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ORIGINAL ARTICLE

The efficacy of subcutaneous slow-release melatonin implants in the prevention of canine flank alopecia recurrence is uncertain: A double-blind, randomized, placebo-controlled study

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Abstract

Background: Canine flank alopecia (CFA) is characterized by seasonally recurring noninflammatory, occasionally hyperpigmented alopecia predominantly in the thoracolumbar area. Previous studies suggest that reduced production of endogenous melatonin may play a role in the pathogenesis of this condition, and placebo-controlled studies on the efficacy of preventative melatonin treatment are lacking.

Objective: To evaluate the efficacy of subcutaneous slow-release melatonin implants in the prevention of CFA recurrence.

Animals: Twenty-one client-owned dogs with a history of CFA were included in the study.

Materials and Methods: At time (T)0, a general physical and dermatological examination was performed on each dog, blood was collected for serum biochemistry analysis and two skin biopsies were taken from alopecic areas on the nonsedated affected dogs after subcutaneous injection with 2% lidocaine. Dogs with normal blood work and histological results compatible with CFA were included in the study. Participating dogs were randomly assigned to receive either placebo or 18 mg melatonin subcutaneously in the interscapular area, approximately 2 months before expected CFA onset (T1). CFA recurrence was scored qualitatively as complete, ≤50% recurrence, or no recurrence at 5 and 7 months after the intervention (T2 and T3, respectively).

Results: At T3, in dogs treated with placebo (nine of 17), the percentages for complete recurrence, ≤50% recurrence and no recurrence were 44%, 0% and 56%, respectively. In dogs treated with melatonin (eight of 17), these percentages were 25%, 50% and 25%, respectively. There were no statistically significant differences in the scores between melatonin-treated dogs and placebo-treated dogs ($p = 0.40$). In three of eight melatonin-treated dogs, mild transient swelling was observed at the injection site.

This study was presented in part at the European Veterinary Dermatology Congress, 2021, Virtual Congress.

Conclusions: This study did not provide evidence that an 18 mg melatonin implant treatment, although well-tolerated, is efficacious in preventing recurrence of CFA in affected dogs.

INTRODUCTION

Canine flank alopecia (CFA) is a dermatological condition characterized by recurrent nonpruritic, nonscarring and noninflammatory alopecia generally in the thoracolumbar area.[1–4] This visually distinctive, usually well-circumscribed, occasionally hyperpigmented alopecia can be either unilateral or bilateral. In contrast to most endocrine alopecias, both hair quality and quantity in the nonaffected areas are normal.[1,2] CFA is seen in both males and females, intact and neutered.[1–4] First CFA onset is usually between 3 and 6 years of age[1–3] and occurs between November and April in the Northern Hemisphere.[1–4] In the following 3–8 months, hair usually will regrow spontaneously, yet in some dogs, the alopecia may become permanent.[3,4] Numerous breeds can be affected, yet some breeds are more prone to developing CFA (e.g. English bulldog, Rhodesian ridgeback and Staffordshire bull terrier),[1–5] indicating that genetic predisposition could be a risk factor for CFA. Because CFA-affected dogs are otherwise healthy, and an association with other internal or metabolic diseases has not been established, benign neglect is often the treatment of choice.[1,2,4] As many owners perceive the recurring condition as cosmetically undesirable, a safe and effective treatment would be of great value.

The pathogenesis of CFA remains unclear. Melatonin is known to play a role in the physiology of hair growth.[6–8] It is an endogenous neurohormone produced mainly in the pineal gland; when daylight declines, melatonin levels increase. The onset of CFA is in the months with shorter day length.[8] Thus, a decline in daylight exposure appears to trigger the onset of CFA, which might suggest that melatonin is involved in the pathogenesis.

Several studies support the hypothesis that melatonin is an effective treatment of CFA. One study showed promising results with subcutaneous melatonin implants,[9] and a few case studies implicated oral melatonin as a good treatment choice.[8,10] A study on winter fur growth in adult male raccoon dogs (Nyctereutes procyonoides) revealed an increased hair density of the undercoat after melatonin implants were administered.[11]

There are several studies on this topic in other species. In some mammalian species, the haircoat consists of an outer layer of guard hairs and an inner layer of soft, finer undercoat which serves to insulate and grows thicker in the winter. Subcutaneous melatonin implants in female mink yielded a winter coat maturity 6–7 weeks earlier than in the control animals.[12]

The aim of this randomized, double-blind, placebo-controlled clinical trial was to evaluate the efficacy of subcutaneously applied, slow-release melatonin implants in the prevention of CFA recurrence in dogs.

