

Sensitivity and specificity of a shortened elimination diet protocol for the diagnosis of food-induced atopic dermatitis (FIAD)

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Background – The gold standard to diagnose food allergy in dogs is an eight week elimination diet trial (EDT) followed by a re-challenge. A recent study demonstrated that a shorter EDT is possible if prednisolone is administered initially.

Hypothesis/Objectives – The goal was to evaluate the sensitivity and specificity of the EDT based on the number of relapses after prednisolone discontinuation. In addition, the aim was to determine whether the initial treatment length or the replacement of prednisolone with oclacitinib would influence the outcome.

Animals – Eighty-seven dogs with atopic dermatitis.

Methods and materials – Dogs were fed an elimination diet and treated with either prednisolone or oclacitinib for two to three weeks. Relapsing dogs were treated a second time. In the absence of a relapse after two weeks off medication, dogs then were challenged. Dogs never achieving two weeks off treatment without relapse received the regular EDT.

Results – Fifty-eight of 87 dogs completed the study. Thirty-nine of 58 dogs received prednisolone; 21 of these were diagnosed with FIAD and had no relapse ($n = 14$), one relapse ($n = 6$) or two relapses ($n = 1$). Nineteen of 58 dogs received oclacitinib; 11 of these were deemed food-allergic and had no relapse ($n = 7$) or two relapses ($n = 4$). The initial treatment duration did not influence the outcome. The threshold of one relapse or less for the diagnosis of FIAD was associated with a sensitivity of 95% for prednisolone and 63% for oclacitinib. The specificity was 100% for both drugs.

Conclusion and clinical importance – Initial prednisolone or oclacitinib use in EDT shortens the time to diagnosis of FIAD.

Introduction

Cutaneous adverse food reactions (CAFRs) are a common cause of skin disease in dogs, and the pathogenesis can involve nonimmunological (i.e. food intolerance) and immunological (i.e. food allergy) processes. The prevalence of canine food allergy varies depending on the studies and specific variables measured.¹ A recent study showed that among all dogs presented to a veterinarian, the prevalence was 1–2% and among those with skin diseases it was $\leq 24\%$. In dogs diagnosed with atopic dermatitis (AD), food-induced atopic dermatitis (FIAD) prevalence was $\leq 50\%$ (9–50%).²

In human medicine, the double-blinded, placebo-controlled food challenge (DBPCFC) represents the current gold standard and the only way to establish or rule out an adverse reaction to a food.^{3,4} Unfortunately, double-blinded, placebo-controlled tests are not feasible in

veterinary medicine as single-food extracts are not commercially available. Therefore, an elimination diet trial (EDT) remains the gold standard for the diagnosis of FIAD in dogs, and to date there are no specific serological or intracutaneous tests for the diagnosis available.⁵

The diagnosis of FIAD is based on the improvement of skin lesions and pruritus during the restrictive phase and a relapse of clinical signs after a challenge with the original diet.² The success of an EDT depends, therefore, on the owner's compliance and their ability to identify a recurrence of the clinical signs.⁶ The interpretation of EDTs can be affected by several factors leading to false-positive or false-negative test results.⁷ The duration of an EDT often varies yet an evidence-based review showed that at least an eight week EDT is needed to diagnose FIAD in $>90\%$ of dogs.⁶ A recent study demonstrated that a shorter EDT is possible if the initial allergic pruritus and inflammation are controlled with a short course of glucocorticoids.⁷ The authors proposed that the shortened trial is likely to improve owner compliance and facilitate the diagnosis of food allergy.

The goal of the present study was to assess the sensitivity and specificity of the newly published shortened protocol for the diagnosis of FIAD in dogs relapsing less

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than two times after the initial treatment. Additionally, we wanted to assess whether the length of the initial anti-inflammatory treatment (prednisolone or oclacitinib) influenced the diagnostic outcome of this protocol.

