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Intralesional Therapy of Alopecia Areata by 1% Lactic Acid Solution Versus Triamcinolone Acetoind Injection
(Interventional ,Case Controlled ,Single Blinded, Comparative Study)

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Abstract
Background: *Alopecia areata is a common autoimmune disease encountered in daily clinical practice, where many topical and systemic therapies had been advocated. Lactic acid had been used as a topical therapy for many dermatoses.*
Objective: *To assess the effectiveness of intralesional 1% lactic acid solution in treatment of patchy alopecia areata in comparison with standard mode of therapy like intralesional triamcinolone acetonide injectable suspension.*
Patients and Methods: *This interventional ,case controlled , single blinded, comparative, therapeutic study conducted in Department of Dermatology. Baghdad Teaching Hospital, Baghdad, Iraq between December 2011 and July 2013.*
Fifty patient, with patchy alopecia areata were enrolled, total number of lesions were 128 patches. The patients were divided into 2 groups according to type of treatment:
Group (A) *(triamcinolone acetonide injectable suspension): Twenty five patient (70)patches were included in this group. Intralesional injection was done every 4 weeks in 52(74.29%) patches, while 18(25.71%) patches were left as control group.*
Group (B)*(lactic acid 1% solution): Twenty five patient (58patches) were included in this group. Lactic acid solution 1% was injected every 4 weeks intralesionally in 42(72.4%) patches,while16(27.6%) patches were left as control. Treatment continued for 3 months. Follow up was don for further 3 months without treatment for both groups .*
Results: ***Group A****: Thirty (57.7%) of treated patches showed complete hair regrowth at the end of third month of treatment while after 3 months of follow up, 42(80.8%)patches showed complete hair regrowth, while 10(19.2%) patches showed partial hair regrowth. The remaining 18(25.7%) patches (control group): hair regrowth seen in 3(4.3%)patches. No relapse noticed during 3 months of follow up.*
Group B*:Sixteen (38.1%) of treated patches showed complete hair regrowth at the end of third month of treatment while after 3 months of follow up, 33(78.6%)patches showed complete hair regrowth ,7(16.6%)patches remained partial pigmented hair,1(2.4%)patch partial fine hair growth and 1(2.4%)patch with no hair regrowth. Regarding the control group:16 (27.6%) patches hair regrowth was noticed in 5(8.6%) patches during 3 months follow up. No relapse noticed during three months of follow up.*
When the 2 groups compared with each other, ***Group A*** *showed rapid hair growth in first 3 months ,and when compared with* ***Group B****, it was statistical significant, while at the end of 3 months of follow up when 2 groups compared, still triamcinolone acetoinde* ***(Group B)*** *was faster ,it not reach statistical different.*
Conclusion*: Triamcinolone acetoind and lactic acid 1%solusion intralesional injections of alopecia areata are effective comparable to each other's but lactic acid is cost effective with no important side effects.*
Keywords: *alopecia areata, triamcinolone acetoind, lactic acid.*

I. Introduction

Alopecia areata(AA) is an autoimmune chronic inflammatory disease that involves the hair follicle and sometimes the nails, characterized by rapid and complete loss of hair in one or more round or oval patches, usually on the scalp, bearded area, eyebrows, eyelashes, and less commonly, on other hairy areas of the body.[1,2]were its pathology is not well elucidated but the autoimmune etiology is the most favored (Oligoclonal and auto-reactive T-lymphocytes are present in the peribulbar inflammatory infiltrate, and many patients respond to immune-modulating drugs. [3-5].The early phase of hair loss appears to be mediated by type 1 cytokines, including interleukin (IL)-2, interferon (IFN)-γ, and tumor necrosis factor (TNF)-α.[2]

There are many modes of therapy including topical and systemic types and all of them seem to be effective like a topical Diclofenac sodium gel 1%[6], Benzoyl peroxide gel 5%[6], onion juice[7],Lactic acid[8,9], topical steroids[10]electrical current[11],photochemotherapy[12]intralesional steroid (triamcinolone acetonide), systemic steroid[13]Immunotherapy[14], zinc sulfate[15], cyclosporine[16], Methotrexate[17], Excimer laser[18] and Fractional photothermolysis laser.[19]

The lactic acid 15% solution had been used as an effective topical therapy for alopecia areata.[8,9]

Accordingly ,the present work was arranged to evaluate the effectiveness and safety of intralesional lactic acid 1% solution in comparison with intralesional triamcinolone acetoind injectable suspension in treatment of alopecia areata.

