Latanoprost in the treatment of eyelash alopecia in alopecia areata universalis

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Abstract

Objectives The aim of this study was to test the efficacy of latanoprost in eyelash alopecia areata (AA).

Design This study is a 2-year prospective, non-blinded, non-randomized, bilateral eyelash alopecia controlled study.

Setting The setting of this study was Trichology Unit, Virgen Macarena University Hospital, Seville, Spain.

Patients We conducted a survey of 54 subjects with AA universalis treated with the protocol of the Trichology Unit of our Department. Control group comprised 10 subjects who received injections of 0.5 mg/cm² of triamcinolone acetonide (TAC) in their eyebrows and 1 mg/cm² of TAC injections in affected scalp. The treatment group included 44 subjects who received the same treatment as the control group in scalp and eyebrows but they also applied a drop of latanoprost 0.005% (50 μg/mL) ophthalmic solution in their eyelid margins every night. Subjects were reviewed every 3 months for 2 years.

Results Forty subjects finished the study and four subjects were lost to follow-up. In the treatment arm of this study, the course was well tolerated and uncomplicated. Both investigators and patients evaluated the regrowth. The results we obtained were: complete regrowth in 17.5%, moderate regrowth in 27.5%, slight regrowth in 30% and without response in 25%. Moderate and total regrowth constituted a cosmetically acceptable response. The therapy was continuous and the response remained without any side effects. No patients had cosmetically acceptable eyelash regrowth in the control group.

Conclusions Latanoprost may be an effective drug in the treatment of eyelash AA because it induces acceptable responses (total and moderate) in 45% of the patients. A formal, blinded prospective unilateral controlled study will permit further understanding about this promising therapeutic agent for eyelash AA.

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Keywords

alopecia areata, eyelash, latanoprost, treatment

Introduction

Alopecia areata (AA) is an autoimmune disease whose target is the hair follicle. The disease is often clinically characterized by non-scarring and patchy hair loss. The scalp is the most frequent location of the disease, but any hair-bearing area can be affected. Eyelashes and eyebrows have a protective function as well as a cosmetic function. Apart from this protective function, eyelashes establish personal identity, and therefore patients with eyelash-loss often have a loss of identity.

Methods

There are several protocols of treatment for AA of the scalp with varied results. In the Trichology Unit of our Department of Dermatology, we employ the following treatment for AA universalis, totalis and some cases of ophiasis, all with eyelash-loss. In children under 40 kg, we only use biotin 10–20 mg/day, zinc aspartate 100 mg/day and local injections of 1 mg/cm² triamcinolone acetonide (TAC) diluted 50% in saline solution in each eyebrow every 3 months, and topical 0.025% clobetasol propionate twice a day in the scalp. In children and adults over 40 kg, we treat the affected scalp with 1 mg/cm² TAC every 3 months. Total dose of TAC (mg) is 2/3 of the weight of the patient, that is, 40 mg for a weight of 60 kg. With this protocol, we had observed acceptable eyelash regrowth in less than 3% of the patients, who were in all cases adults in the first 3 or 6 months of treatment. Nevertheless, spontaneous remission could explain this response.
We performed a 2-year, prospective, non-blinded, non-randomized, controlled survey with patients with AA universalis who had never before received treatment in their eyelashes. The wash-out period for other medication used as treatment of AA was of 12 months. The aim of the study was to test the efficacy of once daily topical latanoprost in the treatment of eyelash AA in individuals with AA universalis. Subjects were grouped into two categories:

- A control group comprising subjects who refused to be treated with latanoprost and who were treated in scalp and eyebrows following the protocol of the Unit.
- A treated group comprising patients who received the treatment protocol and they also spread a drop of latanoprost 0.005% (50 µg/mL) ophthalmic solution in each eye across the border of their lids every day using a cotton-applicator or their finger. To avoid iridal hyperpigmentation or other possible complications, we recommended patients with blue eyes to use the cotton-applicator. We prolonged the treatment for 2 years despite eyelash regrowth because this effect is reversible.

