

Effects of otic betamethasone on intradermal testing in normal dogs

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What is known about the topic of this paper

- Otic glucocorticoids are commonly used to treat otitis externa secondary to atopic disease.
- Otic betamethasone administered for 2 weeks at manufacturer's recommended doses does not induce adrenal gland suppression.
- It is uncertain if otic glucocorticoids may interfere with intradermal tests for atopic dermatitis.

What this paper adds to the field of veterinary dermatology

- Otic betamethasone administered 2 weeks at manufacturer's recommended doses in normal dogs caused a significant reduction in skin reactivity to *Dermatophagoides farinae*, *Cynodon dactylon* and to histamine 1 : 100 000 w/v.
 - This reduction was observed despite normal adrenal gland response to adrenocorticotrophic hormone.
 - Although statistically significant, the reduction was within the limits of variability of the intradermal testing and was too small to be clinically relevant.
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Abstract

Otitis externa is common in atopic dogs and is frequently treated using potent glucocorticoids topically. These preparations can cause adrenal suppression and affect skin test reactivity. The purpose of this study was to determine if an otic product containing betamethasone could decrease skin reactivity in normal dogs.

Sixteen laboratory beagles were used in a cross-over, blinded trial. Dogs were enrolled in two groups; one received placebo and the other a betamethasone-containing otic preparation (Otomax®) twice daily for 2 weeks. After a 4-week wash-out period, treatments were switched. Dogs were intradermally tested on days 0 and 14 of each treatment period with histamine phosphate (1 : 100 000 and 1 : 200 000 w/v) and allergens common in the area. Adrenocorticotrophic hormone (ACTH) stimulation tests were done before and after treatment to investigate adrenal suppression.

After 2 weeks of otic betamethasone, *Dermatophagoides farinae* ($P = 0.0034$), *Cynodon dactylon* ($P = 0.0459$) and histamine 1 : 100 000 w/v ($P = 0.0028$) reactions were significantly reduced. Pre-treatment post-ACTH serum cortisol levels and those obtained after both treatments did not differ statistically

($P = 0.6362$). Betamethasone induced a slight but statistically significant elevation ($P = 0.0002$) of serum alkaline phosphatase. Despite the increase, values were within normal range.

It is concluded that, although otic betamethasone did not suppress adrenal glands, it mildly suppressed intradermal reactions to 1 : 100 000 w/v histamine, *D. farinae* and *C. dactylon*.

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Introduction

Otitis externa is common in dogs with atopic dermatitis (AD), and its treatment usually involves the use of topical otic preparations containing potent glucocorticoids such as betamethasone or dexamethasone. Almost two decades ago, local administration of this type of glucocorticoids in topical otic preparations was shown to suppress the HPA axis in normal dogs.¹ After this and other studies^{2,3} it was concluded that application of some glucocorticoids in topical, ophthalmic and otic formulations could result in adrenal suppression for periods up to 2–8 weeks depending on the formulation.⁴ If the preparation is sufficiently potent to cause adrenal suppression for these time periods, it is likely that it could also be capable of suppressing skin reactions in patients undergoing intradermal testing (IDT) for AD.

Intradermal testing remains a common procedure at dermatology referral centres to evaluate dogs with suspected AD. More importantly, the success of hyposensitization treatment depends largely on the accuracy of the IDT in identifying antigens that are responsible for clinical signs. Reduction in the number of false-negative and false-positive reactions on the IDT may improve the response rate to hyposensitization treatment.^{5,6} A wash-out period of 2 weeks for topical corticosteroid preparations and of 8 weeks for systemic preparations has been proposed to avoid inhibition of skin reactions to allergens.⁷ A more recent report studied the length of time needed for resolution of adrenal suppression after treatment with two otic glucocorticoid preparations in normal small-breed dogs (less than 14 kg body weight) without evidence of otitis.⁸ The results of the study of Ghubash *et al.*⁸ demonstrated that small-breed dogs with normal ears treated with betamethasone, at the manufacturer's prescribed dosage, did not exhibit a suppressed adrenocortical response after 2 weeks of treatment, whereas dogs receiving dexamethasone showed variable adrenal suppression that persisted 2 weeks after cessation of treatment in two of the seven dogs treated. Thus, we hypothesized that a similar treatment of otic betamethasone would not interfere with IDT. The purpose of this study was to determine if recent

