The Efficacy of Azelaic Acid 20% Cream in the Treatment of Scalp Alopecia Areata

Mudheher I. Salih, **Dindar S. Qurtas**
Department of Medicine, College of Medicine, Hawler Medical University, Erbil, Iraq.
Corresponding author: mudheher1985@gmail.com

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ABSTRACT

Alopecia areata (AA) is a common, inflammatory, non-scarring type of hair loss that affects persons of both sexes and all age groups, with prevalence in the general population of approximately 0.1–0.2%. It is characterized by variable clinical presentations, ranging from single or multiple well-circumscribed patches of hair loss to extensive involvement with the complete absence of body and scalp hair. Alopecia areata (AA) is an autoimmune disease of the hair follicle. Its pathogenesis is associated with loss of follicular immune privilege and T-cell mediated inflammatory response, leading to interruption of the hair growth cycle. The diagnosis of alopecia areata is usually based on clinical manifestations in addition to using SALT score. Currently, there is no treatment for AA approved by the US Food and Drugs Administration. However, several treatment modalities for AA have been introduced with variable outcomes. Although topical and systemic immunomodulators are the mainstay options, there is still a lack of high-quality randomized controlled trials (RCTs) supporting these treatment modalities. Topical Corticosteroids (TCs) are considered the first-line therapy for patch-type AA. High-potency TCs such as 0.05% clobetasol propionate in different forms or 0.25% desoximetasone cream are usually prescribed in adults with response rates of approximately 47% and 60%, respectively. Azelaic acid is a dicarboxylic acid, derived from the fungus *Pityrosporum ovale*, which is naturally derived from grains such as wheat and barley. Finally, Azelaic acid is an effective topical therapy for patchy AA in 20%.

Keywords: alopecia areata, Topical corticosteroid, Azelaic acid, Diagnosis of alopecia areata.

فاعلية كريم حامض الازيليك 20% في علاج داء الثعلبة في فروة الراس

الملخص

الثعلبة البقعية هي نوع شائع من انواع تساقط الشعر الالتهابي وغير المندوب ويصيب الاشخاص من كلا الجنسيين وجميع الفئات العمرية، ويبلغ معدل انتشارة في عموم السكان حوالي (0,1 – 0,2%) يتميز بالعروض السريرية المتغيرة، والتي تتراوح من بقعة فردية أو متعددة من تساقط الشعر الى مشاركة واسعة النطاق مع الغياب التام لشعر الجسم وفروة الراس. الثعلبة البقعية هي مرض مناعي ذاتي يصيب بصيلات الشعر يرتبط نشاته بفقدان الامتياز المناعي الجريبي والاستجابة الالتهابية بواسطة الخلايا التائية، مما يودي الى انقطاع نمو دورة نمو الشعر. يعتمد تشخيص داء الثعلبة عادة على المظاهر السريرية بالاضافة الى استخدام مقياس SALT حاليا، لا يوجد علاج لمرض الثعلبة البقعية معتمدة من اداراة الغذاء والدواء الامريكية. ومع ذلك فقد تم تقديم العديد من طرق العلاج مع نتائج متغيرة. على الرغم من ان معدلات المناعه الموضعية والجهازية هي الخيارات الاساسية، لا يزال هناك نقص في التجارب المعشاة ذات الشواهد عالية الجودة (RCTS) التي تدعم طرائق العلاج هذة. تعتبر الكوتيكوسيرويدات الموضعية (TCs) العلاج الاول للرقعة من النةع AA. عادة ما يتم وصف ادوية عالية الفعالية مثل بربيونات كلوبيتاس05و 0 % باشكال صيدلانية مختلفة أو كريم ديسوكسيميتازون.0,025 % للبالغين بمعدلات استجابه تقارب 47% و 60% على التوالي. أن حامض الازليك هو حامض ثنائي الكابوكسيل مشتق من

فطر *Pityrosporum ovale* ، وهو مشتق بشكل طبيعي من الحبوب مثل القمح والشعير. أخيرا، يعد حامض الازليك علاجا موضعيا فعالا لعلاج الثعلبة البقعية AAغيرالمكتمل .20%.

