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Comparative Study Between Minoxidil 5% and Micro-Botulinum Toxin Effectiveness in Treatment of Female Pattern Androgenetic Alopecia with Dermoscopic Evaluation

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Abstract:

Introduction: Female pattern hair loss (FPHL) can have a detrimental effect on patients' sense of self-worth and quality of life, which is among the most frequent causes for hair consultations. Their expectations regarding the outcomes of therapy are frequently more positive than the reality. Therefore, it is essential to emphasize during the initial consultation that improvement and regrowth are not always attainable, and that the primary management goal is to arrest development and prevent further thinning.

Aim of the study: Compare the effectiveness of intralesional minoxidil (MS) 5% vs botulinum toxin (BTX-A) in the management of FPHL with dermoscopic evaluation.

Subjects and Methods: This is a prospective interventional comparative study. Ten patients received two sessions of BTX-A, each session consisting of 50 units, with an interval of four months between the two sessions. The other ten patients took three sessions of MS 5% injection with three weeks' intervals between the sessions. Dermoscopic examination was performed before and during each session and at the end of the last session.

Results: Both BTX-A and MS are effective in the treatment of FPHL. There was statistically insignificant alteration ($p \leq .05$) according to baseline score (S1), score at the end of treatment sessions (S2), and score four months follow up after the last session (S3) between both groups.

Conclusion: BTX-A and MS are equally effective in the treatment of FPHL.

Keywords: FPHL; BTX-A; Minoxidil.

1. Introduction

Feminine pattern baldness is a prevalent, non-scarring kind of baldness in which the terminal hair follicles gradually shrink. Caucasians have a higher risk than Asians and Africans do, and the incidence rises with age [1].

There is still debate about whether or not androgens contribute to the beginning of FPHL. Some women with typical amounts of circulating androgens still get FPHL. Inhibitors of androgen metabolism, such as thyroxin and prolactin, may have a role in the development of FPHL. Insulin resistance and other symptoms of metabolic syndrome have been linked to FPHL, which may be caused by vascular impairment owing to hyperglycemia along with the resulting damage to hair follicles [2].

Dihydrotestosterone (DHT) is released when testosterone is converted by the enzyme 5-alpha reductase (5-α reductase)., Increased activity of type II 5α-reductase, and thus an excessive production of DHT, was observed in the hair follicles (HFs) of people with FPHL. Excessive DHT causes the miniaturization of hair, reducing the anagen phase and increasing the telogen phase, leading to hair loss and decreased hair density [3].

In addition to hereditary considerations, environmental factors can play a role in FPHL. Psychological stress, smoking, diabetes mellitus, hypertension, many deliveries, an absence of photoprotection and a high income are all environmental variables that have been linked to FPHL [2].

Baldness is characterized by shrinkage of the hair follicle and a mild to moderate peri- peri-infundibular lymphohistiocytic [4]. The best-researched medicinal treatment for men's and women's pattern hair loss is topical minoxidil (MS), which is very successful and well tolerated in randomized controlled studies. Hair development is stimulated because the telogen (rest) phase of hair follicles is shortened and the anagen (growth) phase is lengthened, MS also acts as a vasodilator by stimulating the body's natural release of vascular endothelial growth factor (VEGF), that may raise blood vessel density along with the size of dermal papillae [5]. Micro-needling is a more invasive process that can help medication absorption deep into the

skin when combined with other therapies like MS or platelet-rich plasma [6].

The combination of MS as well as spironolactone was found in research to be useful in treating FPHL [7]. Also, resistant cases not responding to therapies may benefit from a hair transplantation, which is considered both efficient as well as safe [2].

BTA has been approved by FDA and tested for treatment of different conditions, such as wrinkles and migraines', as it relax muscles surrounding the head and improve oxygen and blood flow to the alopecia affected sites, as well as inhibits the activation of DHT which is activated by hypoxic state so finally it leads to decreased hair loss. In addition, hair follicles can enter the growth phase in response to a high oxygen concentration, which leads to hair regeneration [8].

2. Subjects and Methods

2.1 Subjects

This study is a prospective comparative study conducted on 20 cases with FPHL. Persons were obtained from the outpatient clinic of Dermatology, STDs and Andrology department, Fayoum University hospitals. This trial was conducted over 10 months from August 2020 to May 2021. The individuals were split up into two groups, each consisting of ten individuals.

Inclusion criteria

Female patients of the age group (20-45) complaining of FPHL clinically and dermoscopically.

Exclusion criteria

- Patients having any other dermatological or systemic diseases.
- Patients on treatment that could affect the hair cycle.
- Patients with a history of bleeding disorders or on anticoagulant therapy.
- Personal or family history of keloid.
- Pregnancy or lactation.

