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Study of the Effectiveness and Safety of Botulinum Toxin Type- A for Treatment of Androgenetic Alopecia in men

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ABSTRACT
Background: Up to 80% of men and 50% of women have androgenetic alopecia (AGA), a non-scarring hair loss condition that is marked by a gradual shrinkage of the hair follicle, throughout adolescence and beyond puberty,
Aim and objectives: This study aimed to assess the efficiency and security of using type A botulinum toxin (BTA) to treat androgenetic alopecia in males,
Subjects and methods: This interventional research was conducted in Dermatology, Venereology and Andrology Department Outpatient Clinic, Al-Azhar University Hospital (Damietta) and Mubarak Hospital in Giza (Ministry of Heath). This study included 20 patients with androgenetic alopecia grade II-IV according to Norwood Hamilton criteria,
Result: There was statistically significant decrease of vellous hair count between first session 48.6 to 39.7 second session and 31.25 at third session with percent of change is the highest between 1st and 3rd session (35.7%) then between second and third session (21.3%) and the lowest percent of change was detected between 1st session and 2nd session (18.3%).There was statistically significant increase of mean hair thickness between first & second session 56.30 & 66.20 and 78.2 at third session with percent of change is the highest between 1st and 3rd session (38.9%), then second and third session (18.1%) and between 1st session and 2nd session (17.6%),
Conclusion: The results of the current research showed that BTA is a safe and successful treatment for AGA and has outstanding outcomes. These findings provide an innovative theoretical framework and therapeutic approach for the management of AGA,
Keywords: Androgenetic alopecia (AGA).

INTRODUCTION

The most common and upsetting clinical complaint dermatologist's face in medical practice is hair loss. The three most prevalent kinds of hair loss are alopecia areata, telogen effluvium, and androgenetic alopecia (AGA) [(1)]. AGA is a non-scarring hair loss condition that affects up to 80% of men and 50% of women throughout adolescence and the years following puberty, is characterized by a gradual shrinkage of the hair follicle [(2)]. As a consequence of the combination of hereditary and environmental variables, AGA has a complex etiology. The number of hair follicles per unit area does not change even as the terminal hairs change into intermediate and eventually vellus hairs [(3)].

The enzyme 5α-reductase, found in hair follicles, transforms testosterone into the more powerful dihydrotestosterone (DHT). The hair follicles' diminution is caused by this DHT. The only FDA-approved therapy of AGA is oral finasteride and topical minoxidil. A 5α-reductase inhibitor known as finasteride stops the conversion of testosterone to DHT. Oral minoxidil is a vasodilator and an antihypertensive. Minoxidil's method of action is intricate. It causes the activation of potassium channels, the creation of prostaglandins and vascular endothelial growth factors in the dermal papilla, and an increase in the anagen to telogen ratio [(4)].

The most typical clinical issue dermatologists see is androgenetic alopecia. More individualized therapeutic methods for AGA are required since the effectiveness and safety of existing medicinal treatments for AGA are still restricted. As a result, BTA injection or BTA injection paired with oral finasteride (FNS) was used to treat individuals with AGA in research. It was discovered that BTA and FNS together had a more potent therapeutic effect than BTA alone [(5)].

In this study, participants were injected with BTA for two times with 4 months interval, we aimed to decrease the duration of treatment, the cost, the local side effects that result from repeated injection of BTA as inflammation, edema, erythema and blisters and systemic side reactions as headache, nausea, fever and chest tightness. The study's objective is to assess the efficacy and security of using botulinum toxin type A (BTA) to treat androgenetic alopecia in males. Participants are individuals who meet the Norwood Hamilton criteria for androgenetic alopecia, grades II–IV. Intramuscular injections of type A botulinum toxin are of interest. The goal is to enhance hair growth.

PATIENTS AND METHODS

This study was one group of twenty patients was quasi experimental study as we trying to detect the effect of an intervention (injection of Botulinum Toxin Type- A). This study was done in Dermatology, Venereology and Andrology Department Outpatient Clinic, Al-Azhar University Hospital [Damietta] and Mubarak Hospital in Giza (Ministry of Heath).

Inclusion criteria: Male patients only, age from 20 to 40 years and patient with AGA (diagnosis is evaluated following Norwood Hamilton grade II-IV criteria).

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Exclusion criteria: Patient with history of treatment with drugs that interfere with BTA within the past six months, such as anticoagulants, non-steroidal anti-inflammatory drugs, certain antibiotics, severe hepatic, renal, or cardiac diseases, eye, skin, or neuromuscular system diseases (such as Myasthenia gravis), infection, inflammation, or unhealed wounds on the skin near the injection site (as aminoglycosides).