Subjects were reviewed every 3 months for 2 years. They were also reviewed by an Ophthalmologist, at least at pre-treatment baseline and at 1 year of the treatment. Subjects were referred for any eye-related concern possibly attributed to latanoprost. We took photographs in each review, including the basal visit (CM) with a DermLite photo adapted to a Nikon Coolpix 4500. Two investigators made a non-blinded evaluation of the responses based on the pictures taken in each visit (CP and RR). Every subject was evaluated by the two investigators and in two cases where there was a difference of opinion, they were reviewed by the responsible of study (CM). The responses to the treatment were grouped into four categories: total (80–100% regrowth), moderate (between 30% and 79% regrowth), slight (some eyelashes: 1–29%) and no regrowth (0%). This grouping is identical to our previously published scalp hair-regrowth scale,¹ which has been accepted by other authors. Both investigators and subjects used the same scheme. Moderate and total regrowth constituted a ‘cosmetically acceptable response’. We also considered ‘recurrence or relapse’ the worsening of the previous condition.

Results
A total of 54 patients with AA universalis participated in the survey (three patients under 40 kg: two girls and one boy; 51 patient over 40 kg: 27 women and 24 men). All but three patients (two women and one girl with blue eyes) had dark eyes (brown or black). Forty subjects finished the study while four subjects from the treated group withdrew for different reasons non-related to latanoprost: one case of worsened diabetes at 6 months (46-year-old male patient) and another case of arterial hypertension at 9 months (52-year-old male patient), both related to steroidal treatment, and two cases of voluntarily withdraw for lack of response at 6 months (23-year-old female patient and 31-year-old female patient).

The control group consisted of 10 patients (three females and seven males, with a mean age of 35.8 years; range 18–46), who refused treatment with latanoprost. The wash-out period for other medications was the same in the control and the study group. There were no children in the control group. Subjects in the control group received treatment in scalp and eyebrows following the protocol of our Unit.

The treatment group was comprised of 44 patients (18 males and 26 females), with a mean age of 30.9 years (range 9–54). Three patients were children less than 14 years of age but with a weight greater than 40 kg (two girls and one boy). There were no patients with glaucoma in the treated group. Subjects reported complete compliance of treatment. Three men had difficulties applying the drop in the free border of lids and they put it on their conjunctiva, then closed their eyes and then spread the fluid across the border of their lids. These patients were reviewed by an Ophthalmologist on each 3 months.

The results of eyelash regrowth in treated subjects are shown in Fig. 1. Complete regrowth was shown in 17.5% of the subjects (Fig. 2) and 27.5% had moderate regrowth (Fig. 3), 30% had slight regrowth and 25% showed no response after 2 years of treatment. The majority of patients with cosmetically acceptable regrowth were very satisfied with the treatment and the response was maintained throughout the study period. The investigators’s opinion agreed with the satisfaction of the patient in the majority of cases. The average time needed to induce eyelash regrowth was from 3 to 6 months. Eyelashes did not appear in subjects of the control group. Therefore, the regrowth, in our opinion, was not caused by intralesiona steroids or spontaneous regrowth that can be observed in patients with AA. We did not find any differences in the response between patients who used latanoprost in their eyelid margins and patients who applied a drop of latanoprost in

![Figure 1](image-url)
their conjunctiva, although it cannot be considered statistically significant because the sample size was short.

We did not find any difference between the response to intraleisional injection of TAC in eyebrows and scalp in study and control groups. All the patients with complete response to latanoprost were in the group of complete response to TAC in eyebrows in the study group but patients with moderate and slight responses to latanoprost showed more regrowth in eyelashes than in eyebrows. Therefore, the response does not seem to correlate with TAC injections.

Latanoprost was well tolerated and we did not observe any hyperpigmentation at eyelid or iris or increased number of visible hairs in canthal area despite the continued use of the drug. We observed that the newly appeared eyelashes grew in different directions\(^3\) in all patients to a greater or lesser extent (Fig. 4).

Some subjects lost some eyelashes during the study despite using latanoprost. Recurrences occurred in 17.5% of the subjects, mainly in the slight response group. The only case of recurrence in the moderate response group showed later regrowth during the following 3 months. In all cases, recurrences were transient and eyelashes reappeared during the 2 years in which the patient was still applying the drug (Fig. 5).