II. Patients And Methods

This was interventional ,case controlled ,single blinded ,comparative study that was conducted in the Department of Dermatology. Baghdad Teaching Hospital, Medical City, Baghdad, Iraq between December 2011 and July 2013.

Fifty patients with patchy AA(128 patches) were enrolled in this study, 30(60%) patients were males and 20(40%) patients were females. The diagnosis of alopecia areata was done clinically. They were divided into 2 groups, according to type of therapy.

Group A (triamcinolone acetonide injectable suspension):Twenty five patient with (70)patches were included in this group. Fourteen (56%) patients were males and 11(44%) were females .Intralesional triamcinolone acetonide was injected every 4 weeks in 52(74.29%) patches, while 18(25.71%) patches were left as a control placebo group.

Group B (lactic acid 1% solution**):** Twenty five patient with (58 patches) were included in this group. Sixteen (64%) patients were males and 9 (36%) were females. Lactic acid solution 1% was injected every 4 weeks intralesionally in 42 (72.4%) patches, while 16 (27.6%) patches were left as a control placebo group.
Treatment of both groups continued for 3 months, and another 3 months after cessation of therapy as follow up period.

Group C: They are 34 patches from both groups left without treatment as a control placebo group:18 patches from **Group A**, 16 patches from **Group B**.

A history was taken from each patient regarding the following: age, gender, duration of AA, prior history of AA, history of emotional stress, history of BCG vaccination, personal or family history of the same condition and atopy or other autoimmune disorders e.g. vitiligo, connective tissue diseases, diabetes mellitus, , lichen planus, thyroid diseases and ulcerative colitis.

Physical examination was performed for each patient emphasized on the following: site, size, number, exclamation's mark hair, color of the hair, nail changes (pitting, ridging, mottled lunula, Beau's line and others), scar of previous BCG vaccination.

Photographs were taken for each patient at each visit by GT-N7000 mobile GALAXY Note 1, at the same place, distance and illumination.

Only patients with patchy AA of up to 4 months duration were enrolled. While Alopecia totalis, universalis, ophiasis, sisaipho, Down's syndrome with AA, diabetic patients were excluded from the study. All cases had received no treatment for at least 2 months before starting therapy.

The nature and aim of this study were explained for each patient. Formal consent was taken from each patient before starting the trial after a full explanation for the nature of the disease, causes, prognosis, the drug, the method of treatment, duration of follow up and the possible side effects. As well as the need of pre-and post-treatment photographs. The ethical approval was given by the Scientific Council of Dermatology &Venereology-Arab Board for Medical Specializations.
Patients were divided into two groups:

Group A: was given intralesional triamcinolone acetonide injectable suspension (40mg/ml, IBN HAYYAN PHARMA-HOMS-SYRIA) which was diluted with distal water to half, mixed well and intradermal injection was carried out by insulin syringe (26 gage).

Group B: was given lactic acid solution (CH3.CHOH.COOH) 88% concentration PH (6.84), made in GAINLAND CHEMICAL COMPANY, U.K.
It was diluted with distal water to have a final concentration of 1%, it was also injected intradermal by insulin syringe(26 gage).

Patients were allocated to receive either intralesional steroid, or intralesional lactic acid every 4 weeks, for 3 months, then follow up for another 3 months without therapy.
Patients were followed up for 3 months.They were seen every month. Patients were evaluated clinically by looking for any hair regrowth, which was categorized according to the following scoring:

Grade 0: those patches with no hair growth.

Grade IA: those with partial hair regrowth with villous hair (fine, thin, short).

Grade IB: those with partial hair regrowth with coarse, pigmented hair.

Grade II: those patches with complete hair regrowth with terminal hair (coarse, pigmented, long).
During each visit of follow up, any adverse effects were recorded of both drugs like: pain, erythema, itching and others. .

