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Is Bimatoprost Effective In Increasing Satisfaction In Patients At Least 12 Years Old With Eyelash Hypotrichosis?

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Is Bimatoprost Effective In Increasing Satisfaction In Patients At Least 12 Years Old With Eyelash Hypotrichosis?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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ABSTRACT

OBJECTIVE: The objective of this systematic review is to determine whether or not bimatoprost 0.03% improves satisfaction in patients at least 12 years old with eyelash hypotrichosis.

STUDY DESIGN: Systematic review of three multicenter, double-masked, randomized, parallel group studies, all published in English between 2015 and 2016.

DATA SOURCES: All three studies used in this review were researched via PubMed and were published in peer-reviewed journals.

OUTCOMES MEASURED: Patient satisfaction was measured using the Eyelash Satisfaction Questionnaire (ESQ) in all three studies.

RESULTS: Wirta et al. (*J Clin Aesthet Dermatol*. 2015;8:11–20.) found a statistically significant relationship between bimatoprost 0.03% and satisfaction with a p=0.004. Borchert et al. (*Clin Ophthalmol*. 2016;10:419-29. doi:10.2147/OPTH.S89561) did not indicate a p-value but 78.2% of subjects treated with bimatoprost 0.03% and 65% of subjects in the control were found to have an increase in satisfaction of eyelash growth at the end of the study. The study conducted by Glaser et al. (*Br J Dermatol*. 2015;172(5):1384-94.) did not find a statistically significant relationship between bimatoprost 0.03% and satisfaction with p=0.25.

CONCLUSIONS: The results of these studies show that the objective question remains inconclusive in regard to increasing patient satisfaction after the use of bimatoprost 0.03% as only one out of the three studies showed a statistically significant relationship. Further studies should be conducted with researchers not employed by the pharmaceutical company who manufactures the product.

KEY WORDS: bimatoprost, eyelash

INTRODUCTION

Eyelash hypotrichosis is a condition that is characterized by reduced hair growth, specifically of the eyelashes. Hypotrichosis is often used interchangeably with the term alopecia areata which is a condition of the skin that causes sudden hair loss in various parts of the body.[1] The presentation of eyelash hypotrichosis is an inadequate amount of hair at the margin of the upper eyelids while alopecia areata presents as hair loss on the body, scalp, eyebrows or eyelashes. Eyelashes are considered terminal hair, in which the hair is coarse, thick and pigmented, versus vellus hair which is the soft, short and non-pigmented hair, such as those found on the face.[2] The function of eyelashes is very versatile. Eyelashes provide a barrier, protecting the eyes from foreign bodies and perspiration by triggering the corneal reflex if touched. Eyelashes are also cosmetically appealing, and the length of eyelashes signifies beauty and femininity in most cultures while increasing the attractiveness of a person.[2]

Causes of eyelash hypotrichosis include genetics, chemotherapy induced, advanced age or trauma to the face including trichotillomania.[2] Eyelash hypotrichosis is a common side effect among chemotherapy drugs. Since hair cells are rapidly dividing, chemotherapy drugs destroy those cells, causing hair loss.[3] The prevalence of eyelash hypotrichosis is unknown, although, chemotherapy induced hair loss, including eyelashes will be the result of approximately sixty-five percent of patients undergoing chemotherapy.[4] As stated previously, eyelashes have a physical and cosmetic component attached to them and eyelash hypotrichosis or alopecia areata may lead to a negative impact on the patient's quality of life including an impairment in psycho-social functioning as well as negatively affecting the self-image of a person.[5]

Unfortunately, the number of healthcare visits for eyelash hypotrichosis has not been identified; however, there is an estimated 2.4 million doctor office visits in the United States are

for alopecia areata.[6] The cost of eyelash hypotrichosis has not been identified, but the out-of-pocket costs associated with alopecia areata is approximately $1,354 per year.[7] This cost includes hair appointments, vitamins, insurance deductibles, office visits, transportation and wigs for patients with alopecia areata.[7]

