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Original Research Article

Randomised controlled study for comparing the efficacy of tretinoin 0.05% cream alone versus tretinoin combined with microdermabrasion in adult patients of alopecia areata

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ABSTRACT

Background: Alopecia areata is non-scarring autoimmune disease. It is characterized by discrete patches of non-scarring hair loss and may involve scalp, eyebrows, eyelashes, beard, axillary hair and pubic hair. Therapeutic armamentarium is expanding with detailed elucidation of patho-mechanisms and emergence of new drugs like janus kinase inhibitors.
Methods: An interventional prospective study was conducted on the patients which were randomized into two groups (19 patients each) by lottery system, patients of group A were treated with tretinoin 0.05% cream whereas in group B patients microdermabrasion (MDA) was performed at baseline, 3rd, 6th, 9th and 12th weeks in addition to the application of tretinoin 0.05% cream daily.
Results: The mean GPI% in Group A was 6.26±5.13 and group B was 32.63±15.29% which is significantly higher at the end of 2 weeks (p=0.001). At 8 weeks, mean GPI in group A was 10.95±6.79 and in group B was 51.42±12.42 which was also significantly higher (p=0.026) as compared to group A. Similarly mean VAS in group A at 2 weeks and 8 weeks (0.62±0.51 and 1.1±0.67) and in group B was (3.27±1.53 and 5.16±1.26) which was significantly higher with difference in p value at 2 weeks between the two groups was p=0.001 and at 8 weeks was p=0.017. There was significant change in GPI and VAS at 8 weeks, in group A as compared to group B.
Conclusions: This study revealed that tretinoin was more effective than the combination with MDA.

Keywords: Alopecia areata, Tretinoin, MDA

INTRODUCTION

Alopecia areata (AA) is a common non-scarring autoimmune disease with prevalence of 0.1-0.2% in the general population. It accounts for 0.7-3% of the consultations seen in dermatological outpatient settings.[1] It is characterized by discrete patches of non-scarring hair loss and may involve scalp, eyebrows, eyelashes, beard, axillary hair and pubic hair. Rarely, it can present as alopecia areata universalis, the most severe variant wherein there is loss of all the terminal hairs of the body. Although, primarily it affects the terminal hairs but there may be associated nail findings such as pitting, longitudinal striations and beau's lines.[2] There are known

association of AA with other autoimmune disorders like diabetes mellitus, thyroid disorders, vitiligo etc. Spontaneous remission has been observed in 34-50% of patients within a year but most people seek active treatment due to associated anxiety and cosmetic concern.[4] Therapeutic armamentarium is expanding with detailed elucidation of patho-mechanisms and emergence of new drugs like janus kinase inhibitors. The newer agents are costly and find its role in usually refractory course of disease. Intralesional corticosteroids still remain the first line treatment in most cases with limited disease but dark side of the treatment is associated pain dyspigmentation, telangiectasia and atrophy, making them less desirable to both patients and physicians.[3,5] There is still a scope to explore time tested topical therapies in limited AA that has proven safety and efficacy in other autoimmune dermatoses. One of such agents are topical retinoids. Recent studies from the past have revealed successful use of topical tretinoin in contributing significant regrowth of hairs in AA of pediatric age group. Topical retinoids are the drugs with anti-inflammatory, immunomodulatory and counter irritant properties with better safety profile as compared to other irritants and topical steroids. On the basis of encouraging results of topical tretinoin in pediatric patients, we decided to evaluate its usefulness in adult AA. The absorption of the drug is less in adults as compared to pediatric population and thus therapeutic effects may be diminished, so we intended to achieve better transdermal delivery of the drug by means of MDA.[6] This study was aimed to compare the efficacy of tretinoin 0.05% cream alone verses 0.05% tretinoin cream combined with MDA in adult patients of AA.

METHODS

This was an interventional controlled prospective study. The participants were recruited over a period of 1 year (from 1 Jan 2018 to 31 dec 2018) at the OPD of tertiary care centre. This study comprises patients of AA, who were treatment naive and duration of disease of at least 1 month. Patient of both gender and age above 18 years, who has given informed consent were included in the study. History of chemoradiation for any cause, patient on any therapy for AA in last 1 month, patient with extensive AA (>5 patches of alopecia areata) and with known sensitivity to tretinoin were excluded from the study. Randomized sampling was done and patients were enrolled in the study until reaching the calculated sample size of 38. The patients were randomized into two groups (19 patients each) by lottery system, in patients of group A MDA was performed at baseline, 3rd, 6th, 9th and 12th weeks in addition to the application of tretinoin 0.05% cream daily whereas patients in group B were treated with tretinoin 0.05% cream alone.

