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Research Article

EFFICACY AND SAFETY OF COMBINATION THERAPY OF TOPICAL 17 α-ESTRADIOL AND TOPICAL MINOXIDIL ON FEMALE PATTERN HAIR LOSS: A PROSPECTIVE STUDY

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A B S T R A C T

Background: Female pattern hair loss (FPHL) has replaced androgenetic alopecia (AGA) in women and is being widely used in the recent years. The most common differential diagnosis is chronic telogen effluvium. The prevalence of the FPHL might be still lower in the Asian people. Proper data are not available from the Indian subcontinent. Medical therapy should be started as soon as possible since it effectively stops hair loss rather than boosting regrowth. Minoxidil remains the first-line treatment, while anti-androgens are the second-line treatment. The **goal** of this study was to see if a combined medication of topical 17α-stradiol and minoxidil may help patients with FPHL in Northern India. **Material and methods:** This study was conducted at Department of Skin and VD, Nalanda Medical College and Hospital, Patna, during Mar 2019 to Feb 2020 i.e. 12 months on 50 patients with female pattern hair loss. **Results:** Studied 50 patients of FPHL in skin outpatients in a tertiary care centre and found that mean age of patients were 45.25±15.98 years and maximum patients belong to age group 20-30 years i.e. 24 (48%). Most commonly observed adverse effect was pain (04%) followed by fever, Folliulitis, itching & seborrheic dermatitis i.e. 02%. **Conclusion:** Despite the study's limitations, we discovered that a combination of topical 0.025 percent 17α-stradiol and topical 3 percent minoxidil exhibited clear clinical effectiveness. As a result, this combination therapy for FPHL is an effective and safe therapeutic option that may be implemented quickly in a clinical context.

INTRODUCTION

"Diffuse alopecia in women" was the term used to signalize the disease in the early days. Joseph Plenck, was the first person to identify the miniaturization of hair follicles and in his book "Doctrina de Morbis Cutaneis" (Vienna, 1776) he mentioned it as "calvities". Female Androgenetic Alopecia was the term used after 1942 to describe patterned hair loss in women. Female pattern hair loss (FPHL) has replaced androgenetic alopecia (AGA) in women and is being widely used in the recent years [1]. The most common differential diagnosis is chronic telogen effluvium [1]. In a study by Norwood the prevalence of this condition was estimated to be 19 percent approximately 1000 Caucasian women. A study conducted in korea projected that the prevalence in Korean women of this condition was 5.6%. Prevalence accelerates with advancing age. The prevalence of the FPHL might be still lower in the Asian people. Proper data are not available from the Indian subcontinent [2-3].

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FPHL tends to occur in genetically pre-disposed females with alteration in hair follicle cycling and miniaturization of hair follicles which ends up in conversion of terminal hair to vellus hair follicles. The duration of anagen phase shrinks from 3 to 6 years to few weeks or months, the duration of telogen remains unaltered or elongates to more than 3 months resulting in a swifter turnover of anagen hair and excessive proportion of telogen hair from 5-10% to nearly 15-20% [5]. The androgen receptor (AR) and the enzymes, 5α-reductase I, II, and aromatase, are accumulated in the outer root sheath and dermal papillae of hair follicles of people affected with AGA. Female frontal hair follicles contain AR receptor that is 40% lower than that in the males [5]. The protective role of oestrogen is shown by the increased prevalence of FPHL in postmenopausal women. Aromatase inhibitors are shown to induce FPHL by reducing oestrogen content and topical oestrogen applications are beneficial in FPHL. Few studies have shown inhibition of hair growth in murine animal models by oestrogens [6]. Minoxidil 2% twice daily was approved by the FDA in 1991 for FPHL and a 5% minoxidil foam once daily was approved in 2014 [7]. Side effects include allergic or irritant contact dermatitis mostly due to vehicle propylene glycol, hypertrichosis of the forehead or face [8]. The goal of

this study was to see if a combined medication of topical 0.025 percent 17α-stradiol and 3 percent minoxidil may help patients with FPHL in Northern India.