2.2 Methods

All patients were subjected to:

- History taking.
- General and local examination.

- FPHL severity index scoring at baseline (S1), at the end of treatment sessions (S2), and four months follow-up after the last session (S3).

Patients were divided into:

- **Group 1:** Dermapen is equipped with a disposable head that is personalized for each patient and can be sterilized after each session. The head is plastic and has 12 needles, which are made of stainless steel, which is strong and nontoxic, with automatic vertical movements and adjustable depth of penetration of 2mm. we used 12 needles from the cartridge. After loading (3-5) ml of MS into the derma-pen injector syringe, the device was dragged along the treatment area in linear strokes while being lifted in between. The goal was to achieve pinpoint bleeding at the site of treatment. After that, a gauze dipped in saline was used to wipe the scalp clean. We see each patient for a total of three appointments, spaced out by three weeks. As a facial treatment machine, we employ a two-in-one Hydra Injector Derma Pen Nano Mesotherapy Microneedle derma-pen Mesogun.
- **Group 2:** each patient has two sessions with a 4-month interval. Each patient had an injection of 50 units of neuronox (BTX-A) diluted with 5 mL saline intradermal using an insulin syringe. We start the injection 3 ml away from the frontal hairline, injecting points with 2cm intervals. After injection, we instruct the patient to apply an ice pack for 10 minutes, avoid leaning forward for 4 hours, refrain from using tight hair ties, and not wash their hair on the day of the injection. Each patient was injected with dexamethasone ampoule to control any allergic reaction from BTX-A.

2.3 Statistical analysis:

Data collected and coded to facilitate data manipulation and double entered into Microsoft Access, and data analysis performed using the Statistical Package of Social Science (SPSS) software version 22 in Windows 7 (SPSS Inc., Chicago, IL, USA). Simple descriptive analysis in the form of numbers and percentages of qualitative data, and arithmetic means as central tendency measurement, standard deviations as a measure of dispersion of quantitative parametric data. For quantitative parametric data, the Independent samples t-test was used to compare quantitative measures between two

independent groups. One-way ANOVA test was used to compare quantitative measures between more than two independent groups of quantitative data. For quantitative non-parametric data, the Kruskal-Wallis test was used to compare more than two independent groups. For qualitative data, the Chi-square test was used to compare two or more qualitative groups. The *P*-value< 0.05 was considered statistically significant.

3. Results

Table 1 showed that Hirsutism was significant in the BTX-A group (p <0.05). Other demographic data were non-significant.

Table 1: Comparison between the two investigated groups about age (years) and risk factors

Risk factors		Group 1((MS)) (n=10)	Group 2(BTX -A) (n=10)	test of sig.	p
Age (years)	Min. – Max.	27.0 – 40.0	21.0 – 50.0	t=2.015	0.059
	Mean ± SD	33.20 ± 5.18	39.50 ± 8.42		
	Median (IQR)	31.50 (30.0 – 39.0)	40.0 (35.0 – 45.0)		
Family history	No	2 (20%)	2 (20%)	<0.000	^{FE}p= 1
	Yes	8 (80%)	8 (80%)		
Hirsutism	No	10 (100%)	5 (50%)	6.667*	^{FE}p= 0.033*
	Yes	0 (0%)	5 (50%)		
Acne	No	9 (90%)	8 (80%)	0.392	^{FE}p= 1
	Yes	1 (10%)	2 (20%)		
Menstrual history	Regular	10 (100%)	8 (80%)	2.222	^{FE}p= 0.474
	Irregular	0 (0%)	2 (20%)		
Method of contraception	Single	1 (10%)	1 (10%)	2.713	^{MC}p= 0.73
	IUD	7 (70%)	6 (60%)		
	Oral Contraceptive	2 (20%)	0 (0%)		
	Pills	0 (0%)	1 (10%)		

*SD: Standard deviation; IQR: Inter Quartile Range; t: Student t-test; χ^2: Chi square test; FE: Fisher Exact; MC: Monte Carlo test; p: p-value for comparing group 1 and 2. *: Statistically significant at p less than or equal to 0.05.*

There was no statistically significant difference between the score items of the two groups (**Table 2**).

Table 2: Comparison between the diverse investigated durations regarding score (S1, S2, and S3) in each group.