Detailed history, clinical examination, dermoscopy and photographic documentation were carried out for all patients at baseline according to predesigned performa. Relevant laboratory investigations for screening associated comorbidities were carried out when indicated. Trichoscopic findings and hair counts in the treated area were recorded at the subsequent visits at 2nd, 4th, 6th and 8th weeks. Assessment of all the patients was done by trichoscopic findings, visual acuity score (VAS) and global photographic index (GPI).

At the end of the study, results were compared in both groups. We used student's (unpaired) t test to compare the quantitative parameters between the groups. The difference of proportion was compared by chi-squared test. Fisher's exact test has been used to compare the categorical variables between 2 or more groups. P<0.05 was considered to be statistically significant.

RESULTS

We enrolled 38 patients in our study and divided them into two treatment groups, group A (Figure 1) received local application of tretinoin 0.05% cream daily with MDA done at every visit whereas group B (Figure 2) received tretinoin 0.05% cream daily for 8 weeks. Both groups were comparable in clinicodemographic profiles (Table 1). Mean age in both groups were statistically similar i.e., group A (38.89±15.34) years and in group B (33.05±12.02) years; (p=0.226) thus eliminating the bias of age on our treatment. There was male preponderance in our study with 27 males (71%) and 11 (29%) females. Mean number of bald patches in tretinoin with MDA was same i.e., 1.42±0.83 at 2 weeks and 8 weeks and in tretinoin was 1.26±0.56 at 2 weeks and 8 weeks. P value was statistically significant (<0.05).

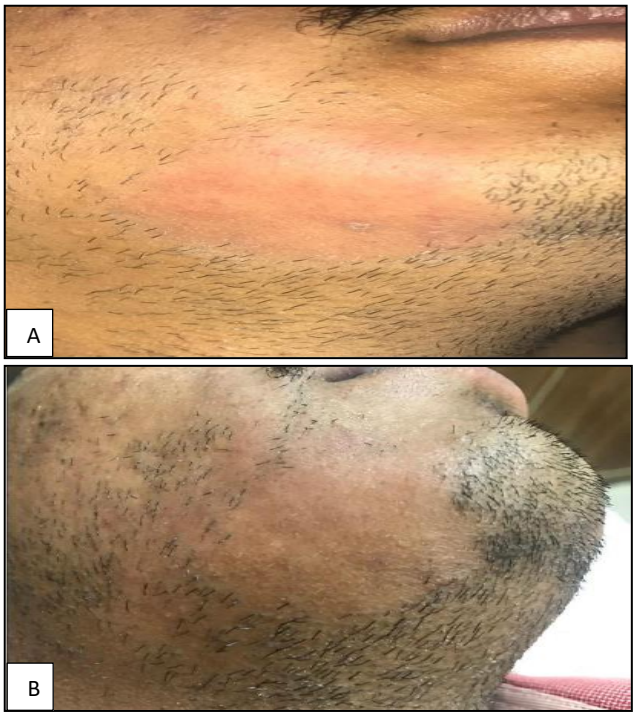

Figure 1 (A and B): localized patch of alopecia areata present over chin at 2 weeks and localized patch of alopecia areata present over chin at 8 weeks.

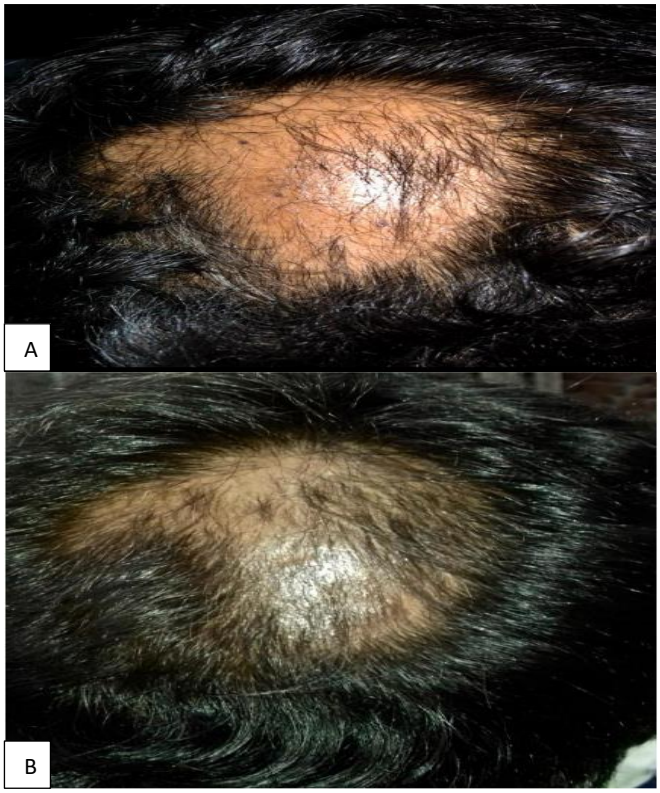

Figure 2 (A and B): localized patch of alopecia areata over scalp at 2 weeks and localized patch of alopecia areata over scalp at 8 weeks.