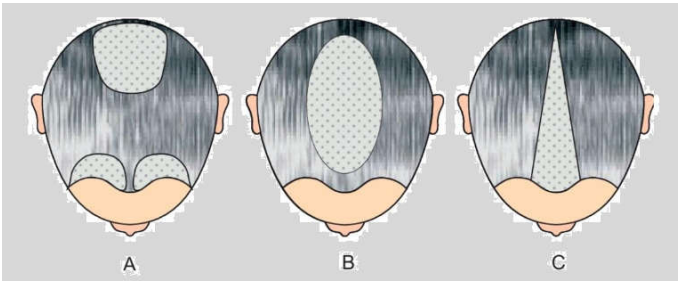

Fig 1 Androgenic alopecia in females. A: Hamilton's male pattern type, B: Ludwig's diffuse vertical thinning type & C: Oslen's Christmas tree type of hair loss

MATERIAL AND METHODS

Place of study: Department of Dermatology, Nalanda Medical College & Hospital, Patna. ***Type of study:*** Non-Randomised Prospective Interventional Study. ***Target population:*** Patients attending Dermatology outpatient department. ***Study population:*** Patients with Female pattern hair loss attending Dermatology outpatient department. ***Duration:*** 1 year from Mar 2019 to Feb 2020.Sample size: Sample size is calculated based on the formula 4pq/d2, P= Prevalence of disease, q= 1-P, d= Allowable error, P: 13% [4], q: 100-13= 87, Sample size: 45 + 10% Non –responders, Sample size taken as 50.

Inclusion criteria: Females with female pattern hair loss (Sinclair scale – Grade 2 and above)**,** Age: 18 - 50 years & patients willing for the procedure and willing to sign informed consent.

Exclusion criteria: Platelet/Bleeding Disorders, Malignancy, Keloidal Tendency, Pregnancy and Lactation, Positive Viral Markers (HIV 1 & 2, Hepatitis B/ Positive RPR, Anticoagulant Therapy & Thyroid Dysfunction.

An informed and written consent was obtained. Complete history regarding the onset, duration, co-existence of other systemic illness, past history of treatment for female pattern hair loss and other systemic illness if any were noted. Histories of use of minoxidil, hair supplements, immunosuppressive drugs, blood thinning agents were noted. Hepatitis-B and C co-infection were also screened for. 50 patients with female pattern hair loss, satisfying the inclusion criteria, attending our skin outpatient department were selected. Proper counseling was given and motivation of the patient was assessed. Clinical photographs of the alopecia were taken at screening visit and also at each visit after obtaining informed consent from the patients.

Grading of alopecia: The grade of hair loss was done by a non - treating dermatologist depending on the patient's pattern of hair loss –Sinclair 5-point scale.

Table 1 Sinclair 5- point visual analogue scale which assesses the degree of hair loss using the midline part.

Grade	Features
1	Normal. This pattern is found in all girls prior to puberty but in only 45% of women aged 80 or more.
2	Shows a widening of the central part
3	Shows a widening of the central part and thinning of the hair on either side of the central part
4	Reveals the emergence of a diffuse hair loss over the top of the scalp
5	Indicates advanced hair loss

Assessment: Clinical response to the treatment was monitored by patient's satisfaction score, physician assessment scale, and photography. Patient satisfaction score: Patients were asked to grade their satisfaction at 0 month, after 2 settings & 6 months after combination therapy. Satisfactions are like: 0 – Poor, 1 – Fair, 2 – Good, 3 – Very good & 4 – Excellent. ***Data analysis:*** The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value <0.05 is considered as significant level.

RESULTS

This Non-Randomised Prospective Interventional Study conducted on patients with female pattern hair loss attending dermatology outpatient department of a tertiary care centre from Mar 2019 to Feb 2020 in 50 patients.