**Comment**

Latanoprost is a prostaglandin F-2\(\alpha\) analogue that is used in the treatment of open angle glaucoma. Since 1996, when it was introduced for the treatment of glaucoma, several side effects have been reported: irreversible hyperpigmentation at iris and eyelid, conjunctival hyperaemia, uveitis, eyelash curling, increased number, thickness and pigmentation of lashes and regional skin.\(^3,4\)

Prostaglandin F receptors are expressed in all ocular tissues.\(^5\) The eyelash hair follicles also have a cell population that expresses these receptors in the dermal papilla and outer root sheath. These cells might be the target of latanoprost and hypertrichosis could be induced by several mechanisms.\(^6\) Studies report that the average time needed to induce hypertrichosis varies from 2 or 3 days to several weeks. Notwithstanding, Stecchi \etal.\(^7\) showed no hypertrichotic effect in patients who had applied latanoprost for 6 months.

In one reported case of a 53-year-old woman with eyelash alopecia caused by allergic reaction to ibuprofen, complete eyelash regrowth occurred after applying latanoprost for 8 weeks as a part of her glaucoma treatment.\(^8\) There are very few reports of latanoprost being used in the treatment of AA. Mehta \etal.\(^9\) reported that an 11-year-old girl with AA who

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**Figure 2** Total regrowth in a patient with eyelash alopecia areata (AA). (a) Basal visit; (b) at 3 months; (c) at 6 months.

**Figure 3** A case of moderate regrowth. (a) Basal; (b) at 3 months; (c) at 6 months; (d) at 12 months and (e) at 24 months.
was treated with topical latanoprost once a day developed new eyelashes eight weeks after she started the treatment. Nevertheless, Ross et al.\textsuperscript{10} reported no significant regrowth in eyebrow AA (not eyelash AA) using latanoprost drops twice a day for 12 weeks.

In this study, 45\% of patients with bilateral eyelash AA demonstrated acceptable responses using latanoprost 0.005\% (50 \(\mu\)g/mL) ophthalmic solution once a day. However, there are some limitations in this study: this is not a blinded study, we did not compare the treated group with placebo and we did not randomize the subjects included. The ophthalmological explorations at baseline and quarterly when was considered necessary showed no kind of side effects, even in the three subjects who applied the drug directly to the eye before smearing it on their eyelids. Nevertheless, while no untoward side effects were observed with use of latanoprost in our study population, recently we have observed a case of diffuse eyelid hypertrichosis with direct application of drug to the eyelid margin after 3 and 6 months of treatment (Fig. 6).

![Figure 4](image1.png) **Figure 4** (a–e) Eyelashes with different directions and length in five cases with total and moderate regrowth using latanoprost.

![Figure 5](image2.png) **Figure 5** (a) Moderate regrowth after 9 months of using latanoprost; (b) recurrence at 12 months; (c, d): regrowth at 18 and 24 months after daily use of latanoprost.

![Figure 6](image3.png) **Figure 6** Men with bilateral eyelash alopecia that developed diffuse eyelid hypertrichosis. (a) Basal; (b) at 3 months; (c) at 6 months.
The good responses obtained suggest that this drug is effective in the treatment of this kind of AA. However, the new prosta-
glandin F agonists like bimatoprost and travoprost, which have shown to cause hypertrichosis more frequently than latanoprost,\(^{11}\) may prove to be yet more beneficial for the treatment of eyelash AA.

**Author contributions**
Prof Camacho had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Camacho-Martı´nez: study concept and design. Coronel-Pe´rez, Rodrı´guez-Rey, Camacho-Martı´nez: acquisition of data. Coronel-Pe´rez: drafting of the manuscript. Camacho-Martı´nez: critical revision of the manuscript for important intellectual content. Coronel-Pe´rez, Rodrı´guez-Rey, Camacho-Martı´nez: administrative, technical and material support. Camacho-Martı´nez: study supervision.

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None.

**References**