Study procedure

Pre-operative procedure: Patients' age, weight, comorbidities and treatment were carefully checked. Basic dermoscope and recording of an objective assessment score for the scalp photos. High risk consent - showing the adverse effects- was taken from all subjects involved in this study.

Operative technique: Botulinum toxin type A (BTA) is administered intramuscularly utilizing an insulin syringe with a 40 U/ml capacity. Participants received BTA injection for two times within a four-month interval and followed up after three months. The scalp is sterilized, 30 injection target locations (positioned in the periauricular, frontal, temporal, and occipital muscles) are characterized with gentian violet, and each injection site is 1.5 to 2 cm apart.

Study assessment: Dermoscopy and an objective assessment score of the scalp photos are used to evaluate effectiveness (at baseline, before 2nd injection & 3 months after last injection as follow-up for treatment). Two dermatological experts grade the head shots. They reviewed the photographs of the scalp before each session and at the conclusion of the follow-up. Appraisal of patients' own performance: A questionnaire was filled out by patients. Evaluation of side effects, which may include swelling, erythema, edema, and blisters at the injection site as well as systemic side effects such nausea, headaches, fever, and chest tightness were recorded.

Duration of the study: 7 months per patient.

Data collection: Demographic data, comorbidities, drugs, basic and follow-up of scalp photographs and questionnaires of patient s satisfaction were recorded.

Ethical Approval: The study was approved by the Ethics Board of Al-Azhar University and the patients were given all the information they need about the trial. An informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

SPSS software, version 18 (SPSS Inc., PASW, SPSS Inc., Chicago) was utilized to analyze the data. Number and percentage were utilized to describe qualitative data. Mean was used to describe quantitative data. Standard deviation for data that are regularly distributed utilizing the Kolmogorov-Smirnov test for normality. The acquired findings' significance was assessed at 0.05 level. To compare two paired readings of scattered data, the paired t test was performed.

RESULTS

key:

1 (Before njection)
2 (4 months after 1st session)
3 (3 months after 2nd session)

Table (1) showed that the mean age of patients was 34.25 years ranging from 20 to 39 years, 65% were from Mansoura, 65% were professional worker and 95% were married.

Table (1): Socio-demographic features of the cases under study

	n=20	%
Age/years		
Mean ± SD (Min-Max)	34.25 ± 4.48 (20-39)	
Residence		
Cairo	7	35.0
Mansoura	13	65.0
Occupation		
Manual worker	6	30.0
Student	1	5.0
Professional worker	13	65.0
Marital status		
Single	1	5.0
Married	19	95.0

Table (2) showed that mean duration of the disease was 12.2 years ranging from 4 to 20 years.

Table (2): disease duration distribution among studied cases

	n=20	%
Duration/years		
Mean ± SD (Min-Max)	12.2±3.91 (4-20)	

Table (3) illustrated that there was statistically significant decrease of vellous hair count between (1) 48.6 to 39.7 (2) and 31.25 at (3) with percent of change was the highest between (1) and (3) (35.7%) then between (2)and (3) (21.3%) and the lowest percent of change was detected between 1 and 2 (18.3%).

Table (3): comparison of change in vellous hair number during different sessions of treatment

	1	2	3	within group significance	% of change
Vellous hair Mean ± SD	48.60±7.23	39.70±7.53	31.25±5.37	p1<0.001* p2<0.001* p3<0.001*	18.3% 35.7% 21.3%

p1: distinction between 1& 2, p2: distinction between 1&3, p3: distinction between 2&3, Used test Paired t test, *statistically significant

Table (4) demonstrated that there was statistically significant increase of terminal hair count between (1) 105.6 to 131.85 (2) and 157.55 at (3) with percent of change was the highest between 1 and 3 (49.2%), then between 1 and 2 (24.9%) and then between 2 and 3 (19.5%).

Table (4): comparison of change in terminal hair number during different sessions of treatment

	1	2	3	within group significance	% of change
Terminal hair Mean ± SD	105.60±12.30	131.85±15.36	157.55±11.24	p1<0.001* p2<0.001* p3<0.001*	24.9% 49.2% 19.5%

p1: variation between 1&2, p2: variation between 1&3, p3: variation between 2&3, Used test Paired t test, *statistically significant.

Table (5) showed that there was statistically significant increase of mean hair thickness between (1) & (2) 56.30 & 66.20 and 78.2 at (3) with percent of change was the highest between 1 and 3 (38.9%), then (2) and (3) (18.1%) and between 1 and 2 (17.6%).

