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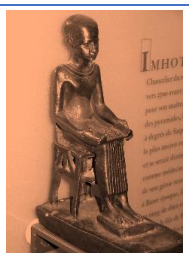

Original Article

Comparative Study between Intralesional Pentoxifylline and Steroid in Localized Alopecia Areata

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ABSTRACT

Background: Alopecia Areata [AA] is a classic autoimmune disorder, with a fluctuating course and no definitive treatment with guaranteed outcome. Intralesional corticosteroids are the most commonly prescribed treatment for patchy AA, but with a typical outcome of localized regression**.**

The Aim of the work: This study aimed to evaluate the efficacy and safety of intralesional injection of pentoxifylline in localized alopecia areata compared to intralesional injection of triamcinolone acetonide [TrA].

Patients and Methods: Thirty patients with localized alopecia areata, involving at least two patches, were included in this study. In each patient, one patch was treated with intralesional pentoxifylline [PTX] and another patch with intralesional corticosteroids [ILCs]. Assessments were conducted every four weeks for a total of 15 weeks. Evaluation was completed at baseline, post-treatment, clinically using the SALT score, dermoscopically, and photographically.

Results: Both treatment protocols resulted in significant improvement of SALT score and dermoscopic findings post-treatment. Comparison of the two treatment modalities revealed a 100% hair regrowth rate after intralesional corticosteroids [ILC] and a 60% improvement after intralesional pentoxifylline [PTX], with a statistically significant difference. Adverse effects included temporary pain during injection. Both treatment strategies demonstrated efficacy in the management of patchy alopecia areata, with the highest effectiveness observed following the ILCs procedure due to greater and earlier hair regrowth.

Conclusion: Pentoxifylline is a potent and safe therapeutic approach for alopecia areata and can be used as an alternative to intralesional corticosteroid injection.

Keywords: Alopecia Areata; Intralesional; Steroids; Pentoxifylline.

INTRODUCTION

Alopecia areata [AA] is an autoimmune disorder characterized by non-scarring hair loss. It affects both sexes and all age groups, with approximately 2% of the population experiencing it at some point in their lives [1].

Studies have reported that the majority of patients develop the disease before the age of 40 [2].

The exact pathophysiology of alopecia areata remains unknown. The most widely accepted theory is that alopecia areata is a lymphocyte-mediated autoimmune condition that is likely to occur in genetically predisposed individuals [3].

Alopecia areata occurs due to a white blood cell attack on hair follicles [HFs] and disruption of their immune privilege, resulting in temporary hair loss that can last from weeks to many years and impose a significant psychological burden [4].

The management of AA depends primarily on the patient's age and the extent of hair loss, which involves addressing the psychological needs of the patients and providing treatment to those requiring intervention [5].

Intralesional corticosteroids are commonly used in AA. Steroids with low solubility are preferred for their slow absorption from the injection site, promoting maximum local action with minimal systemic effects. Immunosuppression is the primary mechanism of action. Corticosteroids suppress the lymphocyte-mediated immune attack on the hair follicle [6].

Pentoxifylline is a methylxanthine derivative with various anti-inflammatory effects, approved by the Food and Drug Administration [FDA] for the treatment of intermittent claudication. Studies have shown that it has diverse physiological effects at the cellular level, which may be significant in treating a diverse range of diseases [7].

Pentoxifylline affects almost all factors responsible for blood viscosity and is indeed the first known hemorheologically active drug [8]. Pentoxifylline [PTX] has anti-inflammatory effects by inhibiting pro-inflammatory cytokines [9]. PTX efficiently interferes with the activation and cell adhesion of T lymphocytes **[10, 11]**, reduces the surface expression of ICAM-1 **[12]**, suppresses natural killer cell-mediated cytotoxicity **[13]**, and enhances the T-helper type 2 [Th2] response as evidenced by elevated Th2 cytokine levels **[14]**.