MATERIALS AND METHODS

Ethics

The study was conducted in accordance with the guidelines for Good Clinical Practice (VICH GL9).

We obtained written informed consent from the participating owners, and all data were anonymised.

Study design

This double-blind, randomized, placebo-controlled clinical trial was performed between February 2019 and July 2020, at a private veterinary practice in Noord-Brabant, the Netherlands, and the University Clinic for Companion Animal Health Utrecht, the Netherlands.

The inclusion criteria were otherwise healthy dogs with a history of at least two consecutive CFA episodes, with onset each year between November and April, followed by either full or partial hair regrowth within 8 months following the previous CFA episode. Dogs were excluded if they were on any CFA treatment (e.g. oral melatonin) at the start of the study and those dogs that developed persistent CFA between time (T)0 (baseline) and T1 (point of intervention) were subsequently excluded from further analysis.

Study dogs were followed up for 17 months: at T0, baseline (active CFA); T1, approximately 10 months after T0 (i.e. 2 months before the next anticipated onset of CFA in the following season) (intervention); T2, 5 months after intervention (month of anticipated CFA recurrence); and T3, 7 months after intervention (month of anticipated most extensive CFA recurrence).

Data collection protocol

A schematic timeline of the study phases is shown in Figure 1.

At T0, a questionnaire to evaluate eligibility was obtained from the owner. Alopecia was assessed qualitatively on both sides and photographed by the investigator. Additionally, a general physical and dermatological examination was performed. Two blood samples were drawn for haematological and serum biochemical investigation, including testing for total T4 serum concentration. Two biopsies were taken with a 6 mm disposable punch from the affected alopecic skin after subcutaneous injection with 2% lidocaine. All skin biopsies were fixed in 10% neutral buffered formalin, routinely processed and stained with haematoxylin and eosin. After processing, these were examined by a board-certified anatomical pathologist and histological

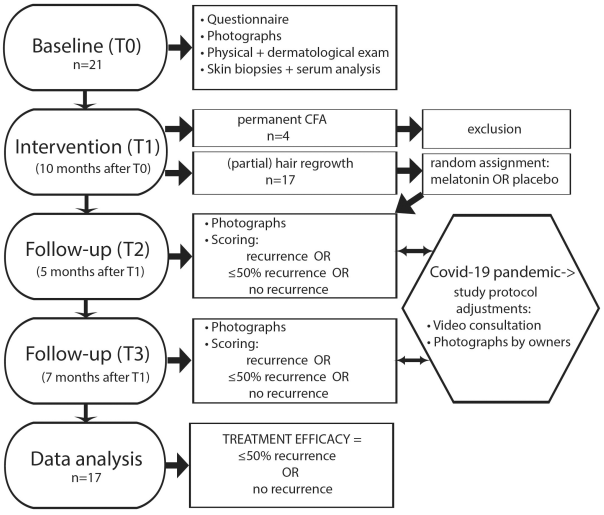

FIGURE 1 Schematic timeline of the study phases

changes were compared to the descriptions of CFA.[13,14] The blood tests were performed by a specialized laboratory (IDEXX BV; Hoofddorp, the Netherlands).

The diagnosis was confirmed when the history, clinical findings and histopathological evaluation were consistent with CFA, and the routine blood tests were normal.

At T1, after qualitatively assessing and photographing hair regrowth on both sides, dogs were randomly assigned to receive either placebo or melatonin by subcutaneous injection in the interscapular area, using an implanter gun.

At T2 and T3, CFA recurrence was photographed and assessed on both sides, using the predefined qualitative scores: complete recurrence, ≤50% recurrence or no recurrence, respectively. As the alopecic areas are not always sharply marginated, quantitative measurement in cm^2 of these areas is difficult. Consequently, we defined ≤50% recurrence as markedly smaller alopecic areas (both sides combined) when compared to the alopecia developing in previous years and this was considered an effective result. Therefore, the ≤50% recurrence and no recurrence were pooled together.

Between T2 and T3, the study protocol was affected by the COVID-19 pandemic regulations. The Dutch government measures prevented owners from visiting the clinic. To comply with these measures, we made appropriate study protocol adjustments: physical consultations were converted into video consultations, and photographs of the dogs' flanks were taken by the owners. We ensured both owner's and investigator's safety, and data integrity (Figure 1).