Table 1. Concentrations of allergenic extracts and histamine used in the study

Extract	Concentration
House dust	1 : 1000 w/v
<i>Dermatophagoides farinae</i>	500 biological units mL ⁻¹
<i>Dermatophagoides pteronyssinus</i>	500 biological units mL ⁻¹
<i>Artemisia vulgaris</i>	10000 biological units mL ⁻¹
<i>Ctenocephalides felis</i>	1 : 1000 w/v
<i>Cynodon dactylon</i>	1 : 200 w/v
<i>Rumex acetosella</i>	1 : 200 w/v
Histamine phosphate 1	1 : 100 000 w/v
Histamine phosphate 2	1 : 200 000 w/v

otic application of a suspension containing 0.088% betamethasone may inhibit IDT reactivity to intradermal allergens and histamine in normal dogs.

Materials and methods

Dogs

Sixteen clinically normal laboratory beagles (ten females, six males; age range 1–5 years) were used in the study. The dogs had no previous history of otitis externa or dermatological disease and had not received oral, parenteral or topical corticosteroids in the 3 months prior to the beginning of the study. The dogs were dewormed periodically, were normal on physical examination, otoscopy and external ear canal cytology. Dogs were housed individually in indoor–outdoor pens and were fed commercial dry food with water always available. Pens were cleaned daily with high pressure water but dogs had soft bedding and were walked twice a day in an external facility. No limitation of allergen exposure was intended. All procedures applied in this study were approved by the Committee of Animal Ethics of the University of Cordoba.

Study design

The study was designed as a crossover-blinded clinical trial in which the investigator reading the IDT results was not aware of the treatments. Dogs were randomly enrolled in two groups; one received a placebo treatment (Epitoc®, Virbac, Barcelona, Spain) and the other a betamethasone-containing preparation (Otomax®; Schering-Plough, Madrid, Spain) twice daily for 2 weeks. This product is formulated as a suspension containing per ml 0.88 mg of betamethasone valerate, 8.8 mg of clotrimazole and 2640 UI of gentamicin. The volume administered was based on the manufacturer's recommendations (four drops for dogs less than 14 kg and eight drops for dogs more than 15 kg). A wash-out period of 4 weeks was observed; then treatments were switched. The 4-week period was selected based on previous studies determining the effect of topical⁸ and systemic⁹ exogenous glucocorticoids.

Evaluation of intradermal skin testing reactions

Each dog was intradermally tested on days 0 and 14 of each treatment period with histamine phosphate (1 : 100 000 and 1 : 200 000 w/v) and several common allergens (Table 1). Buffered saline with phenol was used as negative control. All allergens were provided diluted in buffered saline with phenol by the same manufacturer (Inmunotek SL, Madrid, Spain). Allergens were stored at 5 °C as recommended by the laboratory and the same batch was used throughout the study. Dogs were sedated (xylazine 0.25 mg kg⁻¹ IV, Rompun®, Bayer, Barcelona, Spain), and a volume of 0.05 mL of each solution was injected intradermally on the clipped lateral thorax using a 26-gauge needle. Reactions were evaluated at 15 min by objective measurement in millimetres of the wheal reaction determined as the average of two perpendicular axes. All intradermal injections and evaluation of responses were performed by the same investigator, who was blinded to the treatment allocation. Subjective evaluation was not performed.

Laboratory testing

On days 0 and 14 of each treatment period, all dogs had blood collected for total cell counts, and biochemical parameters most likely to be affected by glucocorticoid absorption were monitored. On the days before and after ending treatments adrenocorticotrophic hormone (ACTH) stimulation tests were performed using synthetic ACTH (Nuvachten®; Laboratory Padrós; Barcelona, Spain) (0.25 mg dog⁻¹ IM). Serum samples were collected before and 1 h after ACTH administration.

Statistics

Laboratory results and IDT response to histamine and allergens before and after otic treatment were included in the database. For statistical analysis, time and treatment sequences were catalogued as level 1: baseline prior to otic betamethasone; level 2: end of betamethasone treatment; level 3: baseline prior to placebo treatment; and level 4: end of placebo treatment. Differences between treatments and times were analysed by the Student *t*-test (two-tail test) looking for heterogeneity of the mean. Differences were considered significant at a *P* ≤ 0.05. All IDT scores and laboratory results passed the Kolmogorov–Smirnov normality test. All statistical analyses were performed using STATGRAPHICS version 7 plus software (Manugistics Inc., Rockville, MD, USA).