Methods and materials

Dogs with AD were included in the study. The diagnosis of AD was made based on generally accepted criteria, namely exclusion of resembling diseases such as ectoparasite infestation, bacterial and yeast infections and fulfilment of at least five of eight criteria.^{8,9} All dogs were put on EDT based on the recently published protocol with slight adaptations.⁷ Briefly, all dogs received a diet developed for the diagnosis of food allergy (the dry, hydrolysed diet Anallergenic, Royal Canin; Aimargues, France; or the canned single kangaroo protein diet, Dog Sana Kangaroo, Vet-Concept; Föhren, Germany) and were divided into two groups. Dogs in Group A received either two or three weeks of prednisolone (Prednisolone, Streuli Pharma AG; Uznach, Switzerland; dosage: 1 mg/kg for three days, reduction to 0.5 mg/kg for five or 10 days and further reduction to 0.5 mg/kg every other day for six or eight days). These two different prednisolone treatment durations were meant to test whether one protocol is associated with less relapse in dogs subsequently diagnosed as food-allergic dogs.

Group B consisted of a smaller number of dogs. In this group prednisolone was replaced by oclacitinib. The dosage of oclacitinib (Apoquel, Zoetis; Delémont, Switzerland) was 0.4–0.6 mg/kg twice daily for two weeks, followed by 0.4–0.6 mg/kg once daily for another week.

Other systemic treatments were not allowed. Topicals were allowed if the treatment was started before enrollment and continued without any changes during the study period.

After this initial treatment, based on the results of a recent study,⁷ it was expected that the pruritus would be controlled [Hill's pruritus Visual Analog Scale (pVAS) <2.5],¹⁰ and that the prednisolone or oclacitinib treatment could be discontinued. The owners then monitored the pruritus and were instructed to inform the investigators of any deterioration in the dogs' pruritus and/or condition. This deterioration was assessed by the descriptor "The disease of my dog is not at all controlled. The quality of life of my dog is impaired. It is necessary to change the treatment and/or to visit the doctor" already used in the previous study.⁷ This was because one of the goals of the study was to test the performance of this EDT protocol under practice conditions. A descriptor was considered more user-friendly than a numerical assessment such as pVAS. Dogs not relapsing during two drug-free weeks were challenged with the regular food.

A second course of prednisolone or oclacitinib was administered to dogs experiencing a worsening of the pruritus after cessation of the medications (0.5 mg/kg prednisolone once daily for dogs in Group A and 0.4–0.6 mg/kg oclacitinib once daily for dogs in Group B for one more week). These dogs were challenged with the former food two weeks after cessation of the medication (so four to six weeks after beginning the EDT), if they did not relapse during that time. In all others a standard eight week EDT was completed.

A final diagnosis of FIAD was confirmed in dogs that were improved with two drug-free weeks and that relapsed after the reintroduction of the regular food. The improvement was either after four to five weeks (if no deterioration was seen after the first drug discontinuation), or after six to seven weeks (in dogs relapsing during the first drug-free period). In dogs that did not improve after completion of an eight week elimination diet, FIAD was considered to be ruled out. Figure 1 presents a summary of the study protocol.

Analyses and statistics

The first goal was to assess whether the length of the initial prednisolone treatment influences the number of relapses in dogs subsequently diagnosed as FIAD dogs. A Fisher's exact test was used to achieve this. To determine the sensitivity, specificity, positive and negative predictive values, our hypothesis was that dogs with FIAD

should have no or only one relapse after the initial treatment. Prednisolone and oclacitinib were analysed separately to assess if either was associated with a better outcome.

Results

Of 87 dogs initially included in the study, 58 followed the protocol and ultimately completed the study. For details on the reasons for the 29 drop-outs and final outcome, see Figure 2. Twenty-one female dogs (14 of 21 spayed) and 37 male dogs (17 of 37 castrated) were included. Ages ranged from 1- to 13-year-old, with a median age of 4 years. French bulldogs were over-represented ($n = 13$).