Table 2 Patient demographic and hair loss features at baseline

Variables	No. of patients		Percentage
Age in years			
<20 years	04		08%
20-30 years	24		48%
30-40 years	15		30%
40-50 years	07		14%
Total	50		100%
Mean age ± SD	45.25±15.98 years		
Family history of AGA			
Yes	27		54%
No	23		46%
Previous Rx History			
No	28		56%
Yes	22		44%
Pattern and Grading of hair loss			
FPHL Sinclair	Grade 4	12	24%
5 point scale	Grade 3	26	52%
	Grade 2	12	24%
	Grade 1	00	00%
Average amounts of drugs prescribed for daily (ml)			
Minoxidil			1.13±0.56 ml
17α-estradiol			2.57±0.89 ml

Studied 50 patients of FPHL in skin outpatients in a tertiary care centre and found that mean age of patients were 45.25±15.98 years and maximum patient belong to age group 20-30 years i.e. 24 (48%) and minimum from 40-50 years i.e. 07 (14%) respectively. On the basis of FPHL Sinclair 5 point scale mostly belong to Grade 3 i.e. 52%.

Table 3 Outcome of treatment in studied patients

Grade	Before Rx	After 2 sittings	After 6 months
I	00.00%	00.00%	10.00%
II	17.00%	17.00%	78.00%
III	58.00%	68.00%	12.00%
IV	25.00%	15.00%	00.00%

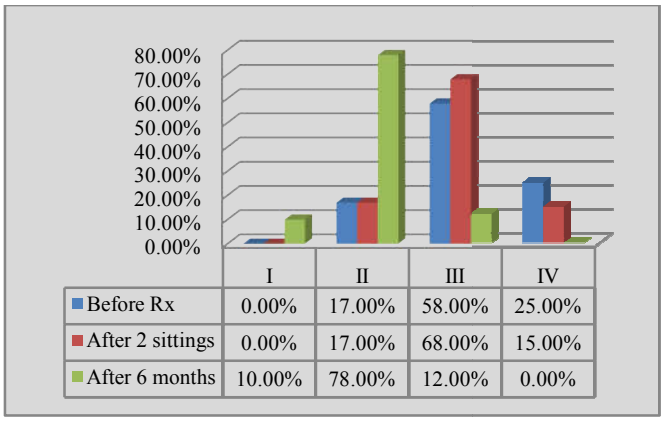

Fig 2 Outcome of treatment in studied patients

Table 4 Physician Assessment Scale in studied patients

Physician Assessment Scale after 2 sittings		
Value	No. of patients	Percentage
0	26	52%
1	24	42%
Physician assessment scale at the end of 6 months (follow up)		
1	21	42%
2	22	44%
3	07	14%

26 patients showed no improvement after 2 sittings. 24 patients showed mild improvement after 2 sittings. Majority of the patients showed moderate response (44.00%) & 7 patients showed good response at the end of 6 months.

Table 5 Patient Satisfaction Score in studied patients

Patient Satisfaction Score after 2 sittings		
Value	No. of patients	Percentage
0	30	60%
1	20	40%
Patient satisfaction score at the end of 6 months (follow up)		
0	05	10%
1	34	68%
2	11	22%

Majority of the patients (68.00%) felt fair response at the end of 6 months & 11 Patients felt good response at the end of 6 months.

Table 6 Adverse effects during and post treatment in studied patients

Adverse effects	No. of patients	Percentage
Nil	44	88%
Fever	01	02%
Folliculitis	01	02%
Itching	01	02%
Pain	02	04%
Seborrheic dermatitis	01	02%
Total	50	100%

