Research Article

Topical Bimatoprost (0.03%) Versus Topical Mometasone Furoate (0.1%) in Treatment of Alopecia Areata

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Abstract

Background: Alopecia areata is a prevalent, immune-mediated disease that targets anagen hair follicles in gentically predisposed individuals. Their are various treatment modalities of different Ecco Ay and safety for treatment of this chronic ailment. Bimatoprost, a prostamide analog have been recognised with the potential of increaed hair growth and can be used as an alternative treatment option.

Objective: To compare the efficacy and safety of bimatoprost 0.03% with mometasone furoate 0.1%in the treatment of AA involving eyebrows, scalp and beard.

Methods: This was a randomized single-blinded clinical trial done in the Dermatology Outpatient Department of Nishtar Hospital Multan (NHM). The duration of the study was from August 2020 to March 2021. 60 patients with patchy AA having upto 5 patches with a maximum diameter of 5cm in longest dimension involving eyebrows, scalp and beard were included in the study and were randomly assigned to either Group A (topical bimatoprost 0.03% solution twice daily) or Group B (topical mometasone furoate 0.1% cream once daily) for a period of 3 months. Patients were called for assessment monthly (every 4 weeks) and clinical photographs of the site of treatment were taken. Response to the treatment was assessed clinically by subjective improvement of hair growth at the site of hair loss by two physicians as no, mild, moderate and good hair re-growth depending on the percentage of hair re-growth. The data was analyzed through SPSS version 21.

Results: At the end of 3 months of treatment, 29 out of 30 (97%) patients of Group B responded to the treatment, while 24 out of 30 (80%) Group A patients responded to the treatment. The response to both treatments was found statistically significant and the p-value was 0.000. Group B treated patients were better in their percentage of hair re-growth, speed of recovery, patient satisfaction and were devoid of any documented side effects.

Conclusion: Bimatoprost 0.03% solution (topical), owing to its safety and efficacy represent a better therapeutic option for the treatment of AA involving eyebrows, scalp and beard.

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Introduction:

Alopecia Areata (AA) is a prevalent, chronic inflammatory disorder that causes non-cicatricial alopecia. This autoimmune disease primarily targets anagen hair follicles in genetically predisposed individuals.[1] Both males and females are affected by this disease without any age or race preponderance[2] and it has a psychological impact on the patient especially if the

patient is female[3] or hairs of the facial area are affected. Alopecia Areata clinically manifests as well-circumscribed, skin-colored patches of hair loss. Hair loss can be localized or diffuse, most often it affects the scalp and beard but any hair-bearing area can be involved. Various treatment modalities have been elucidated as a treatment option for alopecia areata but none of them is generally demonstrated as curative or preventive. Among many, topical and intralesional steroids are the mainstay of treatment used for Alopecia areata.[4] The major drawback of long-term use of topical and systemic steroids is their cutaneous and systemic side-effects when used for a long duration.[5] Bimatoprost is an FDA-approved drug, initially recommended for the treatment of ocular hypertension and open-angle glaucoma.[6] It is a prostamide F2α analog with the potential of increased hair growth. It is believed that it directs its effects by stimulating the prostamide receptors within the follicles themselves leading to changes in the hair cycle by stimulating follicles to enter anagen earlier and remain there for longer.[6] Accordingly, several types of studies have been done over the years to explore the potentials of this remedial methodology. Anyhow, the results were conflicting and were generally revolved around AA of the eyelashes.[7-11] In a recent study, the role of bimatoprost is postulated as more efficacious and safe as compared to conventional therapies in the treatment of scalp Alopecia Areata.[12]

Previously, a national comprehensive review have documented that latanoprost can be an efficient agent in scalp Alopecia Areata13 but no study exploring the role of bimatoprost in alopecia areata has yet been conducted in Pakistan. Therefore, motivated by the work of Zaheret al[12] and to treat this distressing disease in an effective way, a trial to know the safety and efficacy of topical bimatoprost (0.03%) in comparison with topical mometasone furoate (0.1%) in the treatment of limited patchy AA involving eyebrows, beard and scalp has been conducted in Multan.

Methods:

After approval from the Ethical Review Board of the Hospital, A randomized single-blinded clinical trial in which patient was unaware with the type of treatment given to them in each group in the Dermatology Outpatient Department of Nishtar Hospital Multan (NHM). The duration of the study was from August 2020 to March 2021. Before enrolling the patients in the study, an informed written consent was obtained from all patients.

