



Intralesional Platelet-rich Plasma Therapy vs Intralesional Triamcinolone Acetonide for the Treatment of Alopecia Areata

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ABSTRACT

Introduction: Alopecia areata (AA) is a common autoimmune condition causing hair loss. Platelet-rich plasma (PRP) has emerged as a new treatment modality in dermatology, and preliminary evidence has suggested that it might have a beneficial role in hair growth.

Aims and objectives: To compare the efficacy of intralesional PRP therapy vs intralesional triamcinolone acetonide (TrA) for the treatment of AA in a randomized, single-blinded, placebo and active-controlled parallel study.

Materials and methods: Thirty AA patients were randomized into two groups to receive intralesional injections of PRP or TrA. Half the number of patches in each patient were treated and other half were injected with placebo (normal saline). A total of three treatments were given for each patient at one month intervals. The evaluation was done by severity of alopecia tool (SALT) scoring, dermoscopic evaluation of dystrophic hair, and patient satisfaction. Patients were followed up for 6 months.

Observations and results: Intralesional TrA was found to give better results as compared with intralesional PRP.

Conclusion: Intralesional TrA gives superior results in AA as compared with intralesional PRP.

Keywords: Alopecia areata, Intralesional triamcinolone acetonide, Platelet-rich plasma therapy.

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INTRODUCTION

Alopecia areata (AA) does not destroy hair follicles, and therefore, the potential for regrowth of hair is retained

for many years, and is possibly lifelong.¹ A variety of therapeutic options are available. Search for new modalities continues as there is a high relapse rate.

Intralesional corticosteroids are the most popular drugs available for the treatment of AA.² But localized atrophy is a common complication, particularly if TrA is used.¹ Other therapies like topical minoxidil, anthralin, immunotherapy, topical/systemic corticosteroids, cyclosporine, and Psoralen and Ultra Violet-A light therapy are commonly used with varying success.

Platelet-rich plasma (PRP) is an autologous concentration of platelets in concentrated plasma.³ Recently, there have been a few studies investigating the clinical results of PRP applications as treatment for AA. It is hypothesized that growth factors released from platelets may act on stem cells in the bulge area of the follicles, stimulating the development of new follicles and promoting neovascularization in cases of AA.⁴

So, PRP is a potential useful therapeutic tool for alopecias, without major adverse effects. A study has been carried out to evaluate the effectiveness of intralesional PRP in cases of AA and compare its efficacy with the most popular treatment option, i.e., intralesional TrA.

AIMS AND OBJECTIVES

- To compare the efficacy and safety of intralesional PRP vs intralesional TrA for the treatment of stable scalp AA.
- To compare the overall patient satisfaction in the two treatment groups.

MATERIALS AND METHODS

Ethical Considerations

The study design was approved by the Institutional Ethics Review Committee. Written informed consent was obtained from each subject prior to enrollment in the study.

Study Area

The study was conducted in the outpatient department (OPD) of a tertiary care center situated in Navi Mumbai, in the periphery of Mumbai, the capital of Maharashtra state in India.

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Duration

The study was conducted over a period of 22 months from February 2014 to November 2015.

Inclusion Criteria

- Patients with patches of AA over scalp
- Patients with stable AA—patient denying history of increase in patch size or of development of new patches and a negative hair pull test
- Patients with a minimum of two patches
- Patients with a normal platelet count (>1.5–4.5 lakh/cu.mm)
- Patients willing to be part of the study after informed consent

Exclusion Criteria

- Patients below 15 years of age
- Patients with active AA
- Patients with alopecia totalis/universalis
- Patients who have been treated with topical agents in the past 15 days or intralesional/systemic agents in the past 1 month
- Pregnant and lactating women
- Unwilling patients

Patients

- A sample size of 30 patients fulfilling the inclusion and exclusion criteria was taken in the study.
- Patients were selected from Dermatology OPD, MGM Hospital, Kamothe, Navi Mumbai, Maharashtra, India.
- A written informed consent was taken from all selected patients.
- Patients were explained the procedure, possible side effects, and postprocedure care.
- Information sheet was given to all patients. It was explained to them that they can drop out of the study at any given point of time for any reason. It will not affect their further management in any way.
- All patients were photographed prior to starting the study and at last follow-up visit.