Data were statistically described in terms of range, mean, standard deviation (±SD) and frequencies (number of patches and cases) and relative frequencies (percentages). Chi square was done for comparison between discrete data (gender, site response, etc...) while t test was done for continuous one (age and duration). P value less than 0.05 was considered significant. All statistical calculations were done using computer statistical programs SPSS ver.20 (Statistical Package for the Social Science; SPSS Inc. Chicago, IL, USA).

III. Results

There were no significant differences for all demographic criteria between the three groups (Table-1).
Group A: Thirty (57.7%) of treated patches showed complete hair regrowth at the end of third month of treatment, while 8 (15.4%) patches showed partial course, pigmented hair regrowth and 14(26.9)patches showed partial fine hair at the end of third month of treatment. At the end of three months of follow up , 42(80.8%) patches showed complete hair regrowth and 10(19.2%) patches showed partial course, pigmented hair regrowth (Table-2)(Figure-1).

Group B: Sixteen (38.1%) patches showed complete hair regrowth, 25(59.5%) patches showed partial course pigmented hair and 1(2.4%)patch show no hair regrowth at the end of three months of treatment. At the end of three months of follow up,33(78.6%)patches showed complete hair regrowth,7(16.6%) patches showed partial course pigmented hair,1(2.4%) patch showed partial fine hair and 1(2.4%) patch showed no hair regrowth (Table-2)(Figure-2).

Group C: During three months of treatment showed in these patches ,while during follow up partial course pigmented hair regrowth in 8(23%)patches(Table-2).
Table three showing local side effects of intralesional triamcinolone in patients within Group A and intralesional lactic acid in patients within Group B.

Table -1: Showing demographic features of patients in both groups.

Parameter		Group A	Group B	P value
Gender	Male	14 (56%)	16 (64%)	0.387
	Female	11 (44%)	9 (36%)	
Age	Mean	28.08	28.04	0.128
	SD	10.062	7.503	
Duration	Mean	6.44	7.36	0.327
	SD	3.852	3.729	
Positive personal history of AA		9 (36%)	7 (28%)	0.381
Psychological distress		24 (96%)	23 (92%)	0.5
Family history of AA		10 (40%)	6(24%)	0.182
Nail changes		3 (12.0%)	0 (0.0%)	0.117
History of BCG		25 (100.0%)	25 (100.0%)	*
Site	Scalp	18 (72.0%)	18 (72.0%)	1.0
	Beard	6 (24.0%)	6 (24.0%)	1.0
	Mustache	1 (4.0%)	1 (4.0%)	1.0

* No statistics are computed because History of BCG is a constant

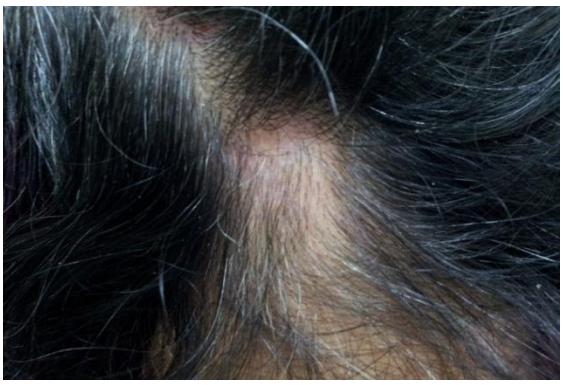
Table -2: Showing the response to treatment in patients in Group A ,B, and C.

Visits	Response	Group A		Group B		Group C		P value
		No.	%	No.	%	No.	%	
Second visit	No response	13	25.0%	22	52.4%	**34**	100.0%	**0.0001**
	Partial (Fine hair)	4	7.7%	6	14.3%	**0**	0.0%	
	Partial (Course hair)	35	67.3%	14	33.3%	**0**	0.0%	
	P value	**0.335**						
Third visit	No response	1	1.9%	1	2.4%	**34**	100.0%	**0.0001**
	Partial (Fine hair)	17	32.7%	15	35.7%	**0**	0.0%	
	Partial (Course hair)	29	55.8%	25	59.5%	**0**	0.0%	
	Complete	5	9.6%	1	2.4%	**0**	0.0%	
	P value	**0.706**						
Fourth visit	No response	0	0.0%	1	2.4%	**34**	100.0%	**0.0001**
	Partial (Fine hair)	14	26.9%	0	0.0%	**0**	0.0%	
	Partial (Course hair)	8	15.4%	25	59.5%	**0**	0.0%	
	Complete	30	57.7%	16	38.1%	**0**	0.0%	
	P value	**0.001**						
Follow up	No response	0	0.0%	1	2.4%	**26**	76.5%	**0.0001**
	Partial (Fine hair)	0	0.0%	1	2.4%	0	0.0%	
	Partial (Course hair)	10	19.2%	7	16.6%	8	23.5%	
	Complete	42	80.8%	33	78.6%	0	0.0%	
	P value	**0.128**						