	Score	S1	S2	S3	Fr	p
Group 1 (MS)	Min. – Max.	5.0 – 20.0	5.0 – 17.0	5.0 – 17.0	12.8	0.002*
	Mean ± SD.	16.70 ± 4.40	10.80 ± 3.85	10.80 ± 3.85		
	Median (IQR)	18.50 (16.0 – 19.0)	10.0 (9.0 – 14.0)	10.0 (9.0 – 14.0)		
	P-values	p_1=0.007*, p_2=0.007*, p_3=1.000				
Group 2 (BTX-A)	Min. – Max.	9.0 – 18.0	5.0 – 11.0	5.0 – 11.0	20*	<0.001*
	Mean ± SD.	16.20 ± 2.82	8.40 ± 1.90	8.40 ± 1.90		
	Median (IQR)	17.0 (16.0 – 18.0)	9.0 (9.0 – 9.0)	9.0 (9.0 – 9.0)		
	P-values	p_1=0.001*, p_2=0.001*, p_3=1.000				

Fr: Friedman test, Sig. bet. periods have been performed utilizing Post Hoc Test (Dunn's). p: p-value for comparing the two investigated periods. p_1: p value for comparing between Baseline and 1st Follow-up. p_2: p-value for comparing between Baseline and 2nd Follow-up. p_3: p value for comparing among 1st Follow up and 2nd Follow up.

In group 1, there was a high statistically significant variation among S1 and both S2 and S3, while no significant variation between S2 and S3. In g**roup 2, t**here was a high statistically significant variation between (S1) and both (S2) and (S3), while no significant variance between S2 and S3 (**Figure 1).**

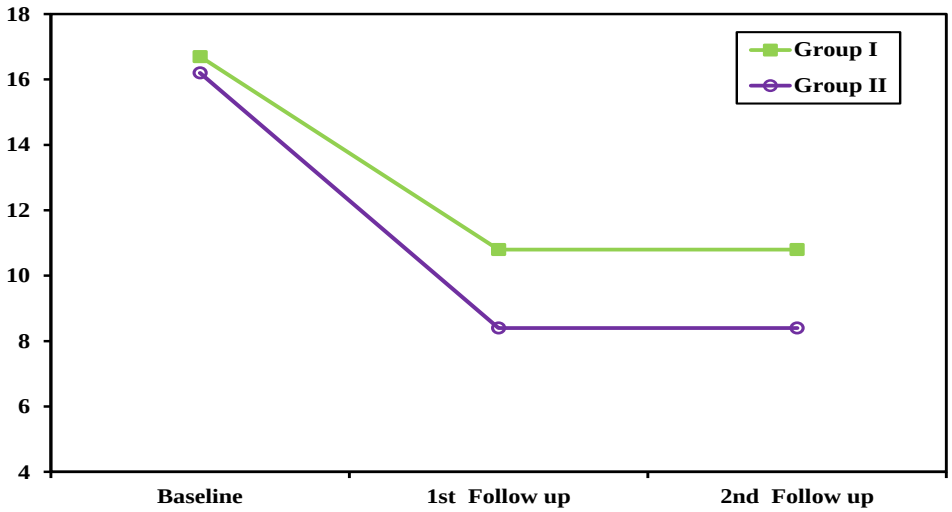

Figure 1: Comparison between the different studied periods according to score in each group.

There was no statistically significant difference regarding baseline score, score at the end of the treatment sessions and score four months after the last session between both groups (**Table 3).**

Table 3: Comparison between the two investigated groups regarding score.

Score		Group I (number=10)	Group II (number=10)	U	p
Baseline	Min. – Max.	5.0 – 20.0	9.0 – 18.0	33.0	0.218
	Mean ± SD.	16.70 ± 4.40	16.20 ± 2.82		
	Median (IQR)	18.50 (16.0 – 19.0)	17.0 (16.0 – 18.0)		
1st Follow-up	Min. – Max.	5.0 – 17.0	5.0 – 11.0	31.50	0.165
	Mean ± SD.	10.80 ± 3.85	8.40 ± 1.90		
	Median (IQR)	10.0 (9.0 – 14.0)	9.0 (9.0 – 9.0)		
2nd Follow-up	Min. – Max.	5.0 – 17.0	5.0 – 11.0	31.50	0.165
	Mean ± SD.	10.80 ± 3.85	8.40 ± 1.90		
	Median (IQR)	10.0 (9.0 – 14.0)	9.0 (9.0 – 9.0)		
Improvement	Min. – Max.	-2.0 – 11.0	4.0 – 9.0	4.0	0.529
	Mean ± SD	5.90 ± 4.36	7.80 ± 1.55		
	Median (IQR)	7.50 (2.0 – 10.0)	8.0 (7.0 – 9.0)		

*U: Mann-Whitney test. p: p-value for comparing groups I and II, *: Statistically significant at p-value less than or equal to 0.05. SD: Standard deviation, IQR: Interquartile Range.*

There was a higher statistically significant difference concerning nausea in the BTX-A group; other side effects (pain, erythema, itching, headache and inflammation) were non-significant between the two groups (**Table 4**).