Preparation of PRP

- All patients were sent to the blood bank located within MGM Hospital for preparation of PRP.
- After taking informed consent, patients' 20 cc blood was obtained by venipuncture in two tubes containing 0.9 mL of anticoagulant citrate dextrose A.
- After blood collection, the tubes were made to stand vertically for half an hour.
- The citrated blood was then centrifuged in Heraeus Cryofuge 5500i centrifuge at 1000 rpm for 12 minutes (soft spin) at 22°C.

- After the first step, each tube gave 3 mL of plasma (containing buffy coat with platelets and leukocytes).
- Subsequently, this 6 mL plasma was taken up from both the tubes using a sterile micropipette and was transferred to another sterile tube.
- A second round of centrifugation was performed at 2000 rpm for 10 minutes (hard spin) at 22°C.
- The pellet containing platelets accumulated at the bottom and the platelet-poor plasma surfaced to the top. The upper 2 mL was discarded and the lower 4 mL was used to resuspend the platelets.
- The suspended pellet in 4 mL of plasma was used as PRP.
- The platelet count was then checked to ensure adequate amount of platelets in PRP.

Procedure

- Randomization of the patients was done by using random number table and it was known only to the one doing the procedure.
- Patients were divided into two groups of 15 patients each.
- One group received intralesional PRP and the other group received intralesional TrA.
- Half of the patches in each patient were treated, whereas the other half were given placebo (normal saline). In case of odd number of patches, more number of patches were treated and less number were given placebo.
- The alopecia patches in each patient were randomized to receive intralesional PRP or intralesional TrA.
- Three monthly therapies were given.
- New patches developing during the course of the study were treated, but not included in the study evaluation.

Procedure for Injecting

- Area was cleaned by betadine solution and normal saline.
- 0.1ml of PRP/intralesional TrA/normal saline was injected into the dermis of affected patches at multiple points 1 cm apart.
- Treated site was again cleaned and left open.
- Patients were followed up for a total of 6 months.
- Evaluation was done at:
 - T0—1st visit (1st injection)
 - T1—2nd visit (2nd injection)
 - T2—3rd visit (3rd injection)
 - T3—4th visit (6 months after 1st injection)

Evaluation

Evaluation was done by a non-treating dermatologist at every visit.

Table 1: Age and sex distribution

Age	PRP				ILS				Total
	Male		Female		Male		Female		
	n	%	n	%	n	%	n	%	
Below 20	2	13	1	7	3	20	0	0	6
21–30	3	20	2	13	4	27	2	13	11
31–40	3	20	2	13	3	20	1	7	9
41–50	0	0	1	7	0	0	2	13	3
51–60	0	0	1	7	0	0	0	0	1
Total	8	53	7	47	10	67	5	33	30

Severity of Alopecia Tool Scoring

The proportion of scalp involvement is determined by dividing the scalp into five regions and estimating the percentage of the scalp surface that all the alopecic area would occupy if placed together. These five were named as regions:

1. S1: <25% hair loss
2. S2: 25 to 49% hair loss
3. S3: 50 to 74% hair loss
4. S4: 75 to 99% hair loss
 - a. A: 75 to 95% hair loss
 - b. B: 96 to 99% hair loss
5. S5: 100% hair loss

Severity of alopecia tool scoring was done at every visit.

Body Hair Loss

- B0: No body hair loss
- B1: Some body hair loss
- B2: 100% body hair loss (excluding scalp)

This involved a complete physical examination and included facial, axillary, truncal, genital, and extremity hair evaluation.

Nail Involvement

- No: No nail involvement
- N1: Some nail involvement
- N2: Twenty nail dystrophy/trachyonychia (i.e., all 20 nails)

Nail assessment was done at every visit to look for any improvement, worsening, or no change.

