human epidermis and of detection of VEGF-A in epidermal cells harvested from atopic humans,⁷ the authors chose the tape-stripping technique due to its noninvasiveness and ease of use. In the present study, the lack of expression of VEGF-A in the blood of healthy and atopic dogs compared to tape-strip samples likely indicates that VEGF-A is locally produced by keratinocytes and it has an autocrine/paracrine action on the cutaneous tissues.²³ All of the atopic dogs in the present study had a mild to moderate CADESI-04 score, and it is possible that the level of clinical severity was not high enough to lead to a significant difference between the stratum corneum VEGF-A concentrations in atopic and healthy skin. In addition, the relatively mild degree of inflammation in atopic dogs as reflected by CADESI-04 scores may not have been high enough to induce a large amount of VEGF-A from the keratinocytes and thus led to a lack of correlation between VEGF-A concentrations and the severity of disease. Thus, it is possible that more severe CADESI-04 scores may lead to a significant increase in the stratum corneum VEGF-A concentrations; however, further studies are needed to support this hypothesis.

Limitations of the present study include the small sample size and the lack of external validation of the VEGF ELISA kit for epidermal cell extracts; a larger sample size may allow for a better evaluation of the role that VEGF-A plays in atopic dogs. In addition, future studies may consider alternatives to the tape-stripping technique to evaluate concentrations of VEGF-A by using more sensitive methodology (skin biopsy samples with immunohistochemical evaluation, flow cytometer and/or PCR). Another limitation of this study is that although VEGF-A and isoform 164 are the only VEGF forms currently studied in dogs,¹⁹ it is possible that other variants of VEGF (VEGF-C and VEGF-D) and different VEGF isoforms (120, 182 and 188)¹⁹ may be more prevalent in skin or/and blood of healthy and allergic dogs. Unfortunately, validated, commercially available, canine-specific ELISAs for additional variants and isoforms are not currently available. Another possible study direction could be the evaluation of VEGF, mRNA and/or protein circulating in serum/plasma exosomes.^{24–26}

Acknowledgments

The authors thank Kim Ahrens and Rachel Wilkes for helping with the BSA and ELISA analysis.

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Résumé

Contexte – Le VEGF (vascular endothelial growth factor) est une cytokine impliquée dans l'angiogenèse. Chez l'homme atteint de dermatite atopique (AD), le VEGF a été détecté dans le *stratum corneum* et le sang.

Objectif – Évaluer l'expression de VEGF-A dans le serum et le *stratum corneum* des chiens sains et atopiques, et, si possible, évaluer la corrélation avec la sévérité de l'atteinte chez le chien atopique.

Sujets – Quinze chiens atopiques et 15 chiens sains de propriétaires.

Matériels et méthodes – La sévérité des signes cliniques associés à l'AD a été évaluée par un CADESI-04

(Canine Atopic Dermatitis Extent and Severity Index). Pour tous les chiens, un échantillon sanguin a été prélevé pour récolte du serum. L'abrasion cutanée par ruban adhésif (15 fois) a été réalisée sur peaux lésionnelles sur la zone péri-oculaire gauche. Un test ELISA commercial VEGF-A, spécifique du chien a été réalisé pour tous les échantillons.

Résultats – Le VEGF-A était indétectable dans le sérum. Dans le *stratum corneum*, il n'y avait pas de différence significative dans les concentrations de VEGF-A entre les chiens sains (médiane: 89.4±59.5 pg/ml) et les chiens atopiques (médiane: 100.3±77.1 pg/ml) ($P = 0.71$). Il n'y avait pas de corrélation entre les concentrations de VEGF-A entre le *stratum corneum* et les scores de CADESI-04.

Conclusions et importance clinique – Le rôle du VEGF dans l'AD canine n'est pas clair. A cause de nombreuses variables, les isotypes de VEGF-C et VEGF-D ou VEGF-A devaient être explorés dans la peau pour mieux évaluer le rôle du VEGF dans l'atopie canine. L'épaisseur totale des biopsies cutanées, la biologie moléculaire et l'histopathologie sont nécessaires pour étudier davantage l'expression de VEGF cutané.

Resumen

Introducción – el factor de crecimiento endotelial vascular (VEGF) es una citoquina implicada principalmente en la angiogénesis. En la dermatitis atópica humana (AD), se ha detectado VEGF en el estrato córneo y la sangre.