INTRODUCTION

Alopecia areata (AA) is a common, inflammatory, non-scarring type of hair loss that affects persons of both sexes and all age groups, with prevalence in the general population of approximately 0.1–0.2%. It is characterized by variable clinical presentations, ranging from single or multiple well-circumscribed patches of hair loss to extensive involvement with the complete absence of body and scalp hair (1). The condition is associated with a variety of inflammatory and immune-mediated diseases, such as atopic dermatitis, allergic rhinitis, lupus erythematosus, psoriasis, thyroid disease, rheumatoid arthritis, celiac disease, and type 1 diabetes mellitus (2).

TCs are considered the first-line therapy for patch-type AA. High-potency TCs such as 0.05% clobetasol propionate (3).

Azelaic acid is a dicarboxylic acid, derived from the fungus Pityrosporum ovale, which is naturally derived from grains such as wheat and barley (4). Azelaic acid is an effective topical therapy for patchy AA (5).

This study focused about the efficacy of azelaic acid in comparison with traditional therapy and its novel role in the treatment of scalp alopecia areata.

METHODS:

Study design: To achieve the aim of the present study, An Interventional Prospective study was conducted at the Erbil Dermatology Teaching Centre (EDTC) between March 2021 to March 2022.

Sample size & Sampling:

The patients who are diagnosed to have scalp Alopecia Areata were enrolled in this study. The patients were collected from EDTC. The patients were divided into two groups: group A includes fifteen patients on topical Clobetasol propionate 0.05% cream; group B includes fifteen patients on topical Azelaic acid 20% cream. Both treatment groups were followed up for a period of twelve weeks with monthly check-up visits.

The assessment of both therapies in the clinical course of the disease was assessed using the SALT score each month as shown in (Appendix I)(6) and the obtained data were processed by using a special software system (SPSS) Statistical Package for the Social Sciences.

Data collection:

The main sources of data were obtained directly from grouped patients by researcher interviewing them, using specially prepared questionnaire as shown in (Appendix II). Each patient was enrolled in this study coded by number.

Ethical Consideration:

*** Information sheet:** (as shown in Appendix III)

*** Consent Form:** (as shown in Appendix IX)

RESULTS:

The study includes 30 individuals; 15 individuals in group A and 15 in group B.

Table (1) demonstrates the comparison of age, weight, height, BMI, and duration and shows that the individuals

in group A are older, heavier but shorter than that in group B. BMI is higher among group A than in group B. Group A has a longer duration than group B. The differences between study groups concerning all the variables are statistically non-significant.

Table (1): The comparison of age, weight, height, BMI, and duration.

	Group A	Group B	p-value*
	Mean ± SD	Mean ± SD	
Age	21.533±13.216	21.200±15.543	0.950
Weight	61.667±40.286	52.333±24.106	0.448
Height	141.600±32.264	144.133±29.413	0.824
BMI	23.733±7.622	23.533±4.668	0.932
Duration	2.867±1.586	2.200±1.474	0.243

*(unpaired)t-test

Figure (1) demonstrates the distribution of study groups according to gender and illustrates that the male gender represents 7(46.7%) and 6(40.0%) of groups A and B respectively, while the females constitute 8(53.3%) and 9(60.0%) of group A and B in that same order.