Dermoscopic Evaluation

It was done by a non-treating dermatologist. Evaluation was intended to determine the number of dystrophic hair in the patch. Markers for dystrophic hair included exclamation mark hair, black dots, yellow dots, coudability hair. The percentage of dystrophic hair was calculated on a 4-point scale:

1. 3: >50%
2. 2: 30 to 49%

3. 1: 1 to 29%
4. 0: no dystrophic hair

Patient Satisfaction

Based on the improvement perceived by the patients, they were asked to rate the improvement in hair growth on a 10-point scale:

- 7 and above: excellent response
- Between 4 and 6: good response
- 3 or less than 4: poor response

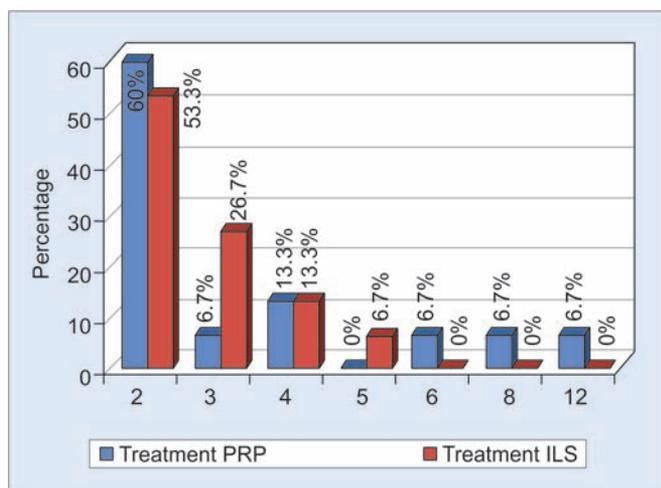
Data analysis was done by using statistical tests, such as unpaired t-test, paired t-test and chi-square test. Level of significance was set at 0.05. All p-values <0.05 were treated as significant. Statistical Package for the Social Sciences version 17.0 was used for data analysis.

OBSERVATION AND RESULTS

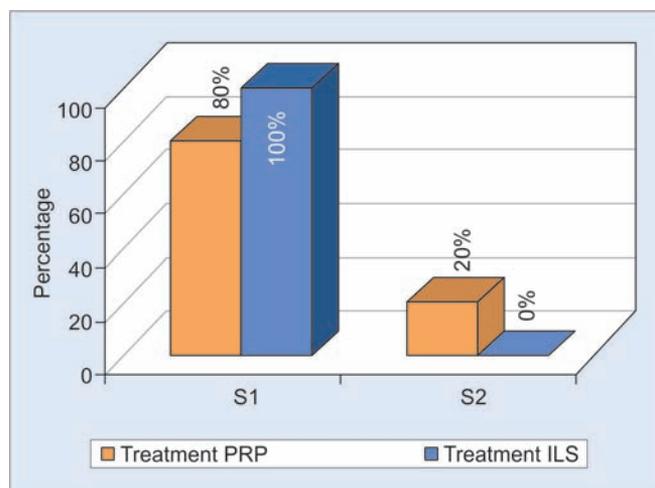
Out of the total 30 patients, 27 patients completed the study and 3 were dropouts. Assessment for hair regrowth was done by a blinded observer using SALT score and by another blinded observer for dermoscopic improvement. Also, subjective evaluation was done by the patient. Analysis of data was done by statistical tests mentioned above. Age and sex distribution has been depicted in Table 1. The disease duration of the patients enrolled in the study varied from less than 1 month to more than 6 months, depicted in Table 2. The number of patches of alopecia areata in the patients enrolled in the study varied from two to twelve, depicted in Graph 1. The extent of hair loss in patients, calculated by SALT score is depicted in Graph 2. Some patients gave history of similar episodes of patchy hair loss in the past, depicted in Table 3.

Table 2: Total disease duration of patients enrolled in the study

Duration	PRP (%)		ILS (%)		Total
≤1 month	2	13.3	4	26.7	6
1–6 months	10	66.7	11	73.3	21
>6 months	3	20.0	0	0.0	3
Total	15	100.0	15	100.0	30



Graph 1: Number of patches in all patients enrolled in the study



Graph 2: Extent of hair loss calculated using the SALT score

Table 3: Total number of prior episodes in each group of patients

		PRP		ILS		Total
		n	%	n	%	
Number of prior episodes	None	14	93.3	11	73.3	25
	One	1	6.7	2	13.3	3
	Two	0	0.0	1	6.7	1
	Multiple	0	0.0	1	6.7	1
Total		15	100.0	15	100.0	30

Table 4: Dermoscopic improvement (active)

	PRP				ILS			
	Before		After		Before		After	
	n	%	n	%	n	%	n	%
G0	2	15.4	7	53.8	1	7.1	11	78.6
G1	6	46.2	6	46.2	7	50.0	1	7.1
G2	1	7.7	0	0.0	5	35.7	2	14.3
G3	4	30.8	0	0.0	1	7.1	0	0.0
Total	13	100.0	13	100.0	14	100.0	14	100.0

Association of Infection with Onset of AA

No such association was seen in the study as none of the patients gave any history of, or symptoms suggestive of, any infection prior to onset of hair loss.