Results

There were no significant differences between groups for IDT results at each time point, indicating that there was no order of treatment effect. The data from both groups were pooled to analyse treatment effect.

Baseline results were compared with those obtained at the end of glucocorticoid or placebo treatments (Fig. 1). There were no significant differences in IDT scores of allergens and histamine dilutions tested at the end of placebo treatment although mean IDT reactions were variably lower. In contrast, after 2 weeks of otic betamethasone *D. farinae* (*P* = 0.0034), *C. dactylon* (*P* = 0.0459) and histamine 1 : 100 000 (*P* = 0.0028) reactions were significantly reduced (Table 2). Baseline results before betamethasone and placebo treatments showed no significant differences, indicating that the 4-week period before switching treatments was appropriate.

As for IDT results, laboratory data showed no significant differences between groups at each time point and were pooled. Haematology results did not differ significantly after comparing placebo and otic betamethasone treatments (Table 3). Adrenocorticotrophic hormone stimulation tests performed at the end of each treatment period were normal in all dogs (post-ACTH cortisol values > 6 µg dL⁻¹ and < 17 µg dL⁻¹). Comparison of baseline post-ACTH serum cortisol levels and those obtained after otic betamethasone or placebo treatment was not statistically significant (Table 4).

Concerning the serum parameters monitored, the 2-week administration of otic betamethasone induced a statistically significant (*P* = 0.0002) elevation of serum ALP levels. However, concentrations remained within the normal laboratory range in all dogs (Table 4).

Discussion

In this study we found no significant differences in IDT scores at the end of placebo treatment, whereas after 2 weeks of otic betamethasone *D. farinae*, *C. dactylon* and histamine 1 : 100 000 w/v reactions were significantly reduced. Although statistically significant, the magnitude of the reduction in mean IDT scores was within the range

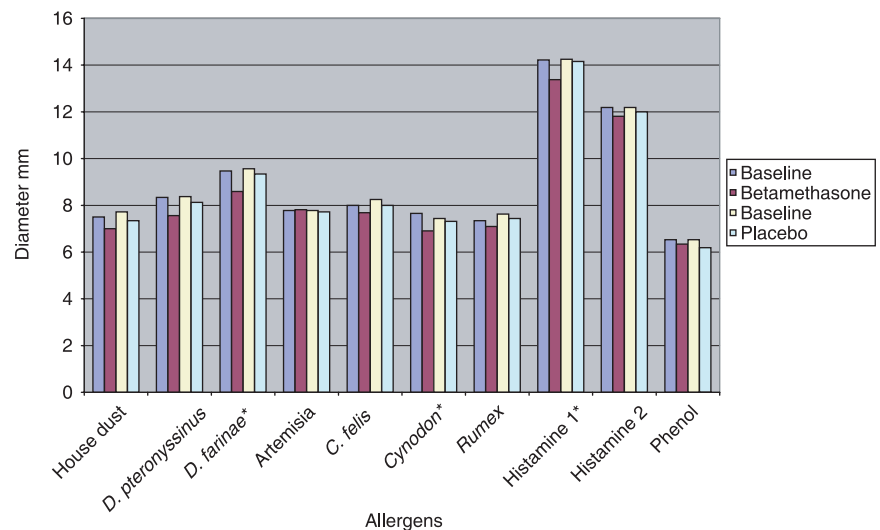


Figure 1. Mean skin test reactivity (mm) for each allergen and histamine before and after 2 weeks of treatment with otic betamethasone or placebo. Histamine 1 = histamine 1 : 100 000 w/v; histamine 2 = histamine 1 : 200 000 w/v. *Indicates a significant ($P \leq 0.05$) difference from baseline.

Table 2. Mean $\pm$ standard deviation of intradermal testing results before and after otic betamethasone and placebo treatments; *Indicates a significant ($P \leq 0.05$) difference from baseline. All results were normally distributed (Kolmogorov–Smirnov normality test); $N = 16$