To date, there is no known definitive treatment for eyelash hypotrichosis. Additionally, there is no known cure or FDA-approved treatments for alopecia areata. There are, however, off label uses for corticosteroids, calcineurin inhibitors, immunotherapies and hair-growth-stimulating solutions for alopecia areata. [8] Many patients have reported these treatments as ineffective while some patients could not tolerate the side effects, therefore, needing additional treatment options.[8] Corticosteroids are the most common type of medication prescribed for alopecia areata, which includes oral, topical and injectable. This treatment worked well for some patients, but many have stated that corticosteroids worked very little to none.[8] Fortunately, for patients with eyelash hypotrichosis, there is now an FDA-approved treatment, bimatoprost 0.03%. Bimatoprost is a synthetic prostamide F2 alpha analogue and its use for eyelash hypotrichosis was empirically discovered in patients being treated with bimatoprost for increased intraocular pressure in patients with open-angle glaucoma.[9] As stated previously, many patients reported the treatments above were ineffective for alopecia areata, but the same has not been reported for bimatoprost 0.03%.

OBJECTIVE:

The objective of this systematic review is to determine whether or not bimatoprost 0.03% improves satisfaction in patients at least 12 years old with eyelash hypotrichosis.

METHODS

This systematic review analyzes three randomized control trials (RCTs) to assess patient satisfaction of bimatoprost 0.03% for the treatment of eyelash hypotrichosis compared with a vehicle in patients at least 12 years old.

All three articles were found through PubMed using the key words bimatoprost and eyelash. The articles selected for review were published in English and were published in peer-reviewed journals. Each article was selected based on its relevance to the clinical question and if they included patient orientated outcomes (POEMS). The inclusion criteria consisted of all articles being published in English and dated 2008 or later. Studies were excluded from this review if published in another language other than English, dated before 2008 or if bimatoprost was used for other indications. All three articles used p-value, EER, CER, ARR, NNT, ABI and RBI statistics. Please see Table 1 for the outline of demographics and characteristics of each study.

For this selective evidence-based medicine review, the author chose three randomized control studies (RCTs) that were selected, reviewed and analyzed based on population, intervention, comparison groups and outcomes measured. This review included a population of patients at least 12 years of age with idiopathic or chemotherapy induced eyelash hypotrichosis. The intervention in these studies involved an application of bimatoprost 0.03% ophthalmic solution to the margin of the upper eyelids. The patients receiving bimatoprost 0.03% were compared to the experimental group in which patients applied a vehicle to the margin of the upper eyelids. Each of the three studies measured the satisfaction of the patients in both the treatment and control group using the Eyelash Satisfaction Questionnaire (ESQ) which is a self-reported assessment of satisfaction.

Table 1. Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W /D	Interventions
Wirta[5] (2015)	Double blind RCT	130	≥ 18	≥ 18 yo w/ chemo-induced eyelash hypotrichosis Tx'd for Stage I-IIIA solid tumors w/ curative intent or rcv'd front-line tx for stage I - II DLBCL or HL; resolution of chemo related AE's except for hair loss; completed chemo 4-16 wks prior to study baseline; Had Eastern Cooperative Oncology group performance status of 0 or 1 & no evidence of mets or anticipated need for further chemo during study period	If they did not have a GEA score of 1 or 2, or if they did not have a ESQ score of 1 or 2 in certain categories. Subjects w/ unequal GEA scores for the RT and LT eyelashes, uncontrolled systemic disease or known ocular disease or abnormality.	7	Bimatoprost 0.03%
Borchert[10] (2016)	Double blind RCT	65	12-17	12-17 yo Healthy, Chemo or alopecia areata induced eyelash hypotrichosis; GEA score 1-3, visual acuity of 20/100; IOP ≤20mmhg; completed chemo 4 wks; chemo related AE's resolved/managed;	Positive Preg test; Gross asymmetry of eyelash prominence, uncontrolled systemic disease, trichotillomania or known ocular disease	1	Bimatoprost 0.03%
Glaser[11] (2015)	Double blind RCT	130	≥ 18	≥ 18 yo w/ score of 1-2 on GEA and ESQ; visual acuity of 20/100; IOP ≤20 mmhg; Inadequate eyelashes after chemo, tx for stage 1,2 or 3a cancer; last chemo was 4-16wks prior to baseline, considered ca free	Any eye disease or abnormality; hx of eye surgery	14	Bimatoprost 0.03%

OUTCOMES MEASURED

The outcomes measured in this selective evidence-based review were based on patient-reported questionnaires that were completed throughout and at the end of the bimatoprost 0.03% ophthalmic treatment.