Study product

As no melatonin implants approved for use in dogs were available in the EU at the start of the study, we used 18 mg slow-release Melatonin implants (Melovine, CEVA Santé Animale; Libourne, France) authorized in Spain (1274 ES) for subcutaneous injection (SSRM), containing 18 mg melatonin and excipients: ethylcellulose, quinoline lacquer, vegetable fatty oils and dibutyl phthalate, and a Melovine implanter gun. Melatonin is released progressively from these implants over 3–4 months.[15] Melovine is approved for estrous induction in small ruminants. The 18 mg dosage was based on empirical dose recommendations for a US melatonin implant (Dermatonin, Melatek LLC; Prairie di Sac, WI, USA), data on the melatonin absorption and bioavailability are lacking used for the treatment of various alopecia disorders in dogs.[16]

Randomization and blinding

Randomization and blinding were performed by the veterinary pharmacy of Utrecht University, using blocked random allocation of clusters of five patients to prevent seasonal effects and ensure comparable group size. The commercial implants were packed per 25 in a strip. From this strip, 12 implants were removed for the placebo treatments by randomization. The strip then was placed in the implanter gun for administration and sealed with nontransparent tape. Both investigators and owners were blinded to group assignment. Group assignment was revealed to the investigators after collected data were analysed and interpreted.

Tolerance

We asked the owners to monitor and report possible adverse reactions during the study, to assess melatonin tolerance. We assessed and noted these adverse reactions at T2 and T3.

Statistical analysis

Treatment efficacy was defined as either ≤50% recurrence or no recurrence observed at T3. Thus, the ≤50% recurrence and no-recurrence groups were pooled together. The statistical analysis was performed by an independent statistician. With an alpha of 0.05, a desired power of 85%, a minimum of 10 dogs per group was required. The observed CFA recurrence scores in the treatment groups were tested against the null hypothesis that there is no difference in treatment efficacy scores between the SSRM group and placebo group, using Pearson's chi-square test. The *p*-value was the probability of the observed CFA recurrence under the null hypothesis; $p < 0.05$ was considered statistically significant. All calculations were performed with SPSS STATISTICS 25 for Windows (SPSS Benelux BV; Gorinchem, the Netherlands).

RESULTS

Between February 2019 and July 2019, 21 dogs were included (T0). The most represented breeds were Rhodesian ridgeback (29%) and Staffordshire bull terrier (19%). Other breeds were English bulldog, French bulldog, German shorthaired pointer, Wetterhoun,

old English bulldog, Bouvier des Flandres and mixed breeds.

All dogs presented with a bilaterally symmetrical flank alopecia. The areas of alopecia were not always identical. In 41% of the dogs, hyperpigmentation of the alopecic skin was noted and in only 29% of the dogs were the alopecic areas well-demarcated.

Histological interpretation of all skin biopsies demonstrated some degree of infundibular orthokeratotic hyperkeratosis. More specifically, a variable number of hair follicles revealed widened keratin-filled infundibulae with a foot-like configuration overlying deeper atrophic follicles, compatible with the description of CFA.[13] The distribution of the follicular stages was highly variable between dogs: in nine dogs, follicles were predominantly in the anagen stage (≤90% of follicles); in six dogs the hair follicles were between 5% and 30% anagen follicles; while in the other six dogs, follicles were exclusively in telogen or kenogen stage.

Between T0 and T1, four dogs had progressed into permanent CFA. These dogs (age range 4–9 years, weight 6–28 kg, number of previous CFA episodes ranged from three to nine) were excluded from the study at this time point because they no longer met the inclusion criteria.

At T1, 81% of the 21 dogs were included, of which 47% had experienced four or more previous consecutive CFA episodes, 18% had experienced three episodes, and 35% had experienced two episodes. Age, weight, breed, sex and the number of CFA episodes before the study are shown in Table 1.

CLINICAL ASSESSMENT

At T1, 53% (nine of 17) dogs were randomly assigned to receive placebo and 47% (eight of 17) dogs to receive melatonin (Table 1).

At T2, in the placebo-treated group, the percentages for recurrence, ≤50% recurrence and no recurrence were 33% (three of nine dogs), 0% (zero of nine) and 67% (six of nine dogs), respectively. In the melatonin-treated group, these percentages were 25% (two of eight dogs), 25% (two of eight dogs) and 50% (four of eight dogs), respectively.