THE AIM OF THE WORK

This study aimed to evaluate the efficacy and safety of intralesional injection of pentoxifylline compared to intralesional injection of triamcinolone acetonide [TrA] for the treatment of localized alopecia areata.

PATIENTS AND METHODS

This interventional comparative study was conducted from November 2019 to March 2021. The study enrolled 30 patients with localized alopecia areata recruited from outpatient clinics of the Dermatology and Venereology Department at Al-Zahraa University Hospital. Informed written consent was obtained from all patients after receiving approval from the Research Ethics Committee of the Faculty of Medicine for Women at Al-Azhar University. Patients with localized AA [at least 2 patches] either in remission or recently diagnosed and patients aged 16 years or older were included in the study. Patients with alopecia areata affecting more than 50% of the scalp were excluded, as well as pregnant women, lactating mothers, and those with needle phobia. Patients with bleeding disorders, immuno-suppressed patients, and those on immunosuppressive medications were also excluded from the study.

All patients underwent comprehensive medical history taking, general physical examination, dermatological assessment, and clinical evaluations to assess the extent of alopecia areata using the SALT score, photography, and dermoscopy. Patients were instructed to keep their hair as short as possible, and the affected areas were prepared by cleaning with alcohol. Patients who could not tolerate the discomfort received 2% lidocaine cream [prilocaine cream] under occlusion, applied one hour before the procedure. Patients were randomly divided into two groups. Patients in the pentoxifylline group received intralesional injections of pentoxifylline at a dose of 0.05 mL per patch alone, with a maximum of 20 mg per session [5 sessions, 3 weeks apart]. Patients in the steroid group were treated with intralesional injections of Triamcinolone acetonide [5mg/ml]. Digital photographs were taken at baseline, between sessions, at the end of treatment, and during follow-up to assess treatment efficacy and recurrence. Assessment of treatment response was conducted using the Severity of Alopecia Tool [SALT score], dermoscopy, and photographs.

Statistical Analysis: The analysis was conducted using SPSS version 26. Numeric data were presented as mean ± standard deviation [SD] for normally distributed variables, or as median and interquartile range [IQR] for those not normally distributed. Categorical variables were summarized using frequencies and percentages. The normality of the data was assessed with the Kolmogorov-Smirnov test. For normally distributed numeric variables, independent samples t-tests were employed to compare between two groups, whereas the Mann-Whitney U test was utilized for non-normally distributed numeric variables. Associations between categorical variables were examined using either the Chi-square test or Fisher's exact test [if more than 20% of cells had an expected count less than 5]. The correlation between numeric variables was evaluated using Pearson's correlation coefficient for normally distributed data and Spearman's rank correlation coefficient for non-normally distributed data. A P-value of less than 0.05 was considered statistically significant.

RESULTS

Thirty patients with localized alopecia areata were included in the study. The participants consisted of both genders [28 males [93.3%] and 2 females [6.7%]], with an age range of 16 to 58 years and a mean ± SD of 30.33 ± 11.60 years [Table 1]. When comparing the SALT scores between the steroid group and PTX group, there was a statistically significant difference between the two groups before treatment [P-value = 0.002]. There was no statistically significant difference between the two groups at the end of the study [one month after the last session] [P-value = 0.568]. However, there was a highly statistically

significant difference between both groups based on the SALT score categories [p-value = 0.002]. When comparing the reduction in SALT scores between both groups, there was a highly statistically significant difference between the steroid group and PTX group [P-value = 0.001] [Table 2]. There was no statistically significant difference between the steroid group and PTX group in yellow dots, black dots, exclamation marks, and vellus hair [p-values = 1.000, 0.432, 0.405, 0.598, respectively] before treatment. After treatment, there was also no statistically significant difference between both groups in exclamation marks, broken hair, and vellus hair [p-values = 0.197, 0.389, 0.426, respectively] [Table 3]. There was no statistically significant correlation between SALT score reduction and the age of the studied cases in the steroid group, PTX group, and all patients [Table 4].