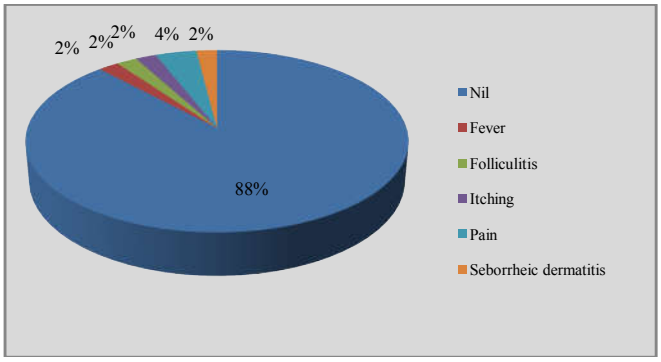

Fig 3 Adverse effects during and post treatment in studied patients

Most commonly observed adverse effect was pain (04%) followed by Fever, Folliculitis, itching & Seborrheic dermatitis i.e. 02%.

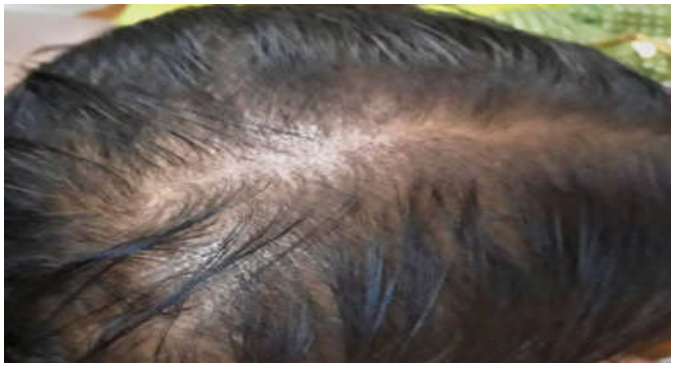

Fig 4 Before treatment

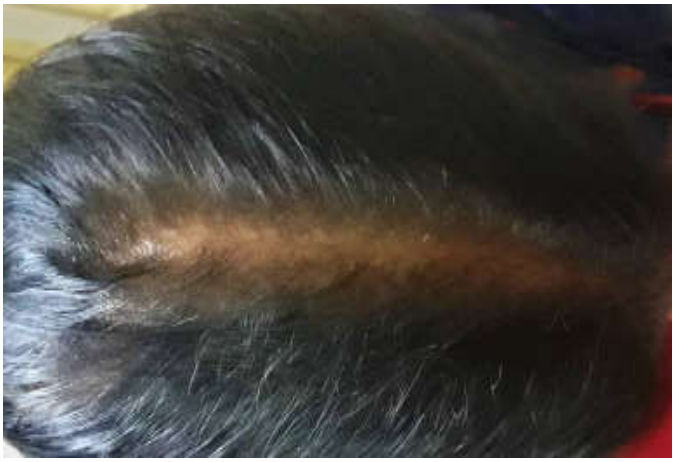

Fig 5 After 6 months

DISCUSSION

In our study, majority of the patients belonged to 20 – 30 years (48%). In a study by Ranneva *et al* [9] study, the mean age of patients was 34.63 years. In similar results, a study by Mansuri Uzzaif *et al* [10] study reported majority of patients in the category < 30 years (70%). In a study by Tawfik *et al* [11] study, the mean age of patients was 29.3. The mean age of the patient approached for treatment in our study was 45.25±15.98 years. At the end of 6 months (follow up), majority of patients had improved to one higher grade (71%). 10% patients had 2 grade improvement. Most of the patients who did not show improvement in grade had decrease in hair fall post treatment. Improvement in the grade of hair loss was statistically significant (p - <0.0005) post treatment. Olsen EA *et al* [1] also show comparable results to present study. Our study is supported by Gkini MA *et al* [12] study in which hair loss decreased and good response to treatment seen after 3 sessions of treatment. 88% of patients did not report any adverse effects during the entire treatment period. Pain was the frequently reported complaint (4%). Pain was the frequent complaint noted in Jha AK *et al* [13] study. Less common adverse effect reported in our study includes folliculitis, itching, fever. In contrast, Seborrheic dermatitis was the most reported adverse effect in Mansuri Uzzaif *et al* [10] study. Also Mansuri Uzzaif *et al* [10], 60 % of patients showed good response to treatment during the follow up period. Most of the patients reported decrease in hair fall post treatment which was also reported by most of the patients in Gkini *et al* [12] study.