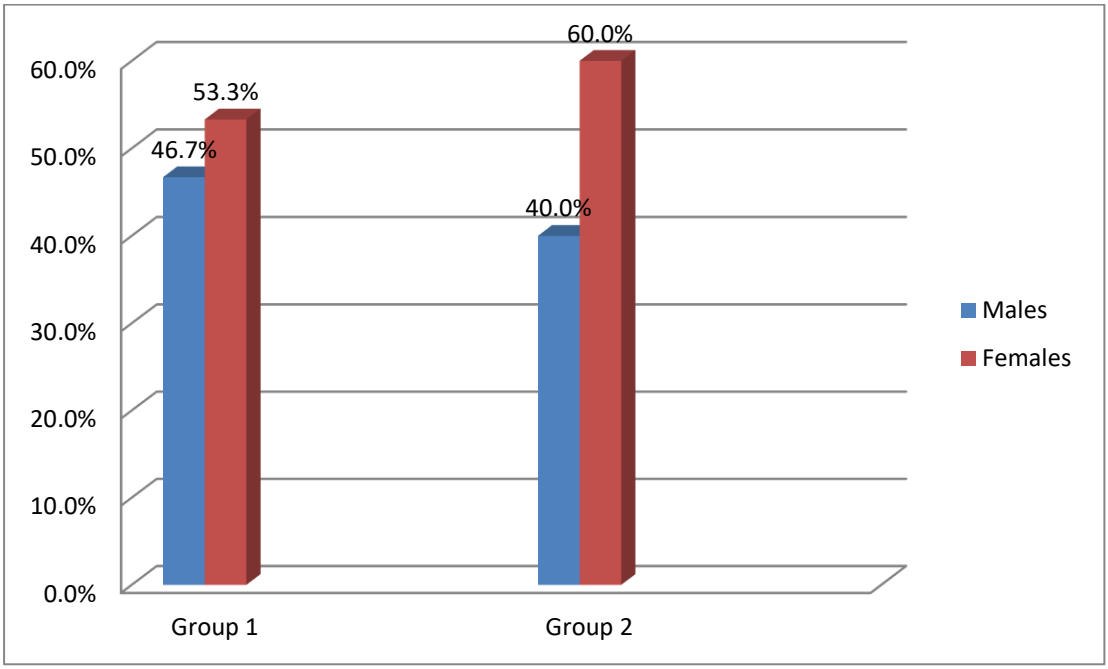

Figure (1): The distribution of study groups according to gender.

Table (2) shows the comparisons between study groups concerning socio-demographic characteristics and displays non-significant differences between group A and group B.

Table (2): The comparisons between study groups.

Socio-demographic characteristics		Group A		Group B		p-value
		No.	%	No.	%	
Social status	Single	7	46.67%	5	33.3.%	0.456*
	Married	5	33.3.%	5	33.3.%	1.000*
	Divorced	0	0.00%	1	6.67%	1.000**
	Child	3	20.00%	4	26.67%	1.000**
Economical status	Poor	4	26.67%	4	26.67%	1.000**
	Moderate	5	33.3.%	9	60.00%	0.143*
	Good	2	13.33%	2	13.33%	1.000**
	Very good	4	26.67%	0	0.00%	0.100**
Address	Inside Erbil	9	60.00%	0	0.00%	0.000**
	Outside Erbil	6	40.0%	15	100.0%	
Jobs	Child	4	26.67%	5	33.3.%	1.000**
	Student	4	26.67%	3	20.00%	1.000**
	Gov. employee	1	6.67%	1	6.67%	1.000**
	Private employee	2	13.33%	4	26.67%	0.651**
	Retired	0	0.00%	0	0.00%	1.000**
	Jobless	1	6.67%	2	13.33%	1.000**

*(chi-square)test **fissure exact test

Table (3) shows the comparisons between study groups regarding the physical examination and demonstrates non-significant differences between group A and group B.

Table (3): The comparisons between study groups regarding the physical examination.

Physical examination		Group A		Group B		p-value
		No.	%	No.	%	
Erythema	Yes	1	6.67%	1	6.67%	1.000**
	No	14	93.33%	14	93.33%	
Scale	Yes	0	0.00%	0	0.00%	1.000**
	No	15	100.0%	15	100.0%	
Short hair	Yes	8	53.33%	10	66.67%	0.456*

	No	7	46.67%	5	33.3.%	
Area involved	Vertex	2	13.33%	3	20.00%	0.645**
	Occipital	8	53.33%	8	53.33%	1.000*
	Frontal	1	6.67%	1	6.67%	1.000**
	Temporal	4	26.67%	3	20.00%	1.000**
	Peripheral	0	0.00%	0	0.00%	1.000**
Nail involvement	Yes	2	13.33%	0	0.00%	0.483**
	No	13	86.67%	15	100.0%	
Exclamation mark hair	Yes	2	13.33%	2	13.33%	1.000**
	No	13	86.67%	13	86.67%	
Hair pull at patch edges	Easily detached	5	33.3.%	3	20.00%	0.682**
	Normal	10	66.67%	12	80.00%	

*(chi-square)test **fissure exact test

Figure (2) illustrates the distribution of study groups according to family history and shows that 9(73.3%) and 5(33.3%) of group A and group B respectively have a positive family history. The difference is statistically non-significant between the groups.