60 patients were selected by using epi-info software with p=0.6011, out of which 33(55.0%)were males, and 27(45.0%) were Females aged 5–45 years, with AA patches located on the scalp, eyebrows and beard were enrolled in this study. All recruited patients had a maximum of 5 patches of hair loss with a maximum size of individual patches up to 5cm in longest dimension. Patients having alopecia universalis, alopecia totalis, ophiasis and those who had received treatment for AA within[6] weeks prior to the study were excluded. Patients with associated systemic and/or other dermatological diseases (thyroid disease, atopic eczema on the basis of history and clinical examination) and those having known sensitivity to bimatoprost or mometasone furoate were not included in the study. The patients who came with spontaneous hair re-growth at the site of hair loss, were also excluded.

After detailed history taking and clinical examination, patients were enrolled and all the information was recorded on pre-designed Proforma. The diagnosis of AA patches was based on clinical grounds.

60 patients of AA were selected for this study who met the inclusion and exclusion criteria and freely gave their informed consent. They were divided into two groups, each comprising of 30 patients. Randomization was done according to the serial number. Patients were randomly selected for Group A and Group B regardless of their age and gender. Group A patients were instructed to apply topical mometasone furoate 0.1% cream, over the affected area once a day for 3 months duration. Patients of Group B were advised to apply 1 to 2 drops of 0.03% bimatoprost solution (topical) with a cotton-tipped applicator over the affected area twice a day for a period of 3 months.

Patients were called for assessment monthly (every 4 weeks) for a period of 3 months and each time clinical photographs were taken. Response to therapy was assessed clinically by subjective improvement of hair re-growth at the site of hair loss. All assessments were performed by two physicians who were blind to the therapy by comparing serial photographs of patients with their pre-treatment photographs. Hair re-growth was

recorded as No growth if no changes in the size of patches or further loss have occurred, Mild if less than 30% hair re-grow, Moderate if 30 to 50% hair re-grow, Good if more than 50% hairs re-grow. At the end of 3 months, patients were inquired about their satisfaction regarding efficacy of the treatment. Side effects were cautiously recorded for each group. The primary data was collected from patients and ana-lyzed through SPSS version 21. The frequencies, per-centages, mean and standard deviation were used to describe the data. The t- test was used to check the effec-tiveness of treatments given to both groups at 5% level of significance. The confidence interval for this study is set at 95%. The calculated p value ≤ 0.05 will be con-sidered as significant.

Results:

About 100 patients with hair loss due to Alopecia Areata visited the outpatient department, of which eighty gave consent and twenty were excluded depending upon exclusion criteria. In current study 60 patients, 33 males (55%) and 27 females (45%) were enrolled. There was a preponderance of age group 16-26 years (23, 38% cases), followed by 27-37 years (18, 30% cases), 5-15years (15, 25%) and more than 38 years (4, 6.7% cases) of age with mean and S.D 21.87± 10.39. All the enrolled participants successfully completed the study.83% of patients were residents of Multan, others were from nearby areas like Khanewal, Vehari, etc.

The characteristics of Alopecia Areata patches are described in Table 1.

Table 1: *Characteristics of Alopecia Areata Patches.*

Variable		Frequency	Mean ± S.D
Disease Duration	1-4 months	44 (73.3%)	1.30 ± 0.53
	5-10 months	14 (23.3%)	
	>10 months	(3.3%)	
Site of Hair loss	Scalp	40 (66.7%)	1.90 ± 1.33
	Beard	16 (26.7%)	
	Eyebrows	4 (6.6%)	
Number of Patches	1	25 (41.7%)	2.07 ± 1.20
	2	17 (28.3%)	
	3	12 (20%)	
	4	1 (1.7%)	
	5	5 (8.3%)	

