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Original Research Article

Comparative Study of 0.1% Betamethasone Valerate Ointment Vs 2% Tofacitinib Gel in Childhood Alopecia Areata

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Abstract

Aim: The aim of the present study was to compare 0.1% betamethasone valerate ointment vs 2% tofacitinib gel in childhood alopecia areata.

Methods: This study was done in the Department of Pharmacology and Department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna, Bihar, India, for one year. The study was conducted after approval from Institutional Ethical Committee, Patna Medical College, Patna.

Results: There was male predominance in both the groups. 36.67% and 20% were the family history on both the groups respectively. The median (interquartile range) regrowth score was significantly lower in the latanoprost group as compared to the betamethasone group at the end of 16 weeks (1 [0–4.5] vs. 5 [1–5], P = 0.02). 27 subjects completed 16 weeks follow-up. Similar results were obtained on the per-protocol analysis. None of the subjects in either group had a relapse at the end of 24 weeks. Erythema was the only adverse effect observed in the group A while erythema, skin atrophy, telangiectasia, dermatitis and pustules were observed in the group B.

Conclusion: Alopecia areata is a common yet challenging condition to manage in the Pediatric Dermatology clinic while many patients with localized AA will respond well to first-line treatment with topical or intralesional corticosteroids, some patients will require more aggressive or second-line therapy. Pediatric age of onset, more extensive disease (scalp involvement more than 50%, phasis, or AT/AU), and recalcitrance to initial therapies may highlight patients who will prove to be challenging to manage.

Keywords: 0.1% betamethasone valerate ointment, 2% tofacitinib gel, childhood alopecia areata

Introduction

Alopecia areata has a variable course and uncertain natural history. All patients of alopecia areata may not require treatment. Spontaneous regrowth in some cases with limited disease process is well known. [1,2] Although diverse therapeutic options are available, none of them is satisfactory. Moreover, it is not yet identifiable as to which patient of alopecia areata will progress into extensive disease or alopecia totalize/ universalis and will require intervention. In these patients too, the ideal and effective treatment protocol is yet to be evolved.

Alopecia areata (AA) is a non-scarring, recurrent, auto-immune and inflammatory scalp and/or body hair loss condition. AA is further characterized into two types; the first one is alopecia totalize which is hair loss of either patches or total hair loss of scalp and second one is alopecia universalis which is 100% hair loss of scalp and body hair. Hair loss can be caused by various factors such as genetics, hormones, stress, and infectious disease and so on. [3] But T-Lymphocytes play a key role in AA as they attack the hair follicles around them and cause inflammation and ultimately leading to hair loss. [4] Tofacitinib citrate (TFC) is a Janus kinase (JAK) inhibitor. Recent studies have shown that JAK inhibitors are an upcoming treatment for AA due to their faster mechanism of action and lesser side effect. AA is caused when the hair follicles start presenting major histocompatibility complexes which take part in the activation of JAK-STAT

pathway which leads to T-cell-mediated inflammation. JAK inhibitors block this pathway thus inhibiting the inflammation. [5] TFC was initially introduced in 2012 for the treatment of rheumatoid arthritis. TFC inhibits JAK3 enzyme therefore, it is used to treat various dermatological conditions which is regulated by JAK1/3, such as AA, psoriasis and dermatitis. [6]

A genetic predisposition to AA is supported by the frequent history of affected family members. Several genomes- wide studies have identified potential polymorphisms associated with disease. The strongest evidence is for a single nucleoid polymorphism in PTPN22, with weaker data supporting polymorphisms in FAS, FASL, PTPN22, CTLA4, and IL2RA. [7] Several potential triggers of disease onset and flares have been identified. Viral infections associated with initial presentation and recurrence of AA include Epstein–Barr virus (EBV), hepatitis B and C viruses, and swine flu. [8] Vaccines are another reported trigger, with many different vaccines implicated including influenza, hepatitis, and coronaviruses. [9-11]

Potent or super potent class of topical steroids are the first choice of treatment in cases of pediatric AA. According to a recently published metanalysis, [12] the level of evidence regarding their efficacy is fairly good (level II according to The Oxford 2011 Levels of Evidence), in the sense that there are the number of observational studies in its support. It reported 81% response rate, but showed that more than half of the patients had relapsed on stoppage of therapy. [13] Topical steroids must be used for 2 3 months after improvement in hair growth and gradually tapered. Washing the head or the applied area 12 h after application may reduce the incidence of scalp folliculitis in children.[14] Intralesional steroid injections are poorly tolerated due to fear of pain and are generally not used, except in some older children or adolescents with localized lesions.