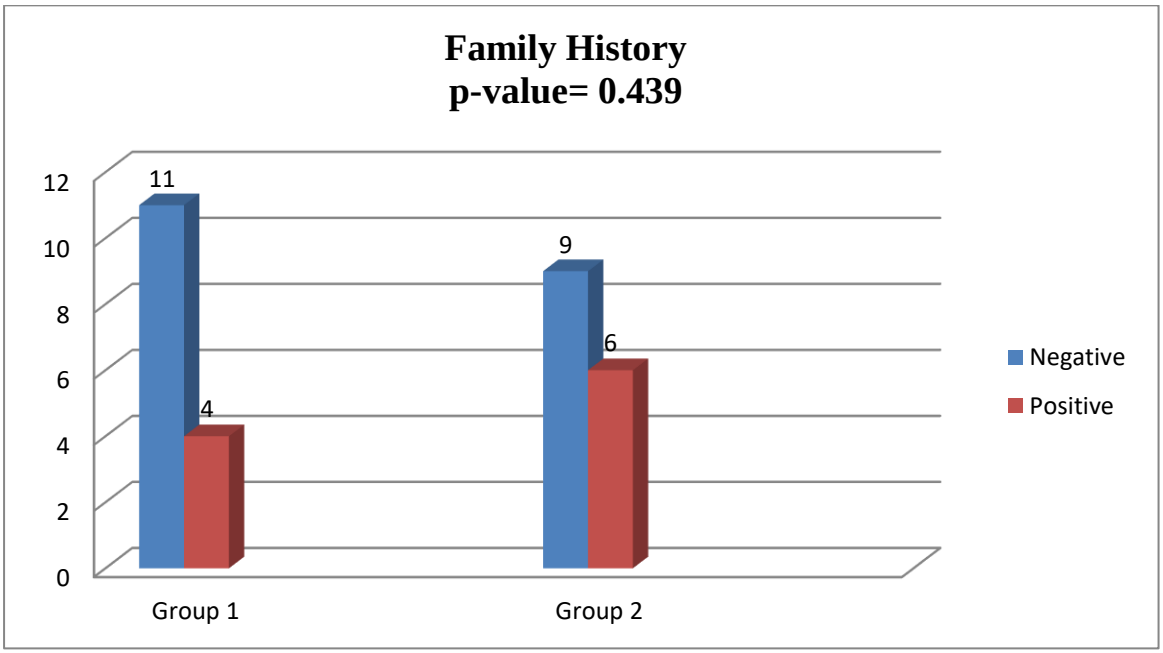

Figure (2): The distribution of study groups according to family history.

Table (4) shows the comparison between study groups regarding SALT score at the baseline, 4 weeks, 8 weeks, and 12 weeks visits and reveals non-significant differences.

Table (4a): The comparison between study groups regarding the SALT score.

SALT score	Group A	Group B	p-value*
	Mean ± SD	Mean ± SD	
Baseline	7.933±3.595	5.667±4.801	0.096
4 weeks visit	7.200±3.189	5.167±2.922	0.079
8 weeks visit	5.400±2.995	3.900±2.894	0.174
12 weeks visit	4.267±3.348	2.700±2.016	0.132

*(un-paired)t-test

Table (4b) demonstrates the comparison between the baseline and 12weeks visits for each study group concerning SALT score depicts that the mean of the SALT score for both groups at 12 weeks visit is lower than that of the baseline visit in a statistically significant way.