Table [1]: Demographic data of the studied cases

		Total no. = 30
Sex	**Females**	2 [6.7%]
	Males	28 [93.3%]
Age	**Mean ± SD**	30.33 ± 11.60
	Range	16 – 58
Duration [m]	**Median [IQR]**	4 [2 – 8]
	Range	1 – 24

Table [2]: Comparison between PTX group and steroid group regarding SALT score before and at the end of the study

		Steroid group	PTX group	Test value	P-value
		No. = 30	**No. = 30**		
Salt score % [before]	**Median; IQR]**	3.6; [2.4 – 6.3]	1.9; [1.2 – 3.6]	-3.062	0.002
	Min. – Max.	0.54 – 32	0.72 – 6		
S category [before]	**S0**	0 [0.0%]	0 [0.0%]	1.017	0.313
	S1	29 [96.7%]	30 [100.0%]		
	S2	1 [3.3%]	0 [0.0%]		
Salt score % [after]	**Median; [IQR]**	0.85; [0 – 1.8]	0.81; [0.4 – 1.68]	-0.571	0.568
	Min. – Max.	0 – 8.4	0.12 – 4		
S category [after]	**S0**	8 [26.7%]	0 [0.0%]	9.231	0.002
	S1	22 [73.3%]	30 [100.0%]		
	S2	0 [0.0%]	0 [0.0%]		
SALT reduction	**Median; [IQR]**	80; [66.67 – 100]	50; [30 – 75]	-3.424	0.001
	Min. – Max.	15 – 100	0 – 93.33		

Table [3]: Dermoscopic findings in steroid group versus PTX group before and after treatment

	Steroid group	PTX group	Test value	P-value
	No. = 30	**No. = 30**		
Dermoscopic before				
Yellow dots	26 [86.7%]	26 [86.7%]	0.000	1.000
Black dots	16 [53.3%]	19 [63.3%]	0.617	0.432
Exclamation mark	19 [63.3%]	22 [73.3%]	0.693	0.405
Broken hair	5 [16.7%]	12 [40.0%]	4.022	0.045
Vellus hair	19 [63.3%]	17 [56.7%]	0.278*	0.598
Terminal hair	11 [36.7%]	4 [13.3%]	4.356	0.037
Dermoscopic after				
Yellow dots	9 [30.0%]	22 [73.3%]	11.279	0.001
Black dots	3 [10.0%]	10 [33.3%]	4.812	0.028
Exclamation mark	4 [13.3%]	8 [26.7%]	1.667	0.197
Broken hair	2 [6.7%]	4 [13.3%]	0.741	0.389
Vellus hair	13 [43.3%]	10 [33.3%]	0.635	0.426
Terminal hair	30 [100.0%]	18 [60.0%]	15.000	0.000

Table [4]: Correlation of SALT score reduction with age, duration [months] and satisfaction score of the studied cases

	SALT reduction					
	Steroid group		**PTX group**		**All**	
	r	**P-value**	**r**	**P-value**	**r**	**P-value**
Age	0.084	0.659	-0.214	0.257	-0.044	0.741
Duration [m]	-0.244	0.194	**-0.476****	**0.008**	**-0.348****	**0.007**
Satisfaction score	**0.883****	**0.000**	**0.846****	**0.000**	**0.899****	**0.000**

Illustrated cases

No [1]