In all three studies, patient satisfaction was measured using the Eyelash Satisfaction Questionnaire (ESQ). This is a patient-reported outcome measure that consists of 23 questions measured on a five-point scale. The scale included: 1- very much disagree, 2- disagree, 3- neutral, 4- agree, 5- very much agree. The 23 questions consisted of three domains which assessed various outcomes. The Wirta et al.[5] study focused on Domain 2 of the ESQ which assessed satisfaction with subjective attributes of eyelashes such as attractiveness, confidence and professionalism.[11] In this study, subjects were assessed with the ESQ before and after treatment. In a pediatric study by Borchert et al.,[10] only subject's aged 12-17 assessed their eyelashes with the ESQ as well. These subjects were evaluated at screening and months 1-5 of the study.[10] The last study by Glaser et al.[11] also measured patient satisfaction using the ESQ five-point scale Domain 2 before and after treatment.

RESULTS

This systematic review analyzed three randomized control studies to determine if bimatoprost 0.03% can increase satisfaction in patients at least 12 years old who have eyelash hypotrichosis. Each study consisted of a treatment group with bimatoprost 0.03% applied to the upper eyelid margins and a control group with a vehicle applied to the upper eyelid margins.

In the Wirta et al.[5] study, 130 patients with chemotherapy induced eyelash hypotrichosis were randomized with a web response system of an automatic interactive voice to either bimatoprost 0.03% (n=96) or a vehicle group (n=34). Patients, investigators and their staff were

blind to treatment assignment for the entire treatment period. Each subject was asked to place one drop of treatment or vehicle to a sterile, single-use applicator and then brush it on the upper eyelid margins once every evening. Excluded subjects were those with unequal Global Eyelash Assessment (GEA) scores for the left and right eyelashes, uncontrolled systemic disease or known ocular disease. Eye examinations such as intraocular pressure and iris color were conducted throughout the study. Conjunctival hyperemia was the most common adverse reaction of bimatoprost, followed by punctate keratitis, upper respiratory tract infection and eye pruritus, respectively. The study reported one death following the first administration of bimatoprost, but investigators attribute this due to an elective surgery and not related to the study medication.[5]

Wirta et al.[5] compared baseline and 6 months ESQ Domain 2 scores of subjects and increased satisfaction was considered if there was a ≥ 3-point improvement. At the end of the 6 months, Wirta et al.[5] found that there was an increase in satisfaction in 46.9% (46 patients) versus 18.2% (6 patients) for bimatoprost 0.03% and vehicle, respectively. The p-value was considered to be statistically significant at p=0.004 and NNT was calculated to be 4. Table 2 includes detailed calculations for this study.

Table 2. NNT Calculations For Satisfaction of Bimatoprost 0.03% To Improve Eyelash Hypotrichosis By Wirta et al.[5]

CER	EER	Relative Benefit Increase (RBI)	Absolute Benefit Increase (ABI)	Number Needed To Treat (NNT)	P-value
0.182 = 18.2%	**0.469= 46.9%**	**1.576**	**0.287**	**4**	**0.004**

Borchert et al.[10] studied 62 pediatrics aged 12-17 years old with eyelash hypotrichosis who were randomized 2:1 to either receive bimatoprost 0.03% (n=42) or vehicle (n=20). Patients, investigators and their staff were blind to treatment assignment for the entire treatment

period of 5 months. Subjects or their guardians were instructed to place one drop of treatment or vehicle to a sterile, single-use applicator and then brush it on the upper eyelid margins once every evening. Subjects were excluded from this study if there was gross asymmetry of eyelash prominence between right and left eyes, uncontrolled systemic disease, suspected or known trichotillomania or ocular disease appreciated. Adverse effects were monitored at each study entry and physical exams performed including eye examinations of IOP, visual acuity and iris color at baseline, and months 1 and 4.[10]

This study used Pearson's chi-square and dichotomized the ESQ score responses into two groups: satisfied and not satisfied/neutral.[10] The results showed that mean scores improved from baseline in both treatment groups for satisfaction.[10] This study showed that 78.2% (33 patients) of subjects in the treatment group were satisfied versus 65% (13 patients) of subjects in the control group. There was no p-value calculated for subject satisfaction and NNT was calculated to be 8. Table 3 includes detailed calculations for review.