Table (5): comparison of change in hair thickness during different sessions of treatment

	1	2	3	within group significance	% of change
Hair thickness/mm Mean ± SD	56.30±6.89	66.20±7.84	78.20±10.75	p1<0.001* p2<0.001* p3<0.001*	17.6% 38.9% 18.1%

p1: variation between 1&2, p2: variation between 1&3, p3: variation between 2&3, Used test Paired t test, *statistically significant

Figures (1, 2) showed that there was statistically significant increase of mean hair density between (1) & (2) 156 &168.7 and 183.6 at (3) with percent of change was the highest between (1) and (3) (17.7%), then between (2)and (3) (8.9%) and then between (1) and(3) (8.1%).

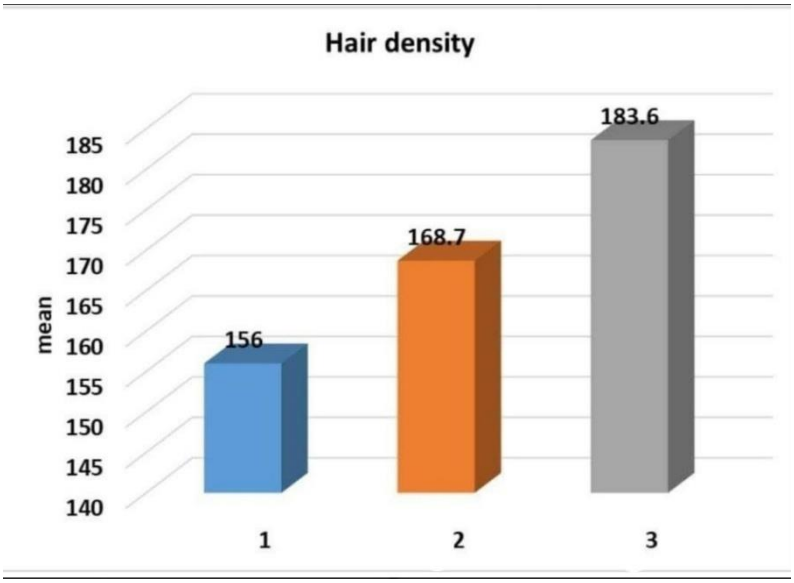

Figure (1): mean hair density between different sessions

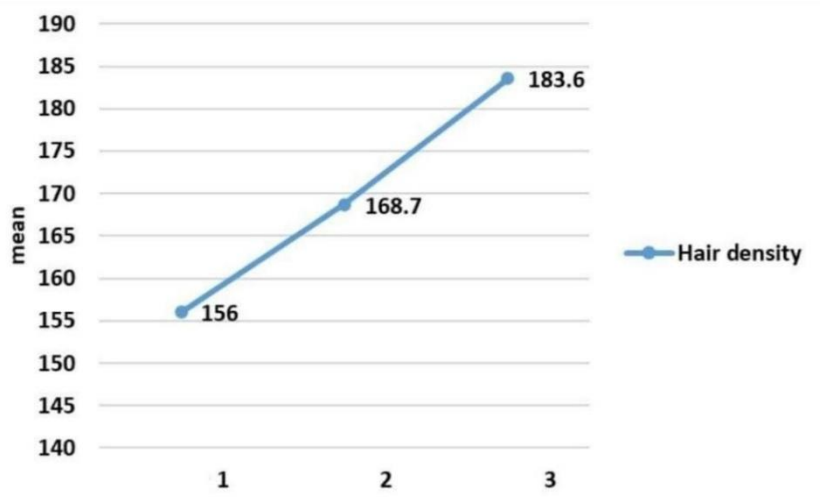

Figure (2): line graph showing hair density change during different sessions.

DISCUSSION

Mostly, botulinum toxin type A (BTA), a very strong neurotoxin that specifically inhibits the release of acetylcholine at the neuromuscular junction, is used in the management of numerous dermatological disorders [(6)]. The recent development of an alternate method involves injecting BTA into the scalps of AGA sufferers [(5)].

This study's primary objective was to assess the efficacy and safety of utilizing botulinum toxin type A (BTA) to treat androgenetic alopecia in males. This interventional study was conducted in Dermatology, Venereology and Andrology Department Outpatient Clinic, Al-Azhar University Hospital (Damietta) and Mubarak Hospital in Giza (Ministry of Heath) on 20 patients with androgenetic alopecia grade II-IV according to Norwood Hamilton criteria.

Regarding sociodemographic characteristics of the studied cases, we found that the median age of the researched cases was 34.25 years ranging from 20 to 39 years, 65% from Mansoura, 65% professional worker and 95% married. The mean duration of the disease was 12.2 years ranging from 4 to 20 years.