Thirty-nine of 58 dogs received prednisolone, 15 for two weeks initially and 24 for three weeks. Nineteen of 58 dogs received oclacitinib for three weeks. Fifty-two of 58 dogs received the hydrolysed diet (Anallergenic, Royal Canin), while the rest (six dogs) received the canned single kangaroo protein diet (Dog Sana Kangaroo, Vet-Concept).

Group A: prednisolone-treated dogs

A final diagnosis of FIAD was made in 21 dogs; 14 of these did not deteriorate after cessation of prednisolone, six dogs relapsed once and one dog relapsed twice. In nine of 14 dogs that did not relapse after discontinuation of prednisolone, food challenge then was performed after another two medication-free weeks. This meant that the duration of EDT could be limited to four to five weeks (depending on how long prednisolone was administered initially). In the remaining five of 14 dogs, the owners decided to challenge later ($\text{EDT} \leq 12$ weeks) and none of these dogs showed a relapse under EDT until provocation with the old food was begun.

In the seven dogs that relapsed once or twice, the challenge was performed immediately after the two weeks off prednisolone in four dogs, whereas three dogs were challenged after three weeks off medication. Fisher's exact test was applied to determine whether the initial duration of the prednisolone treatment influenced the number of relapses, and $P = 0.74$ suggested that the duration does not markedly influence the outcome.

A threshold was set at a maximum of one relapse for the exclusion of the diagnosis of FIAD. In the FIAD group only one of 21 dogs experienced more than one relapses and the sensitivity was consequently 95%. However, a diagnosis of FIAD was ruled out in 18 dogs, all of which relapsed more than once. The specificity for the diagnosis of FIAD was consequently 100%. The positive predictive value of the diagnostic tool "up to one relapse" was 100%, while the negative predictive value was 95%.

Group B: oclacitinib-treated dogs

In this group, the diagnosis of FIAD was made in 11 of 19 dogs; of these seven were without any relapse and four had two relapses. Only three of seven dogs were challenged after two medication-free weeks and EDT was therefore reduced to five weeks' duration; the other four dogs, which did not relapse after cessation of oclacitinib, were kept on the diet longer without any relapse.

Food allergy was ruled out in eight dogs, three with two relapses, another three with three relapses and two