At T3, in the placebo-treated group, these percentages were 44% (four of nine dogs), 0% (zero of nine dogs) and 56% (five of nine dogs), respectively. In the melatonin-treated group, these percentages were 25% (two of eight dogs), 50% (four of eight dogs) and 25% (two of eight dogs), respectively (Figure 2).

At T2 and T3, in all dogs in either the treated or placebo group with either recurrence or ≤50% recurrence, we observed that the alopecic areas were bilateral, symmetrical and not identical in size and shape. We also noted hyperpigmentation of the affected areas in

TABLE 1 Characteristics of dogs included in the study at onset (T1)

Variables	All dogs (*n* = 17)	Placebo group (*n* = 9)	Melatonin group (*n* = 8)
Age (years)			
Median	5	5	5
Mean	5.3	5.3	5.3
Range	2–9	2–9	2–9
Weight (kg)			
Median	34	30	39
Mean	32.9	29.7	36.5
Range	8–56	8–45	12–56
Breed			
Rhodesian ridgeback	6	3	3
Staffordshire bull terrier	4	1	3
English bulldog	1	1	0
French bulldog	2	1	1
Wetterhoun	1	1	0
Old English bulldog	1	0	1
Bouvier des Flandres	1	1	0
Mixed breed	1	1	0
Sex			
Male (Mc)	0 (8)	0 (5)	0 (3)
Female (Fs)	2 (7)	1 (3)	1 (4)
Number of previous CFA episodes			
Median	3	3	4
Mean	3.3	3	3.6
Range	2–5	2–5	2–5

Abbreviations: Mc, castrated male; Fs, spayed female.

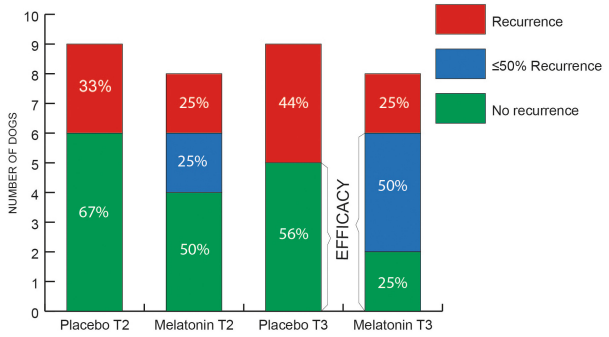

FIGURE 2 Number and percentage of dogs that showed recurrence, ≤50% recurrence and no recurrence, respectively, for the placebo-treated group compared to the melatonin-treated group at T2 and T3 in canine flank alopecia (CFA)-affected dogs included in the study.
Treatment efficacy indicated at T3.

33% of the placebo-treated group compared to 50% of the melatonin-treated group.

At T3, there were no statistically significant differences in the efficacy of treatment with melatonin as compared with the dogs which received placebo (Pearson's chi-square test, $p = 0.4$). The results at T2 and T3 are shown in Figure 2.

Tolerability

In 38% (three of eight) melatonin-treated dogs, we observed mild swelling at the injection site, which resolved spontaneously within 4 weeks post-treatment. No other adverse effects of either treatments were recorded.

DISCUSSION

To the best of our knowledge, this is the first double-blind, randomized, placebo-controlled study to evaluate the efficacy of an 18 mg SSRM implant in the prevention of CFA recurrence in dogs. Our findings did not support the efficacy of this treatment as compared to placebo in affected dogs when consideration was given to the recurrence of alopecia in <50% of affected skin or no recurrence of alopecia at all.

When comparing our results to those of previous studies, it should be noted that recent data on the efficacy of melatonin implants in the prevention of CFA recurrence are lacking. Paradis (1995) found in an open pilot study that subcutaneous melatonin implants or injections with melatonin in soybean oil were efficacious (alopecic areas were smaller and of shorter duration compared to previous years) in nine of nine dogs.[9] By contrast, we observed a lower efficacy rate (75%). Several possible explanations can be hypothesized for the discrepancy in findings. First, in the study by Paradis, higher melatonin doses were used (36 mg melatonin and 25 mg melatonin in six and three of nine dogs, respectively), while in the present study, 18 mg melatonin was used in all eight dogs. In neither study was the hormone administered on a mg/kg basis. Secondly, in the study by Paradis possible bias (both randomization and blinding were lacking) and low statistical power (small sample size) should be considered.

It is possible that some dogs could have developed hypothyroidism between T0 and T1. However, we considered this unlikely as none of the affected dogs had developed changes in hair quality or quantity in the nonaffected skin or other clinical signs consistent with hypothyroidism, and thus, blood tests were not repeated at T1.