Objetivo – evaluar la expresión de VEGF-A en el suero y el estrato córneo de perros sanos y atópicos, y su posible correlación con la gravedad de la enfermedad en perros atópicos.

Animales – quince perros atópicos y 15 sanos, de propiedad privada.

Métodos y materiales – la gravedad de los signos clínicos asociados con la AD se evaluó con el índice de severidad y extensión de la dermatitis atópica canina (CADESI-04). Para todos los perros, se obtuvo una sola muestra de sangre y se recogió el suero. Se realizó obtención de muestras con cinta adhesiva (15 veces) en el área periocular izquierda (piel lesionada). Se realizó una prueba de ELISA comercial específica de VEGF-A específico para perros en todas las muestras.

Resultados – el factor de crecimiento endotelial vascular A fue indetectable en el suero. En el estrato córneo, no hubo diferencias significativas en las concentraciones de VEGF-A entre perros sanos (media 89,4 ± 59,5 pg/ml) y atópicos (media 100, 3±77,1 pg/ml) ($P = 0,71$). No hubo correlación entre las concentraciones de VEGF-A en el estrato córneo y las puntuaciones CADESI-04.

Conclusiones e importancia clínica – el papel de VEGF en la AD canina no está claro. Debido a la presencia de muchas variantes, los isótopos VEGF-C y VEGF-D o VEGF-A deben explorarse en la piel para evaluar mejor el papel del VEGF en la atopía canina. Biopsias de piel de espesor completo, pruebas de biología molecular e investigación histopatológica pueden ser necesarias para evaluar aún más la expresión cutánea de VEGF.

Zusammenfassung

Hintergrund – Der Vascular endothelial Growth Factor (VEGF) ist ein Zytokin, welches in erster Linie bei der Angiogenese involviert ist. Bei der atopischen Dermatitis des Menschen (AD) wurde VEGF im Stratum corneum und im Blut gefunden.

Ziel – Eine Evaluierung der VEGF-A Exprimierung im Serum und im Stratum corneum von gesunden sowie atopischen Hunden und die mögliche Korrelation der Schwere der Krankheit bei atopischen Hunden.

Tier – Fünfzehn atopische und 15 gesunde Hunde in Privatbesitz.

Methoden und Materialien – Die Schwere der klinischen Zeichen, die mit AD einhergehen wurde mittels Canine Atopic Dermatitis Extent and Severity Index (CADESI-04) evaluiert. Bei allen Hunden wurde eine einzige Blutabnahme durchgeführt und Serum gesammelt. Am linken Auge wurde periokulär (läsionale Haut) mittels Klebestreifen gestrippt (15 Mal). Es wurde ein kommerziell verfügbarer Hunde-spezifischer VEGF-A Enzym-linked-Immunsorbent Assay an allen Proben durchgeführt.

Ergebnisse – Der Vascular endothelial Growth Factor war im Serum nicht nachweisbar. Im Stratum corneum bestand kein signifikanter Unterschied zwischen den VEGF-A Konzentrationen zwischen den gesunden (Durchschnitt: 89,4±59,5 pg/mL) und atopischen Hunden (Durchschnitt 100,3±77,1 pg/mL; ($P = 0,71$). Es bestand keine Korrelation zwischen den VEGF-A Konzentrationen im Stratum corneum und den CADESI-04 Werten.

Schlussfolgerungen und klinische Bedeutung – Die Rolle von VEGF bei der caninen AD ist unklar. Aufgrund vieler Varianten, sollten VEGF-C und VEGF-D oder VEGF-A Isoptope in der Haut untersucht werden, um die Rolle von VEGF bei der Atopie des Hundes besser zu evaluieren. Hautbiopsien, molekularbiologische Untersuchungen und eine histopathologische Untersuchung könnte nötig sein, um die Exprimierung von VEGF in der Haut besser zu erfassen.