Hair re-growth after 1 Month of treatment was seen in 16 out of 30 (53%) patients of group A, all were having mild hair re-growth and those in group B showed hair re-growth in 28 out of 30 (93%) patients (13, 43% mild re-growth, 14, 47% moderate hair re-growth, 1, 3% good hair re-growth). After 2 months of treatment, 23 out of 30 (77%) cases of corticosteroid cream treated patient showed hair re-growth, while 29 out of 30 (97%) cases of bimatoprost 0.03% solution showed hair re-growth. After completion of therapy at 3 months, 24 out of 30 patients (80%) in group A were documented as having hair re-growth out of which 9 (30%) patients were having mild hair re-growth, 7(23%) moderate hair re-growth and 8 (26%) good hair re-growth. Group B treated patients showed hair re-growth in 29 out of 30 (97%) patients out of which 4 (13%) cases showed mild hair re-growth, 5 (16%) moderate and 20 (66%) cases were documented with good hair re-growth. Percentages of group B treated patients were higher than group A and patient of group B showed more responders with higher percentages of hair re-growth at end of 1 month which demonstrates the early response of therapy, results were statistically significant (Table 1).No hair re-growth was documented in 6 out of 30 (20%) AA patients treated with topical corticosteroid cream and in 1 out of 30 (3%) AA patients treated with topical bimatoprost 0.03% solution at the end of 3 months (Table 1).Hair re-growth in Alopecia Areata patches after 3 months of treatment depending upon the site of involvement is described in Table 3.

As regards side effects, 3 out of 30 (10%) patients belonging to group A reported either burning or itching after application of the medication on the site of hair loss, while 4 out of 30 (13%) patients of group A were demonstrated either having mild atrophy and/or hyperpigmentation reported by the examining physician. However, no side effects were stated in any of the group B treated patients. At the end of treatment (3 months), patients of group B were more satisfied (97%) than group A (80%). We applied t test to check the efficacy of treatment given to Group A and Group B after one month, two months and three months. The p value obtained for the treatment given to both groups after one month is p=0.001 with confidence interval [1.80, 2.20], the p value obtained for the treatment given to both groups after two month is p=0.001 with confidence interval [2.44, 2.96] and similarly the p value obtained for the treatment given to both groups after three month is p=0.000 with confidence interval [2.74, 3.30] which are significant at 5% level of significance. It denotes the fact that both topical treatments are effective for the treatment of alopecia areata but the percentage of hair re-growth and speed of recovery

Table 2: *Treatment effectiveness in Group A & Group B*

		No	Mild	Mode-rate	Good	P-value
1 Month	Group A	14 (47%)	16 (53%)	0	0	0.001
	Group B	2 (7%)	13 (43%)	14 (47%)	1 (3%)	0.001
2 Month	Group A	7 (23%)	13 (43%)	10 (33%)	0	0.001
	Group B	1 (3%)	4 (13%)	10 (33%)	15 (50%)	0.001
3 Month	Group A	6 (20%)	9 (30%)	7 (23%)	8 (26%)	0.000
	Group B	1 (3%)	4 (13%)	5 (16%)	20 (66%)	0.000

is better in Group B treated patients(Table 2).

It was also noticed that all bimatoprost treated patients had pigmented and thick hairs at the site of hair loss (Figure 2), while those of group A (mometasone furoate) treated patients had thin, white to slightly pigmented hairs (Figure 1) that later became pigmented.

Figure 1. *A 25- year-old male patient with beard AA treated with mometasone furoate 0.1% cream (Group A). A. Alopecia Areata patch at baseline B. Alopecia Areata patch after 3 months of treatment.*

Fig.2. *A 35- year-old male patient with beard AA treated with bimatoprost solution (Group B). C. Alopecia Areata patch at baseline D. Alopecia Areata patch after 3 months of treatment.*

Table 3: *Hair Re-growth after 3 months of treatment*

		Scalp	Eye Brows	Beard
Group A	No	4(19%)	0	2(29%)
	Mild	5(24%)	1(50%)	3(43%)
	Moderate	5(24%)	0	2(29%)
	Good	7(34%)	1(50%)	0
Group B	No	1(6%)	0	0
	Mild	3(16%)	0	1(12%)
	Moderate	3(16%)	0	2(23%)
	Good	12(64%)	2(100%)	6(67%)

Discussion:

Despite the availability of various treatment modalities for the management of AA, it remains hard to treat. Uptill now, topical and injectable corticosteroids are recommended as first line treatment for limited AA both in children and adults[4,14,15] but the side effects with the use of corticosteroids (topical or intralesional) are diverse[5,16] and intrigue a researcher to search such therapeutic options which are effective and devoid of adverse effects. To our knowledge, this is the first study in our area evaluating the potentials of bimatoprost 0.03% in the treatment of AA.