Family History

Only one patient enrolled in the study, from the ILS group, gave family history of AA.

Nail Involvement

Three (10%) patients had nail involvement which was in the form of pitting of nail plate. Of these, 1 was from the ILS group and two were from the PRP group.

Body Hair Involvement

Two (6.7%) patients had body hair involvement, one patient in each group.

Evaluation of Hair Regrowth by SALT Scoring

Thirteen (43.33%) patients had complete hair regrowth, of which 3 (20%) were from the PRP group and 10 (66.67%) were from the ILS group.

The association between treatment given and response was tested using chi-square test for association. The result indicates that there is significant difference in the proportion of responses between intralesional TrA and intralesional PRP therapy

Table 5: Dermoscopic improvement (placebo)

	PRP				ILS			
	Before		After		Before		After	
	n	%	n	%	n	%	n	%
G0	3	23.1	9	69.2	3	21.4	13	92.9
G1	7	53.8	4	30.8	8	57.1	1	7.1
G2	1	7.7	0	0.0	1	7.1	0	0.0
G3	2	15.4	0	0.0	2	14.3	0	0.0
Total	13	100.0	13	100.0	14	100.0	14	100.0

Table 6: Patient satisfaction score

		Patient satisfaction score					Total
		0%	10%	30%	60%	100%	
Treatment	PRP	8	2	0	1	2	13
	ILS	1	1	1	0	11	14
Total		9	3	1	1	13	27

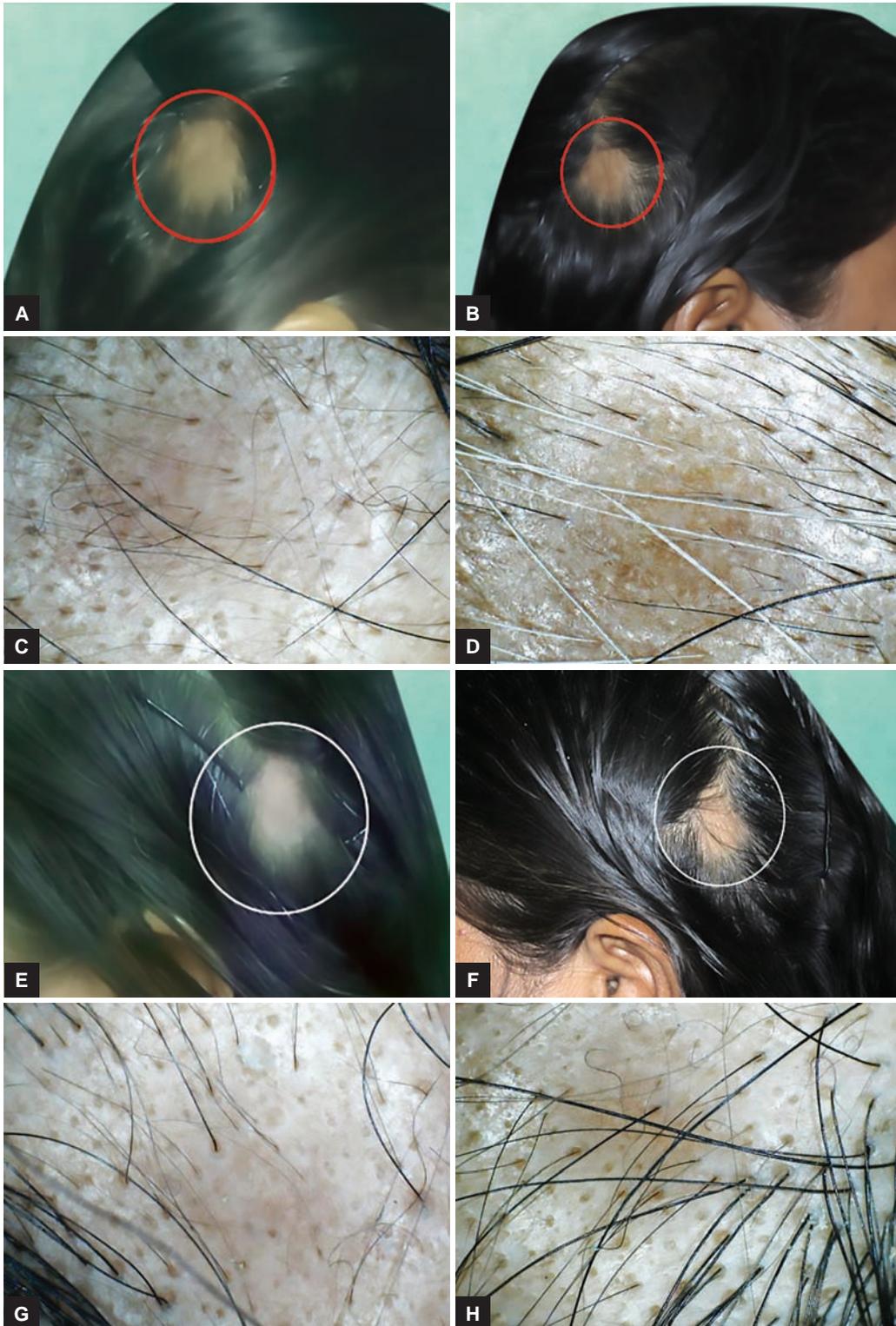
Chi-square = 13.897, $p < 0.05$, significant