The aim of the present study was to compare 0.1% betamethasone valerate ointment vs 2% tofacitinib gel in childhood alopecia areata.

Materials and Methods

This study was done in the Department of Pharmacology and Department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna, Bihar, India, for one year. The study was conducted after approval from Institutional Ethical Committee, Patna Medical College, Patna.

Inclusion Criteria:

1. Patients of either sex

2. Patients aged 2-12 years with mild to moderate patchy alopecia areata, with a duration of disease less than two months.

Exclusion Criteria:

1. Patients with history of previous systemic or local treatment,

2. Patients with severe alopecia areata,

3. Patients with any known severe systemic disease,

4. Patients with a known sensitivity to the study drug or class of study drug.

Study Design: This was prospective open label study conducted in the department of Pharmacology, Patna Medical College and Hospital, Patna in 60 patients visiting OPD of department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna over a period of 6 months fulfilling the inclusion criteria. Written informed consent was taken from all the patients guardians included in my study.

Study Procedure: The disease was diagnosed on the basis of clinical features. Patients were randomly allocated into two groups. Group A, having 30 patients were given topical 0.1% Betamethasone ointment whereas Group B, having 30 patients were given 2% topical Tofacitinib gel.

The study was carried out over a 12 week period. During this treatment period patients were assigned to either 0.1% Betamethasone valerate or 2% Tofacitinib to be applied to the affected areas twice daily for 12 weeks followed by monthly follow up visits. The baseline assessment of alopecia grading was performed using a 6-point scale score: S0 = No alopecia, S1 = hair loss <10%, S2 =hair loss 11–25%, S3 = hair loss 26–50%, S4 = hair loss 51–75% and S5 = hair loss > 75%.

Efficacy was evaluated on an intention-to-treat basis, using a hair regrowth score (RGS) with a scale ranging from 0 (regrowth < 10%) to 1 (11–25%), 2 (26–50%), 3 (51–75%) and 4 (regrowth> 75%). The safety and tolerability of Betamethasone and Tofacitinib was assessed by monitoring adverse events at follow up visits throughout the study.

Statistical Analysis: All the values were taken as mean and ±SEM. The primary efficacy measurement was the mean change in the alopecia grading and to compare the hair regrowth rate by using hair regrowth score (RGS).

Results

Table 1: Demographic characteristics of study patients

Baseline characteristics	Group A (n=30)	Group B (n=30)	P
Age (years)	10 (2-12)	11 (2-12)	0.89
Gender (male:female)	19:11	20:10	1.00
Total area involved by AA (cm^2)	5 (2.1-15.9)	9.9 (4.2-14.2)	0.19
Duration of disease (months)	3 (2-4.5)	3 (1-6)	0.79
Family history of alopecia	11 (36.67)	6 (20.0)	0.21
Family history of atopy	6 (20)	5 (16.67)	0.71
Personal history of atopy	11 (36.67)	6 (20)	0.21
Elevated TSH	3 (10)	1 (3.33)	0.30
Positive ANA	2 (6.67)	0	0.15

There was male predominance in both the groups. 36.67% and 20% were the family history on both the groups respectively.

Table 2: Outcomes of the study

Outcome	Group A (n=30)	Group B (n=30)	Estimated difference (95% CI)	P
Intention-to-treat analysis	n=25	n=25		
Primary outcome				
Percentage reduction in an area with hair loss between baseline and 16 weeks	11.1 (0-99.1)	100 (13.6-100)	-	0.02
Other outcomes				
Complete response	8 (26.67)	17 (56.67)	0.32 (0.05-0.53)	0.02
Hair RGS at 16 weeks	1 (0-4.5)	5 (1-5)	-	0.02
Primary outcome				
Percentage reduction in an area with hair loss between baseline and 16 weeks	71.7 (0-100)	100 (50.8-100)	-	0.03
Other outcomes				
Complete response	9 (30)	18 (60)	0.32 (0.03-0.55)	0.03
Hair RGS at 16 weeks	3 (0-5)	5 (3-5)	-	0.03

The median (interquartile range) regrowth score was significantly lower in the latanoprost group as compared to the betamethasone group at the end of 16 weeks (1 [0–4.5] vs. 5 [1–5], P = 0.02). 27 subjects completed 16 weeks follow-up. Similar results were obtained on the per-protocol analysis.