Topical bimatoprost is FDA recommended first line remedy for the treatment of eyelash hypotrichosis.[6,17] Although, exact mode of action by which it causes hypertrichosis is not yet clear but it is hypothesized after many studies conducted in mice that it targets the PG receptors on the hair follicles and influences the hair growth cycle by increasing the number of hair follicles in anagen phase, reducing the telogen and late catagen phase follicles and by lengthening the interval of the anagen phase.[6,9]

In present study, if the same postulated effects of Bimatoprost that were used for eyelash hypotrichosis if applied over the hair follicles present on the scalp, beard and eyebrows, it could be able to produce significant proportion of hair regrowth and it was documented in the group B patients treated with bimatoprost as high percentage of hair re-growth on eyebrows, scalp and beard as compared to group A, mometasone furoate treated patients. This much good response of bimatoprost is also supported by a recent study on rabbit eyelashes which showed that bimatoprost increases the number of eyelashes within the same hair follicle.[18] These animal studies alsodenoted the expanded lash thickness and

darkness due to the bimatoprost induced melanogenesis and increased breadth of the hair bulb and dermal papilla[6] and documented in current study by production of pigmented hairs with bimtoprost in all patients at 1st month follow up after starting therapy while the hairs were white to slightly pigmented in corticosteroid treated patients. Effectiveness of Bimatoprost by inducing high percentage of hair re-growth on eyebrows[10,19,20] and scalp[11,21] was supported by other investigators. No data regarding prostamide analog directed studies on beard is available but the results are comparable in both effectiveness and safety with the results of the same drug used for other areas.[9,10,12,17,19-21]

A recent study conducted in India by Sonalietal[11] suggested that prostaglandin analogue (latanoprost 0.005%), which is a drug closely related to prostamide analog is less effective but safe than topical corticosteroids (betamethasone dipropionate 0.05%). This difference can be due to the use of different drug because latanoprost is less effective in causing hypertrichosis than bimatoprost[22] because for being pharmacologically active latanoprost needs to be converted in to an active metabolite, which explains its low efficacy. This less effectiveness of latanoprost is also supported by a previous study which documented that latanoprost is not effective is the treatment of alopecia areata involving eyelashes and eyebrows.[23]

Some of former studies of the same drug (Bimatoprost) on AA involving eyelashes have inconsistent results suggesting that drug is ineffective.[7,8] There are many possibilities why these differences occurred. First, patients enrolled in these studies had more severe disease with more than 50% involvement of the area, suggesting that drug is only efficacious for limited AA. Second, drug application frequency was low. Third, as drug was instilled into the eyes[9], drug may wash away or spill out which is not possible when drug is applied with an applicator over the eyebrows, scalp and beard.

Bimatoprost solution (0.03%) did not show any side effects during the whole duration of the current study which obviously accentuates its high safety profile. These results are in accordance with a number of previous researches in which no side effects were documented with use of prostamide analogue for treatment of AA on scalp[12] and eyebrows.[20,24] Although, a few transitory side effects were documented by other investigators like slight skin hyperpigmentation[25], mild pruritus but no hyperpigmentation[10] where eyebrow hypotrichosis was treated with topical bimatoprost and conjunctival erythema, eye irritation[7,26] were reported with treatment of eyelash AA, when drops were instilled into the eyes. Only drawback to the treatment with bimatoprost is the cost of the bimatoprost solution which is many times higher than the mometasone furoate cream.

So, this trial has revealed that the use of prostamide analog in AA is beneficial in many ways. First, by inducing higher percentage of hair re-growth obtained at the end of 1st, 2nd and 3rd month than topical corticosteroid. Second, the Speed of hair re-growth and patients satisfaction was better with group B treated patients and third, no side effects were reported with the use of topical bimatoprost solution. Due to this much effectiveness and safety of topical bimatoprost, it should be a preferred therapeutic agent for the treatment of limited patchy AA.

Our study also has a few limitations, the duration of the study was short and no post-treatment follow-up was done to assess the relapse of the disease in successfully treated patients. Another limitation was we used the hair re-growth percentage by subjective improvement in the area with hair loss as the primary outcome. We did not assess the Severity of the Alopecia Tool (SALT) score which is a more widely used and validated measure of assessing hair loss in alopecia areata.

Conclusion:

So, the current study advocates that although, both treatments are effective and can be used in treatment of AA but treatment with Bimatoprostis much more efficacious and have high safety profile in term of showing higher percentage of hair re-growth, speedy recovery, patient's satisfaction and no side effects. That's why it should be preferred over mometasone furoate for the treatment of patchy AA regardless of the site of involvement.

Further such studies are necessary with large sample size and long term follow up after completion of treatment to enlighten the safety and efficacy of Bimatoprost in treatment of AA.

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