Dermoscopic improvement in active and placebo patches are depicted in Tables 4 and 5 respectively.

Side effects: None of the patients enrolled in the study showed any adverse effect to therapy.

Patient satisfaction: As depicted in Table 6, 2 (13.33%) patients from PRP group were 100% satisfied, whereas 11 (73.33%) patients from the ILS group were 100% satisfied with the therapy.

The association between treatment given and patient satisfaction was tested using Pearson's chi-square test.

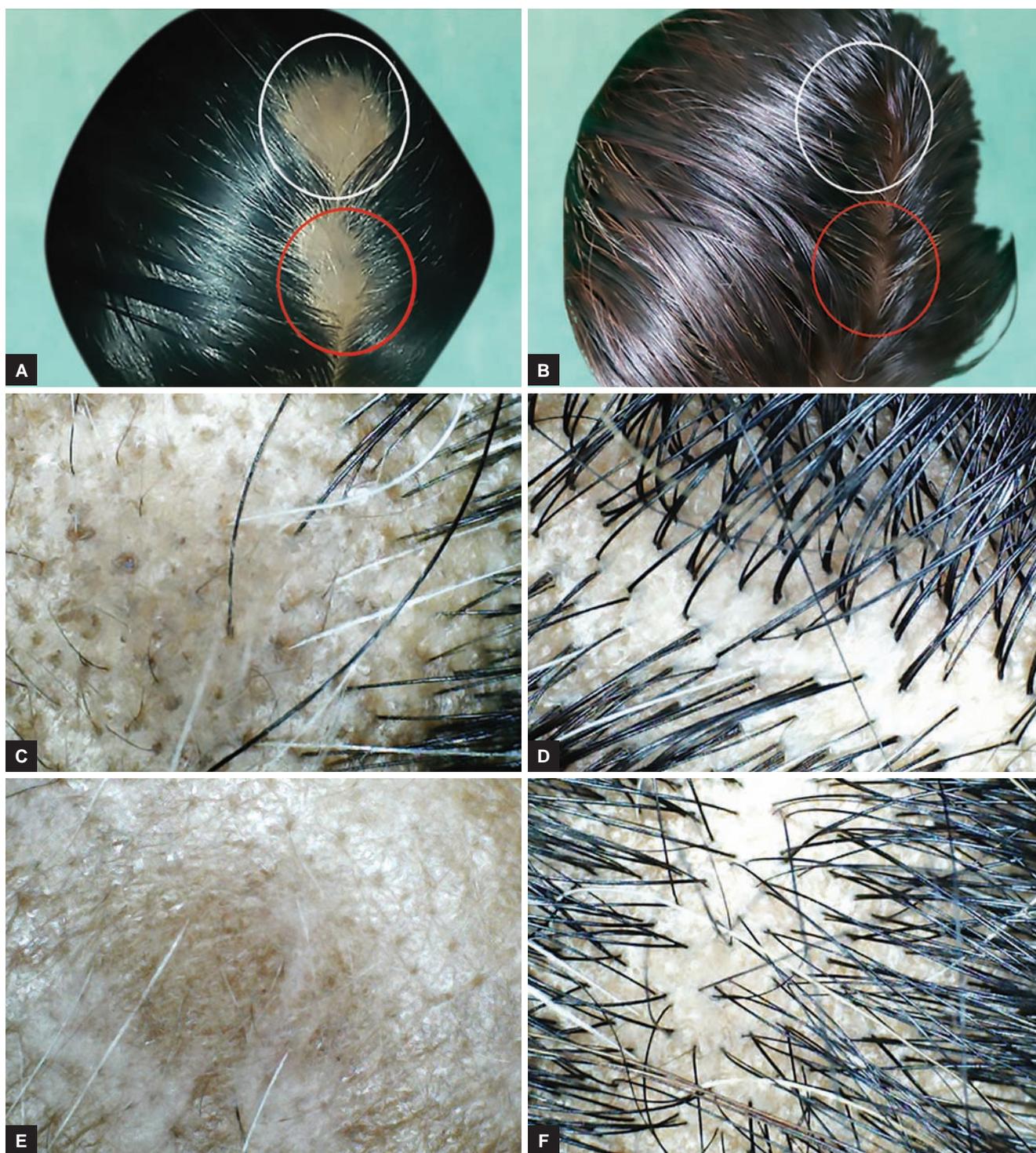


Figs 1A to H: Patient on PRP. 51 years/F, presented with two bald patches on the scalp since 15 months. No similar complaints in past. No body hair involvement. No nail involvement. No treatment taken in the past. No similar complaints in family members. H/o asthma in sister. Ix: WNL. Evaluation:

- SALT score: 0%
- Dermoscopic grading
 - Active patch G3 to G0
 - Placebo patch G3 to G1
- Patient satisfaction 60%

The result indicates that there is a significant difference in patient satisfaction between intralesional triamcinolone and intralesional PRP therapy.

Figures 1 and 2 compare two patients, one from each treatment group, highlighting the difference in treatment response.