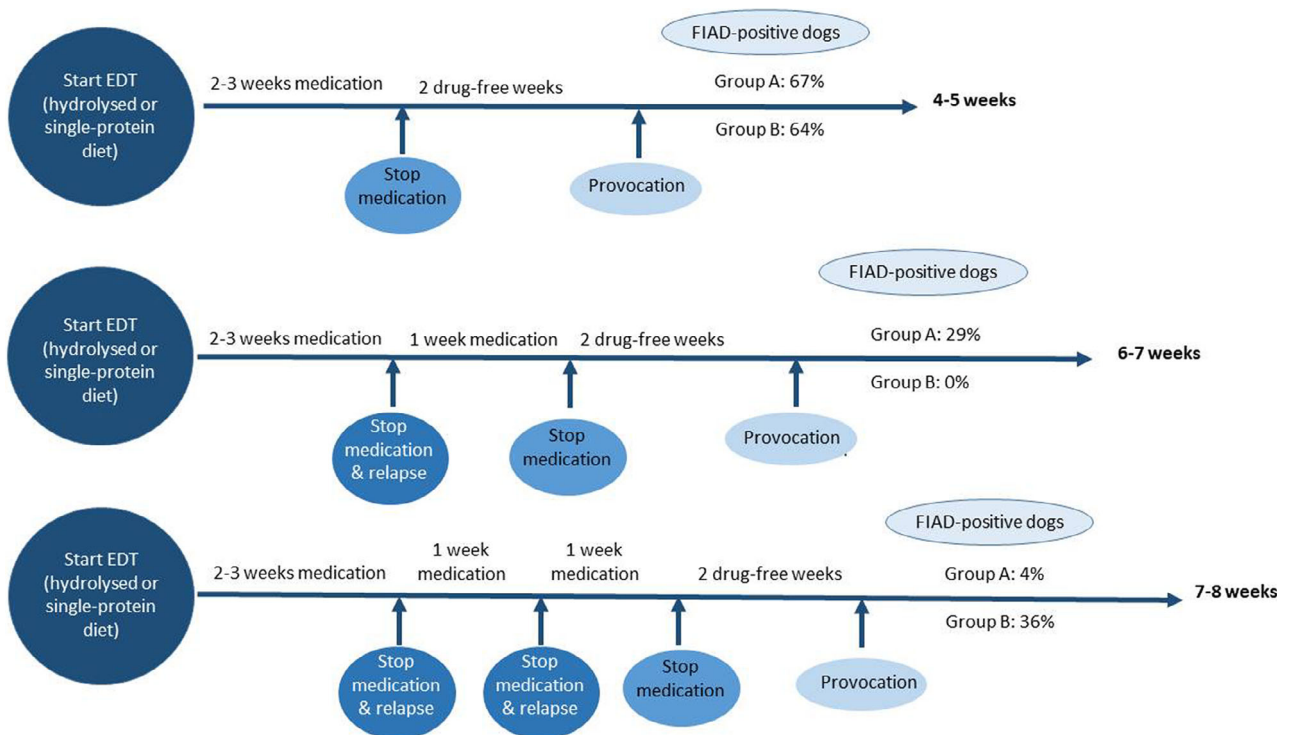


Figure 1. Overview of the protocol.

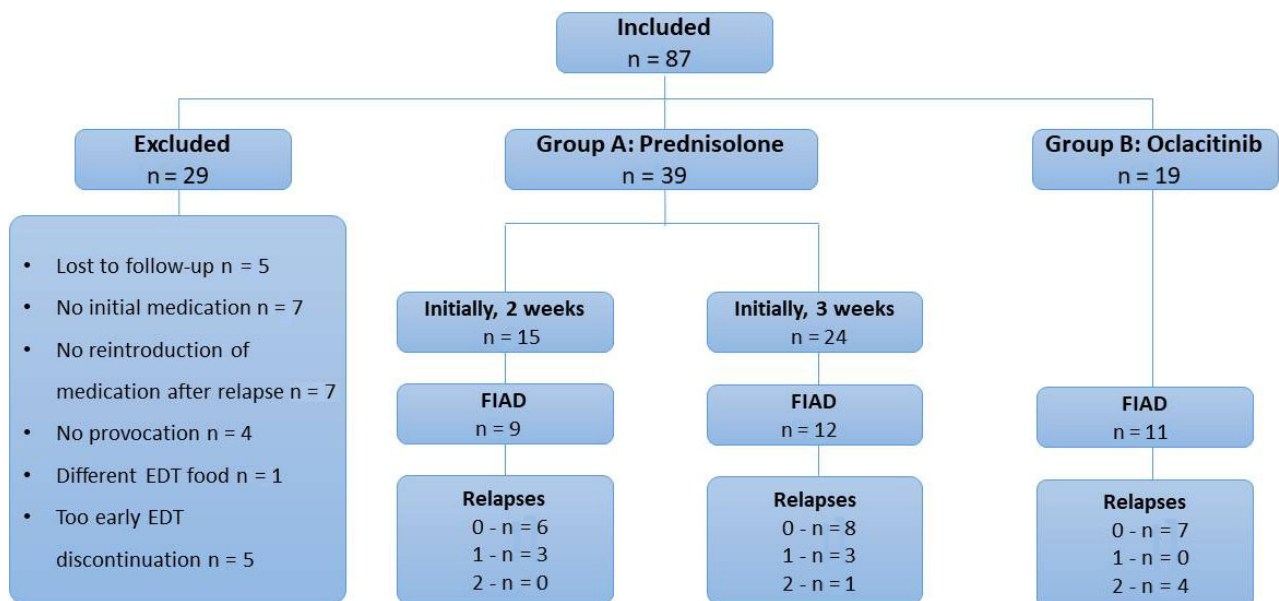


Figure 2. Main results and final diagnoses.

with four relapses. When applying the threshold used above for oclacitinib, the sensitivity was 63% and the specificity 100%; the positive predictive value was 63% while the negative predictive value was 100%.