Table (4b):

	Study groups	**Baseline visit**	**12 week visit**	**p-value**
SALT Score	Group A	7.933±3.595	4.267±3.348	**0.007***
	Group B	5.667±4.801	2.700±2.016	**0.036***

DISCUSSION:

Alopecia areata (AA) is a common, inflammatory, non-scarring type of hair loss that affects persons of both sexes and all age groups. It is characterized by variable clinical presentations, ranging from single or multiple well-circumscribed patches of hair loss to extensive involvement with complete absence of body and scalp hair (1). The condition is associated with a variety of inflammatory and immune-mediated diseases, such as atopic dermatitis, allergic rhinitis, lupus erythematous, psoriasis, thyroid disease, rheumatoid arthritis, celiac disease and type 1 diabetes mellitus (2). Several therapies are available for the treatment of AA, including corticosteroids (topical, systemic or injectable modalities) and topical immunotherapies (diphenylcyclopropenone or squaric acid Dibutyl ester), but these are characterized by unpredictable efficacy and durability (7, 8). Alopecia areata (AA) has been generally considered a cell-mediated tissue-specific autoimmune hair disease (9, 10, 11).

TCs are considered the first-line therapy for patch-type AA. High-potency TCs such as 0.05% clobetasol propionate (3). Azelaic acid is a dicarboxylic acid, derived from the fungus Pityrosporum ovale, which is naturally derived from grains such as wheat and barley (4). Azelaic acid is an effective topical therapy for patchy AA (5).

Characteristics of grouped Population:

The present study was performed to evaluate the efficacy of topical Azelaic acid 20% in the treatment of Alopecia Areata by collecting the patients who are diagnosed to have scalp Alopecia Areata with certain criteria to be enrolled in this study.

The current study involved the patients who are diagnosed to have scalp Alopecia Areata will be enrolled in this study. The patients will be collected from EDTC. The patients will be divided into two groups: group A includes fifteen patients on topical Clobetasol propionate 0.05% cream; group B includes fifteen patients on topical Azelaic acid 20% cream. Both treatment groups will be followed up for a period of twelve weeks with a monthly check-up visit. Both drugs will be applied topically once daily at night.

This study showed that the differences between study groups concerning all the variables (age, weight, height, BMI, and duration) are statistically non-significant {(0.95), (0.448), (0.824), (0.932), (0.243)} respectively. The assessment of both therapies in the clinical course of the disease will be assessed using the SALT score with physical and dermoscopic examinations each month (6).

The present study showed the comparisons between study groups concerning socio-demographic characteristics (Economical status, Address Jobs), physical examination (erythema, scale, short hair, area involved, nail involvement, exclamation mark hair, hair pull at patch edges) and family history demonstrates non-significant differences between group A and group B. Pascher *et al.*,1970 (12) was agreed with this study.

The SALT is a tool used by clinicians to assess the severity of AA through an estimate of the percent of scalp hair loss (0%-100%). A visual aid shows four images of the scalp divided into quadrants (i.e., left side, right side, top, and back). The percent of hair loss is assessed in each quadrant and the final SALT score is obtained by multiplying an assigned weight for each quadrant by the percent of hair loss in each quadrant, specifically, SALT score= 0.18×percent_left side + 0.18×percent_right side + 0.4×percent_top + 0.24×percent_back (13).

The present study showed the comparison between study groups regarding SALT score at the baseline, 4 weeks, 8 weeks, and 12 weeks visits and reveals non-significant differences (p= 0.096, 0.079, 0.174, 0.132) respectively. Hordinsky M and Donati A, 2014 (14) agreed with this study. while the comparison between the baseline and 12 weeks visits for each study group concerning SALT score depicts that the mean of the SALT score for both groups at 12 weeks visit is lower than that of baseline visit in a statistically significant way (Group A, p=0.007, Group B, p=0.036). De Oliveira *et al.,* 2019 (15) agreed with this study and showed that need chronic administration maintains response. Lee and Lee, 2017(8) disagreed with this study and show the superiority of topical clobetasol compared to other medications.

Finally, the results showed that topical Azelaic acid 20% has an acceptable efficacy in comparison to topical clobetasol 0.05% in the treatment of localized Alopecia Areata on the scalp and can be considered as a therapeutic option for this condition.