Table 3: Adverse effects of treatment in the study groups

Adverse effect	Group A (n=30)	Group B (n=30)	P
Any adverse effect	4 (16.0)	4 (16.0)	1.00
Erythema	5 (16.67)	1 (3.33)	0.13
Skin atrophy	0	4 (13.33)	0.09
Telangiectasia	0	2 (6.67)	0.17
Dermatitis	0	1 (3.33)	0.33
Pustules	0	2 (6.67)	0.17

None of the subjects in either group had a relapse at the end of 24 weeks. Erythema was the only adverse effect observed in the group A while erythema, skin atrophy, telangiectasia, dermatitis and pustules were observed in the group B.

Discussion

Disturbance of hair follicle cycling lie at the heart of most hair growth disorders, and have dramatic effects on visible hair growth and hair shaft shedding. If the anagen phase is prematurely terminated and catagen occurs too early, the affected skin shows largely catagen and/ or follicles, and loosely anchored club hairs that are eventually shed (i.e., the normal anagen/ telogen ratio of approximately 4.5:1 changes in favour of telogen). Considering that our scalp skin alone has approximately 100,000 hair follicles, even relatively small shifts in the percentage of anagen versus telogen follicles have major effects on hair growth and shedding. [15]

At any given time, approximately 0.2 % of the population has alopecia areata and approximately 1.7 % of the population experience an episode of alopecia areata during their lifetime. However, there are great geographic and ethnic variations in the

incidence and prevalence of the disease; this is also seen with respect to the immunogenetic background of patients with alopecia areata. [16] It can affect all ages, but the prevalence appears higher in children compared to adults (1.92%, 1.47%). [17] The sex incidence is probably equal.

Alopecia areata is a chronic, organ- specific autoimmune disease, probably mediated by autoreactive T cells, which affects hair follicles and sometimes the nails. [18] There is an increased frequency of other autoimmune diseases, notably autoimmune thyroid disease in affected adults, and of organ- specific auto antibodies in patients with alopecia areata. Hair follicle auto antibodies are also found in some patients with alopecia areata although it is unlikely that these auto antibodies are of importance in the primary pathogenesis of alopecia areata. There was male predominance in both the groups. 36.67% and 20% were the family history on both the groups respectively. The median (interquartile range) regrowth score was significantly lower in the latanoprost group as compared to the betamethasone group at the end of 16 weeks (1 [0–4.5] vs. 5 [1–5], P = 0.02). 27 subjects completed 16 weeks follow-up. Similar results were obtained on the per-protocol analysis. None of the subjects in either group had a relapse at the end of 24 weeks. Erythema was the only adverse effect observed in the group A while erythema, skin atrophy, telangiectasia, dermatitis and pustules were observed in the group B.

In a recent study by Zaher et al [19], bimatoprost, a PGF2α analogue was shown to be more effective than topical mometasone furoate cream in the treatment of localized alopecia areata. Pasricha et al [20] treated a single patient with 5 mg of betamethasone twice weekly with a rapid re-growth of hair all over the scalp in 3 months. Sharma [21] administered oral prednisolone as pulses in doses of 300 mg at 4 weeks intervals. Cosmetically acceptable hair growth was seen in 58.3% patients at 4 months of treatment and relapse was seen in 2 patients after stoppage of therapy at 3 and 9 months respectively. In another study, Sharma et al [22] have reported complete hair growth in 26.6% of patients and a good response in 36.6% of patients treated with oral mini-pulse with dexamethasone.

Conclusion

Alopecia areata is a common yet challenging condition to manage in the Pediatric Dermatology clinic while many patients with localized AA will respond well to first-line treatment with topical or intralesional corticosteroids, some patients will require more aggressive or second-line therapy. Pediatric age of onset, more extensive disease (scalp involvement more than 50%, ophiasis, or AT/AU), and recalcitrance to initial therapies may highlight patients who will prove to be challenging to manage.

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