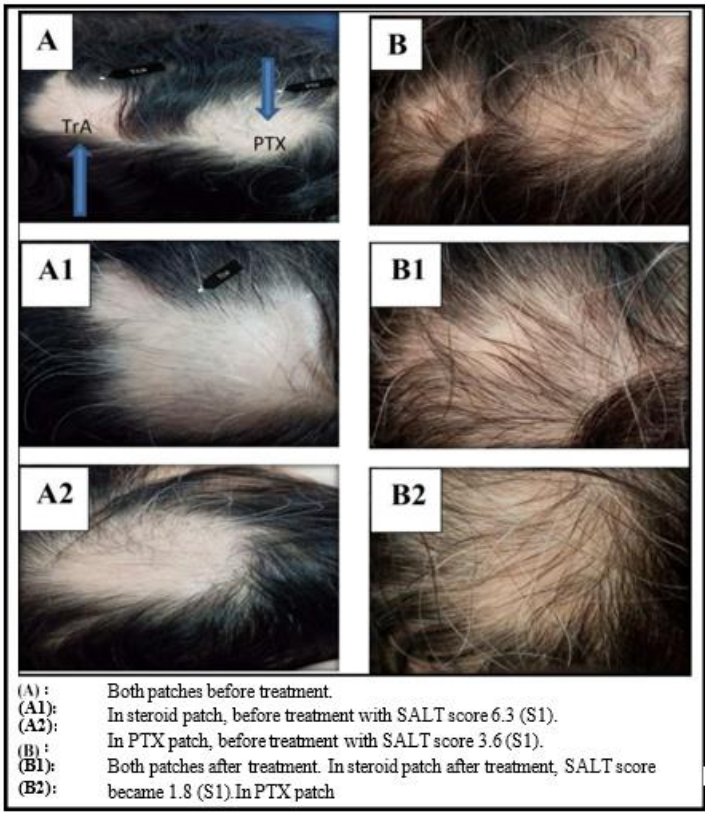

Figure [1]: patchy AA over scalp. one patch treated by intralesional TrA injection and another patch treated by intralesional PTX injection.

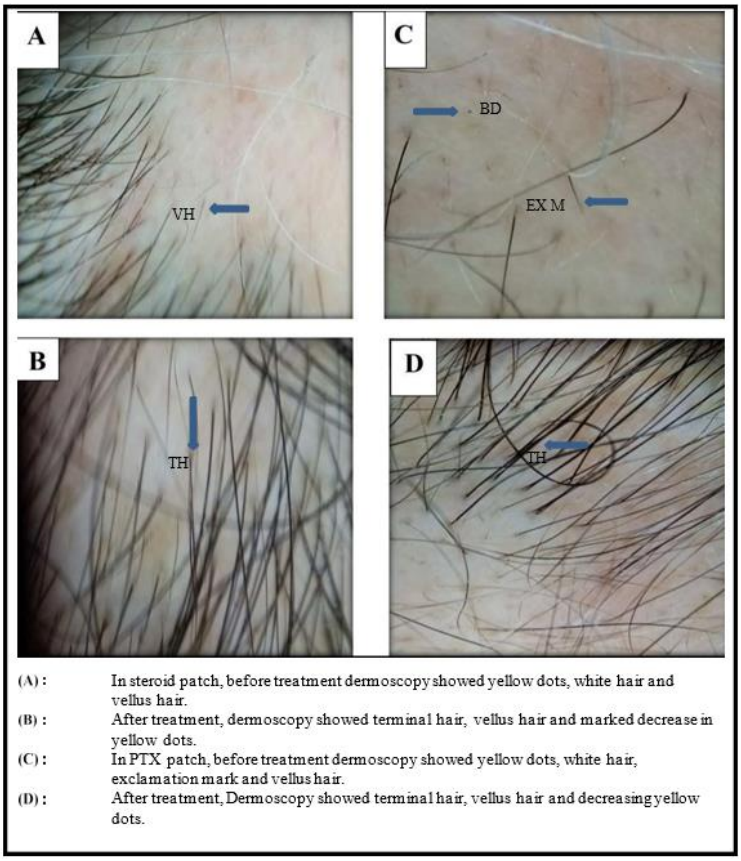

Figure [2]: Patchy AA over scalp one patch treated by intralesional TrA injection and another patch treated by intralesional PTX injection

No [2]