要約

背景 – 血管内皮増殖因子(VEGF)は、主に血管新生に関与するサイトカインである。VEGFは人のアトピー性皮膚炎(AD)において角層および血液で検出されている。

目的 – 本研究の目的は、健康およびアトピー犬の血清および角層におけるVEGF-A発現を評価し、アトピー

一犬の疾患重症度との可能な相関を評価することである。

被験動物 – アトピー犬15頭と健常飼育犬15頭。

材料と方法 – ADに関連する臨床徴候の重症度を、犬アトピー性皮膚炎の程度および重症度指数(CADESI-04)で評価した。すべての犬において、単一の血液サンプルを採取し、血清を収集した。左眼周囲領域(病変部皮膚)においてテープストリッピング(15回)を実施した。市販の犬特異的VEGF-A酵素結合免疫吸着アッセイをすべてのサンプルにおいて実施した。

結果 – VEGF-Aは血清では検出されなかった。角層では、健常犬(中央値:89.4±59.5 pg/ml)およびアトピー犬(中央値:100.3±77.1pg/ml)間に、VEGF-A濃度に有意差はなかった。(P = 0.71)。角層VEGF-A濃度およびCADESI-04スコア間に相関関係はなかった。

結論と臨床的重要性 – 犬ADにおけるVEGFの役割は不明である。多くの変異体があるため、犬アトピーにおけるVEGFの役割をよりよく評価するため、VEGF-CおよびVEGF-DまたはVEGF-A同位体を皮膚で調査する必要がある。皮膚のVEGF発現をさらに評価するには、全層皮膚生検、分子生物学および組織病理学的調査が必要な場合がある。

摘要

背景 – 血管内皮生长因子(VEGF)是一种细胞因子,主要参与血管生成。在人类的异位性皮炎(AD)中,可在角质层和血液中检测到VEGF。

目的 – 评估VEGF-A在健康犬和异位性犬血清和角质层中的表达,及探究其与异位性犬疾病严重程度的关系。

动物 – 15只异位性皮炎患犬和15只健康私家犬。

方法和材料 – 用犬异位性皮炎程度和严重性指数(CADESI-04)评估与AD相关临床症状的严重程度。对所有犬进行单次血样采集并收集血清;在左眼周区域(病变皮肤)上胶带采集样本(15次)。对所有样品进行市售的犬特异性VEGF-A酶联免疫吸附测定。

结果 – 在血清中检测不到血管内皮生长因子-A。在健康犬(平均值:89.4±59.5 pg/ml)和异位性犬(平均值:100.3±77.1pg/ml)之间,角质层中的VEGF-A浓度无显著差异(P = 0.71)。角质层VEGF-A浓度与CADESI-04评分之间无相关性。

结论和临床价值 – VEGF在犬AD中的作用尚不明确。由于存在许多变异,应该在皮肤中探索VEGF-C、VEGF-D或VEGF-A同位素,以更好地评估VEGF在犬异位性皮炎中的作用。可能需要进行全层皮肤活检、分子生物学和组织病理学检查,才能进一步评估皮肤VEGF的表达。

Resumo

Contexto – O fator de crescimento endotelial vascular (VEGF) é uma citocina envolvida primariamente na angiogênese. Na dermatite atópica (DA) humana, o VEGF foi detectado no estrato córneo e no sangue.

Objetivo – Avaliar a expressão de VEGF-A no soro e no estrato córneo de cães saudáveis e atópicos, e sua possível correlação com a gravidade da doença em cães atópicos.

Animais – Quinze cães atópicos e 15 saudáveis, de proprietários.

Métodos e materiais – A gravidade dos sinais clínicos associados à DA foi avaliada com o Índice de Extensão e Gravidade da Dermatite Atópica Canina (*Canine Atopic Dermatitis Extent and Severity Index* - CADESI-04). Para todos os cães, coletou-se uma única amostra de sangue e o soro foi extraído. Realizou-se impressão por fita adesiva (15 vezes) na área periocular esquerda (pele lesional). Um ensaio imunossorvente ligado a enzima VEGF-A específico para cães, disponível no mercado, foi realizado com todas as amostras.

Resultados – O fator A de crescimento endotelial vascular não foi detectado no soro. No estrato córneo, não houve diferença significativa nas concentrações de VEGF-A entre cães saudáveis (média: 89,4±59.5 pg/ml) e cães atópicos (média 100,3±77,1pg/ml) (P = 0.71). Não houve correlação entre as concentrações de VEGF-A no estrato córneo e os escores CADESI-04.

Conclusões e importância clínica – O papel do VEGF na DA canina não é claro. Devido a muitas variantes, os isótopos de VEGF-C e VEGF-D ou VEGF-A devem ser explorados na pele para avaliar melhor o papel do VEGF na atopia canina. Biópsia cutânea de espessura total, biologia molecular e investigação histopatológica podem ser necessárias para melhor avaliar a expressão cutânea de VEGF.