Figs 2A to F: Patient on ILS. 42 years/F, presented with two bald patches on the scalp since 2 months. No similar complaints in past. No body hair involvement. No nail involvement. Topical herbal treatment taken in the past with partial improvement. No similar complaints in family members. H/o atopic dermatitis and vitiligo in daughter. Ix: Hb: 10.9; rest WNL. Evaluation:

- SALT score: 100%
- Dermoscopic grading
 - Active patch G1 to G0
 - Placebo patch G0 to G0
- Patient satisfaction 100%

DISCUSSION

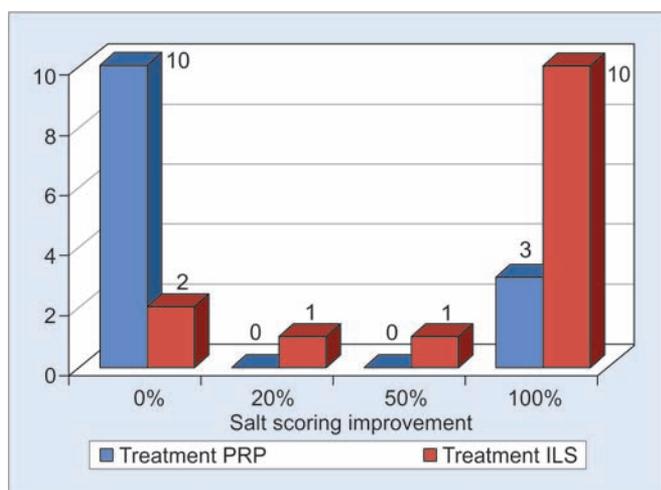
The practice of using PRP in dermatology is new and there are not many reports in the dermatology literature ascribing the benefits of this practice. It is therefore, subject

to both overuse and over expectations, as well as over concerns and misunderstandings.⁵ In 2013, Trink et al⁶ performed a randomized, double-blind, placebo- and active-controlled, half-head study on 45 patients and

evaluated the efficacy of PRP in patients with AA. Both triamcinolone and PRP led to increased hair regrowth compared with the untreated side of the scalp. Additionally, patients treated with PRP had significantly increased hair regrowth compared with those treated with triamcinolone.