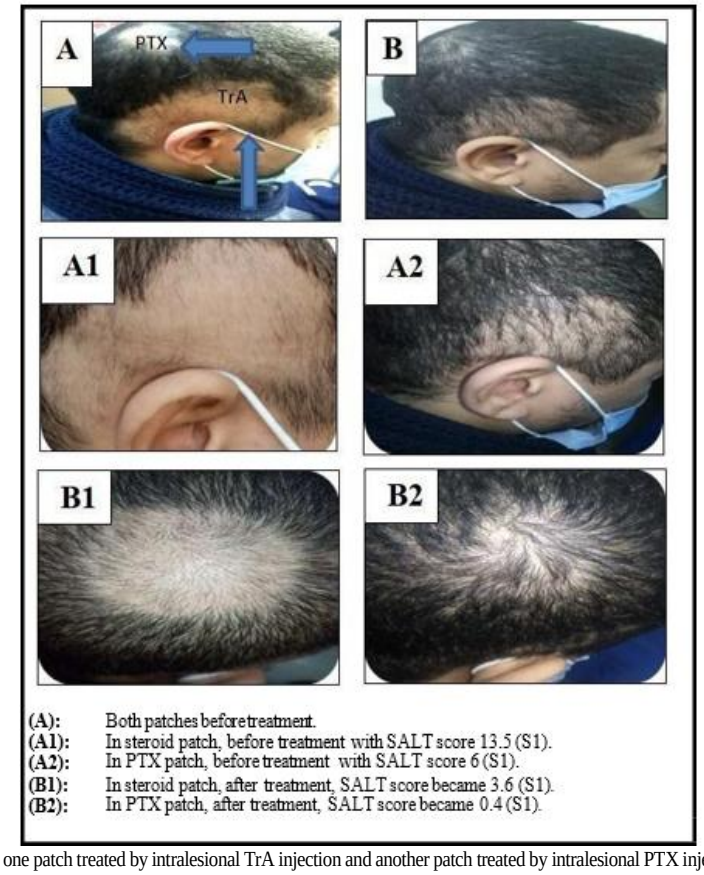

Figure [3]: Patchy AA over scalp one patch treated by intralesional TrA injection and another patch treated by intralesional PTX injection.

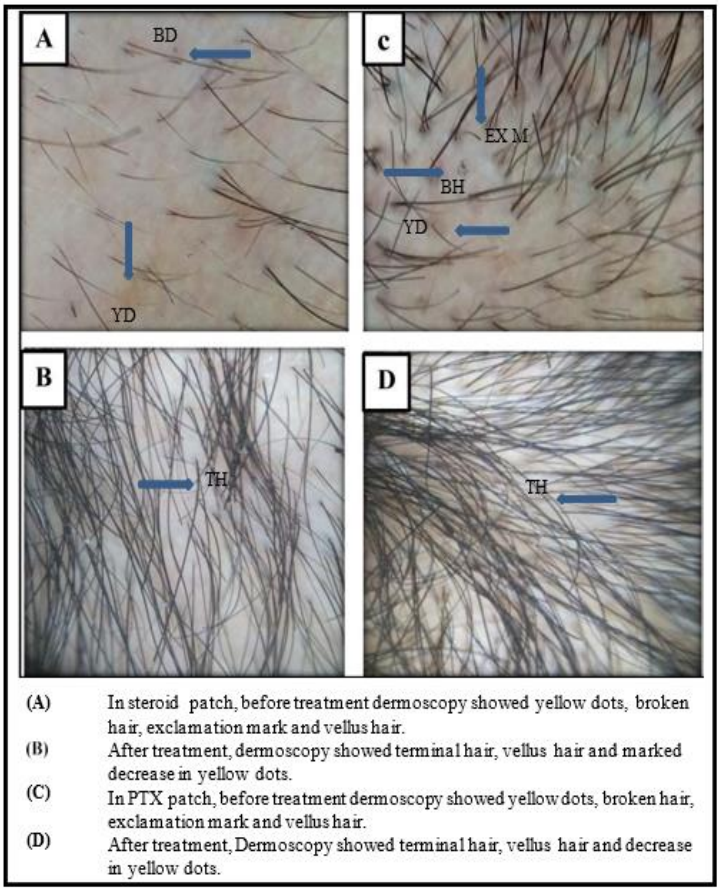

Figure [4]: Patchy AA over scalp one patch treated by intralesional TrA injection and another patch treated by intralesional PTX injection. VH = vellus hair; EX M = exclamation mark; BD = black dot TH = terminal hair; YD = yellow dot; BH = broken hair