Discussion

For decades, the recommended duration of an EDT was set from eight up to ten weeks.⁶ One explanation for the need of such a long period was a self-perpetuating inflammatory process, which had to be overcome by long-term

elimination of allergen exposure.⁶ A recent study showed that EDT duration could be successfully reduced by adding a short course of prednisolone in the initial EDT phase to switch off as many inflammatory pathways as possible, as soon as possible.⁷

The main goal of this study was to determine the sensitivity and specificity of this newly published shortened protocol for the diagnosis of FIAD in dogs relapsing one time or less during EDT. Based on the results, one can suggest that dogs relapsing more than twice are very unlikely to have food allergy. We assessed a positive

predictive value of the diagnostic tool “one or less than one relapse” of 100% while the negative predictive value was 95%.

Therefore, we confirmed the results of Favrot *et al.*, and showed that this EDT protocol can markedly reduce the duration of EDT in most allergic dogs. In most of the dogs with FIAD, provocation was started after four weeks and a diagnosis could be made within six weeks. Unfortunately, not all FIAD dogs that did not deteriorate after cessation of medication were challenged by the owners immediately after two medication-free weeks; however, in nine dogs this was successfully done and therefore EDT duration could be significantly reduced to only four to five weeks. This short EDT duration also markedly improves owner’s compliance.

The two other questions were whether the medication type and duration of therapy given in the beginning of EDT influences the outcomes. First, dogs were treated with either prednisolone for two or three weeks, or oclacitinib for three weeks. The positive predictive value of the diagnostic tool “one or less than one relapse” to diagnose FIAD was 100% in all groups and the negative predictive value was 95% when using prednisolone, compared to 63% positive and 100% negative predictive values when using oclacitinib. Therefore, as already discussed herein and expected by Favrot *et al.*,^{7,11} prednisolone seems to be the better option for most dogs, probably as a consequence of the more rapid and broader anti-inflammatory effects of glucocorticoids.⁷

Second, we wanted to assess the influence of the initial treatment duration. In their study, Favrot *et al.* mentioned that some dogs got a rapid relapse and pronounced cutaneous inflammation after cessation of prednisolone and asked whether a longer initial treatment (up to four weeks) would permit a better and faster diagnosis of FIAD. In our study, there was no statistical difference in the number of relapses between the two different schedules of prednisolone for two or three weeks, respectively, and therefore we conclude that this duration can be adapted to the severity and needs of each single patient.

By contrast with Favrot *et al.*, dogs receiving the kangaroo-based diet (Dog Sana Kangaroo, Vet-Concept) also were included. Six dogs received this single protein canned diet and 52 dogs received a commercial dry hydrolysed diet (Anallergenic, Royal Canin). The small number of dogs receiving the canned food precluded any meaningful statistical interpretation. As shown previously, the hydrolysed diet worked very well and was well-tolerated.¹² We did not observe any adverse effects with the canned ED which also was well-tolerated by all dogs.

The goal of this study was not to evaluate the prevalence of FIAD, and instead to assess the sensitivity and specificity of a proposed shortened EDT protocol of a recently released study and to test it in daily practice.⁷ In our study the proposed protocol was adapted with regard to type and duration of medication by adding oclacitinib and a canned food diet to better meet the owner’s wishes. In dogs relapsing twice, FIAD can be ruled out, providing that the protocols were followed correctly.

These protocols could be useful in daily practice and reduce EDT duration.

Conclusions

This protocol is able to shorten the duration of EDT with a high specificity, when used in conjunction with an initial treatment of prednisolone and oclacitinib. The sensitivity of the protocol is higher for prednisolone. The study protocol was designed in such a way that it can be very easily used in daily practice; nevertheless, the use of a more objective scoring system (such as Canine Atopic Dermatitis Extent and Severity Index or pVAS) to grade the outcome would have enhanced the significance of the study.