Table-3: Showing local side effects of intralesional triamcinolone in patients within Group A and intralesional lactic acid in patients within Group B.

Side effects	Group A		Group B		P value
	No.	%	No.	%	
Pain	**5**	**20%**	**25**	**100%**	**0.0001**
Itching	**10**	**40%**	**10**	**40%**	**0.613**
Erythema	**5**	**20%**	**0**	**0%**	**0.025**
Swelling	**0**	**0%**	**2**	**8%**	***1**
Necrosis	**0**	**0%**	**1**	**4%**	**1**

A:Before treatment.



B:After three months of treatment.

C:After three months of follow up.
Figure-1 A,B,C: patient treated with intralesional triamcinolone acetoind.

A:Before treatment.

B:After three months of treatment.

C:After three months of follow up.
Figure-2:A,B,C:patient treated with intralesional1% lactic acid solution.

IV. Discussion

Many topical and systemic therapies have been tried in treatment of alopecia areata, which are grouped into irritants, immune inhibitors, immune enhancers[1-3] and others[3] with uncertain mode of action.

Intralesional triamcinolone acetoid is preferred by many dermatologists in cases of AA involving less than 50% of the scalp [1],but if used in wrong technique or given in high dose might give all side effects of corticosteroid especially skin atrophy.

Topical lactic acid solusion15%,12% cream had been used effectively as mode of therapy of alopecia areata[8,9] ,but many patients have no compliance for daily topical application and prefer use intralesional injections at distant intervals ,hence the present work was arranged.

In the current study patients divided into groups (A, B) where the patients are comparable in their ages, gender, duration of disease, severity and activity of the disease. This indicates a good match between the two groups. The response of AA to intralesional triamcinolone acetonide injectable suspension was good achieving 57.7% complete hair growth of the patches treated at the end of third month of treatment and 38.1% complete hair growth of the treated patches in patients treated with intralesional 1%lactic acid at the third month of therapy. The difference in response between the treated patches in group A and the comparison patches in group B was statistically significant at the end of the course of the treatment (p -value 0.03). while at the end of three months follow up without therapy , the response rate in group A was 80.8% and in group B 76.8% complete hair growth which was insignificant statistically (p- value 0.128).

Regarding the side effects, triamcinolone acetoind at the present work showed no significant side effect, but if used in wrong technique or given in high dose it might give all side effects of corticosteroid .In case of lactic acid solution no important side effects were observed.

Regarding the relapse rate ,during the course of therapy and follow up period ,no relapse was recorded.

Regarding the mechanism, corticosteroid well known antinflammatory and interfere with local immunity of the skin and this help in recovery of the disease.[1]

Lactic acid has been used in treatment of many skin disease like topical treatment of alopecia areata and vitiligo, in these diseases gave high recovery rate and the mechanisms could be suggested by spontaneous secretion of vascular endothelial growth factor (VEGF) by human reconstructed epidermis (Sharquie 2013). VEGF is a multifunctional angiogenic cytokine involved in angiogensis and wound healing, and this cytokine will enhance and stimulate the growth of hair follicles result in recovery of alopecia areata.[20]

As reaction of lactic acid in treatment AA is not well elucidated, hence we recommended doing a small punch biopsy to see the changes that may occur during treatment and healing process. Lactic acid could be delivered through roller rather than intralesional injection by a syringe to minimize the pain and local reactions.

In conclusions ,triamcinolone acetoind and lactic acid 1%solusion intralesional injections of alopecia areata are effective comparable to each other's but lactic acid is cost effective with no important side effects .

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