Taking this study into consideration, we formulated our study to compare the safety and efficacy of intralesional TrA vs intralesional PRP for the treatment of scalp AA. Very few similar studies have been published in literature so far. According to the assessment criteria used by us, i.e., SALT scoring, dermoscopic evaluation and patient satisfaction, significant proportion of difference (p-value <0.05) has been found between intralesional PRP therapy and intralesional TrA 5 mg/mL groups. The response was better in patients treated with intralesional TrA 5 mg/mL, with 10 out of 15 (66.67%) patients showing 100% hair regrowth by the end of 6 months in contrast to only 3 out of 15 (20%) patients showing complete hair regrowth in the intralesional PRP therapy group; 10 out of 15 (66.67%) patients showed no response with PRP therapy in contrast to only 2 (13.33%) patients showing no response with Intralesional TrA. This association between treatment given and improvement in SALT score is depicted in Graph 3.

On dermoscopic examination also, better result was seen in the intralesional TrA group with more number of patients showing reduced dystrophic hair at the end of the therapy; 11 out of 15 (78.6%) patients in the ILS group achieved grade 0, i.e., no dystrophic hair, by the end of therapy; 11 out of 15 (78.6%) patients in the intralesional TrA group achieving the same result. Comparable results were seen even in the placebo patches with 13 (92.9%) patients of intralesional TrA group achieving grade 0 by the end of therapy in contrast to only 9 (69.2%) patients achieving similar results in the PRP group.



Graph 3: Association between treatment given and improvement SALT score

The results of our study are in contrast to the study conducted by Trink et al⁶ in which better results were seen in patients treated with intralesional PRP therapy. In another similar study done by Shumez et al,⁷ better results were seen with intralesional PRP therapy but the results were statistically insignificant.

Surprisingly, it was also noticed that when treatment given led to hair regrowth in the active patch, placebo patches in which normal saline was injected also showed similar hair regrowth. This finding was consistent with both the therapies.

The overall patient satisfaction was better in the intralesional TrA group with 11 (73.3%) patients being 100% satisfied in contrast to only 2 (13.33%) patients of PRP group.

The PRP preparations are being extensively used in wound healing and tissue repair despite insufficient evidence. Blinded multicenter, randomized controlled studies are the need of the hour. There are no universally established standards for collection, quality control and administration of the product.

Transforming growth factor beta (TGF- β) and platelet-derived growth factor (PDGF) have been purported to be the most active contents in PRP for hair growth. So far, their biological actions are not fully known.⁵ Mode of growth factor release and dynamics of the hair follicle environment may be important determinants of their outcome.

The TGF- β , in particular, is released in a latent form and requires activation for it to exert any biologic effects.⁸ Whether latent TGF- β can be activated and, if activated, whether it is quantitatively adequate to produce a desired biologic effect, is still unknown. The PDGF can promote several biologic effects. The mitogenic actions of PDGF, as well as its expression by malignant cells, suggest that it may have a role in malignant transformation.⁹

CONCLUSION

The assessment criteria used in this study have shown significant proportion of difference (p-value <0.05) between intralesional PRP and intralesional TrA 5 mg/mL for the treatment of scalp AA. This study showed that:

- Intralesional PRP therapy was not found to be efficacious standalone therapy for the treatment of scalp AA.
- Response of intralesional TrA 5 mg/mL for the treatment of scalp AA was found to be better as compared with that of intralesional PRP therapy, with 10 out of 15 (66.67%) patients showing 100% hair regrowth by

the end of 6 months in contrast to only 3 out of 15 (20%) patients showing complete hair regrowth in the intralesional PRP therapy group.

- Overall patient satisfaction was better in patients of intralesional TrA 5 mg/mL group as compared with intralesional PRP therapy.

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