Table 1: Clinical and demographic profiles of patients in both groups.

Variables		Group A	Group B
Mean age (Years)		38.89±15.34	33.05±12.02
Male: Female		14:5	13:6
Number of bald patches		1.42±0.83	1.26±0.56
Duration of the disease (Months)	<12	16	17
	>12	3	2
	Mean duration	8.73±4.67	8.2±4.2
Associations	Vitiligo	1 patient	1 patient
	Atopic dermatitis	7 patients	8 patients
Family history		15 patients	15 patients
Nail changes		47.36%	31.57%

Trichoscopic examination of all the patients revealed findings such as exclamation mark hair, angular hair, upright regrowing hair, clustered short vellus hair, broken hair, yellow dot and black dot (Table 2). Patients of both groups were also evaluated on the basis of global photographic index (GPI%) and visual analogue scale (VAS). The mean GPI% in group A was 6.26±5.13 and group-B was 32.63±15.29 % which is significantly higher at the end of 2 weeks (p=0.001). At 8 weeks, mean GPI in Group A was 10.95±6.79 and in group B was 51.42±12.42 which was also significantly higher (p=0.026) as compared to group A.

Table 2: Trichoscopic findings.

Variables	Group A	Group B
Mean ± SD	8 weeks	8 weeks
Exclamation mark	0.79±0.53	1.37±0.83
Tapered hair	0.63±0.59	1.36±0.83
Angular hair	0.47±0.51	0.95±0.84
Upright regrowing hair	16.53±8.59	59.84±10.55
Clustered short vellus hair	1.68±1	1±0.86
Broken hair	2.21±0.91	0.42±0.50
Yellow dot	0.58±0.50	0.47±0.61
Black dot	0.74±0.65	0.74±0.56

Similarly mean VAS in group A at 2 weeks and 8 weeks (0.62±0.51 and1.1±0.67) and in group B was (3.27±1.53 and 5.16±1.26) which was significantly higher with difference in p value at 2 weeks between the two groups was p=0.001 and at 8 weeks was p=0.017. There was significant change in GPI and VAS at 8 weeks, in group A as compared to group B.

No serious complication was reported by patients in both the groups.

DISCUSSION

Alopecia areata is a challenging condition to manage, especially in those patients not responding spontaneously. A variety of treatments have been tried but no therapy is considered to be the gold standard. Tretinoin induces irritant contact dermatitis thus diverting the immune arm to a different target, it's use in pediatric AA is well known but is still unexplored in adults. It is plausible that this phenomenon contributes to the hair regrowth in alopecic patch. There are various ways to enhance penetration to increase the bioavailability at the site (chemical as well as physical). Our study explored the use of topical tretinoin in adult AA due to its better compliance and safety profile in comparison to intralesional steroids.[6] MDA has also shown a role in enhancing transdermal delivery of topical medications applied over the skin, thus indirectly increasing the efficacy of the topical drugs.[7]

Trichoscopy has been established as an essential tool in the diagnosis of various hair disorders. Lacarrubba et al first described videodermoscopic features of AA, and since then, it has been widely used due to it's ease and non-invasiveness.[9] A study done by Inui et al of 300 patients with AA, in different stages and different subtypes of the disease, identified yellow dots (YD), black dots (BD), broken hairs (BH), coudability hairs, and clustered short vellus hairs as the most common features.[10] Exclamation mark hair and yellow dots were the most sensitive markers, and black dots, tapering hairs, and broken hairs were the most specific markers for the disease.

Baseline trichoscopic findings of our study match the studies conducted by Guttikonda et al and KaradagKöse and Güleç and Mane et al.[10,11] The baseline findings indicate similar activity and severity profile of the disease in our patients as recruited in other interventional studies.

Black dots (cadaverous hairs) are the remnants of broken hair (BH) and tapering hair (TH) seen in 65% of our patients and in 58% of the cases in study done by Guttikonda et al.[8] They are not specific to AA as they are also seen in other conditions such as trichotillomania. In our study BH, clustered short vellus hair (SVH) were seen more in group A as compared to group B probably due to trauma caused by MDA in AA.

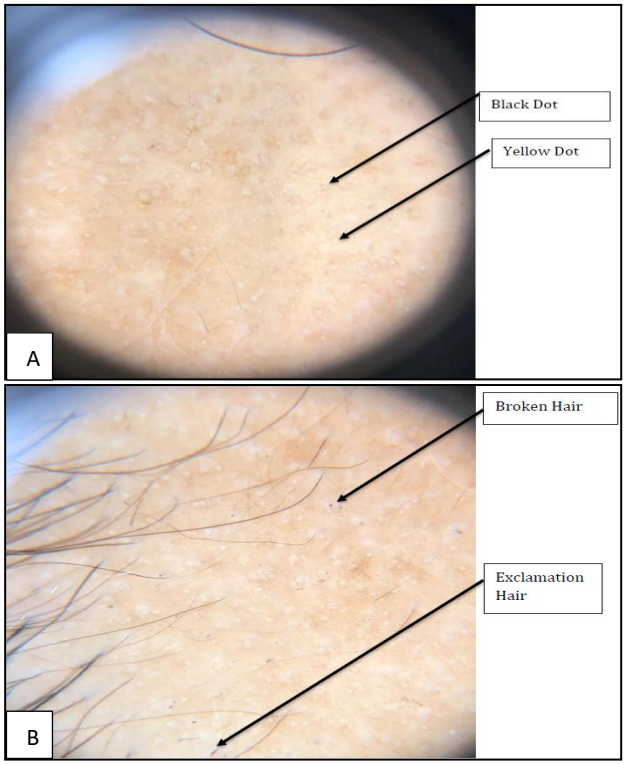

Figure 3 (A and B): Dermoscopy of alopecia areata, showing-black dots and yellow dots and dermoscopy of alopecia areata showing-broken hair and exclamation hair.

Frequent features of AA patch i.e., exclamation hairs (Figure 3 B), angulated hair, upright regrowing hair, yellow dots and black dots (Figure 3 A) were mostly seen in group B as compared to group A. Studies of Inui et al and Peter et al reported slightly lower incidences of TH as compared to 70% patients in our study.[10]

Lacarrubba et al described two patterns of hair regrowth in some patients with chronic AA, one was homogeneous and <10 mm long hair indicating early disease remission (upright vellus hair) and second was short vellus hair (SVH) with characteristic circular hair pattern pigtail hair (PTH) that were usually lost after few weeks.[9] Regrowth of SVH after treatment can be seen on trichoscopy before they can be perceived by the naked eye. While some studies like Guttikonda et al found SCH in 66% of patients, Peter et al and Mane et al.[11,12] Found a lower incidence of SVH. This variation in the incidence may be attributed to the difference in exposure of patients to various treatment modalities before being included in the study.

In our study there was hair count improvement in both group A and group B i.e., 16.53±8.59 and 59.84±10.55 respectively at 8 weeks. In contrast to 12-week study of Dhurat et al which showed that dermaroller along with minoxidil treated group was statistically superior to minoxidil treated group in promoting hair growth in men with AGA and they suggest release of platelet derived growth factor, epidermal growth factor is increasing through platelet activation and skin wound regeneration mechanism.

There was significant change in VAS and this finding was in concordance with Dhurat et al. There was statistical difference ($p<0.05$) for the variables like GPI%, hair count, VAS score, exclamation hair, upright hair, broken hair, short vellus hair, black dot and yellow dot at 2 weeks and 8 wks.

In our study, we used MDA to enhance the delivery of tretinoin but there was a lack of appropriate response. This can be attributed to microtrauma and inflammation that is produced by the procedure. D'Ovidio et al reported Koebner phenomenon in AA which explained that MDA produces microtrauma, induces heat shock protein, which modifies antigenicity of follicular targets, and also enhances cytotoxicity of T cells and NK cells. It affects the catagen phase of hair cycle as well as the superficial bulbar keratinocytes. Conventionally, it can induce controlled irritation of scalp (contact immunotherapy), cleansing of plugged follicular canals and it was said to improve blood flow.[13]

In our study, tretinoin was more effective than the combination with MDA. This was supported by the study done by Baldwin et al which demonstrated action associated with tretinoin, including keratolytic activity, collagenesis, and other mechanisms associated with the activation of nuclear retinoic acid receptors (RARα, RARβ, and RARγ). The results concluded that MDA should not be used in the patients who have positive Koebner's phenomenon and used cautiously in diseases known to exhibit Koebnerization. They described new formulations of topical tretinoin that have been designed to reduce irritation potential and its use in acne, for photodamage and alopecia areata.[14]

CONCLUSION

Our study was unique in its class as no Indian study of adult AA has studied the comparative effect of MDA and tretinoin. This limitation of our study was a small number

of cases due to a short duration which could be improved by extending the study for a longer duration.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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