Table 3. NNT Calculations For Satisfaction of Bimatoprost 0.03% To Improve Eyelash Hypotrichosis By Borchert et al.[10]

CER	EER	Relative Benefit Increase (RBI)	Absolute Benefit increase (ABI)	Number Needed To Treat (NNT)	P-value
0.65 = 65%	**0.785= 78.5%**	**0.207**	**0.135**	**8**	**Not calculated**

Glaser et al.[11] analyzed 129 subjects with chemotherapy-induced eyelash hypotrichosis who were randomized to either receive bimatoprost 0.03% (n=96) or vehicle (n=33). All patients, investigators and staff were blind to treatment assignment for the entire study. Subjects were instructed to place one drop of treatment or vehicle to a sterile, single-use applicator and then apply it to the upper eyelid margins once every evening. In this study, subjects were excluded if they had any eye abnormality or disease or a history of eye surgery. Primary efficacy

was based on at least a 3-point increase from baseline in the total score for ESQ domain 2. Glaser et al.[11] found an increase in satisfaction in 47.9% (46 patients) versus 36.4% (12 patients) for bimatoprost 0.03% and vehicle, respectively. The p-value was considered to not be statistically significant at p=0.25 and NNT was calculated to be 9. Table 4 includes detailed calculations.

Table 4. NNT Calculations For Satisfaction of Bimatoprost 0.03% To Improve Eyelash Hypotrichosis By Glaser et al.[11]

CER	EER	Relative Benefit Increase (RBI)	Absolute Benefit Increase (ABI)	Number Needed To Treat (NNT)	P-value
0.365 =36.5%	**0.479 =47.9%**	**0.315**	**0.115**	**9**	**0.25**

DISCUSSION

This systematic review analyzes the results of bimatoprost 0.03% for patients with eyelash hypotrichosis. Only one of the three studies show statistical significance for the use of bimatoprost 0.03% in patients with eyelash hypotrichosis. In the Wirta et al.[5] study, p= 0.004 is statistically significant and suggestive of increased satisfaction of eyelash growth with the use of bimatoprost 0.03%. In the Borchert et al.[10] study, no p-value was calculated, but 78.2% of subjects in the experimental group and 65% of subjects in the control group expressed satisfaction after treatment of bimatoprost 0.03%. These percentages were used to calculate the NNT. Based upon no provided p-value and the small NNT compared against a small sample size, there is not enough information to conclude whether or not this study led patients to increased satisfaction. On the other hand, the Glaser et al.[11] study was found to not be statistically significant with p=0.25.

Currently, bimatoprost 0.03% is marketed by only one pharmaceutical company, Allergan which is sold under the name, Latisse. Since Latisse is used for cosmetic purposes

only, insurance companies do not cover the product. Patients can purchase Latisse out of pocket with a prescription for a monthly cost of approximately $120.00.[12] At this cost, most patients may not be able to afford this monthly price. According to Banaszek,[12] patients with glaucoma using Lumigan, should not use Latisse as it would double the dose of bimatoprost 0.03%. This is because Lumigan and Latisse are the same exact drug, just packaged and administered differently.[12]

Acknowledging limitations to these studies is very important. In all three studies, subjects were instructed to apply bimatoprost 0.03% every evening in the same fashion. If subjects did not follow these instructions closely, the results could have been skewed. In the Wirta et al.[5] study, 125 subjects out of a total of 130 subjects had a history of breast cancer. Since most subjects in the Wirta et al.[5] study were found to have breast cancer, the results of this study may have had a different outcome if the type of cancer was more diverse. Additionally, there is overlap between the researchers for all three studies and this may limit the generalizability of the results.

CONCLUSIONS

The results from this selective evidence-based review indicate that bimatoprost 0.03% increases patient satisfaction in only one out of the three studies. Based upon this, the answer to the objective question remains inconclusive in regard to increasing patient satisfaction and further research should be conducted. The outcomes could have been affected by drug adherence and correct application of bimatoprost 0.03%. Subjects or their parents were expected to apply the treatment every evening in a specific fashion. The outcomes may have also been affected by the researchers as each study disclosed that they were consultants, investigators or employees of Allergan, the pharmaceutical company that produces Latisse. Future research of

bimatoprost 0.03% for eyelash hypotrichosis should be conducted without any affiliation to Allergan pharmaceuticals to eliminate any bias that may occur.

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