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RÉSUMÉ

Contexte – Le gold standard du diagnostic de l'allergie alimentaire du chien est un régime d'éviction de huit semaines (EDT) suivi d'un test de provocation. Une étude récente a montré qu'un EDT plus court est possible si la prednisolone est administrée initialement.

Hypothèses/Objectifs – Le but est d'évaluer la sensibilité et la spécificité de l'EDT basé sur le nombre de récurrences après l'arrêt de la prednisolone. En outre, l'objectif était de déterminer si la longueur du traitement initial ou le remplacement de la prednisolone par l'ocacitinib pourrait influencer l'issue.

Sujets – Quatre vingt sept chiens avec dermatite atopique.

Matériels et méthodes – Les chiens ont été nourris par un régime d'éviction et traités soit avec de la prednisolone ou de l'ocacitinib pendant deux à trois semaines. Les chiens récidivants ont été traités une deuxième fois. En l'absence de récurrence après deux semaines sans traitement, les chiens étaient provoqués. Les chiens n'ayant jamais atteints deux semaines sans traitement sans rechute ont reçu l'EDT classique.

Résultats – Cinquante-huit des 87 chiens ont complété l'étude. Trente-neuf des 58 chiens ont reçu de la prednisolone ; 21 d'entre eux ont été diagnostiqués avec FIAD et n'ont pas eu de récurrence (n=14), une récurrence (n=6) ou deux récurrences (n = 1). Dix neuf des 58 chiens ont reçu de l'ocacitinib ; 11 ont été considérés allergiques alimentaires et n'ont pas récidivés (n=7) ou deux récurrences (n = 4). La durée du traitement initial n'a pas influencé l'issue. La survenue d'une récurrence ou moins pour le diagnostic de FIAD a été associé à une sensibilité de 95% pour la prednisolone et 63% pour l'ocacitinib. La spécificité était de 100% pour les deux traitements.

Conclusion – La prednisolone et l'ocacitinib, utilisées en initiation des EDT, raccourcissent la durée du diagnostic de FIAD.

RESUMEN

Introducción – el estándar de referencia para diagnosticar la alergia alimentaria en perros es una prueba de dieta de eliminación (EDT) de ocho semanas seguida de una nueva exposición. Un estudio reciente demostró que es posible una EDT más corta si se administra prednisolona inicialmente.

Hipótesis/Objetivos – el objetivo era evaluar la sensibilidad y la especificidad de EDT según el número de recaídas después de la suspensión de la prednisolona. Además, el objetivo era determinar si la duración del tratamiento inicial o el reemplazo de prednisolona por oclacitinib influirían en el resultado.

Animales – ochenta y siete perros con dermatitis atópica.

Métodos y materiales – los perros fueron alimentados con una dieta de eliminación y tratados con prednisolona u oclacitinib durante dos o tres semanas. Los perros que recayeron fueron tratados por segunda vez. En ausencia de una recaída después de dos semanas sin medicación, los perros fueron expuestos nuevamente. Los perros que nunca lograron estar sin recaída tras dos semanas sin tratamiento recibieron la EDT regular.

Resultados – Cincuenta y ocho de 87 perros completaron el estudio. Treinta y nueve de 58 perros recibieron prednisolona; 21 de ellos fueron diagnosticados con reacción adversa a alimentos (FIAD) y no tuvieron recaídas (n = 14), una recaída (n = 6) o dos recaídas (n = 1). Diecinueve de 58 perros recibieron oclacitinib; 11 de estos fueron considerados alérgicos a los alimentos y no tuvieron recaídas (n = 7) o dos recaídas (n = 4). La duración del tratamiento inicial no influyó en el resultado. El umbral de una recaída o menos para el diagnóstico de FIAD se asoció con una sensibilidad del 95% para prednisolona y del 63% para oclacitinib. La especificidad fue del 100% para ambos fármacos.