CONCLUSION

In this study assessing the efficacy and safety profile of topical 17α-Estradiol and topical Minoxidil in the treatment of female pattern hair loss, majority of the patients showed hair re-growth with decrease in hair fall post treatment and few patients showed decrease in hair fall despite having no improvement in grade of hair loss. Majority of the patients did not experience any adverse effect during and after treatment signifying the safety profile of the treatment procedure. The significant outcome by treating patients of FPHL topical 17α-Estradiol and topical Minoxidil will improve the social and emotional aspect of patient' life, thus, topical 17α-Estradiol and topical Minoxidil can be considered as an option in the treatment of female pattern hair loss with a good safety profile. However, many factors may play a role in the development of female pattern hair loss and multimodality approach may be the best therapeutic option for prevention of hair fall and hair re-growth.

References

1. Olsen EA. Female pattern hair loss: Clinical features and potential hormonal factors; JAAD; September 2001, Volume 45, Issue 3, Supplement, Pages S70–S80.
2. Norwood OT "Incidence of female androgenetic alopecia (female pattern alopecia)," Dermatologic Surgery, vol. 27, no. 1, pp. 53–54, 2001.
3. Paik JH, Yoon JB, Sim WY, Kim BS, and Kim NI, "The prevalence and types of androgenetic alopecia in Korean men and women," *Br J Dermatol*, vol. 145, no. 1, pp. 95–99, 2001.
4. Birch M.P., Messenger J.F., Messenger A.G. Hair density, hair diameter and the prevalence of female pattern hair loss. Br J Dermatol. 2001; 144:297–304.
5. Martinez-Jacobo L, Villarreal-Villarreal CD, Ortiz-López R, Ocampo-Candiani J, Rojas-Martínez A. Genetic and molecular aspects of androgenetic alopecia. *Indian J Dermatol Venereol Leprol* 2018; 84:263-8.
6. Banka *et al*., 2013; N. Banka, M.J. Bunagan, J. Shapiro; Pattern hair loss in men: Diagnosis and medical treatment; Dermatol Clin, 31 (2013), pp. 129-140.
7. Varothai S, Bergfeld WF. Androgenetic alopecia: An evidence‐based treatment update. *Am J Clin Dermatol* 2014;15:217‐30.
8. Herskovitz I, Tosti A. Female pattern hair loss. *Int J* Endocrinol Metab 2013;11:e9860.
9. Evgeniya Ranneva; Hair restoration; clinical study to evaluate the efficacy of a combined treatment between specific meso hair cocktail class III device and micro needling device in different baldness patterns; J Cosmo Trichol 2017, 3:3(Suppl) DOI :10.4172/2471-9323-C1-006.
10. Mansuri UU, Vaaruni R, Parmar KS, Shah BJ. A comparative study of treatment modalities in female androgenetic alopecia. *Int J Res Med Sci* 2016; 4:1229-36.
11. Tawfik, Osman. Journal of Cosmetic Dermatology 2017. The effect of autologous activated platelet-rich plasma injection on female pattern hair loss: A randomized placebo-controlled study.
12. Gkini MA, Kouskoukis AE, Tripsianis G, Rigopoulos D, Kouskoukis K; Study of platelet-rich plasma injections in the treatment of androgenetic alopecia through an one-year period; J Cutan Aesthet Surg. 2014 Oct-Dec;7(4):213-9. doi: 10.4103/0974-2077.150743.
13. Jha AK, Udayan UK, Roy PK, Amar AKJ, Chaudhary RKP; Original article: Platelet-rich plasma with micro needling in androgenetic alopecia along with dermoscopic pre- and post-treatment evaluation. *J Cosmet Dermatol*. 2018 Jun;17(3):313-318.

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