DISCUSSION

Alopecia areata is an autoimmune disease that presents as discrete patches of non-scarring hair loss on skin with typical appearance [15].

Although the etiopathogenesis of alopecia areata is poorly understood, most research suggests that it is associated with the immune cycle [16].

The primary treatments include systemic corticosteroids, photochemotherapy, and other immunosuppressive agents. Spontaneous resolution occurs in up to 80% of patients with localized patchy hair loss of short duration [<1 year] [17].

El-Taweel *et al.* [18] observed hair regrowth in 71% of patients with AA treated with triamcinolone acetonide injections every two weeks, compared to 7% of control subjects injected with isotonic saline.

Alkhalifah *et al.* [19] conducted a study on 290 patients with AA, showing improvement in 61% of patients after 1-2 intralesional steroid injections.

Ranawaka *et al.* [20] used intralesional corticosteroid injection with a concentration of 10 mg/mL every two weeks for 5 sessions and demonstrated hair regrowth in 64% of patients. However, our results regarding the clinical response to intralesional corticosteroid [ILCS] treatment were better than all the aforementioned studies.

In our study, we not only relied on clinical response assessment but also on dermoscopic findings. There was a significant reduction in all dermoscopic features of AA at the end of the sessions in both groups. By comparing the improvement in dermoscopic findings between the two groups at the end of the study, there was a statistically significant difference in black dots and highly significant differences in yellow dots and terminal hair after treatment, with better improvement seen in the steroid group than the PTX group.

In the current study, we utilized dermoscopy to provide more objective results. There was a significant improvement in all dermoscopic findings, which was noticeable from the first session and became more significant by the end of the study.

This is consistent with the studies of **Srivastava et al.** [21] and **Ganjoo and Thappa** [22], who demonstrated an early response to intralesional corticosteroids by dermoscopy. Similarly, **Albalat et al** [23] reported a statistically significant improvement in dermoscopic findings after treatment.

In our study, the patients' age ranged between 16 and 58 years, with a mean age of 30.33 ± 11.60 years, in agreement with a study by **Darwin et al.** [24], who stated that AA can occur at any age, with a median age at diagnosis of 33. Patients within these age ranges are more suitable for intralesional injections.

This is also supported by **Aksu Cerman et al.,** [25] who found no statistically significant differences in age among AA patients, with a mean age at diagnosis of 31.21 ± 9.60 years.

The patients were randomly selected, with 28 males [93.3%] and 2 females [6.7%], which aligns closely with the study by **Metwally et al.** [26], who conducted research on 25 males [92.6%] and 2 females [7.4%] with a mean age of 31.07 ± 10.19 years [ranging from 18 to 50 years].

Conclusion:

Both intralesional pentoxifylline and intra-lesional corticosteroid [ILCs] injection are safe and effective modalities in the treatment of localized AA. Pentoxifylline is effective and at the same time less irritating and causes less atrophy compared to ILCs injection. Therefore, pentoxifylline is preferable to be chosen as a treatment option, especially when there is a contraindication to ILCs injection. Dermoscopy is a valuable tool for the dermatologist for the diagnosis, follow-up, and evaluation of response to treatment in AA.

Recommendations:

Further studies with an increasing number of sessions and extended follow-up period are recommended to provide more conclusive results. Additionally, research with alternative treatment modalities for localized alopecia areata is recommended to yield more definitive outcomes.

Conflicts of interest:

There are no conflicts of interest.

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