We did not assess ease of epilation of the hair in this study because hairs in the affected areas may demonstrate either increased or normal epilation.[1] However, this technique may have been used as an adjunctive tool.

We assessed CFA recurrence at 5 and 7 months postintervention (T2 and T3, respectively). Previously, all dogs, with the exception of those which had developed permanent CFA, had complete hair regrowth within 8 months after CFA onset, and therefore, we felt it unnecessary to extend the monitoring period.

An unexpected challenge that we encountered during the ongoing study was the COVID-19 pandemic. The Dutch legislation during this period made direct clinical examinations impossible. Extraordinary measures and pragmatic adjustments to our study protocol were required to ensure the integrity of the study, accurate collection of clinical data and ensuring the safety of both owners and investigators. Accordingly, from February 2020 onwards, the CFA recurrence assessments were conducted via video consultations. The photographs, taken by the owners after this time point, were qualitatively comparable to those taken previously by the investigator.

Several limitations of this study merit consideration. First, at the start of our study, SSRM implants for canine use were not available in the EU. As a consequence of EU regulations, we were restricted to cascade-use of SSRM implants which were approved for estrous induction in small ruminants (Melovine; CEVA Santé Animale).[15] SSRM implants marketed for canine use (Dermatonin; Melatek LLC) containing 8, 12 or 18 mg, respectively, and excipient (polydimethylsiloxane) have a maximum effect after 3–4 months and are available only in the United States or online.[16] Because this product is categorized as a dietary supplement in the United States, it is not subject to strict regulation by the Food and Drug Administration, and data on the absorption and bioavailability of this product are not available. Secondly, the onset of CFA in individuals may vary each year,[1] rendering the timing of intervention (T1) debatable. Considering earlier studies that indicate that melatonin treatment should be started one or 2 months before the anticipated CFA onset,[3,8] we determined T1 based on the time of CFA onset in the previous year. Consequently, our chosen moment of intervention can be considered as justified. Thirdly, the probability of CFA recurrence without treatment is 60%–70%,[4] rendering the assessment of preventative treatment efficacy difficult.

Although limitations must be considered, the contributions of this study to existing knowledge are noteworthy. First, it is known that CFA may be more extensive

each year and can eventually develop into permanent CFA.[1,4] In our study, 19% (four of 21) dogs had developed permanent CFA after the start of the study. These four dogs were older than 4 years of age and had experienced three or more consecutive CFA episodes. These results support findings reported in earlier studies that after several episodes of CFA, the probability of affected dogs developing permanent alopecia will increase. We hypothesize that SSRM treatment could be effective in relatively young (i.e. <4-year-old) dogs before CFA is permanent. Secondly, numerically, the ≤50% recurrence and no recurrence combined were greater in the melatonin group compared to the placebo group when measured at 5 and 7 months after the intervention. Although not statistically significant, these results are promising.

Finally, we did not administer melatonin on a mg/kg basis. However, we did not find higher efficacy rates in the smaller dogs (weight < 20 kg) compared to the larger ones (weight > 30 kg). By contrast, Paradis (2009) suggested that a high dosage of melatonin might be needed to prevent CFA recurrence if modulation of reproductive-hormone secretion is required.[3] In mink, 120 mg implants had a superior effect on early hair growth when compared with 10 mg implants. Therefore, it would be of interest to evaluate preventative CFA treatment efficacy of SSRM implants with optimal dosage regimens based on body weight.

In conclusion, this double-blind, randomized, placebo-controlled study did not provide evidence that the 18 mg SSRM implant treatment is efficacious in preventing CFA recurrence in dogs. The product was safe and well-tolerated. Future studies with larger sample sizes are needed to evaluate both optimal dosage and the preventative effect of licensed SSRM implants in young affected dogs before CFA development is permanent.

AUTHOR CONTRIBUTIONS

Millie Verschuuren: Conceptualization; funding acquisition; investigation; methodology; project administration; writing – original draft. **Yvette M Schlotter:** Conceptualization; supervision; validation; writing – review and editing. **Inge van Geijlswijk:** Supervision; validation; writing – review and editing. **Jaco van der Lugt:** Investigation. **Ronette Gehring:** Supervision; validation; writing – review and editing.

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CONFLICT OF INTEREST

None declared.