Conclusión e importancia clínica – el uso inicial de oclacitinib o prednisolona en EDT acorta el tiempo para el diagnóstico de FIAD.

Zusammenfassung

Hintergrund – Der Goldstandard, um eine Futtermittelallergie bei Hunden zu diagnostizieren, besteht in der Durchführung einer acht-wöchigen Eliminationsdiät (EDT) gefolgt von einer Provokation. Eine jüngste Studie demonstrierte die Möglichkeit einer kürzeren EDT, wenn zu Beginn Prednisolon verabreicht wird.

Hypothese/Ziele – Das Ziel war eine Evaluierung der Sensibilität und der Spezifität der EDT basierend auf der Anzahl der Rezidive nach Ende der Prednisolon Verabreichung. Zusätzlich war es das Ziel herauszufinden, ob die Dauer der Initialtherapie oder der Ersatz des Prednisolons mit Oclacitinib das Ergebnis beeinflussen könnte.

Tiere – Siebenundachtzig Hunde mit atopischer Dermatitis.

Methoden und Materialien – Den Hunden wurde eine Eliminationsdiät gefüttert und entweder Prednisolon oder Oclacitinib für zwei bis drei Wochen verabreicht. Rezidivierende Hunde wurden ein zweites Mal behandelt. Wenn nach zwei Wochen ohne Behandlung kein Rezidiv auftrat, wurde mit den Hunden eine Provokation durchgeführt. Rezidivierende Hunde, die keine zwei Wochen ohne Behandlung durchhielten, bekamen die reguläre EDT.

Ergebnisse – Achtundfünfzig von 87 Hunden beendeten die Studie. Neununddreißig von 58 Hunden erhielten Prednisolon; 21 von diesen wurden mit FIAD diagnostiziert und zeigten kein Rezidiv (n = 14), ein Rezidiv (n = 6) oder zwei Rezidive (n = 1). Neunzehn von 58 Hunden erhielten Oclacitinib; 11 von diesen wurden für

Futtermittelallergiker gehalten und zeigten kein Rezidiv ($n = 7$) oder zwei Rezidive ($n = 4$). Die Eingangsbehandlung beeinflusste das Endergebnis nicht. Der Grenzwert für ein Rezidiv oder weniger zur Diagnose einer FIAD wurde mit einer Sensibilität von 95% für Prednisolon und 63% für Oclacitinib beschrieben. Die Spezifität für beide Wirkstoffe betrug 100%.

Schlussfolgerungen und klinische Bedeutung – Eine Eingangsbehandlung mit Prednisolon oder Oclacitinib verkürzt bei der EDT die Zeit bis zur Diagnose einer FIAD.

要約

背景 – 犬の食物アレルギー診断のゴールドスタンダードは、8週間の除去食試験 (EDT) の後に食物負荷試験を実施することである。最近の研究では、プレドニゾロン初期投与による、より短いEDTが可能であることが示された。

仮説/目的 – 本研究の目的は、プレドニゾロン中止後の再発数に基づく、EDT 感度および特異度を評価することであった。さらに、初期治療期間やプレドニゾロンをオクラシチニブに置き換えることが転帰に影響するかどうかを判断することも目的とした。

供試動物 – アトピー性皮膚炎を有する犬87頭。

材料と方法 – 犬に除去食を与え、プレドニゾロンまたはオクラシチニブを2~3週間投与した。再発した犬には2回目の治療を実施した。2週間の投薬オフ後に再発がない場合、犬はその後負荷試験を実施された。再発せずに2週間の休薬を達成しなかった犬には、通常のEDTを実施した。