Regarding outcomes, the current investigation revealed that there was statistically substantial increase of terminal hair count between first session 105.6 to 131.85 second session and 157.55 at third session with percent of change was the highest between 1st and 3rd session (49.2%), then between 1st session and 2nd session (24.9%) and then between second and third session (19.5%). We also found that there was statistically significant increase of mean hair thickness between first & second session 56.30 & 66.20 and 78.2 at third session with percent of change was the highest between 1st and 3rd session (38.9%), then second and third session (18.1%) and between 1st session and 2nd session (17.6%). The current research also showed that there was statistically substantial decrease of mean hair density between first & second session 156 &168.7 and 183.6 at third session with percent of change was the highest between 1st and 3rd session (17.7%), then between 2nd session and 3rd session (8.9%) and then between first and third session (8.1%).

The current study was supported by **Zhou *et al.*** [(5)] sought to look into the effectiveness and safety of BTA (Botulinum Toxin Type A) in patients with androgenetic alopecia. 63 AGA patients with BTA injection or BTA injection with oral finasteride (FNS) treatment were included in the research. The mean age of BTA groups was 38:47 ± 10.13 years, mean BMI was 23:12 ± 4:54 kg/m^2 and the mean duration was 8:85 ± 7:17 years. As well, the current study was further supported by the pilot study of **Singh *et al.*** [(7)] aimed to assess the effectiveness of botulinum toxin in the treatment of androgenetic alopecia. In the trial, 30 locations on the scalp of 10 male patients with androgenetic alopecia received injections of 5 U of botulinum toxin apiece. According to the research, 8 of the 10 patients showed good to exceptional photographic responses. One patient responded to therapy poorly, while another responded to it fairly after 24 weeks. According to their own assessments, 7 out of 10 patients responded well to very well. Two patients responded to therapy fairly, whereas one patient did not.

As well, **Zhang *et al.*** [(8)] aimed to assess the effectiveness and safety of injecting a tiny dosage of Botox into 24 male outpatients with androgenetic alopecia who are between the ages of 30-45. At 3 months, 10 patients had no evident hair growth (0–10% rise from baseline), 9 patients had clear hair regrowth (>10% improvement), and 5 patients were still experiencing hair loss. Additionally, 19 individuals had a considerable reduction in grease production, which peaked at 3 months. 11 patients demonstrated impressive hair regrowth (>10% rise from baseline). After 6 months of therapy, 8 patients showed very little improvement, and 5 patients showed no response to treatment. Furthermore, in 19 patients whose grease

secretion had significantly decreased at 3 months and whose grease concentration was near to the healthy level, grease secretion progressively returned to the normal condition. Notably, no patient suffered from negative consequences.

Also, **Freund *et al*. [(9)]** reported the findings of an open-label pilot research on the treatment of androgenetic alopecia with botulinum toxin type A (Botox; Allergan, Inc., Irvine, California). There were 50 male participants in the research, ranging in age from 19 to 57. The trial was completed by 40 volunteers, and no negative effects were noted. The percentage of therapeutic response was 75%. Similar to the outcomes seen with Propecia, mean hair counts for the whole cohort increased statistically significantly ($p< 0.0001$) by 18% between baseline and week 48.

An up-to-date comprehensive review and meta-analysis by **English *et al*. [(10)]** the effectiveness and security of intradermal and intramuscular injections of botulinum toxin for androgenic alopecia (AGA). A total of 165 men with AGA were included in five clinical investigations that were part of the meta-analysis. Response rates varied from 75 to 79.1% among the 4 studies examining response rates (i.e., participants with >0% hair changes). Studies that tracked changes in hair count after intramuscular doses found variations between 18 and 20.9%. There were no significant adverse effects recorded.

To understand which injection techniques, result in the greatest results and the processes behind those results, researchers should continue to compare intradermal vs intramuscular injections. To develop a set of best practices for practitioners and patients, it is important to investigate the quantity of botulinum toxin units, the frequency of sessions, and the number of sessions. Last but not least, researchers should think about how various botulinum toxin serotypes affect outcomes.

The results of this research showed that BTA is a safe and successful treatment for the treatment of AGA, and it produces great outcomes. These findings provide an innovative theoretical framework and therapeutic approach for the management of AGA. Our findings need to be confirmed by more comparative studies with bigger sample sizes and longer follow-up in order to uncover risk factors for poor outcomes.

CONCLUSION

The results of this research showed that BTA is a safe, useful, minimally invasive, and successful line of therapy for androgenetic alopecia. Dermoscopy is a useful technique for assessing the efficacy of therapy. These findings provide an innovative theoretical framework and therapeutic approach for the management of AGA.

DECLARATIONS

- **Consent for publication:** I attest that all authors have agreed to submit the work.
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of interest:** no conflicts of interest.

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