	Betamethasone		Placebo	
	Baseline	End of treatment	Baseline	End of treatment
House dust	7.5 $\pm$ 1.30	7.00 $\pm$ 1.29	7.71 $\pm$ 1.03	7.34 $\pm$ 1.23
<i>D. pteronyssinus</i>	8.34 $\pm$ 1.45	7.56 $\pm$ 1.92	8.37 $\pm$ 1.00	8.12 $\pm$ 1.13
<i>D. farinae</i>	9.46 $\pm$ 1.76	*8.59 $\pm$ 1.96	9.56 $\pm$ 1.72	9.34 $\pm$ 1.86
<i>Artemisia vulgaris</i>	7.78 $\pm$ 1.18	7.81 $\pm$ 1.60	7.78 $\pm$ 1.44	7.71 $\pm$ 1.03
<i>Ctenocephalides felis</i>	8.00 $\pm$ 1.90	7.68 $\pm$ 1.36	8.25 $\pm$ 1.44	8.00 $\pm$ 1.76
<i>Cynodon dactylon</i>	7.65 $\pm$ 1.27	*6.90 $\pm$ 1.25	7.43 $\pm$ 1.61	7.31 $\pm$ 1.07
<i>Rumex acetosella</i>	7.34 $\pm$ 1.36	7.09 $\pm$ 1.39	7.62 $\pm$ 1.56	7.43 $\pm$ 1.01
Histamine 1 : 100 000	14.21 $\pm$ 0.51	*13.37 $\pm$ 0.78	14.25 $\pm$ 0.68	14.15 $\pm$ 0.39
Histamine 1 : 200 000	12.18 $\pm$ 0.92	11.81 $\pm$ 1.12	12.18 $\pm$ 1.03	12.00 $\pm$ 0.60
Phenol	6.53 $\pm$ 0.99	6.34 $\pm$ 1.19	6.53 $\pm$ 1.20	6.18 $\pm$ 0.77

Table 3. Mean $\pm$ standard deviation of the haematology results before and after otic betamethasone and placebo treatments. All results were normally distributed (Kolmogorov–Smirnov normality test); $N = 16$

	Betamethasone		Placebo		Normal range
	Baseline	End of treatment	Baseline	End of treatment	
PCV (%)	45.06 $\pm$ 2.56	44.68 $\pm$ 2.65	45.43 $\pm$ 2.85	44.75 $\pm$ 3.35	37–50
WBC ($10^3 \mu\text{L}^{-1}$)	9.71 $\pm$ 2.48	10.04 $\pm$ 2.68	9.85 $\pm$ 2.25	9.31 $\pm$ 2.12	6–12
RBC ($10^6 \mu\text{L}^{-1}$)	5.48 $\pm$ 0.34	5.42 $\pm$ 0.35	5.46 $\pm$ 0.37	5.35 $\pm$ 0.28	5–8
Hb (g dL $^{-1}$)	12.45 $\pm$ 0.55	12.13 $\pm$ 0.92	12.66 $\pm$ 0.69	12.24 $\pm$ 0.81	11–17
Platelets (μL^{-1})	277.5 $\pm$ 62.80	301.68 $\pm$ 93.30	259.50 $\pm$ 54.37	262.25 $\pm$ 55.20	200–400

PCV, packed-cell volume; WBC, white blood cell; RBC, red blood cell.

Table 4. Mean $\pm$ standard deviation of serum biochemical parameters before and after otic betamethasone and placebo treatments. *Indicates a significant ($P \leq 0.05$) difference from baseline. All results were normally distributed (Kolmogorov–Smirnov normality test); $N = 16$

	Betamethasone		Placebo		Normal range
	Baseline	End of treatment	Baseline	End of treatment	
ALP (UI L $^{-1}$)	59.41 $\pm$ 16.19	*78.95 $\pm$ 29.09	56.34 $\pm$ 14.96	56.07 $\pm$ 14.52	< 120
ALT (UI L $^{-1}$)	31.92 $\pm$ 7.39	37.32 $\pm$ 10.73	33.37 $\pm$ 6.64	35.87 $\pm$ 7.55	6–70
Cholesterol (mg dL $^{-1}$)	203.50 $\pm$ 59.13	214.81 $\pm$ 58.94	200.93 $\pm$ 68.64	195.50 $\pm$ 63.04	112–358
Amylase (UI L $^{-1}$)	602.25 $\pm$ 199.06	506.18 $\pm$ 175.02	609.31 $\pm$ 183.38	553.67 $\pm$ 158.28	350–1650
Basal cortisol ($\mu\text{g dL}^{-1}$)	3.49 $\pm$ 1.13	3.06 $\pm$ 1.29	2.87 $\pm$ 1.21	3.57 $\pm$ 1.10	1.1–7.8
Post-ACTH cortisol	13.86 $\pm$ 2.27	13.02 $\pm$ 2.56	12.82 $\pm$ 2.51	13.19 $\pm$ 2.75	< 17

ALP, alkaline phosphatase; ALT, alanine aminotransferase; ACTH, adrenocorticotrophic hormone.

of 0.5–1 mm and for a particular dog and allergen the highest reduction observed in wheal diameter was 3 mm. As in the study of Ghubash *et al.*⁸ otic betamethasone treatment did not cause adrenal suppression in any dog, which seems to indicate that there was no systemic absorption of betamethasone, however, in our study we found a mild but significant increase in ALP serum levels. Thus, one hypothesis is that otic betamethasone absorption could inhibit the skin reaction without causing detectable adrenal suppression and that IDT is more sensitive to the effects of glucocorticoids than ACTH stimulation test. The second explanation could be that the differences found are more inherent to the variability of results with IDT. Both hypotheses seem to be compatible.

Some degree of variability in test results is expected when the same IDT is performed on the same patient.¹⁰ The subjective method of IDT evaluation is most often used on a clinical basis but discrepancies in score assignments are possible, thus only objective measurements were recorded and analysed in this study. Also, the maximal wheal diameter is considered to be a more accurate indicator of the intensity of the IDT reaction and has been used previously in several studies investigating the effect of anaesthetic agents on the IDT.^{10–12} Although there are no specific reports addressing the repeatability of IDT in dogs, this factor may hinder the interpretation of the results. Factors that negatively affect repeatability of the IDT such as batch variability, deterioration during storage and long intervals between tests¹³ were not significant in this study due to the short duration. Also, to minimize variability, all tests were performed and read by the same investigator and the dogs were maintained under the same conditions. Therefore, although some variation is expected when performing multiple IDT, every effort was made in this study to increase repeatability. In a previous study, a 2-mm variation in wheal diameter within the same dog was recorded to a given concentration of histamine.¹¹ This variation was attributed to injection and measurement limitations and is within limits of clinical IDT. However, small variations (2–3 mm) among time points were statistically significant, and could explain the significant differences found. Another fact to address is the reduction in wheal diameter found in all allergens after placebo treatment. Although differences were not statistically significant, this finding needs consideration and might be related to the difficulties to effectively blind all the experimental procedure.

In a previous study the absorption of betamethasone through dog skin was measured *in vitro*. About 10% of the topically applied betamethasone 17-valerate penetrated the skin over a 24-h period.¹⁴ Four drops of Otomax® contain ≈ 0.1193 mg of betamethasone and thus the total daily dosage ranged from $0.0198 \text{ mg kg}^{-1}$ (24 kg dog) to 0.026 mg kg^{-1} (9 kg dog) mg kg^{-1} . This dosage is low compared with those used in previous studies where topical betamethasone-17-valerate induced significant adrenal suppression. Assuming a 10% penetration through normal skin, total daily systemic dosage would range from $1.98 \times 10^{-3} \text{ mg kg}^{-1}$ to $2.6 \times 10^{-4} \text{ mg kg}^{-1}$, and it seems less probable that this low dosage could explain the significant wheal diameter reduction found for some allergens and histamine. In atopic dogs with inflamed ear canals, penetration of otic glucocorticoids might increase

due to alterations in the skin's barrier functions. Although minimal, there were apparent differences in the absorption of hydrocortisone in pruritic vs. normal canine skin.¹⁵ A greater rate of absorption could result in higher serum levels specially if a dog with otitis externa receives a higher than prescribed daily dosage. Unfortunately, private-owned atopic dogs with inflamed ears could not be used in a well-controlled cross-over study design. The use of normal dogs for this study has clear limitations. Until this difficulty could be overcome by experimental models, the preliminary information gained with this study in normal dogs suggests a strict labelled use of otic glucocorticoids before IDT in atopic dogs.

In IDT, histamine phosphate solution is used as positive control at either 1/100 000 or 1/10 000 w/v. A recent study compared both concentrations and concluded that a histamine concentration of 1 : 10 000 w/v gave more consistent results and thus should be used as the standard histamine concentration.¹⁶ In that study, mean wheal diameter of the 1 : 10 000 w/v histamine concentration was 14 mm, whereas the 1 : 100 000 w/v histamine concentration mean wheal diameter was only 11.6 mm. In the present study, a histamine concentration of 1 : 100 000 w/v was used because it is the standard concentration used in our hospital. In our patients, this concentration consistently achieved wheals of ≥ 14 mm in diameter if a glucocorticoid withdrawal period of at least 4 weeks is observed. Thus, a dilution of histamine 1 : 200 000 w/v was tested anticipating that its wheal reaction would be more easily inhibited than the standard 1 : 100 000 w/v dilution. Unexpectedly, at the higher dilution there were no significant differences between baseline and post-betamethasone IDT results. Statistically, the 1 : 200 000 w/v histamine concentration showed more variation at each given time level, whereas the 1 : 100 000 w/v histamine dilution gave more consistent results. It is reasonable to expect higher variations using lower dilutions of histamine. Higher standard deviations would make differences statistically less significant. Also, a similar ratio of inhibition will result in higher absolute wheal diameter reduction for the more concentrated histamine dilution. Thus, it is speculated that there is not a clear biological explanation for this discrepancy and that it is most likely statistically related.

Only *D. farinae* and *C. dactylon* showed a minor but statistically significant reduction on wheal diameter after 2 weeks of otic betamethasone, whereas the rest of allergens showed nonsignificant reductions. With the exception of *Ctenocephalides felis*, the allergens tested were those with a higher frequency of positive IDT reactions in atopic dogs from our geographical area. Although the dogs used were clinically normal some of them showed weak positive responses, especially to *D. farinae* and *Dermatophagoides pteronyssinus*, and other positive reactions were recorded for *Artemisia*, and *C. felis* but not for *C. dactylon*. In normal dogs, the positive reactions found may be categorized as false-positive, irritant reactions or true positives in an asymptomatic dog and these categories can also apply to atopic dogs. The cause of these positive reactions in our dogs is unknown as it is the effect of betamethasone treatment over each of these variables in such a complex test as the IDT. However, in contrast with *D. farinae*, no positive reactions against *C.*

dactylon were found which would point to the variations inherent to IDT and the effect of betamethasone as the more probable explanations for the statistical differences. In any case, mean reduction of wheal diameter was around 1 mm. It is hypothesized that its clinical relevance is most likely limited.

In conclusion, otic betamethasone did not significantly suppress adrenal glands but caused an elevation, within the normal range, of serum ALP levels in the treated group. Betamethasone mildly suppressed IDT reaction to 1 : 100 000 w/v histamine phosphate dilution, *D. farinae* and *C. dactylon* in normal dogs. *D. farinae* reactions were positive in some dogs but since it is not known whether they reflected true-positives, false-positives or irritant reactions, we cannot conclude that a 2-week otic betamethasone treatment would interfere with IDT results in atopic dogs. In spite of statistical significance, the magnitude of the skin reactivity reduction after twice daily otic betamethasone at the manufacturer's recommended dosage is probably too mild to have clinical relevance.

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Résumé Les otites externes sont fréquentes chez les chiens atopiques et sont souvent traitées avec des corticoïdes puissants par voie locale. Ces formulations peuvent provoquer une suppression du fonctionnement des glandes surrénales et modifient les résultats des tests d'intradermoréaction. Le but de cette étude est de déterminer si un produit auriculaire à base de bétaméthasone pouvait diminuer la réactivité cutanée chez des chiens sains. 16 beagles de laboratoire ont été utilisés pour cette étude en aveugle et contre placebo en cross-over. Les chiens ont été divisés en 2 groupes; un a reçu un placebo et l'autre une préparation auriculaire à base de bétaméthasone (Otomax) 2 fois par jour pendant 2 semaines. Après 4 semaines de wash out, les traitements ont été inversés. Les chiens ont été testés par injection intradermique à J0 et J14 pour chaque traitement avec de l'histamine phosphate (1 : 100 000 et 1 : 200 000 w/v) et des aéroallergènes fréquents dans l'environnement. Des tests de stimulation à l'ACTH ont été réalisés avant et après le traitement pour étudier la fonction surrénalienne.

Après 2 semaines de traitement, les réactions à *D. farinae* ($P = 0.0034$), *Cynodon dactylon* ($P = 0.0459$) et à l'histamine 1 : 100 000 w/v ($P = 0.0028$) ont été significativement réduites. Les niveaux de cortisol sérique avant le traitement et après l'injection d'ACTH et les niveaux obtenus après les 2 traitements n'ont pas été différents statistiquement ($P = 0.6362$). La bétaméthasone induit une augmentation modérée mais significative statistiquement ($P = 0.0002$) de la phosphatase alcaline (ALP) sérique. Malgré cette élévation, les valeurs restent dans une moyenne normale. En conclusion, bien que la bétaméthasone en topique auriculaire ne supprime pas le fonctionnement de la glande surrénale, elle supprime en grande partie la réactivité intradermique à l'histamine 1 : 100 000 w/v, *D. farinae* et *C. dactylon*.

Resumen La otitis externa es un fenómeno común en perros atópicos y con frecuencia se trata utilizando potentes glucocorticoides por vía tópica. Estas preparaciones pueden causar supresión de las glándulas

adrenales y pueden afectar la reacción en las pruebas de piel. El propósito de este estudio fue determinar si un producto óptico tópico con betametasona podría reducir la reacción en pruebas de piel en perros normales.

Dieciséis Beagles de laboratorio se utilizaron en un estudio ciego cruzado. Los perros se incluyeron en dos grupos, uno recibiendo placebo y el otro recibiendo una preparación óptica con betametasona (Otomax®) dos veces al día durante dos semanas. Tras un período de 4 semanas de recuperación los tratamientos se intercambiaron. Los perros recibieron una prueba intradérmica en los días 0 y 14 de cada período con fosfato de histamina (1 : 100 000 y 1 : 200 000 masa/volumen) y con alérgenos comunes en el área. Pruebas de estimulación con ACTH se realizaron antes y tras el tratamiento para investigar la posible supresión de las glándulas adrenales. Tras dos semanas de tratamiento con betametasona, las reacciones intradérmicas a *D. farinae* ($P = 0.0034$), *Cynodon dactylon* ($P = 0.0459$) e histamina 1 : 100 000 m/v ($P = 0.0028$) se redujeron de forma significativa. Los niveles de cortisol en suero tras la estimulación con ACTH pretratamientos y posttratamientos no variaron de forma significativa ($P = 0.6362$). El tratamiento con betametasona indujo una elevación ligera pero significativa ($P = 0.0002$) en la fosfatasa alcalina del suero. A pesar de este aumento los valores se situaron dentro del rango normal.

Concluimos que, aunque el tratamiento con betametasona no suprimió las glándulas adrenales, suprimió ligeramente las reacciones intradérmicas a 1 : 100 000 m/v de histamina, *D. farinae*, y *C. dactylon*.

Zusammenfassung Otitis externa kommt bei atopischen Hunden häufig vor und wird oft mit potenten Glukokortikoiden topisch behandelt. Diese Präparate können eine Suppression der Hypophysen-Nebennierenrinden-Achse bewirken und die Hauttestreaktion beeinträchtigen. Das Ziel dieser Studie war es festzustellen, ob ein Ohrpräparat, welches Betamethason beinhaltet, die Hautreaktion bei normalen Hunden herabsetzen konnte. Sechzehn Laborbeagles wurden in einer Crossover-Blindstudie verwendet. Die Hunde wurden in zwei Gruppen eingeteilt; eine bekam Plazebo und die andere ein Ohrprodukt mit Betamethason (Otomax®) zweimal täglich für zwei Wochen. Nach einer 4 wöchigen Wash-out-Phase wurden die Behandlungen getauscht. Die Hunde wurden am Tag 0 und 14 einer jeden Behandlungsperiode mit Histaminphosphat (1 : 100 000 und 1 : 200 000 w/v) und mit Allergenen, die für die Gegend typisch waren, intradermal getestet. ACTH Stimulationstests wurden vor und nach der Behandlung durchgeführt, um eine Suppression der Nebennieren zu ermitteln. Nach einer zweiwöchigen Ohrbehandlung mit Betamethason waren die Reaktionen zu *D. farinae* ($P = 0.0034$), *Cynodon dactylon* ($P = 0.0459$) und Histamin 1 : 100 000 w/v ($P = 0.0028$) signifikant reduziert. Vor der Behandlung waren die post-ACTH Serum Cortisolspiegel nicht signifikant verschieden von denen nach beiden Behandlungen ($P=0.6362$). Betamethason induzierte eine leichte, aber signifikante Erhöhung ($P = 0.0002$) der Alkalinen Phosphatase im Serum (ALP). Trotz der Erhöhung waren die Werte im Normalbereich. Es wurde daraus geschlossen, dass Betamethason als Ohrprodukt zwar die Nebennieren nicht unterdrückt, wohl aber eine milde Unterdrückung der intradermalen Reaktion zu 1 : 100 000 w/v Histamin, *D. farinae* und *C. dactylon* bewirkt.