結果 – 87頭中58頭の犬が研究を完遂した。58頭中39頭の犬がプレドニゾロンを投薬され、21頭が食物アレルギーと診断され、再発なし ($n = 14$)、1回の再発 ($n = 6$) または2回の再発 ($n = 1$) を示した。58頭中19頭がオクラシチニブを投薬され、11頭は食物アレルギーと診断され、再発なし ($n = 7$) または2回の再発 ($n = 4$) を示した。初期治療期間は結果に影響を与えなかった。食物アレルギー診断における1回以下の再発の閾値が、プレドニゾロン95%、オクラシチニブ63%の感度と関連していた。特異度は両剤とも100%であった。

結論と臨床上の重要性 – 食試験におけるプレドニゾロンやオクラシチニブの初期使用は、食物誘発性アレルギー性皮膚炎の診断までの時間を短縮する。

摘要

背景 – 診断犬食物過敏の金標準は8周食物排除試験(EDT), 随后进行再激发试验。最近的一项研究表明, 如果最初给予泼尼松龙, 可能会缩短EDT。

假设/目的 – 目标是根据泼尼松龙停药后的复发次数评价EDT的敏感性和特异性。另一个目的是确定初始治疗时长, 或用奥拉替尼替代泼尼松龙是否会影响结果。

动物 – 87只特异性皮炎犬。

方法和材料 – 犬喂食低敏日粮, 并接受泼尼松龙或奥拉替尼治疗2-3周。对复发犬进行第二次治疗。在停药两周后无复发的情况下, 对犬进行激发。未复发且2周后无法停药的犬接受常规EDT。

结果 – 87只犬中有58只完成了研究。58只犬中的39只接受了泼尼松龙治疗; 其中21只被诊断为FIAD, 无复发($n = 14$)、1次复发($n = 6$)或2次复发($n = 1$)。58只犬中的19只接受了奥拉替尼治疗; 其中11只被认为是食物过敏, 无复发($n = 7$)或2次复发($n = 4$)。初始治疗持续时间不影响结果。对FIAD诊断, 复发阈值一次或更低, 泼尼松龙治疗敏感性为95%, 而奥拉替尼治疗敏感性为63%。两种药物的特异性均为100%。

结论和临床重要性 – 在EDT过程中, 最初使用泼尼松龙或奥拉替尼缩短了诊断FIAD的时间。

Resumo

Contexto – O padrão ouro para se diagnosticar alergia alimentar em cães é a realização de dieta de eliminação (DE) de oito semanas seguido por um desafio dietético. Um estudo recente demonstrou que possível realizar-se uma DE mais curta se a prednisolona for administrada inicialmente.

Hipótese/Objetivos – O objetivo foi avaliar a sensibilidade e especificidade do DE com base no número de recidivas após a descontinuação da prednisolona. Além disso, o objetivo era determinar se a duração do tratamento inicial ou a substituição de prednisolona por oclacitinib influenciaria o resultado.

Animais – Oitenta e sete cães com dermatite atópica.

Métodos e materiais – Os cães foram alimentados com uma dieta de eliminação e tratados com prednisolona ou oclacitinib por duas a três semanas. Cães recidivantes foram tratados uma segunda vez. Na ausência de uma recaída após duas semanas sem medicação, os cães foram desafiados. Os cães que nunca alcançaram duas semanas sem tratamento e sem recidiva receberam a DE regular.

Resultados – Cinquenta e oito de 87 cães completaram o estudo. Trinta e nove de 58 cães receberam prednisolona; 21 deles foram diagnosticados com FIAD e não tiveram recidiva ($n = 14$), uma recaída ($n = 6$) ou duas recidivas ($n = 1$). Dezenove de 58 cães receberam oclacitinib; 11 deles foram considerados alérgicos a alimentos e não tiveram recidiva ($n = 7$) ou tiveram duas recidivas ($n = 4$). A duração do tratamento inicial não influenciou o resultado. O limite de uma recidiva ou menos para o diagnóstico de FIAD foi associado a uma sensibilidade de 95% para prednisolona e 63% para oclacitinib. A especificidade foi de 100% para ambas as drogas.

Conclusão e importância clínica – O uso inicial de prednisolona ou oclacitinib na DE reduz o tempo de diagnóstico da FIAD.