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Résumé

Contexte: L'alopécie récidivante des flancs du chien (AFC) est caractérisée par une alopécie non inflammatoire récurrente de façon saisonnière, parfois hyperpigmentée, principalement dans la région thoraco-lombaire. De précédentes études suggèrent qu'une production réduite de mélatonine endogène peut jouer un rôle dans la pathogénie de cette affection, et des études contrôlées par placebo sur l'efficacité du traitement préventif à la mélatonine font défaut.

Objectif: Évaluer l'efficacité des implants sous-cutanés de mélatonine à libération lente dans la prévention de la récidive de l'AFC.

Animaux: Vingt et un chiens appartenant à des clients ayant des antécédents d'AFC ont été inclus dans l'étude.

Matériels et méthodes: A T0, un examen physique et dermatologique général a été effectué sur chaque chien, du sang a été prélevé pour une analyse biochimique du sérum et deux biopsies cutanées ont été prélevées dans les zones alopéciques sur les chiens affectés non sédatifs après injection sous-cutanée de 2 % lidocaïne. Des chiens avec un bilan sanguin normal et des résultats histologiques compatibles avec l'AFC ont été inclus dans l'étude. Les chiens participants ont été répartis au hasard pour recevoir soit un placebo, soit 18 mg de mélatonine par voie sous-cutanée dans la zone interscapulaire, environ deux mois avant le début prévu de l'AFC (T1). La récidive de l'AFC a été notée qualitativement comme complète, ≤50 % de récidive ou aucune récidive à cinq et sept mois après l'intervention (T2 et T3, respectivement).

Résultats: A T3, chez les chiens traités par placebo (neuf sur 17), les pourcentages de récidive complète, de récidive ≤50 % et d'absence de récidive étaient respectivement de 44 %, 0 % et 56 %. Chez les chiens traités à la mélatonine (huit sur 17), ces pourcentages étaient respectivement de 25 %, 50 % et 25 %. Il n'y avait pas de différences statistiquement significatives dans les scores entre les chiens traités à la mélatonine et les chiens traités au placebo (*p = 0,40*). Chez trois des huit chiens traités à la mélatonine, un léger gonflement transitoire a été observé au site d'injection.

Conclusions: Cette étude n'a pas fourni de preuve qu'un traitement par implant de mélatonine à 18 mg, bien que bien toléré, soit efficace pour prévenir la récidive de l'AFC chez les chiens affectés.

Resumen

Introducción: La alopecia canina de los flanco (CFA, por sus siglas en inglés) se caracteriza por una alopecia estacionalmente recurrente no inflamatoria, ocasionalmente hiperpigmentada, predominantemente en el área toracolumbar. Estudios previos sugieren que la producción reducida de melatonina endógena puede desempeñar un papel en la patogenia de esta afección, y faltan estudios controlados con placebo sobre la eficacia del tratamiento preventivo con melatonina.

Objetivo: evaluar la eficacia de los implantes subcutáneos de melatonina de liberación lenta en la prevención de la recurrencia de la CFA.

Animales: se incluyeron en el estudio veintiún perros de propietarios particulares con antecedentes de CFA.

Materiales y Métodos: En el tiempo (T)0, se realizó un examen físico y dermatológico general a cada perro, se recolectó sangre para análisis de bioquímica sérica y se tomaron dos biopsias de piel de áreas alopécicas en los perros afectados no sedados después de la inyección subcutánea con 2% lidocaína. Se incluyeron en el estudio perros con análisis de sangre normales y resultados histológicos compatibles con CFA. Los perros participantes fueron asignados al azar para recibir placebo o 18 mg de melatonina por vía subcutánea en el área interescapular, aproximadamente dos meses antes del inicio esperado de la CFA (T1). La recurrencia de CFA se calificó cualitativamente como recurrencia completa, ≤50 % o sin recurrencia a los cinco y siete meses después de la intervención (T2 y T3, respectivamente).

Resultados: En T3, en perros tratados con placebo (nueve de 17), los porcentajes de recurrencia completa, ≤50 % de recurrencia y sin recurrencia fueron 44 %, 0 % y 56 %, respectivamente. En perros tratados con melatonina (ocho de 17), estos porcentajes fueron del 25%, 50% y 25%, respectivamente. No hubo diferencias estadísticamente significativas en las puntuaciones entre los perros tratados con melatonina y los perros tratados con placebo ($p = 0{,}40$). En tres de los ocho perros tratados con melatonina, se observó una leve hinchazón transitoria en el lugar de la inyección.