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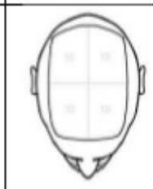
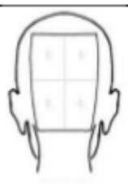
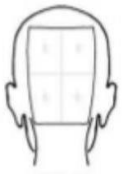
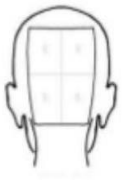
Appendix I (SALT Score)

Appendix II

Questionnaire

Date	Top: 40%	Back: 24%	Left Side:18%	Rt. Side: 18%	Total % of Hair Loss
					
					
					

No.: **Name:** **Age (in years):** **Tel. №:**
Gender: 1. Male 2. Female **Social status:** 1. Single 2. Married 3. Divorced
Economic status: 1. Poor 2. Moderate 3. Good 4. Very good
Address: 1. Inside Erbil 2. Outside Erbil
Job: 1. Child 2. Student 3. Gov. employee 4. Private employee 5. Retired 6. Jobless
Weight (Kg): **Height (Cm):** **BMI:**

History:
Duration:
Previous illness: 1. No 2. Febrile illness 3. Diarrhea 4. Chronic psych stress 5. Others
Symptoms: 1. No 2. Itching 3. Burning 4. Pain 5. Other (specify)
Associated diseases: 1. Vitiligo 2. Thyroid 3. Others
Previous attack: 1. Yes 2. No
If yes, before how long?
Family history:

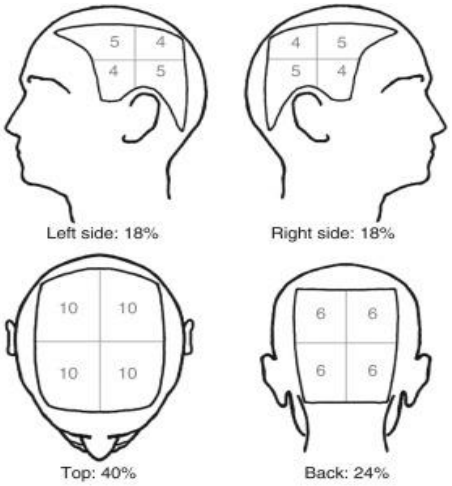
Physical examination:		

Number of patches:		**Size (Cm):**
Erythema: 0. No 1. Yes	**Scale:** 0. No 1. Yes	**Short hairs:** 0. No 1. Yes
Area involved: 1. Vertex 2. Occipital 3. Frontal 4. Temporal 5. Peripheral (circumferential)		
Nail involvement: 1. No 2. Pitting 3. Ridging 4. Beaus lines 5. Red lanula 6. Biting		
Exclamation mark hair: 0. No 1. Yes	**Hair pull at patch edges:** 1. Easily detached 2. Normal	

Salt Score:

1. Baseline
2. 4 weeks
3. 8 weeks
4. 12 weeks

Assessment diagram of SALT score at each visit

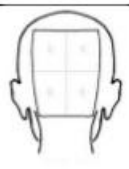
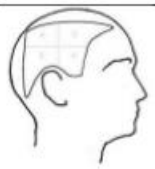
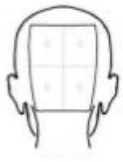


Olsen/Canfield

Salt score			
Site:	Subject:	Visit:	Date:
Quadrant	Percentage involved	Multiplier	Score
Left side		0.18	
Right side		0.18	
Top		0.40	
Back		0.24	
Total			

Follow up diagram of SALT score of each patient

SALT Score: Sequential Analysis

Date	Top: 40%	Back: 24%	Left Side:18%	Rt. Side: 18%	Total % of Hair Loss
					
					
					

Appendix III

Information sheet

I am Mudheher Ibrahim Salih Senior House Officer (SHO) of Dermatology. I have research on the efficacy of topical azelaic acid 20% cream in the treatment of Alopecia Areata of Scalp in Erbil Dermal Teaching Centre. I shall provide this drug as free for you.

Appendix IX : Consent Form

Department of Dermatology

The Efficacy of Topical Azelaic acid 20% Cream in the Treatment of Alopecia Areata of Scalp.

I confirm that I have read and understand the information about the project as provided in the participant information sheet dated in / / 2021.

I confirm that I have had the opportunity to ask questions and the researcher has answered any questions about the study to my satisfaction.

I understand that my participant in voluntary and that I am free to withdraw from the project at any time, without having to give a reason and without any consequences.

I understand that I can withdraw my data from the study at any time.

Signature:

Name: