An Accessible Rabbit Model of Meibomian Gland Dysfunction Induced with Complete Freund's Adjuvant for Anti-Inflammatory Treatment Evaluation.

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Introduction

Meibomian Gland Dysfunction (MGD) is a common eye disease that significantly contributes to evaporative dry eye disease. This disease is characterized by the obstruction of the Meibomian gland orifices, often due to hyperkeratinization of the ductal epithelium, leading to inflammation and altered lipid production necessary for tear film stability.

To better understand the pathophysiology of MGD and evaluate new therapeutic approaches, animal models, particularly rabbit models, are widely used. Rabbits possess a Meibomian gland anatomy that closely resembles that of humans, making them an invaluable model for translational research. A few years ago, researchers developed an accessible rabbit model of MGD induced by complete Freund's adjuvant (CFA). This model is created by injecting CFA into the rabbits' eyelid, which induces symptoms similar to those observed in humans, such as obstructed orifices and gland inflammation. Utilizing this model not only facilitates the study of MGD progression but also allows for the evaluation of potential treatments.

Here, we propose to evaluate the effect of 0.1% dexamethasone eye drops, a corticosteroid, on reducing inflammation, obstruction, and telangiectasia around the glandular orifices in this dry eye model.

Materials and Methods

Animals

Twenty female New Zealand White albino rabbits were allocated in two groups of ten animals. Animals were handled and cared for according to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Induction of MGD and Treatment

Experimental MGD was induced by three subcutaneous injections of CFA (each 50 µL) into the upper eyelid margin on day 1. The two groups received either saline or 0.1% dexamethasone eye drops (50 µL) four times daily from day 1 to day 21.

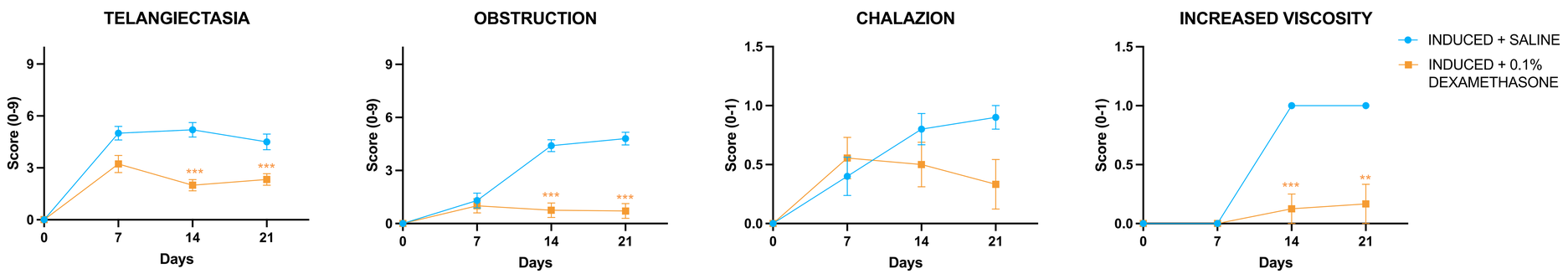
Clinical Evaluations

The rabbits were examined under a slit lamp every week. The evaluation of MGD was based on the presence telangiectasia, of plugged orifices, chalazion, and the increased viscosity of meibum.

Histological Analysis

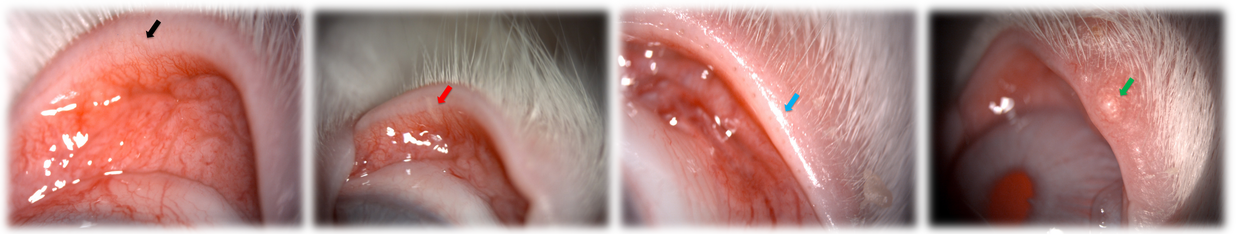
Eyelid tissue included the meibomian gland orifices, was dissected at day 21. The tissue was fixed with Davidson's solution, embedded in paraffin, and vertically cut into 5-µm-thick sections. The sections were stained with Hematoxylin and Eosin (HE) for light microscopic examination.

Results

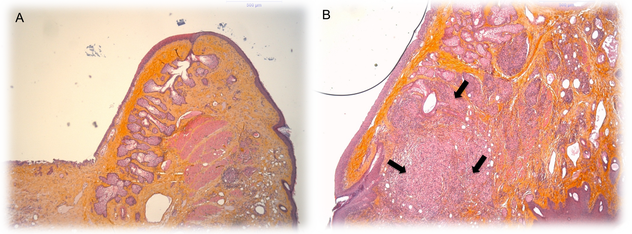


The intensity of telangiectasia was scored in the nasal, central, and temporal regions of the upper eyelid as follows: 0, none; 1, mild; 2, moderate; and 3, severe. The maximum total score was nine.
The number of plugged orifices was scored in the nasal, central, and temporal regions of the upper eyelid as follows: 0, none; 1, fewer than 4 plugged orifices; 2, between 4 and 7 plugged orifices; and 3, more than 7 plugged orifices. The maximum total score was nine.
The chalazion and the increased viscosity of meibum were scored as follows: 0, none; 1, present.

Note: n = 10. All data were presented as the mean ± SEM. *:*p<0.05*, **:*p<0;01*, ***:*p<0.001*.



The rabbit's eyelids, 21 days post-injection with complete Freund's adjuvant, exhibit telangiectasia (*black arrow*), increased meibum viscosity (*red arrow*), occluded gland terminal orifices *(blue arrow)*, and the presence of a chalazion *(green arrow)*.



Light microscopic examination of eyelid tissue sections included the meibomian gland stained with Hematoxylin and Eosin (HE). A: Right eye eyelid 21 days after saline injection. B: Left eye eyelid 21 days after Complete Freund's adjuvant. Here the sample was swollen with inflammatory cells *(black arrow)*.

Conclusions

Rabbits are phylogenetically closer to humans than rodents, making them ideal models for translational research, particularly for the development of new drugs and drug delivery systems. Rabbits have a largely exposed ocular surface and Meibomian gland anatomy comparable to humans, facilitating the use of imaging platforms for dry eye diagnostic tests. Rabbit models of Meibomian gland dysfunction, such as those induced by complete Freund's adjuvant, effectively reproduce symptoms observed in humans, like plugged orifices and telangiectasia, which is crucial for evaluating drug candidates' efficacy. We have seen that 0.1% dexamethasone eye drops reduce inflammation, obstruction, telangiectasia, chalazion, and meibum viscosity. Other active ingredients can be easily tested. This is why the rabbit model of Meibomian gland dysfunction is a valuable tool for researching new treatments and therapeutic approaches.

References

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