Table 4: Comparison between the two investigated groups by side effects**.**

Side effect	Group 1 (MS) (n=10)	Group 2 (BTX-A) (n=10)	$\chi 2$	^{FE}p
Pain	9 (90%)	9 (90%)	0.000	1.000
Erythema	5 (50%)	6 (60%)	0.202	1.000
Headache	5 (50%)	5 (60%)	0.202	1.000
Itching	4 (40%)	0 (0%)	5.000	0.087

Nausea	0 (0%)	5 (50%)	6.667*	0.033*
Inflammation	0 (0%)	3 (30%)	3.529	0.211

4. Discussion

Female pattern hair loss is a frequent kind of hair loss in which the terminal hair follicles gradually shrink in size without leaving any scarring on the scalp. Many studies point to a genetic predisposition as the primary risk factor for AGA, which would make it an androgen-mediated disease [1]. This investigation aimed to compare the efficacy of MS 5% and BTX-A in the management of FPHL. In Group 1, Patients were injected with MS 5% using a derma-pen injector through three sessions of three-week intervals (mini electric nano shuiguang). In Group 2, patients were injected with BTX-A using an insulin syringe through two sessions of four-month intervals and a follow-up for another four months.

Among the study group, the ages ranged from 27 to 40 in Group 1 with a mean age of 33.20 ± 5.18 and from 21-50 in Group 2 with a mean age of 39.50 ± 8.42. Patients were all females, as a cosmetic concern is more remarkable during this age group and in the female gender.

There was no significant difference between the two studied groups according to age, which indicates proper matching of our groups. In BTX-A, there was a statistically significant alteration concerning hirsutism; other variables (age, family history, acne, menstrual history and method of contraception) were not significant. FPHL and hirsutism may be caused by hypersensitivity of androgen receptors to circulating DHT or due to association hyperandrogenic state, as in PCO, virializing tumor or cases who receive treatment with progesterone-containing oral contraceptive pills with a high potential, for example, norethindrone [2].

There was no statistically significant alteration amongst S1, S2 and S3 (total and domains) between both groups. In group 1, there was a statistically significant variance between S1 and both S2, S3, while no alteration amongst S2 and S3, which maintained the effect of MS. MS was proven to stimulate hair development by elongating the hair follicles' anagen (growth) phase and

reducing their telogen (rest) phase [5]. MS also acts as a vasodilator by stimulating the body's natural production of VEGF, which may increase blood vessel density and the size of dermal papillae. This agreed with (Suchonwanit et al., 2019) and (Chen et al., 2020), who used topical (MS) in the treatment of FPHL and found improvement [9, 10].

In group 2, there was a high statistically significant variance between S1 and both S2 and S3, while no difference between S2 and S3. Absence of a statistically significant variance between S2 and S3 indicated a maintained effect of BTX-A. The hypoxic state triggers the production of DHT; however, BTA may relax the muscles surrounding the head, increasing blood flow and oxygen concentration in the area of alopecia, hence reducing hair loss. In addition, a high level of oxygen in the blood can kick-start the hair follicle's growth phase, leading to new hair growth [8]. This agreed with (Shon et al., 2020) and (Zhou et al., 2020), who used BTX-A intradermally and reported improvement of hair loss [11, 12].

There was a higher statistical variance concerning nausea in the BTX-A group, while other side effects (pain, erythema, itching, headache and inflammation) were non-significant between the two groups.

In our study, we injected BTX-A in a more invasive way than MS, which was delivered by derma-pen. anxiety is a natural response to danger. Nausea, as well as additional stomach symptoms, can occur as the brain produces neurotransmitters to prepare the body for combat, but this might disrupt the gut microbiota. There was statistically insignificant variance regarding score improvement with demographic data.

5. Conclusion

BTX-A and MS are equally effective in the treatment of FPHL.

Ethical committee approval: This study was approved by the Research Ethical Committee of Fayoum University. A patient consent form was given to those able to read and accept to participate in the study, explaining the purpose and nature of the study and emphasize that participation in the study is entirely voluntary and withdrawal from the study would not affect the clinical care provided, and confidentiality was assured through coding the data. As well as an oral ascent was also taken from illiterate

participants. Official permission was obtained from the hospital authorities of Fayoum University.

Competing interests: There are no conflicts of interest for the authors.

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