Conclusiones: este estudio no proporcionó evidencia de que un tratamiento con implantes de melatonina de 18 mg, aunque bien tolerado, sea eficaz para prevenir la recurrencia de la CFA en los perros afectados.

Zusammenfassung

Hintergrund: Die Flankenalopezie des Hundes (CFA) ist durch eine saisonal wiederkehrende nicht entzündliche, gelegentlich hyperpigmentierte Alopezie charakterisiert, die hauptsächlich in der Thorakolumbalgegend auftritt. Frühere Studien haben gezeigt, dass eine reduzierte Produktion von endogenem Melatonin eine Rolle bei der Pathogenese dieser Veränderung spielen könnte; wobei Plazebo-kontrollierte Studien über die Wirksamkeit präventativer Melatoninbehandlung fehlen.

Ziel: Eine Evaluierung der Wirksamkeit von subkutanen Slow-release Melatonin Implantaten bei der Verhinderung eines Wiederauftretens der CFA.

Tiere: Einundzwanzig Hunde in Privatbesitz mit der Anamnese einer CFA wurden in die Studie aufgenommen.

Materialien und Methoden: Zum Zeitpunkt (T) 0 wurde eine Allgemein- sowie eine dermatologische Untersuchung bei jedem Hund durchgeführt, es wurden Blut für eine Serumbiochemieanalyse und zwei Hautbiopsien von den haarlosen Stellen entnommen, nachdem den nicht sedierten Hunden mit Hautveränderungen eine subkutane Injektion von 2% Lidocain verabreicht worden war. Hunde mit normalen Blutuntersuchungsergebnissen und histologischen Befunden, die mit einer CFA vereinbar waren, wurden in die Studie aufgenommen. Teilnehmende Hunde wurden zufällig eingeteilt, um entweder Placebo oder 18 mg Melatonin subkutan in der interskapulären Gegend, ungefähr zwei Monate vor dem erwarteten Beginn der CFA (T1) subkutan verabreicht zu bekommen. Ein Wiederauftreten der CFA wurde qualitativ als vollständig, ≤50% Häufigkeit des Wiederauftretens, oder kein Wiederauftreten fünf bzw. sieben Monate nach der Behandlung (T2 bzw. T3) bewertet.

Ergebnisse: Zum T3 lagen die Prozentwerte für ein totales Wiederauftreten, für ein ≤50% iges Wiederauftreten und kein Wiederauftreten bei den Hunden, die mit Plazebo behandelt worden waren (neun von 17), bei 44%, 0% bzw. 56%. Bei Hunden, die mit Melatonin behandelt worden waren (acht von 17), lagen diese Prozentsätze bei 25%, 50% bzw. 25%. Es bestanden keine statistisch signifikanten Unterschiede bei der Auswertung zwischen den Melatonin-behandelten Hunden und jenen, die mit Plazebo behandelt worden waren ($p = 0{,}40$). Bei drei der acht mit Melatonin behandelten Hunde wurde eine milde vorübergehende Schwellung an der Injektionsstelle beobachtet.

Schlussfolgerungen: Diese Studie erbrachte keine Evidenz, dass 18 mg Melatonin Implantate, obwohl sie gut toleriert wurden, das Wiederauftreten einer CFA bei betroffenen Hunden verhindern konnten.

要約

背景: 犬の側腹部脱毛症(CFA)は、主に胸腰部に季節的に繰り返す非炎症性、時に色素沈着性の脱毛症が特徴である。これまでの研究で、内因性メラトニンの産生低下が本疾患の病因に関与している可能性が示唆されているが、メラトニンによる予防的治療の有効性に関するプラセボ対照試験は行われていない。

目的: 本研究の目的は、 CFA の再発予防におけるメラトニン徐放性皮下インプラントの有効性を評価することであった。

対象動物: CFA の既往のあるオーナー所有犬 21 頭を本研究に組み入れた。

材料と方法:　研究初日(T0)に、各犬に対して一般的な身体検査と皮膚科学的検査を行い、血清生化学分析のために採血し、2%リドカインを皮下注射した後、非沈静下の患犬脱毛部から2ヶ所の皮膚生検を行った。血液検査が正常で、組織学的な結果がCFAに適合する犬が研究に参加した。参加した犬は、CFA発症予定日の約2か月前に、プラセボまたは18mgのメラトニンを肩甲骨間部に皮下投与する群に無作為に振り分けられた(T1)。CFAの再発は、介入後5ヶ月および7ヶ月(それぞれT2およびT3)において、完全、50%以下の再発、または再発なしとして定性的にスコア化された。

結果:　T3において、プラセボ投与犬(17頭中9頭)では、完全再発、50%以下の再発、無再発の割合は、それぞれ44%、0%、56%であった。メラトニン治療犬(17頭中8頭)では、これらの割合はそれぞれ25%、50%、25%であった。メラトニンを投与した犬とプラセボを投与した犬の間には、スコアに統計的に有意な差はなかった($p = 0.40$)。メラトニン投与犬8頭中3頭で、注射部位に軽度の一過性の腫脹が観察された。

結論: 本研究は、18mgのメラトニンインプラント治療が、患犬のCFA再発防止に有効であることを示す証拠とはならなかった。

摘要

背景: 犬侧腹脱毛症 (CFA) 的特征为季节性复发的非炎性、偶见色素沉着的脱毛症 , 主要发生在胸腰区。以往的研究认为 , 内源性褪黑素的产生减少可能在这种情况的发病机制中起作用 , 缺乏预防性褪黑素治疗疗效的安慰剂对照研究。

目的: 评价皮下缓释褪黑素植入剂预防 CFA 复发的疗效。
动物: 本研究纳入了21只具有 CFA 病史的私家犬。
材料和方法: 在时间 (T)0 时,对每只犬进行全身体格检查和皮肤病学检查,采集血液进行血清生化分析,并在局部皮下注射2%利多卡因后,从未镇静患犬的脱毛区域采集两份皮肤活检组织。血液检查正常且组织学结果符合 CFA 的犬,被纳入研究。参与研究的犬被随机分配在预期 CFA 发作前约2个月 (T1) 在肩胛间区皮下接受安慰剂或 18 mg 褪黑素。CFA 复发定性评分为完全复发、≤50%复发或干预后5个月和7个月无复发(分别为 T2 和T3)。
结果: 在 T3 时,在接受安慰剂治疗的犬中(17只中的9只),完全复发、≤50%复发和无复发的百分比分别为44%、0%和56%。在接受褪黑素治疗的犬中 (8/17),这些百分比分别为25%、50%和25%。褪黑激素治疗犬和安慰剂治疗犬之间的评分无统计学显著差异 (p = 0.40)。在3/8只褪黑激素处理的犬中,在注射部位观察到一过性轻度肿胀。
结论: 本研究未能证明 18 mg 褪黑素植入有效,尽管耐受性良好。

Resumo

Contexto: A alopecia sazonal do flanco (ASF) é uma doença caracterizada por alopecia sazonal recorrente, não inflamatória e ocasionalmente hiperpigmentada que ocorre predominantemente na região toracolombar. Estudos anteriores sugerem que uma redução na produção de melatonina pode participar na patogênese desta condição, e são escassos os estudos placebo-controle sobre a eficácia do tratamento preventivo com melatonina.

Objetivo: Avaliar a eficácia de implantes de melatonina de liberação lenta na prevenção da recorrência de ASF.

Animais: Vinte e um cães de clientes com histórico de ASF foram incluídos no estudo.

Materiais e métodos: No tempo (T)0, realizou-se uma avaliação física geral e dermatológica de cada animal, coletou-se sangue para análise bioquímica sérica e duas biópsias cutâneas foram coletadas das áreas alopécicas nos cães afetados, sem sedação, após injeção subcutânea de lidocaína 2%. Cães com exames de sangue normais e resultados histológicos compatíveis com ASF foram inclusos no estudo. Os cães participantes foram divididos aleatoriamente para receber placebo ou 18mg de melatonina, por via subcutânea, na região interescapular, aproximadamente dois meses antes do ínicio esperado do quadro de ASF (T1). A recorrência de ASF foi classificada qualitativamente como completa, ≤50% de recorrência, ou nenhuma recorrência em cinco e sete meses após a intervenção (T2 e T3, respectivamente).

Resultados: No T3, os cães tratados com placebo (nove de 17), as porcentagens de recorrência completa, ≤50% de recorrência e nenhuma recorrência foram 44%, 0% e 56%, respectivamente. Não houve diferenças estatísticas nos escores entre cães tratados com melatonina e cães tratados com placebo ($p = 0.40$). Em três de oito cães tratados, observou-se um aumento de volume discreto transitório no local da injeção.

Conclusões: Este estudo não demonstrou evidências de que o tratamento com melatonina, apesar de bem tolerado, é eficaz na prevenção da recorrência de ASF em cães afetados.